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Palliative care for people living with heart and lung disease

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Palliative care for people living with heart and lung disease

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Editorial: Palliative care for people living with heart and lung disease

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Editorial on the Research Topic
Palliative care for people living with heart and lung disease

"Suffering is only intolerable when nobody cares" (1).

Palliative care (PC) takes the publication "The Physical and Mental Distress of the Dying" by Hinton in June 1968 as its symbolic starting point (2). Assessing the distress in those who were thought to die within 6 months, he sowed the seed of the idea of providing care focused on limiting the suffering of those approaching death. Hinton stated, based on interviews with 102 patients approaching death, 14 of whom had heart or renal failure, that the physical distress caused by symptoms in people affected by organ failures was more prevalent (especially in respect to dyspnea, nausea/vomiting) and remained more frequently unaddressed (in the case of breathlessness in 82%), than in people dying of cancer. This paper became one of the founding texts for the development of the hospice movement in the UK. As charities financing hospices were focused on supporting care for people dying of cancer, in its first decades PC was almost exclusively limited to this group of patients.

Unfortunately, over 50 years later, the situation has not yet changed substantially. The provision of PC for people living with non-oncological diseases, despite improving in recent years, remains marginal (3). This is despite the fact that, by signing the World Health Organization resolution on Universal Health Coverage in 2019, all countries have an obligation to provide adequate care including PC to all individuals who need it, across their life course, with access to PC recognized as a fundamental human right.[1,2] Cardiovascular disease, cancer, and chronic respiratory disease are considered to be

1 Available online at: https://www.who.int/health_financing/universal_coverage_definition/en/ (accessed November 2022).

2 Available online at: https://www.who.int/news-room/fact-sheets/detail/palliative-care (accessed November 2022).

the three most common chronic health conditions causing a high risk of suffering and which may require PC (see text footnote 2).

One of the most relevant steps to provide optimal care (in any discipline, and any health-related problem), is timely recognition of the need of an appropriate intervention. Should it not be the same with respect to suffering? The surprise question ("Would you be surprised if a patient were to die within 1 year") has been suggested as a trigger for considering the provision of PC to broader groups of patients (Blum et al.) (4). Adding a second surprise question ("Would I be surprised if this patient is still alive after 12 months") has been proposed in countries with a progressive aging society, such as in the Netherlands, as being more appropriate for the recognition of the probability of a need to start PC based treatment (5). However, as it would not surprise their health care professional if many old and very old people would die, equally it would not surprise them if those in good health were still alive after 12 months. This "surprise" based approach has improved the recognition of the need to begin PC for a higher number of otherwise overlooked people, but it only focuses attention on those at risk of dying. Improving or at least maintaining the best possible quality of life (QoL) must always be the aim in modern health care. A focus on improving QoL should not be delayed until suffering has become unbearable, curative treatment strategies have been exhausted, or the risk of dying has been recognized.

Data from clinical studies and the guidelines of scientific societies recommend the early integration of PC during the course of a disease, concurrent with active treatment in oncology, but this approach is still very much the exception in non-oncological disease (6–10). An Australian group has stated that the need for PC does not correlate with prognosis (11), and should be assessed early in the course of any disease that carries a risk of suffering, using validated tools. This approach is concordant with the different definitions of PC published by globally recognized organizations (e.g., World Health Organization, WHO)[3] stressing that it should be provided to people living with various diseases which cause health-related suffering (*none* of the current definitions mentions the risk of dying or short life expectancy as criteria warranting the provision of PC). The European Society of Cardiology, in its current guidelines for the diagnosis and treatment of acute and chronic heart failure (HF), states that many patients with HF would derive benefits from the early integration of a palliative and supportive approach (12). The systematic review of accessible needs assessment tools presented in the paper by Waller et al. in this issue gives strong hints as to how to implement needs based provision of PC. Those instruments should be used regularly in all units where care is provided for people living with conditions causing a high-risk of suffering, as discussed in papers by Gonzalez-Jaramillo et al. and Hentsch et al., also in this issue (9).

Palliative Care aims to address all of the dimensions in which needs can emerge: physical (caused by symptoms), psychosocial (caused by emotional distress and social isolation) and spiritual (such as coping with existential dilemmas) (13). It is appropriate with any disease and at any age, thus this issue of Frontiers in Cardiovascular Medicine presents papers on PC with different cardiovascular and respiratory diseases causing significant health-related suffering, (like HF; chronic obstructive lung disease, COPD; interstitial lung fibrosis and congenital heart disease) (Hentsch et al.; Bergsträsser et al.; Janowiak et al.). Some of those with common risk factors can coincide (HF and COPD) causing even more prominent suffering than those diseases alone, as presented in the paper by Kowalczys et al. PC is appropriate for any age group, therefore the paper by Bergsträsser et al. discussing care for children living with advanced HF has also been included in this Research Topic. Other papers discuss breathlessness (presenting a case series of people experiencing the side effects of opioids used for breathlessness alleviation) (Sobanski and Currow), non-pharmacological interventions (Pyszora and Lewko), and spiritual care (Kotlińska-Lemieszek et al.) in people living with COPD.

Spirituality is of great significance for many people, especially when coping with a serious disease and at the end of life. Unfortunately, it is usually overlooked in modern medicine but can be an important resource for many people, including those living with HF (14, 15) or COPD (Kotlińska-Lemieszek et al.). To understand that spirituality is of fundamental significance to most people, it is important to be aware that it is a broader than classically perceived religiosity. The European Association for Palliative Care defines spirituality as a dynamic dimension of human life that relates to the way persons (individuals and in a community) experience, express and/or seek meaning, purpose and transcendence, and the way they connect to the moment, to self, to others, to nature, to the significant and/or the sacred (16). A training program for medical students on spiritual care in medicine implemented in a Polish medical university has been described by Fopka-Kowalczyk et al.

An integral part of PC is to give support in decision making to all involved—patients, their relatives and health care professionals. It should be based on in depth communication, not only focused on informing about the potential benefits to be had from therapeutic options, but also the risk of treatment failure, a burden that needs to be calculated in consent for invasive interventions, the probable progression of the disease, and finally the risk of dying. All of these difficult aspects of clinical communication are usually neglected in conversations between ill people and their physicians (17, 18). End-of-life issues are often omitted, even if life is obviously approaching its end. Open, sensitive communication on imminent death with

3 Available online at: https://www.who.int/health-topics/palliative-care.

patients (and their families) can lead to collaborative adjustment of the goals of ongoing therapy. Martínez-Sellés and Grodzicki discuss the matter in this issue of Frontiers, specifically the quality of life driven modification of medical therapy and the activity of implantable devices in patients with advanced HF according to agreed, adjusted goals of care. Therapeutic interventions based on (functional) replacement of an exhausted heart give hope for improving life, but nevertheless come with a high risk of burden and complications. That is why in-depth communication with potential candidates for such treatment is mandatory. This is discussed in the paper by Tenge et al. in a group of patients receiving left ventricular assist devices (LVADs). Ethical challenges and moral dilemmas with respect to the discontinuation of circulatory support are discussed in a paper by Mueller.

Despite undergoing a tremendous evolution in recent years, PC is usually still perceived as a discipline dedicated to those who are dying and are in the last hours of life, when nothing else can be proposed. While much can still be done to improve quality of life during the dying phase, we advocate that disease modifying management incorporate care to assure the best possible quality of life by alleviating symptoms, ensuring compassionate communication, and support for spiritual and existential issues. We hope that this Research Topic of Frontiers in Cardiovascular Medicine will invite you to reflect on how together we can improve care for people with serious heart and lung diseases.

Author contributions

PZS drafted the manuscript. MK and SJG provided edits. All authors contributed to the article and approved the submitted version.

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MINI REVIEW
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Palliative Care in Children With Advanced Heart Disease in a Tertiary Care Environment: A Mini Review

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Palliative care for children continues to evolve. More recently, this has also been true in the field of pediatric cardiology, particularly for children with advanced heart disease. In these children, similarly to children with cancer, treatment successes are offset by the risks of long-term morbidities, including premature death. This mini review aims to provide an overview of current knowledge on children suffering from advanced heart disease, their medical care during various phases of illness (including the palliative and end-of-life phase), symptom burden, experiences of parents, prognostic understanding of parents and physicians, and current status of the involvement of pediatric palliative care. In conclusion, the suffering of these children at the end of their young lives is pronounced and many parents feel prepared neither for medical problems nor for the child's death. An effective and mutually trusting partnership between pediatric cardiology and pediatric palliative care would appear to be a prerequisite for the timely involvement of palliative care in further supporting these children and their families.

Keywords: congenital heart disease, advanced heart disease, pediatrics, palliative care, end-of-life care, pediatric cardiology, symptoms, suffering

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INTRODUCTION

The outcome of children with severe congenital heart disease (CHD) has improved dramatically within the last decades. As a consequence, the population of children with a palliated and rather not repaired heart is growing. Many of these children suffer from a wide range of comorbidities, including associated syndromes. After extensive and repeated cardiac surgery for the underlying heart defect, many experience long-term morbidities, and an increasing number of children are referred to specialized pediatric palliative care (sPPC) services (1, 2). In these children, grouped as advanced heart disease (AHD) in this article, sPPC provides support that addresses the child's and family's most important needs and aims at improving the patient's and family's healthcare-related outcomes. This also includes processes of decision-making known as advance care planning (ACP).

The purpose of this mini review is to draw a picture of the current development and emerging concepts of sPPC in children with AHD and palliative care needs in the form of a summary of the current literature and an outlook on effective partnership between pediatric cardiology and sPPC in the context of tertiary care of well-resourced countries.

Literature

Palliative Care in Children Suffering From Heart Disease

Unlike children suffering from, e.g., cancer, children with cardiac diseases have been rare in sPPC services. Consequently, the medical literature regarding palliative and end-of-life (EOL) care for these children is scant, starting only in 2010. One of the first retrospective studies delivered insight into EOL care and patterns of death for children with AHD (3). In addition to this article from the Children's Hospital Boston, another article focusing on adults with complex CHD was published almost simultaneously and deserves attention (4). Tobler et al. (4) report a retrospective single center study including 48 patients (mean age 37 ± 14 years) with complex CHD who died in hospital unrelated to proximate surgery, two thirds of them in intensive care units (ICU). Circumstances of death, EOL discussions and EOL care are described, yet what strikes readers today is that only a minority of patients were informed and prepared for the terminal stage of their disease. Only 6% of the patients had EOL discussions, while 50% had full resuscitation status and died under full resuscitation efforts. However, as in the pediatric cohort (3), death was to be expected in these adult patients.

In the meantime, change has been emerging. A recent study from Boston compared two cohorts of inpatient pediatric deaths due to AHD from two three-year periods, from 2007 to 2009 and 2015 to 2018 (2). Of a total of 3409 cardiac admissions (2007–2009) and 4032 (2015–2018) in the two groups, 110 and 99 children died, respectively. sPPC involvement was documented more frequently in the later period, with 57 patients (58%) as compared to 19 (17%) in the earlier period.

Patterns and Medical Course of Congenital Heart Disease in Children

CHD is the most frequent birth defect, affecting 0.8% of newborns (5). The spectrum of these defects is broad and ranges from mild and hemodynamically insignificant lesions up to severe and complex conditions sometimes needing multiple interventions during childhood, such as functionally univentricular hearts. The incidence of different heart defects varies, with ventricular septum defects apparently the most common type of CHD. See **Table 1** for an overview of types of CHDs and their severity grading.

Historically, most patients with severe CHD died in early childhood. However, over the past decades, the life expectancy of these children has increased significantly due to the extraordinary advances in the field of congenital heart surgery, interventional pediatric cardiology and pediatric intensive care. Current data demonstrates that approximately 90% of infants born with CHD now reach adulthood (6–8). But even after successful treatment, the burden of disease can be significant for these children, as well as their families, and particularly siblings (9).

A majority of children with AHD and palliative care needs have single-ventricle physiology (approximately half of them with hypoplastic left heart syndrome), followed by Tetralogy of Fallot with pulmonary artresia, double outlet right ventricle, complete atrioventricular canal type, pulmonary vein stenosis and other severe valve diseases. In addition to congenital, mostly structural heart defects, some children suffer from cardiomyopathy, pulmonary hypertension, myocarditis or complications from heart transplantation. In many children (50–70%) the diagnosis is made prenatally (10–13).

In all of these children medical care remains highly complex up to death (2, 3, 11, 13–15). This includes a wide range of interventions and technical support, such as mechanical ventilation, extracorporeal membrane oxygenation (ECMO), a ventricular assist device (VAD), tracheostomy, gastrostomy tubes, and peritoneal drains. Similar findings are reported in the PELICAN (Pediatric End-of Life-Care Needs in Switzerland) study, a nationwide retrospective study in Switzerland that analyses data on the last 4 weeks of life in children (0–18 years) who died in the years 2011 or 2012 due to cardiac, neurological or oncological conditions, or during the neonatal period (11, 16). Children with a cardiac condition (19 of the 149 included patients) had a median age of 0.5 years (0.1–9.1 years), were predominantly hospitalized in an ICU (67%), and underwent several interventions (interventions requiring anesthesia 11 of 19;

TABLE 1 | Severity grading of congenital heart disease (CHD) [modified after Hoffman et al. (5)].

Severe CHD
The majority of these patients present as severely ill in the newborn period or early infancy.
Cyanotic heart disease
• D-transposition of the great arteries
• Tetralogy of Fallot
• Hypoplastic right heart: Tricuspid atresia; Pulmonary atresia with intact ventricular septum; Ebstein anomaly
• Hypoplastic left heart: Aortic atresia; Mitral atresia
• Single ventricle
• Double outlet right ventricle (DORV)
• Truncus arteriosus communis (TAC)
• Total anomalous pulmonary venous connection (TAPVC)
• Critical pulmonary stenosis (PS)
• Miscellaneous uncommon lesions
Acyanotic lesions
• Atrioventricular septal defect (AVSD)
• Large ventricular septal defect (VSD)
• Large persistant ductus arteriosus Botalli (PDA)
• Critical or severe aortic stenosis (AS)
• Severe pulmonary stenosis (PS)
• Critical Coarctation (CoA)
Moderate CHD
These patients require expert care, but less intensive than those with severe CHD. Most conditions are detected during childhood.
• Mild or moderate aortic stenosis or regurgitation (AS/AR)
• Moderate pulmonary stenosis or regurgitation (PS/PR)
• Non-critical CoA
• Large atrial septal defect (ASD)
• Complex forms of VSD
Mild CHD
This is the most numerous group and patients are asymptomatic. They often undergo spontaneous resolution of their lesions.
• Small VSD
• Small PDA
• Mild PS
• Bicuspid aortic valve without AS or AR
• Small or spontaneously closed ASD

mechanical ventilation 14 of 19; ECMO 4 of 19, tube feeding 17 of 19) and received a high range of medications during the last week of life (3–46, including pain medication in 18 of 19 cases).

Most children with AHD die in ICU settings after discontinuation of life-sustaining interventions (2, 3, 11, 14, 15). Prior to death these children often experience a considerable amount of suffering (2, 10, 11, 14, 16).

Symptoms and Suffering in Children With Advanced Heart Disease

Data on symptom burden in children with AHD is limited. A very recent prospective study with 161 hospitalized patients (54% younger than 2 years) provides an overview of the most common symptoms and associated suffering (17). The most frequent symptoms were pain (68%), fatigue (63%) and breathing difficulties (60%). Parents perceived treatment of symptoms as successful for pain (76%) and breathing difficulties (65%). The least relief was achieved in the context of sleep disturbance (24%), sadness or depression (29%), and fatigue (35%). However, most parents reported that the team had addressed symptoms sufficiently. Patients with low functional status were more likely to experience a high symptom burden and suffering. The authors conclude that children with AHD may have an even greater risk of psychiatric morbidity, particularly anxiety and/or depression than the pediatric oncology population (17). Comparably, parent study participants of the above-mentioned PELICAN study reported pain and breathing problems most frequently. When asked to rank the three symptoms that the child suffered from most and were most stressful, parents frequently placed agitation and anxiety in first or second place (16).

An earlier cross-sectional survey that included bereaved parents from two tertiary centers found parents mentioning the poor or fair quality of life (QOL) of their child during its last month of life (14). This is also confirmed by a large study with 475 parents and their 347 children living with mild to complex or severe cardiovascular disease without PPC services being involved (18). Based on self-report, the mean scores of the Pediatric Quality of Life Inventory (PedsQL), which included a cardiac module, were significantly lower than in healthy child norms.

Prognostication and Advance Care Planning

Prognostication in children with AHD seems to be even more challenging than principally assumed (13, 14, 19–21). Particularly in pediatrics, prognostication should not be reduced to questions of "how long" or the binary "curable/incurable," but include a comprehensive conversation about patients' and families' expectations, needs and hopes, their understanding of disease and prognosis and the QOL of the affected child and the whole family (19). Many parents do not realize and struggle to accept that their child has no realistic chance for survival and do not feel prepared for their child's dying and medical problems which may arise prior to death (10, 14).

A longitudinal survey by Morell et al. (13) showed the importance of prognostic understanding in parents, as this was associated with greater preparedness for the child's medical problems. The perspectives of parents and physicians differed significantly concerning prognosis and burden of disease. In particular, parents of children who had had cardiac surgery during the survey reported a significantly poorer understanding of prognosis. This was interpreted as being a result of the day-to-day management of the child's disease in hospital. Nevertheless and as is also well known in pediatric oncology (22, 23), parents of children with complex heart disease wish to receive more information about the disease in general and the child's prognosis, even if this includes "bad news" (13, 16).

In specialties such as cardiology or oncology, where medical and surgical advances have led to tremendous change, parallel planning should be accorded growing importance. This means the introduction of PPC and ACP alongside disease-directed, cure-seeking, life-prolonging treatment and interventions as long as they are in the child's best interest (24).

Early Involvement of Pediatric Palliative Care for Cardiac Patients

Early involvement of PPC could enhance support for patients and their families throughout the course of disease (25, 26). This may also help to move away from the misconception of PPC as EOL care only. Contact with the PPC team may allow more space for hope, which can be important for coping with the most complex situations and promoting a sense of security and trust (27, 28). If there is space for hope, PPC involvement may also provide a space to reflect on feelings of doubt about continuing a burdensome and failing treatment (25).

The aforementioned recent study from Boston (2) listed the following indications for sPPC referral according to their frequency: goals of care and ACP (76%), longitudinal support (70%), symptom management (37%), complex decision-making (34%) and hospice referral or care coordination (3%). In the later period of analysis (2015–2018), sPPC referral occurred earlier, at 69 days instead of the 21 days prior to death reported for the earlier period. Involvement of sPPC was associated with less invasive treatments, such as mechanical ventilation, inotrope treatment, ECMO or VAD, but higher rates of ACP meetings and documentation of resuscitation status. In addition, sPPC had an influence on hospital charges on the day of death and for the 7 days before, which were significantly lower.

Hancock and his team at the University of Michigan carried out a randomized controlled trial that included mothers of infants with prenatal diagnoses of single-ventricle heart disease to study depression, anxiety, coping and QOL at a prenatal visit (baseline assessment) and at neonatal discharge (29). Mothers were randomized to receive early sPPC, including structured evaluation, psychosocial/spiritual and communication support when the infant was admitted for surgery versus standard care. In the cohort of 38 mothers and neonates, 18 received sPPC and 20 standard care. Mothers with early sPPC self-reported better adaptive coping mechanisms, less maternal anxiety, and improved family relationships.

Barriers for the Involvement of Palliative Care

Although pediatric cardiologists and cardiac surgeons feel PPC consultations are helpful, many feel the timing is too late

and at the same time they perceive resistance concerning the involvement of PPC (21). Barriers to PPC are mainly related to the concern of the unintended message given by introducing PPC: "we are giving up on the child" (21). Another barrier to PPC may be due to the unpredictability of these generally rare conditions, which may discourage the discussion of goals of care (26).

DISCUSSION

This mini review leads to the following five salient topics that may be of importance to adult and pediatric cardiologists alike:

(1) Despite tremendous successes in pediatric heart surgery, interventional pediatric cardiology and pediatric intensive care, children with AHD carry a high risk of long-term sequelae, suffering and premature death.
(2) In a palliative phase of the disease and at EOL, the symptom burden of these children is high and often underestimated.
(3) Many parents are not prepared for their child's medical problems and, as a consequence, for their potential death as well as their actual dying.
(4) Prognostic understanding in parents lags behind physicians' understanding.
(5) For these severely ill children and their families sPPC has been shown to provide benefit in terms of support, improvement of QOL and potentially less invasive treatment prior to death.

At a first glance, these five topics contain contradictory information. However, they reflect an important facet of modern medicine: the downsides of success. Success carries the risk of distracting attention from the consequences of that success. This may explain why many parents of children with AHD do not feel prepared for their child's medical problems (13) and, as a consequence also feel unprepared for their child's death (10), even if death is rarely unexpected in these children and adults.

Communication plays a central role in this context as it does in medical care generally. Transparency could help to prevent parents and/or patients from not being or not feeling informed, from missing out on important information or observations, from misconceptions of treatment goals or approaches such as palliative care, and probably from unnecessary surprises. Thus, we need to ask ourselves how it can happen that physicians underestimate symptom-burden, as perceived by parents (13). The same may be true concerning health-related QOL. Furthermore, this extends to the issue of parents not feeling prepared for their child's medical problems, including poor prognosis (13), and dying (10). Morell et al. (13) write: "... if we can improve parent understanding of prognosis, we can improve how prepared parents feel for the medical problems their child is facing." One step in this direction might be a conversation anticipating and addressing uncertainty with the help of "what ifs" (30). This allows parents to express their worries and fears and may help to also initiate ACP. The roadmap for a "what if" conversation developed by Snaman et al. (30) could be a very helpful basis. Besides providing explicit information, the parent-physician relationship appears vital to improving parent understanding and avoiding overly optimistic parental expectations (13, 14, 31).

How could this be achieved and what could be the role of sPPC? In children with complex AHD as in other complex chronic and life-limiting conditions, early involvement of sPPC could help to meet the challenges of many different tasks and requirements and provide continuity and coordination of care. This would also allow conversations about prognosis and, if needed, ACP in times of stability, ideally before scheduled interventions or decompensations (13). As teams for children with complex AHD are naturally large, particularly during hospitalization, including various disciplines from cardiology to heart surgery and intensive care and numerous professions from physicians to nurses, physiotherapists, psychologists, social workers, nutritionists, kindergarten teachers, chaplains and others, continuity and coordination of care reaches its limits. Besides the most urgent medical and nursing requirements, there is a risk that higher-level topics and conversations about a broader perspective will miss out. An sPPC team, not directly involved in these daily, highly complex and specialized medical and nursing requirements could take over tasks of coordination and continuity and facilitate communication, always in close contact with the primary team. The patient's primary team would maintain the lead and medical responsibility. The sPPC team would be involved in the sense of a consultative service, a model of care that is frequently found internationally, especially in tertiary settings (32). Within the scope of practice of such a sPPC team, new roles can emerge allowing a task-shifting and distribution of responsibilities among the different PPC providers. Trustworthy partnership and structured exchange between teams is a prerequisite for a successful integration of sPPC in the care of these children and their families. The misconception that palliative care is EOL care could thus slowly be dispelled, not only for lay people but also for professionals.

More concretely, patients with AHD and their families could benefit from the early involvement of sPPC in several respects: (1) continuous support of the child and the family; (2) improvement of communication, including regular individual information, if appropriate even for the sick child; (3) improvement of prognostic understanding and timely ACP; (4) early anticipation and comprehensive assessment of symptoms and suffering in the affected child and the family; (5) assessment of rare, hitherto little-considered symptoms such as anxiety and fatigue; (6) awareness and improvement of QOL of the child and the family, and (7) support of the attending teams and healthcare professionals.

Future Directions and Conclusion

Declaring early integration of sPPC for children with AHD as a goal would need conceptual work at departmental and institutional levels. To further demonstrate the effects of sPPC interventions and to also overcome persistent barriers, it would be helpful to define and evaluate outcomes as has been done in Boston (2) and is ongoing in a multicenter study in

Switzerland – SPhAERA (Specialized Pediatric Palliative Care: Assessing family, healthcare professionals and health system outcomes in a multi-site context of various settings) (33).

Specialized pediatric palliative care has the potential to improve the QOL of the affected children as well as their families by relieving suffering on different levels and augmenting ACP. EOL experiences of children with AHD and their families can be influenced through earlier awareness and understanding of a prognosis and probably less invasive therapies at EOL. A close collaboration between teams and healthcare professionals may also positively influence the well-being of highly engaged healthcare professionals.

AUTHOR CONTRIBUTIONS

EB developed the concept and structure, and wrote the first draft of the manuscript. SL, KZ, and AO contributed to the writing of the manuscript. All authors reviewed and approved the final manuscript.

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BRIEF RESEARCH REPORT
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Enhancing Palliative Care for Patients With Advanced Heart Failure Through Simple Prognostication Tools: A Comparison of the Surprise Question, the Number of Previous Heart Failure Hospitalizations, and the Seattle Heart Failure Model for Predicting 1-Year Survival

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Background: Score-based survival prediction in patients with advanced heart failure (HF) is complicated. Easy-to-use prognostication tools could inform clinical decision-making and palliative care delivery.

Objective: To compare the prognostic utility of the Seattle HF model (SHFM), the surprise question (SQ), and the number of HF hospitalizations (NoH) within the last 12 months for predicting 1-year survival in patients with advanced HF.

Methods: We retrospectively analyzed data from a cluster-randomized controlled trial of advanced HF patients, predominantly with reduced ejection fraction. Primary outcome was the prognostic discrimination of SHFM, SQ ("Would you be surprised if this patient were to die within 1 year?") answered by HF cardiologists, and NoH, assessed by receiver operating characteristic (ROC) curve analysis. Optimal cut-offs were calculated using Youden's index (SHFM: $<$86% predicted 1-year survival; NoH $\geq$ 2).

Results: Of 535 subjects, 82 (15.3%) had died after 1-year of follow-up. SHFM, SQ, and NoH yielded a similar area under the ROC curve [SHFM: 0.65 (0.60–0.71 95% CI); SQ: 0.58 (0.54–0.63 95% CI); NoH: 0.56 (0.50–0.62 95% CI)] and similar sensitivity [SHFM: 0.76 (0.65–0.84 95% CI); SQ: 0.84 (0.74–0.91 95% CI); NoH: 0.56 (0.45–0.67 95% CI)]. As compared to SHFM, SQ had lower specificity [SQ: 0.33 (0.28–0.37 95% CI) vs. SHFM: 0.55 (0.50–0.60 95% CI)] while NoH had similar specificity [0.56 (0.51–0.61

95% CI)]. SQ combined with NoH showed significantly higher specificity [0.68 (0.64–0.73 95% CI)].

Conclusion: SQ and NoH yielded comparable utility to SHFM for 1-year survival prediction among advanced HF patients, are easy-to-use and could inform bedside decision-making.

Keywords: survival prediction, number of hospitalizations, Seattle Heart Failure Model, advanced heart failure, surprise question, palliative care

INTRODUCTION

Heart Failure (HF) is a life-limiting condition which usually progresses to an advanced stage with debilitating symptoms, emotional burden, and reduced quality-of-life (QOL) (1). Accordingly, current guidelines promote the use of palliative care for patients with advanced HF (2). Palliative care is an interdisciplinary approach aimed to alleviate physical and psychological symptoms and restore and maintain QOL in patients with serious illness and several studies demonstrated its benefit in HF patients (3–5). Palliative care is not limited to end-of-life care and should be integrated early in the disease course for patients with unmet symptoms and needs (3).

Provision of palliative care is not contingent upon a high probability of dying, and should be administered based on clinical necessity. However, clinicians often do not refer patients with advanced heart failure to palliative care until very late in their disease trajectory (6), and better information about prognosis may raise awareness about patients' clinical needs for palliative care. Also, prognostication plays an important role in palliative medicine, in particular when it comes to timing and planning of discharge, referral to hospice, and transition to end-of-life care, as well as to addressing patients' and caregivers' questions and uncertainties (7, 8). Estimates of life expectancy are particularly critical for decision making regarding advanced treatment options for cardiac conditions, such as ICD implantation and transcatheter aortic valve implantation, for which recent guidelines require a minimum life expectancy of 1 year (2).

To date, survival prediction has mostly been approached by means of sophisticated multivariable scores, such as the Seattle Heart Failure Model (SHFM) (2). Although these scores provide fair prognostic discrimination in patients with advanced HF, their utility in clinical practice is limited because they require a large amount of variables some of which are not routinely collected (e.g., lymphocyte count and uric acid) and the use of dedicated calculators.

Simpler prognostic approaches could facilitate the widespread use of survival prediction. The surprise question (SQ), which asks clinicians "Would you be surprised if this patient died in the next 12 months?," and the number of HF hospitalizations within the last 12 months (NoH) are promising prognostic tools which can be easily applied at the bedside by tapping into clinician intuition and basic history-taking. In previous studies of HF patients, both metrics were found to be closely associated with mortality (9–11).

OBJECTIVES

The aim of this study was to compare the discrimination of the SHFM, the SQ, the NoH and the combination of SQ and NoH for prediction of 1-year survival in a population of advanced HF patients.

METHODS

This study was a retrospective, secondary analysis of advanced HF patients with an implantable cardiac defibrillator (ICD) enrolled in the Working to Improve diScussions about DefibrillatOr Management (WISDOM) trial (NCT01459744, NCT01454817). The WISDOM trial was a multisite, single-blinded, cluster-randomized controlled trial to test whether a clinician-centered intervention of educational content and automated reminders increased the likelihood of ICD deactivation conversations and it is described in detail elsewhere (12).

The final inclusion criteria encompassed inpatients, as well as outpatients with advanced HF, an implanted ICD and a high risk of dying according to the following criteria: for inpatients, at least one other HF hospitalization within the last 12 months, or two out of four objective measures (age >70 years, blood urea nitrogen >43 mg/dL, serum creatinine >2.75 mg/dL, systolic blood pressure <115 mmHg) were required; for outpatients, at least two HF hospitalizations within the last 12 months, or New York Heart Association (NYHA) class IV dyspnea, or NYHA class III dyspnea and either at least one HF hospitalization within the last 12 months or two out of four objective measures (age >70 years, blood urea nitrogen >43 mg/dL, serum creatinine >2.75 mg/dL, systolic blood pressure <115 mmHg) were required. The detailed inclusion and exclusion criteria are published separately (13).

For the present study, we included all patients with complete data on SHFM, SQ, NoH and 1-year survival status, which was the outcome of interest. SHFM-predicted survival was calculated from baseline variables (14). Clinical research coordinators collected clinical variables at baseline and ascertained survival status during follow-up. The SQ was answered by attending HF physicians who were board certified in Advanced HF and Transplant Cardiology, Cardiology and Internal Medicine which would require a minimum of approximately 7 years of clinical

experience. The NoH was abstracted manually from electronic medical records.

Statistical analysis was performed using Stata Statistical Software: Release 16 (StataCorp LLC, College Station, TX, United States). Categorical variables are presented as absolute number and percentage. Numerical variables are presented as mean ± standard deviation. Baseline variables were compared using independent *t*-test or Chi-square test, whichever was applicable. Discrimination of the SHFM, SQ, and the NoH for 1-year survival status was assessed by means of receiver operating characteristic (ROC) curve analysis. For the SHFM and the NoH, we empirically determined a cut-off based on Youden's index (15). We compared discrimination for prediction of 1-year survival status of the SHFM, the SQ and the NoH based on area under the ROC curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). To allow for statistical inference regarding the comparison of different prognostic approaches, 95% confidence intervals (95% CI) were computed.

RESULTS

In our sample of 535 patients, 82 (15.3%) had died at 1 year. Population characteristics are detailed in **Table 1**. The mean age was 61.5 ± 13.9 years, 379 patients (70.8%) were male and 286 (52.4%) were White. Overall, the mean left ventricular ejection fraction (LVEF) was 24.3 ± 10.1%. The vast majority of patients [485 (94.9%)] had a reduced LVEF, a minority 10 (2.0%) had mid-range EF, and 16 (3.1%) had preserved LVEF. The average predicted 1-year survival according to the SHFM model at baseline was 86.8% ± 24.9. The SQ was answered with "No, I would not be surprised if this patient was to die within 1 year" in 375 (70.1%) of patients overall. And 246 patients (46.0%) were found to have an NoH ≥ 2 at baseline.

For the SHFM and the NoH, optimal cut-offs based on ROC curve analysis were found to be a predicted survival <86% and ≥2 hospitalizations, respectively. Prognostic performance metrics of the SHFM, the SQ, and the NoH are shown in **Table 2**. The SHFM yielded an area under the ROC curve (AUC) of 0.65 (0.60–0.71 95% CI), a sensitivity of 0.76 (0.65–0.84 95% CI), and a specificity of 0.55 (0.50–0.60 95% CI). The SQ demonstrated a comparable AUC [0.58 (0.54–0.63 95% CI)], similar sensitivity [0.84 (0.74–0.91 95% CI)], but significantly lower specificity [0.33 (0.28–0.37 95% CI)] compared to the SHFM. The NoH demonstrated a comparable AUC [0.56 (0.50–0.62 95% CI)], similar sensitivity [0.56 (0.45–0.67 95% CI)], and similar specificity [0.56 (0.51–0.61 95% CI)] compared to the SHFM. The combination of a positive a SQ and a NoH ≥ 2 showed similar a similar AUC [0.60 (0.54–0.66 95% CI)], lower sensitivity [0.51 (0.40–0.62 95% CI)], but significantly higher specificity [0.68 (0.64–0.73 95% CI)] compared to the SHFM. Of note, the PPV and NPV did not differ significantly between any of the prognostic approaches, with PPVs and NPVs ranging consistently around 20 and 90%, respectively (**Table 2**).

DISCUSSION

In a sample of advanced HF patients at a high risk of dying and of which the vast majority had reduced ejection fraction, two simple single-measure bedside tools, the SQ, the NoH, and the combination of the SQ and NoH performed as well as the complex multivariable SHFM for prediction of 1-year survival status in patients with advanced HF.

The prognostic utility of the SHFM in our study as assessed by the AUC [0.65 (0.60–0.71 95% CI)] was comparable to previous studies of advanced HF populations which reported AUCs ranging from 0.63 to 0.76 (16–18). Three previous studies assessed the SQ in HF populations: Aaronson et al. (19) studied 199 patients presenting to the emergency room with acute HF and found an AUC of 0.68 which was significantly higher than what we found [AUC 0.58 (0.54–0.63 95% CI)]. Straw et al. (9) studied 129 patients hospitalized with acute HF and found a sensitivity of 0.88, which was comparable to our findings [sensitivity 0.84 (0.74–0.91 95% CI)], and a specificity of 0.59, which was significantly higher than in our study [specificity 0.33 (0.28–0.37 95% CI)]. Gonzalez-Jaramillo et al. (10) studied 174 patients recruited from an HF clinic and found a sensitivity of 0.85 (0.69–1.00 95% CI), and a specificity of 0.57 (0.49–0.65 95% CI). Overall, our findings are in line with previous research. Of note, inclusion criteria and event rates varied between those and the present study which limits comparability.

The SHFM is one of the most widely known prognostic models for survival prediction in HF patients, demonstrating robust discrimination in different advanced HF populations and generally considered a gold standard for both clinical practice and research purposes (16–18). It also allows clinicians to estimate the effect of medication and devices such as ICD on mortality (14). For score calculation, users have to access an online application via computer or smartphone (20). The SHFM requires measures of 14 variables including the lymphocyte count and uric acid, which are usually not part of the standard HF laboratory work-up (20). Those requirements severely hinder widespread clinical use of this prognostic tool. Unlike the SHFM, the SQ and the NoH can be easily implemented as part of the routine clinical work-up of advanced HF patients by leveraging clinician intuition and basic history-taking. In our sample, we demonstrated that these simple prediction tools provided similar prognostic discrimination compared to the SHFM. Therefore, we believe that the SQ and the NoH are valuable additions to the "prognostic tool-box" of HF specialists as well as palliative care clinicians, either as quick bedside alternatives, or complementary to more sophisticated approaches.

Previous studies have repeatedly framed the SQ a possible trigger for palliative care referral (19, 21, 22). However, current guidelines and position statements clearly state that palliative care utilization should be based on unmet physical, psychological, social and spiritual needs and poor QOL instead of estimated prognosis (1–3). Yet,

TABLE 1 | Baseline characteristics of the study population overall and stratified for survival status after 1-year follow-up.

	Overall (*N* = 535)	Died (*N* = 82)	Survived (*N* = 453)	*p*-value
Gender, male	379 (70.8)	57 (69.5)	322 (71.1)	0.77
Age – years	61.5 ± 13.9	62.3 ± 13.9	61.4 ± 13.9	0.57
Race/ethnicity*				0.18
White	286 (54.2)	49 (59.8)	237 (53.1)	
Black	213 (40.3)	31 (37.8)	182 (40.8)	
Hispanic	74 (13.9)	10 (12.2)	64 (14.2)	
Other	17 (3.2)	0 (0.0)	17 (3.2)	
LVEF – %	24.3 ± 10.1	22.5 ± 9.0	24.6 ± 10.3	0.10
HF classification**				0.229
HFrEF	485 (94.9)	77 (98.7)	408 (94.2)	
HFmrEF	10 (2.0)	0 (0.0)	10 (2.3)	
HFpEF	16 (3.1)	1 (1.3)	15 (3.5)	
NYHA class				<0.001
I	3 (0.6)	0 (0)	3 (0.7)	
II	43 (8.0)	5 (6.1)	38 (8.4)	
III	412 (77.0)	52 (63.4)	360 (79.5)	
IV	77 (14.4)	25 (30.5)	52 (11.5)	
Ischemic etiology	235 (44.0)	38 (46.3)	197 (43.6)	0.64
VAD/Tx candidate	256 (47.9)	36 (43.9)	220 (48.6)	0.44
Prediction variables				
Surprise question***				0.003
No	375 (70.1)	69 (84.1)	306 (67.5)	
Yes	160 (29.9)	13 (15.9)	147 (32.5)	
Number of HF hospitalizations****				0.046
≥2	246 (46.0)	46 (56.1)	200 (44.2)	
<2	289 (54.0)	36 (43.9)	253 (55.8)	
SHFM predicted 1-year survival				<0.001
<86%	266 (49.7)	62 (75.6)	204 (45.0)	
≥86%	269 (50.3)	20 (24.4)	249 (55.0)	

*Continuous variables are shown as mean ± standard deviation. Categorical variables are shown as number (percentage). HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SHFM, Seattle Heart Failure Model; Tx, transplantation; VAD, ventricular assist device. *Not mutually exclusive. **HF classification according to the Universal Definition and Classification of Heart Failure (27). ***Yes = would be surprised if patient died within 1 year; No = would not be surprised if patient died within 1 year. ****Within the last 12 months before enrollment.*

TABLE 2 | Discrimination of the Seattle Heart Failure Model, the surprise question, the number of hospitalizations and a combination of the latter for prediction of 1-year survival.

	Seattle Heart Failure Model	Surprise question	No. of hospitalizations	Surprise question + No. of hospitalizations
Cut-off	Predicted survival <86%	"No, would not be surprised if patient died."	NoH ≥ 2	"No, would not be surprised" + NoH ≥ 2
AUC	0.65 (0.60, 0.71)	0.58 (0.54, 0.63)	0.56 (0.50, 0.62)	0.60 (0.54, 0.66)
Sensitivity	0.76 (0.65, 0.84)	0.84 (0.74, 0.91)	0.56 (0.45, 0.67)	0.51 (0.40, 0.62)
Specificity	0.55 (0.50, 0.60)	0.33 (0.28, 0.37)	0.56 (0.51, 0.61)	0.68 (0.64, 0.73)
PPV	0.23 (0.18, 0.29)	0.18 (0.15, 0.23)	0.19 (0.14, 0.24)	0.23 (0.17, 0.30)
NPV	0.93 (0.89, 0.95)	0.92 (0.87, 0.96)	0.88 (0.83, 0.91)	0.89 (0.85, 0.92)

Outcome of interest was survival status at 1-year follow up. AUC, area under the receiver operating characteristic curve; NoH, number of heart failure hospitalizations within the last 12 months; NPV, negative predictive value; PPV, positive predictive value; SQ, surprise question; SHFM, Seattle Heart Failure Model.

wide-spread use of evidence-based prognostication, facilitated by simple tools such as the SQ and the NoH, could inform a variety of clinical scenarios and decisions: Estimation of a patient's prognosis is important for improving patients' understanding of their illness trajectory, which remains poor (23), initiating discussions around goals of care and treatment preferences at the end-of-life (24), referring to hospice, which is underused in advanced HF (25),

and engaging in decisions regarding the implantation, continuation or discontinuation of device therapies such as ICD or left ventricular assist devices. The goal of our work is not to imply that referral to palliative care should be based on prognosis; instead we hypothesize that the use of simple tools to determine prognosis might nudge clinicians toward considering palliative care referrals for patients with unmet needs earlier in their illness trajectory. Given the fact that patients with advanced HF are referred to palliative care late (6, 26), we believe that easier tools to flag severely ill patients might create a path to earlier integration of supportive and palliative services into the patient's overall plan of care.

Of note, all prediction tools – and the SQ in particular – are flawed by low specificity translating into a poor positive predictive value. This tendency toward underestimating survival and the generally low accuracy of less than 0.7 AUC for all prognostic approaches under investigation must be kept in mind when applying these tools in clinical practice. Our findings have to be interpreted with caution. As demonstrated previously, the reliability of the SQ depends on training and clinical experience. In our study, the SQ was answered by specialized HF cardiologists – discrimination might be worse when used by other clinicians. Although the inclusion criteria were intended to select patients at high risk of dying, 1-year mortality in our study population was surprisingly low. Low event rates might limit statistical power to detect statistically significant differences. Furthermore, our sample had a rather young mean age, and a high proportion of patients who were candidates for transplantation or VAD which may limit the generalizability of our findings. Readers should bear in mind that the purpose of this retrospective, non-pre-specified study was to explore and compare the prognostic potential of existing approaches, not to develop and validate new prediction models. Thus, our findings should only be considered hypothesis-generating.

CONCLUSION

We found that the SQ, the NoH, and the combination of both could help identify advanced HF patients at increased risk of 1-year mortality; these simple prognostication tools might have the potential to support decision making around advanced HF therapies, inform conversations around goals of care, and raise awareness for unmet palliative care needs.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Program for the Protection of Human Subjects (PPHS) at the Icahn School of Medicine at Mount Sinai. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MB, LG, and NG contributed to conception and design of the study. LG and NG were responsible for investigation, funding acquisition, project administration, and supervision. KM contributed to methodology, data curation, and statistical analysis. MB wrote the first draft and submitted the manuscript. KM, LG, NG, and SP reviewed and edited the manuscript. All authors contributed to the article and approved the submitted version.

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SYSTEMATIC REVIEW
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A Systematic Review of the Development and Implementation of Needs-Based Palliative Care Tools in Heart Failure and Chronic Respiratory Disease

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Background: The impetus to develop and implement tools for non-malignant patient groups is reflected in the increasing number of instruments being developed for heart failure and chronic respiratory diseases. Evidence syntheses of psychometric quality and clinical utility of these tools is required to inform research and clinical practice.

Aims: This systematic review examined palliative care needs tools for people diagnosed with advanced heart failure or chronic respiratory diseases, to determine their: (1) psychometric quality; and (2) acceptability, feasibility and clinical utility when implemented in clinical practice.

Methods: Systematic searches of MEDLINE, CINAHL, Embase, Cochrane and PsycINFO from database inception until June 2021 were undertaken. Additionally, the reference lists of included studies were searched for relevant articles. Psychometric properties of identified measures were evaluated against pre-determined and standard criteria.

Results: Eighteen tools met inclusion criteria: 11 were developed to assess unmet patient palliative care needs. Of those, 6 were generic, 4 were developed for heart failure and 1 was developed for interstitial lung disease. Seven tools identified those who may benefit from palliative care and include general and disease-specific indicators. The psychometric qualities of the tools varied. None met all of the accepted criteria for psychometric rigor in heart failure or respiratory disease populations. There is limited implementation of needs assessment tools in practice.

Conclusion: Several tools were identified, however further validation studies in heart failure and respiratory disease populations are required. Rigorous evaluation to determine the impact of adopting a systematic needs-based approach for heart failure and lung disease on the physical and psychosocial outcomes of patients and carers, as well as the economic costs and benefits to the healthcare system, is required.

Keywords: palliative care, lung disease, heart failure, needs assessment, psychometrics

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INTRODUCTION

Practice guidelines from multiple societies and international policy documents emphasize the importance of delivering equitable and appropriate palliative care to people diagnosed with advanced heart failure (HF) and chronic respiratory diseases, such as chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD) [e.g., (1–5)]. People living with these progressive conditions will eventually experience physical function decline, as well as changes to their psychological, social and spiritual functioning and wellbeing (6–8). Despite comparable mortality rates and symptom burden, fewer people with these conditions are referred to palliative care services and when they are it is typically later compared to those with a cancer diagnosis (9–11). For instance, a Canadian retrospective population-based study reported that significantly fewer patients with COPD received specialist palliative care (SPC) compared to those with lung cancer (20 vs. 57%) (12). A UK population based study of over 92,000 patients with COPD found only 7.8% of the cohort received SPC (13). A systematic review of studies with patients with ILD reported palliative care involvement ranging from 0 to 38% (14). Similar data have been reported for patients with HF in the USA (15, 16), UK (17), Australia (18), Canada (19) and Europe.

A range of patient-, provider- and system- related factors contribute to non-referrals, late or crisis referrals to palliative care for patients with chronic HF and chronic respiratory disease. Patients and families have identified denial, misperception about the potential benefits and purpose of palliative care, and negative previous experiences with services (20, 21). While some providers report feeling comfortable providing a palliative approach (22), for others there is uncertainty about the role of palliative care and when this approach should be introduced (23, 24). Health care providers' poor recognition of their patient's palliative care needs can be impacted by time constraints, a lack of education or training, and awareness or availability of standardized tools and referral pathways (20, 22–25). Some health care providers perceive palliative care is not as useful for non-malignant conditions or that SPC services prioritize patients with cancer (26). Limited availability of SPC services and workforce shortages also limit timely referrals (20, 23, 25, 27). Poor integration of palliative care and cardiology and respiratory services has been reported (28).

In addition to the aforementioned factors, one of the most pertinent barriers to palliative care referrals remains the ongoing reliance on diagnosis and estimated prognosis as the main trigger for palliative care referral (9, 27). Diagnosis-based approaches have contributed to the over-representation of cancer patients in SPC services. Prognosis as a prompt for palliative care is also problematic, given the unpredictable trajectory (29) and evidence of inaccurate estimates by clinicians for patients with progressive chronic diseases (9). For instance, respiratory providers and general practitioners report reliance on the "surprise question" (SQ), which asks clinicians "Would you be surprised if this patient died in the next 12 months?", to promote referrals (30), despite reports of poor to modest prognostic accuracy across studies of patients diagnosed with organ failure, cancer and those attending general practice (31, 32).

A shift from prognosis and diagnosis-based approaches to a needs-based approach for guiding delivery of care has been advocated by international bodies such as Palliative Care Australia and the World Health Organization (WHO). Underpinning this approach is the timely recognition of needs and the delivery of holistic care by non-palliative care specialists to all those with a life-limiting illness. Studies highlight high levels of unmet needs across physical, psychological, social, practical and information domains for patients with HF and COPD, and their carers (33, 34). Therefore, a key component to support the successful integration of a needs-based approach in clinical practice requires the rigorous development, testing and implementation of tools that can accurately assess palliative care needs across a range of settings and diseases (35). Needs assessment tools have been broadly categorized into two groups: those developed to assist in the early identification of individuals who would benefit from palliative care; and those developed to identify and monitor unmet palliative and supportive care needs (35). Factors to consider in tool selection include the: (i) purpose, context and target population being assessed; (ii) the acceptability of the tool to patients, families and health care professionals; (iii) and the psychometric qualities of the instrument (35). Introduction of these tools requires a structured approach, given the potential impact on patients and services, with a particular emphasis on acceptability, feasibility and cost-effectiveness.

AIMS

This systematic review examined palliative care needs tools for people diagnosed with advanced HF or chronic respiratory diseases, to determine their: (1) psychometric quality; and (2) acceptability, feasibility and clinical utility when implemented in clinical practice.

METHODS

Literature Search

The electronic databases Medline, CINAHL, Embase, Psycinfo and Cochrane were searched using a combination of Medical Subject Headings (MeSH) and keywords (see **Supplementary Table 1** for the full search strategy). Major search terms included: "needs assessment," "unmet needs," "palliative care," "hospice and palliative care," in addition to general and more specific search terms for advanced HF and the major types of chronic respiratory disease. Searches were limited to studies published from the earliest records for each database until June 2021 and studies conducted with humans. The reference lists of included studies and the reference lists of relevant review articles were also manually searched to identify any additional studies.

Inclusion and Exclusion Criteria

Studies were included if they: (i) focused on people diagnosed with HF or chronic respiratory disease (e.g., COPD, ILD); (ii) included a tool that aimed to identify individuals for whom a

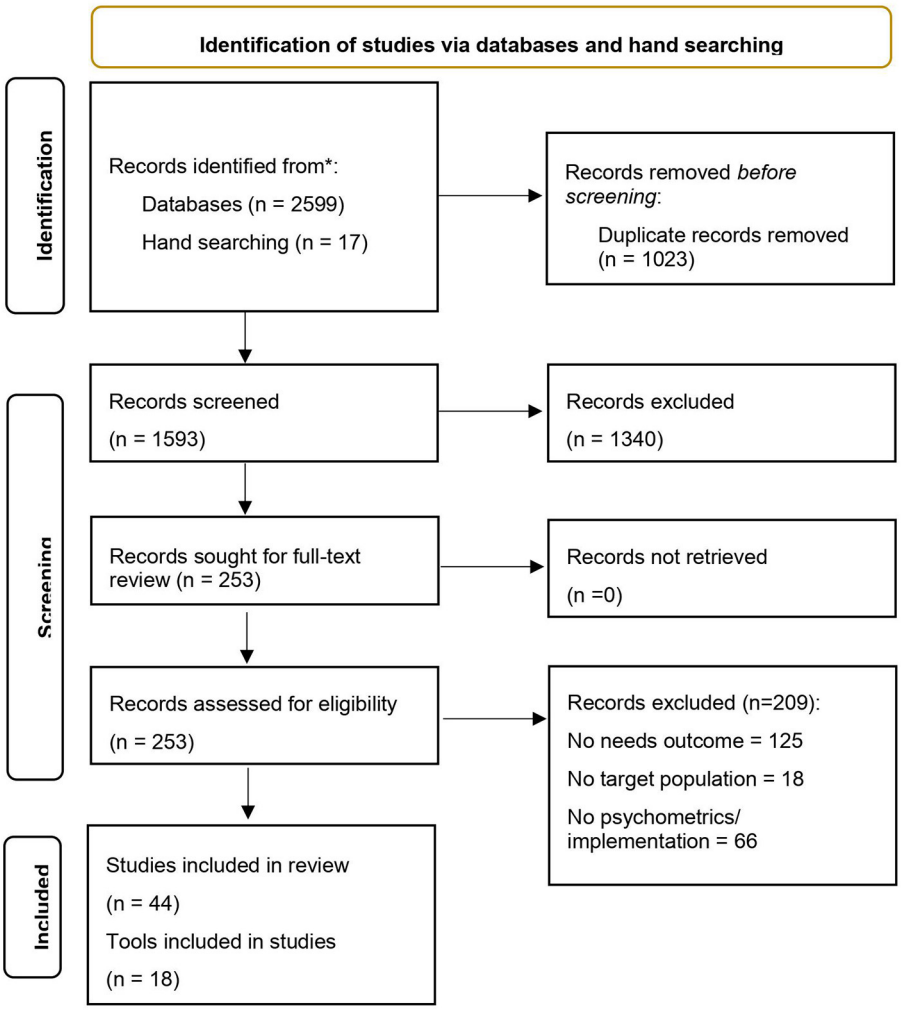

FIGURE 1 | PRISMA flow diagram.

palliative approach is required or assess palliative care needs; (iii) examined psychometric properties, acceptability, feasibility or clinical utility of a palliative care tool; and (iv) included primary collected data. Studies that included a heterogeneous sample of patients including HF and/or chronic respiratory disease patients, were included if they reported outcomes separately for the target population(s); or reported on a sample comprising at least 50% of the target populations.

Studies were excluded if they: (i) were published in a language other than English; (ii) examined tools assessing aspects of health or care other than needs, such as symptoms (e.g., Edmonton Symptom Assessment Scale, St George Respiratory Questionnaire), quality of life (e.g., Minnesota Living with Heart Failure), functional status (e.g., Australian Karnofsky Performance Scale), satisfaction with care (e.g., Quality Care Questionnaire- Palliative Care); (iii) focused on one needs domain, and (iv) were reviews, case studies, commentaries, theses, conference abstracts, protocols or editorials.

Study Screening

Article screening and coding was conducted using the reference management system Covidence. Following removal of duplicate citations, reviewers (AW, BH, KF) independently screened the titles and abstracts of all retrieved studies according to inclusion and exclusion criteria. Discrepancies were resolved by consensus between reviewers, or where there was insufficient detail available to exclude on the basis of study title and abstract, these studies progressed to full-text review. Pairs of reviewers (AW, BH and KF) independently assessed full-text articles for their eligibility for inclusion. Reasons for excluding studies at full-text review were documented (**Figure 1** PRISMA flow diagram of included studies). If discrepancies between reviewers for study inclusion could not be resolved by consensus, a field expert (KC) was consulted as a fourth reviewer to determine inclusion. Three authors (AW, BH and KF) undertook data extraction. Discrepancies were resolved by consensus.

TABLE 1 | Study and sample characteristics used to develop and/or psychometrically test identified tools.

Measure and author(s)	Population	Country, setting	Completion	Domains and items	Question format	Psychometrics
Identify those in need of palliative approach						
CriSTAL Criteria for screening and triaging to appropriate alternative care (36)	Older; any condition; high probability dying in ≤3 months.	Australia USA Netherlands Denmark Ireland Acute	Provider	**29 indicators**: Age≥65; ED admission; ≥2 deterioration criteria, frailty with ≥2 criteria; early warning score>4; presence ≥1 comorbidities; NH placement; cognitive impairment; repeat hospitalization/ICU; abnormal ECG; proteinuria	Presence/absence: "Yes," "No"	Face, content validity (36) Predictive validity (mortality, palliative care referral): retrospective (37, 38); prospective (39) (*additional articles in press*)
GSF PIG Gold Standard Framework Prognostic Indicator Guide (40)	Heart disease COPD	UK Tertiary care	Providers (to determine palliative care needs)	**8 items:** The Surprise Question (SQ); General indicators of decline; Specific clinical indicators related to certain conditions.	Presence/absence: "Yes," "No," "Don't know"	Predictive validity (41, 42) Sensitivity and specificity for COPD; sensitivity and specificity for COPD and HF (mixed patient sample) (43)
NECPAL Palliative Needs World Health Organization Collaborating Center (English translation) (40, 42)	Heart Failure (NECPAL-HF) Respiratory conditions	Spain Tertiary care	Provider	**17 indicators**: SQ, Requests for PC; General indicators (Functional decline, weight decline; Geriatric syndromes; Psychological adjustment Comorbidities Resources/ admissions) Disease-specific indicators	Presence/absence: "Yes," "No"	Predictive validity (HF) (44) Content validity
P-Cares Palliative care and rapid emergency screening Tool (45)	Any ED patient with life limiting illness	USA Emergency Department	Provider Time taken: 1.8 min (average)	Presence life limiting illness: advanced COPD, advanced HF advanced dementia, cancer, end stage renal, end stage liver, septic shock, chance of accelerated death PC needs: frequent visits, uncontrolled symptoms, functional decline, uncertain GOC/care distress, SQ	Presence/absence: "Yes," "No" Score 1+ life-limiting illness and 2+ PC needs indicates PC referral	Inter-rater reliability (46) Face, content validity (45) Criterion validity Acceptability (46) Predictive validity, prognostic utility (47)
ProPal-COPD (48)	COPD	Netherlands Hospital	Patients Providers	**2 patient reported indicators**: Medical Research Council dyspnea (MRC dyspnea); Clinical COPD Questionnaire (CCQ) 10 questions and 3 domains: symptoms, functional status and mental state. **Provider indicators**: SQ, 5 markers COPD severity, presence of comorbidities.	MRC dyspnea: 1 to 5. Higher scores = more severe dyspnea. CCQ: Total score = 6. Higher score = worse health status. Total score > − 1.362 = a high probability for death within 1 year.	Predictive validity (48)
RADPAC RADbound indicators for palliative care needs (49)	COPD Heart failure	Netherlands Primary care	Provider (to identify who requires a palliative care assessment)	General indicators (Functional decline, weight decline; patient-reported concerns Hospital admissions) Disease-specific indicators	Presence/absence: "Yes," "No"	Content validity (49)
SPICT Supportive and Palliative Care Indicators Tool (50)	Heart disease	UK Belgium Primary care Hospital	Provider (to identify who requires a palliative care assessment) Time taken: 4–5 min	**6 general, 21 specific indicators** SQ; General (Functional decline, weight decline; hospital admissions); Requests for PC Living in NH; Persistent symptoms; Disease-specific indicators	"Yes," "No"	Sensitivity and specificity cardiology patients (51) Additional psychometrics available (50, 52–54)
Assess unmet palliative care needs						
CareQol CHF Care-Related Quality of Life survey for Chronic Heart Failure (55, 56)	Heart failure	Netherlands Any	Patient	**20 items, 3 scales**: social and emotional problems; physical limitations; being in safe hands	In last 2 weeks: "never," "seldom," "sometimes," "often," "always," "not applicable."	Internal consistency (55) Face validity (56) Construct validity (55) Criterion validity (55)
HFNAQ Heart Failure Needs Assessment Questionnaire (57)	Heart Failure	Australia Any	Patient Time taken: 10 min	**30 items, 4 domains:** Physical (10 items), Psychological (9 items), Social (8 items), Existential (3 items)	Need for help in last month: 1 ("hardly ever") to 5 ("always")	Internal consistency (57) Content validity (57) Construct validity (57) Concurrent validity (57) Discriminant validity (57)

(Continued)

TABLE 1 | Continued

Measure and author(s)	Population	Country, setting	Completion	Domains and items	Question format	Psychometrics
I-HARP Identification of patients with HeARt failure with PC needs (58)	Heart Failure	Netherlands Primary Secondary Nursing homes	Provider, (in consultation patient/family) Time taken: 34 min (10–60 mins)	**13 items:** physical, daily activities, information, coping, psychological**,** culture/religion, social support, finances, future expectations/worries, carer needs. Open ended question: carer need for information	Presence/absence: "Yes," "No"	Face, content validity (58) Validity and reliability testing planned
NAT: PD-HF Needs Assessment Progressive Disease – Heart Failure (59)	Heart Failure [adapted from original NAT: PD-C (60)]	Australia Netherlands Germany Any	Provider Time taken: 5–10 mins (59) Time taken: 26 min (61)	**18 items, 3 domains:** Patient wellbeing Ability of caregiver/family to care for patients Caregiver/Family wellbeing	Level of concern: "none," "some/potential", "significant" Provider action to manage concern: "directly managed," "managed team," "referral."	Internal consistency (61) Face, content validity (59, 62) Inter-rater reliability (59, 61, 62) Test-retest reliability (61) Concurrent validity (59) Cultural adaptation (61, 62)
NAT:PD-ILD Needs Assessment Progressive Disease for people with Interstitial Lung Disease (63)	ILD [adapted from NAT: PD-C (60)]	UK Any	Provider with patient/carer Time taken: 5–10 min	**22 items, 4 domains:** Red flag symptoms and/or Priority referrals (7) Patient wellbeing (7) Ability of carer to care for patients (6) Carer wellbeing (2) Referral section	Level of concern: "none," "some/potential," "significant" Provider action to manage concern: "directly managed," "managed team," "referral."	Test-retest reliability (64) Face, content validity (63, 65) Construct validity (64) Inter-rater reliability (64)
NEST Needs near the end-of-life scale (66, 67)	Original: Mixed older: heart failure, renal, stroke, dementia, liver, pulmonary diseases (68) Modified: lung transplant (69)	**USA** Emergency department Outpatient Inpatient	Patient Provider	**Original 13 items:** Financial, Access to care, Social connection, Caregiving, Distress, Spirituality, Sense of purpose, Patient-clinician relationship, Clinician communication, Personal acceptance **Modified version 46 items*:*** additional 3 cultural items, 1 open-ended and 9 ESAS items.	Care needs at end of life: 0 ("no need") to 10 ("highest need"); higher scores = higher needs	**Original version:** Feasibility (68) Additional psychometrics available for cancer patients (66, 67, 70) **Modified version** (69) Internal consistency Content validity
PNAP Patient needs Assessment in Palliative Care (71)	End stage chronic diseases	Czech Republic Hospital	Patient Time taken: 45 min (average)	**40 items; 7 domains:** Physical symptoms (12) Social area (6) Respect/support from health professionals (5) Meaning of life (6) Autonomy (7) Share emotions (2) Religious needs (2)	Importance: 1 ("not at all important") to 5 ("very important") Satisfied: 1 ("not met") to 5 ("met in full") Higher score = greater importance/satisfaction	Internal consistency (71) Test-retest reliability Face, content validity Construct validity Convergent validity
IPOS Integrated Palliative Outcome Scale (72, 73)	COPD Heart failure (also: Cancer Dementia HIV/AIDS Kidney, Parkinson, Motor Neuron Disease, Multiple Sclerosis)	**UK** Any	Patient, Carer/proxy, Provider versions Time taken: 10 min	**POS 10 items:** Pain and other symptoms, patient anxiety, family anxiety, information, level support, life worth, self-worth, waste time, personal affairs. Patients open ended item to identify main problem; Staff asked performance status **IPOS 17 items, 3 domains**: Physical, Emotional, Communication/Practical Domains; Patients open ended item to identify main problem	**POS**: Problems, quality of life ≤3 days; Scales: 0 ("no problem") to 4 ("overwhelming problem"); higher score = more problems **IPOS:** Problems last 3 days: 0 ("no at all") to 4 ("overwhelming"). Total Score range 0 to 68; higher values = worse outcome	[see Buasewein et al. and Collins et al. for detailed overviews POS psychometrics (74, 75)] **IPOS (Mixed sample, 7% COPD and HF)** Internal consistency (72) Test-retest reliability (72) Inter-rater reliability (72) Construct validity (72) Face, content validity (76) Responsiveness (72) Further validation in progress

(Continued)

TABLE 1 | Continued

Measure and author(s)	Population	Country, setting	Completion	Domains and items	Question format	Psychometrics
SCNS-SF34 Supportive Care Needs Survey Short Form (original cancer version) (77)	Cardiovascular disease (78) Cystic fibrosis (79)	Australia Germany USA Any	Patient	**34 items, five domains:** Psychological. health system & information, physical & daily living, patient care & support, and sexuality	Level of unmet need last month: 1 ("no need"), 2 ("satisfied need"), 3 ("low need"), 4 ("moderate need"), 5 ("high need"); higher scores = higher levels of unmet need	Internal consistency (78, 79) Additional psychometrics available - cancer only (77)
SPARC Sheffield Profile for Assessment and Referral to Care (80, 81)	Idiopathic pulmonary fibrosis (82) Cancer (81, 83) Stroke (84)	UK Any	Patient Any setting	**45 items:** Communication/ information, Physical, Psychological, Religious and spiritual, Independence and activity, Family and social, Treatment **IPARC version:** 11 items (79)	Level of need last month: 0 ("not at all") to 3 ("very much") Desire for help last month: "Yes," "No" Any score of 3 – referral for further assessment	Internal consistency Face, content validity (81) Convergent and divergent validity Predictive validity (disease progression, mortality) (82)
Unnamed measure (85)	Heart Failure COPD Also oncological disease with metastasis	Bulgaria General practice	Carers	Not reported	"Yes," "No"; multiple choice; Two short answer	Test-retest reliability (85)

Data Extraction

Characteristics for Studies Examining Psychometric Properties of Existing Tools

Study characteristics and the sample used to develop and/or validate each of the included tools were extracted for all psychometric articles: (a) population; (b) country and setting, (c) purpose; (d) tool completion; (e) domains and items; (f) question format and (g) psychometrics. The psychometric properties were evaluated against pre-determined and generally accepted criteria including: reliability (internal consistency, inter-rater reliability and test-retest); validity (face, content, construct, and criterion); responsiveness; and cross-cultural adaptation, summarized in **Table 2**.

Characteristics of Studies Examining Implementation of Existing Tools

Study data extracted from each study implementing the included tools: (a) study design and aims; (b) setting and sample characteristics; (c) evaluation/intervention strategies; and (d) summary of outcomes.

Data Synthesis

A narrative approach was taken to synthesis the psychometric and implementation data of studies examining the included tools.

RESULTS

Search Results

An overview of the search results and study coding process is outlined in **Figure 1** using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram. The initial search yielded 2,616 articles. After removing 1,023 duplicates, 1,593 articles were included in the title and abstract screen. A total of 253 studies were included in the full-text review, of which, 44 met inclusion criteria (30 studies of 18 tools assessing psychometric properties with the target populations; 14 implementation studies) (see **Tables 1**, **2**).

Properties of Identified Tools

Purpose, Population and Context

As seen in **Table 1**, 11 tools have been developed with the primary aim of assessing and monitoring unmet needs across the spectrum of palliative care domains. Generic measures suitable for assessment of needs across a range of chronic diseases included the Integrated Palliative Outcome Scale (IPOS), which is one of the most established and well-validated tools in palliative care, as well as the Needs near the end-of-life scale (NEST); Patient Needs Assessment in Palliative Care (PNAP); Supportive Care Needs Survey Short Form (SCNS-SF34); Sheffield Profile for Assessment and Referral to Care (SPARC) and an unnamed proxy-completed measure. The remaining tools were developed and tested among people diagnosed with HF (Care-Related Quality of Life survey for Chronic Heart Failure [CareQol CHF]; Needs Assessment Tool: Progressive Disease – Heart Failure [NAT: PD-HF]; Heart Failure Needs Assessment Questionnaire [HFNAQ]; and Identification of patients with HeARt failure with PC needs [I-HARP]) or chronic respiratory diseases (Needs

TABLE 2 | Summary of studies summarizing the implementation of tools to identify and assess palliative care needs.

Intervention Studies					
Tool	**References, country**	**Study design, aim**	**Setting, Sample**	**Evaluation/Intervention**	**Summary of outcomes**
Clinical utility (prevalence)					
GSF-PIG	(86), Australia	**Design:** Prospective cohort study **Aim:** To test the prevalence, recognition and outcomes of patients with PC needs in acute care	**Setting:** University hospital **Sample:** Total *N* = 636 (COPD and HF included)	Criteria for initiation of treatment limitation were created using the clinical criteria from the UK GSF prognostic indicator criteria. Audit of hospital electronic database and patient records in two 24-h periods.	27% (*N* = 171) met GSF criteria, of which 12% had COPD and 6% had HF Age, hospital length of stay, GSF COPD criteria increased likelihood in-hospital treatment limitation Hospital mortality (9.9%), highest in patients with GSF HF criteria (30%)
IPOS (German version)	(87), Germany	**Design:** Cross-sectional, implementation study **Aim:** To test the utility of IPOS in assessing palliative care needs in patients with HF	**Setting:** University hospital **Sample:** *N* = 100 HF inpatients	IPOS completed by patients during hospital admission. Two items assessed the comprehensibility and suitability of IPOS.	Patients reported IPOS was: easy to understand (95%); suitable to assess palliative care needs (91%) 56% patients were suitable for SPC co-management (defined by: 2+ items "overwhelming", 3+ items "severe") No significant difference in IPOS total score between NYHA functional class II/III vs. IV, therefore all patients should receive needs assessment
NAT: PD-HF	(17), Australia	**Design:** Prospective cohort study **Aim:** Identify which patients with HF should receive SPC through implementing newly developed PC definition	**Setting: One** community hospital **Sample:** *N* = 272 HF patients (963 assessments)	Index admission assessments including: NAT: PD-HF Prognostic assessments (laboratory, echocardiographic) Physician assessments (physical, AKPS) Medical and drug history Patient measures (QoL, symptom burden, mood disturbance) Carer burden Repeated 4 monthly for 12–21 months	74 (27%) of HF patients had SPC needs Those with SPC need had: worse New York Heart Association class distribution prior to admission; higher % hospitalized in <6months for worsening HF; lower performance status (AKPS); and significant needs on NAT: PD-HF. 24% of those who needed SPC received it
NECPAL-HF	(44), Spain	**Design:** Prospective cohort study **Aim:** To identify HF patients for whom PC may be needed using NECPAL-HF indicators	**Setting:** Ambulatory clinics in three university hospitals **Sample:** *N* = 922 HF patients	NECPAL completed by nurse/physician at a scheduled clinic visit over 4 month period	32.1% (*N* = 297) patients were in need of PC 1 year mortality significantly higher in NECPAL-HF + patients (21.9 vs. 3.8%) The area under the receiver operating characteristics curve for predicting all-cause 1-year mortality was 0.73
NECPAL CCOMS-ICO	(88), Brazil	**Design:** Prospective cohort study **Aim:** To identify the need for palliative care in hospitalized patients with advanced CHF	**Setting:** Hospital **Sample:** *N* = 82 HF patients	NECPAL-HF questionnaire completed by nurse and/or a physician at a scheduled clinic visit over 4 month period	55% in need of PC using NECPAL
SPICT	(51), Belgium	**Design:** Prospective, implementation study **Aim:** To implement and validate SPICT in identifying older hospitalized in need of PC.	**Setting:** Hospital **Sample:** *N* = 209 geriatric patients; *N*=249 cardiology patients	SPICT completed by clinician during hospital admission; Carer contacted 1 year later for survival status and timing death	40% of older people on CUs were SPICT identified. CU SPICT identified patients reported more functional needs and symptoms than SPICT non-identified CU patients. Moderate sensitivity and specificity for CI (0.69 and 0.67 respectively)

(Continued)

TABLE 2 | Continued

Intervention Studies

Tool	Author, year, country	Study design, aim	Setting, Sample	Evaluation/Intervention	Summary of outcomes
Acceptability, feasibility and effectiveness of implementation					
IPOS	(89), UK	**Design:** Single-blind RCT **Aim:** To test the impact of the SIPS intervention on clinical and economic outcomes for older people living with chronic non-cancer conditions	**Setting: Four** general practices **Sample:** *N* = 50 (n= 24 intervention; *N* = 26 control) non-cancer patients (57% circulatory, 35% respiratory)	**Intervention:** usual care + SIPS care, including: palliative care assessment needs/concerns; MD review and management; coordination of care for 12 weeks with up to three-visits/contacts. **Control:** usual care (offered SIPS care at 12 weeks)	Intervention had significantly lower symptom distress than control at 6 and 12 weeks (IPOS) Symptom distress reduced with decreased costs for intervention compared to control (i.e., cost-effective) No significant differences between groups in psychosocial concerns (IPOS), ADLs (Barthel), QoL (EQ5D) or burden (ZBI)
IPOS	(90, 91), Ireland	**Design:** Mixed methods, implementation study **Aim:** To test the feasibility and acceptability of using IPOS, with nurse education and training, to improve the identification and management concerns of CHF patients	**Setting:** Nurse-led CHF disease management clinic in two tertiary referral centers **Sample:** *N* = 38 CHF patients (25 retained); 15 caregivers (10 retained)	**Intervention:** Nurse education and training; IPOS completed by patient at clinic visit; nurse assessed/managed needs and symptoms; implementation strategies included reminders, researcher support and staff engagement.	47% Consent rate (372 screened, 81 approached, 38 recruited) 60% IPOS completion rate 6% IPOS items missing ESAS-r, KCCQ, PHQ-8 and ZBI completion feasible via telephone The intervention and study design was feasible and acceptable. Patients and nurses reported supported identification of unmet needs; enabled holistic assessment; empowered patients.
NAT: PD-HF	(61), Netherlands	**Design:** Mixed methods, implementation pilot trial **Aim:** To test the feasibility and acceptability of Dutch NAT: PD-HF in HF outpatients and preliminary effectiveness of patient outcomes and PC referral	**Setting:** Academic hospital **Sample:** *N* = 23 HF outpatients; *N* = 10 carers; *N* = 8 HF nurses	**Intervention:** Nurses were trained in use of tool the NAT: PD-HF Dutch version; tool implemented during routine home care visit; actions taken by nurses in response	Acceptability: medium score of 7/10 (0 = not at all, 10 = very acceptable) Time taken: average 26 minutes 100% patients had PC needs; 11 (48%) actions taken, 4 (17%) were referred to other team/services Barriers/challenges: Difficult to assess PC needs; limited cultural adaptation; lack of prognostic awareness; role confusion; and lack of inter-disciplinary collaboration
RADPAC	(92–94), UK	**Design:** Cluster randomized controlled trial **Aim:** To test impact of GP training in identifying palliative patients and delivering structured, proactive PC.	**Setting: Two** general practices **Sample:** *N* = 159 (*N* = 80 intervention, *N* = 79 control) Cancer, COPD and CHF patients	**Intervention:** GP training in RADPAC, GP coaching session with PC physician in developing care plans, peer group sessions. Complete RADPAC with patients; medical record audit completed. **Control:** standard care; medical record audit completed.	57 GPs completed training in RADPAC No differences between intervention and control Only 50% intervention GPs identified patients (24% of deceased patients) Identified patients – more GP contact and more deaths at home, fewer hospitalisations 1 year later: trained GPs identified more palliative patients than did untrained GPs and delivered multidimensional palliative care
Supportive care decision aid	(95), UK	**Design:** Before and after, implementation study **Aim:** To test the impact of implementing a supportive care decision aid to identify and address unmet palliative and supportive care needs for patients with IPF.	**Setting:** Outpatient (referral ILD center) **Sample:** *N* = 89 (pre) and *N* = 73 (post) (*N* = 64 deceased) IPF patients	**Intervention:** Tool adapted from renal service tool, refined with expert / MDT input and pilot tested; Pre-implementation audit of hospice referrals, mortality data, medical records ILD service; Post-implementation: decision aid trialed for all patients in ILD clinics over 3 months. Same data collected for post cohort as pre cohort.	Completion rate 49%; Tool completion linked to increase in PC referral (17 vs. 3%). Post-implementation: significant increases in documented discussion PC referral (53 vs. 11%), end-of-life discussions (92 vs. 16%).

AKPS, Australia modified Karnofsky Performance Status; CHF, Chronic Heart Disease; COPD, Chronic Obstructive Pulmonary Disease; GSF, Gold Standards Framework; HF, Heart Failure; ILD, Interstitial Lung Disease; IPF, Idiopathic pulmonary Fibrosis; NAT, PD-HF, Needs Assessment Tool, Progressive Disease – Heart Failure; NECPAL-HF, NECesidades PALiativas; PC, Palliative Care; RADPAC, Radboud indicators for Palliative Care Needs; QoL, Quality of Life; SIPS: short-term integrated palliative and supportive care; SPC, Specialist Palliative Care; UK, United Kingdom.

Assessment Progressive Disease for people with Interstitial Lung Disease [NAT: PD-ILD]). Two of these tools, the NAT: PD-HF and NAT: PD-ILD, included items that assessed the needs of both patients diagnosed with HF or ILDs and their carers within the same instrument.

The remaining seven tools incorporate broader assessments that include general and disease-specific indicators with the primary aim of identifying people with progressive chronic diseases who are at risk of deteriorating and may benefit from palliative care across a range of settings. These include the Supportive and Palliative Care Indicators Tool (SPICT) for application across care settings (50); the Gold Standard Framework Prognostic Indicator Guide (GSF PIG) tested in tertiary care (40); the RADbound indicators for Palliative Care Needs (RADPAC) tool developed to support general practitioners (GPs) (49); and the Palliative Needs WHO Collaborating Center (NECPAL- CCOMs) tool, adapted from the SPICT and GSF PIG (40). Hospital-specific tools include the Criteria for Screening and Triaging to Appropriate alternative care (CrisTAL) tool for older person likely to die within the next 3 months (36); and the Palliative Care and Rapid Emergency Screening (P- CaRES) tool (45). The ProPal-COPD was developed for application for patients with COPD (48).

Reliability

Internal Consistency

Eight tools assessed the internal consistency of the scale. Of these, four reported adequate Cronbach's alphas [exceeding 0.70 (96)] for the total scale and each domain (CareQol CHF, HFNAQ, SCNS-SF34 [in cardiovascular population], PNAP). For the IPOS, SCNS-SF34 (in cystic fibrosis population) and NEST, internal consistency was partially confirmed (Cronbach's alpha of <0.70 for at least one domain).

Test-Retest Reliability

Only four tools examined test-retest reliability. One met the criteria ($k > 0.60$) for the total scale and each domain (PNAP); for the remainder (IPOS, NAT: PD-ILD, unnamed measure) test-retest reliability was partially confirmed ($k < 0.60$ for at least one domain).

Inter-rater Reliability

Inter-rater reliability was assessed for three tools, including the P-Cares, NAT: PD-HF and NAT: PD-ILD using hypothetical case vignettes and video simulated consultations. Inter-rater reliability was confirmed (IRR cutoff of Gwet's AC1 = 0.8) for the P-Cares. At least moderate agreement was found across all items in the NAT: PD-HF (prevalence and bias-adjusted kappa range 0.54-0.90); while inter-rater reliability was partially confirmed for the NAT: PD-ILD (5/16 items had moderate agreement, 11/16 had fair agreement). Inter-rater reliability was explored for the IPOS using patient-staff and staff-staff ratings of 376 patients receiving palliative care in a range of settings in two countries (72). Kappa scores (at least $\geq = 0.4$) were reported for 11 of 17 IPOS items.

Validity

Face and Content Validity

Face and/or content validity was reported for 12 tools. To establish face and content validity, approaches included reviewing previous literature on palliative care needs (CrisTAL, P-Cares, PNAP, RADPAC), adapting items derived from existing tools (CrisTAL, NECPAL, NAT:PD-HF, NAT: PD-ILD, NEST, PNAP, IPOS); and using expert panels and/or focus groups and interviews with health care providers, patients and/or caregivers to derive or refine selected items (CareQol CHF, CrisTAL, NEST, NAT:PD-HF, NAT: PD-ILD, P-Cares, PNAP, IPOS, RADPAC). Some studies employed multiple strategies to select and refine items (HFNAQ, I-HARP, P-Cares, SPARC).

Construct Validity

Adequate construct validity was demonstrated for four tools, with mixed results reported for the NAT: PD-HF. Convergent and divergent validity were examined against other existing tools (CareQol CHF, NAT: PD-HF, NAT: PD-ILD, IPOS, PNAP). Factor analysis was performed to examine construct validity (CareQol CHF, IPOS). Construct validity has also been established for original versions of some tools (e.g., POS, NEST, SPARC, SCNS-SF34). While evidence for construct validity in HF and chronic respiratory disease populations were not available for all tools and all disease-specific subscales reviewed, some authors reported that additional data is forthcoming (e.g., IPOS, I-HARP).

Criterion Validity

Some tools assessing level of unmet need examined criterion validity through comparison with established measures. Adequate criterion validity was established for the CareQol CHF and P-Cares. Three studies of the NAT: PD-HF demonstrated mixed results in relation to construct and criterion validity (17, 59, 61). Other studies focused primarily on examining the predictive validity of tools used to identify those in need of palliative care, particularly in relation to predicting disease progression, mortality and/or palliative care referral (CrisTAL, GSF-PIG, NECPAL, P-Cares, ProPal-COPD, SPARC and SPICT tools).

Responsiveness

There was limited evidence found for tool responsiveness (or sensitivity) to change over time, with only one study examining this psychometric property. A change of 5 points in the total IPOS score was reported to represent a moderate effect size in a mixed palliative population (72).

Administration Mode and Acceptability

Nine tools were completed by health care providers, two included both patient and provider assessment, and seven were self-completed by patients and/or their family or carer proxies. Acceptability was typically evaluated by assessing the length of time taken to complete the tool, reading ease and number of missing items. Where reported, average completion time ranged between 2 min (e.g., P-Cares) and 45 min (e.g., PNAP). Readability was reported for the IPOS, however, no further details

were provided in relation to how this was examined (90). Only one study reported the proportion of missing items. A non-response rate of 6% was reported for the IPOS questionnaire, a value greater than the 5% threshold for acceptability (90). Respondent feedback was also obtained about ease of use, clarity, and comprehensiveness of the items for some tools. Further evidence of acceptability, feasibility and clinical utility of tools when implemented in clinical practice is summarized below and in **Table 2**.

Acceptability, Feasibility and Clinical Utility of Implemented Tools

The feasibility of using tools to identify patients in need of palliative care in a range of settings was explored (**Table 2**). Tools such as the GSF-PIG (86), SPICT (51) and NECPAL (44, 88) were used to identify the proportion of HF and COPD patients in need of palliative care across general practice, hospital and outpatient settings. A prospective cohort study incorporated the NAT: PD-HF in a battery of assessment tools to test a newly developed definition of need for SPC in patients hospitalized with HF (17). Palliative care needs were identified for 27% of patients, however NAT: PD-HF score alone did not significantly predict PC needs. Utility of the German version of the IPOS was reported in a study of hospitalized HF patients, with 56% patients identified as suitable for palliative care (87).

Five studies examined the implementation of the tool(s) alone or as part of a broader intervention on care processes and services outcomes. A pilot implementation trial of a NAT: PD-HF intervention combined with nurse training did not improve communication about PC needs (61). No improvements in symptom burden, physical functioning, care dependency, or caregiver burden, end of life documentation or health care utilization were recorded, however, the intervention was not adequately powered for efficacy testing. In a mixed-methods, implementation study, use of the IPOS in a HF clinic, supported by nurse education and implementation strategies (reminders, staff engagement and research support), was found to be acceptable and feasible (90). Patients and nurses reported the approach improved recognition of needs, facilitated a more holistic assessment and empowered patients; however, some nurses reported uncertainty when it came to addressing identified needs (91). A small before and after study reported benefits of a shared care pathway and supporting tools for patients with HF, including improved access to palliative care, preferred place of death and access to a holistic HF service from point of care to the end of life (97). A cluster randomized controlled trial involved training GPs in identifying patients in need of palliative care and care planning using the RADPAC (93). Among deceased patients in both study groups, no differences were found for out-of-hours contact, GP contacts, place of death, or hospitalisations (93). However, the sub-group of identified patients had more GP contacts, less hospitalisations and were more likely to die at home. Longer-term outcomes, assessed 12-months later found trained GPs identified more palliative patients (most with a cancer diagnosis) and delivered multidimensional palliative care more often than untrained GPs (94). Another before and after implementation study of a supportive care decision aid with ILD patients found that completion was linked to increase in palliative care referral (17 vs. 3%) (95). Significant increases in documented discussions of palliative care referral (53 vs. 11%) and end-of-life discussions (92 vs. 16%) were reported for the post-implementation cohort. Effectiveness and cost-effectiveness were reported in only one trial of a needs-based palliative and supportive care intervention, with significant reductions in symptom distress (measured by IPOS) of older people living with chronic non-cancer (89).

DISCUSSION

This systematic review examined the psychometric quality, acceptability and clinical utility of needs assessment tools in identifying and addressing the palliative care needs of people with HF and chronic respiratory diseases. None of the tools included in this review met all psychometric criteria. Evidence for the acceptability and clinical utility of using the tools in these populations in clinical practice is limited.

A two stage process for needs assessment in routine practice has been proposed in the literature (35, 98). The first stage requires a pragmatic method of identifying those who are currently experiencing, or are likely to develop, palliative care needs (35, 98). Brief tools may be most appropriate for this purpose, particularly in busy settings with limited resources. These tools may also be more feasible for these patients, given the expected gradual, abrupt or intermittent functional decline as they progress toward the end of life. However, no tools identified in this review were designed to provide a brief snapshot of the needs of the target population (i.e., <5 min). The IPOS, NAT: PD-HF and NAT: PD-ILD, with an estimated completion time of 10 min, offer opportunity for development in this area. Alternatively, short provider-completed tools, such as the SPICT, NECPAL and RADPAC, may be useful as a first step in identifying those for whom a palliative approach may be beneficial (98–100). Disadvantages of these tools include their generic nature, that they do not quantify the severity or nature of the palliative care needs, and a lack of action prompts to address needs. Instead, these tools focus primarily on disease-related indicators (98, 99). This could result in under-recognition of holistic needs across psychological, social, cultural, and spiritual domains as defined by the WHO (101).

The second stage should involve the use of tools that facilitate a more comprehensive assessment of the nature and severity of needs patients may experience across domains (35, 98, 100). The mode of administration and potential burden remain important considerations for selection. Self-report tools, such as the HFNAQ, CareQol CHF and PNAP, place the individual patient as the expert, potentially promoting a person-centered approach to care. However, some self-report tools may be too burdensome for patients who are facing the end of their life and/or experiencing severe exacerbations. For instance, the estimated completion time for the PNAP is 45 min. Self-report

tools are also challenging to implement with patients who are acutely unwell or close to death. Tools that rely on proxy ratings, in contrast, can minimize patient burden, but ratings may not always accurately reflect patients' perceptions of what is most important to them or where they want support. Some tools, such as the IPOS, NAT: PD-HF, I-HARP and NAT: PD-ILD were developed to provide a combination of patient-proxy ratings, either through the completion of different versions of the tool (IPOS) or by completing the tool during consultations with patients and/or family members (NATs and IHARP). While the former enables a comparison of ratings to inform care planning, an advantage of the latter approach is that it enables a real-time discussion of what is most important to the patient, as well as the acceptability of actions that providers may suggest to address identified needs. This, however, has implications for time burden, highlighting the importance of exploring impact on time and resources.

Underpinning the development of needs assessment tools, is the perception that these tools can be feasibly implemented so that patients with identified needs can receive appropriate care, leading to an improvement in outcomes. Our review identified few studies examining the acceptability, feasibility and clinical utility of tools in routine practice. This suggests to date, few data report work in this area for for HF and respiratory disease when compared with measures development and descriptive research. Many were single-center, cross-sectional studies aimed at estimating prevalence. The settings in which these tools were implemented varied considerably, with the majority focused on a heterogeneous population in which people with HF or respiratory diseases comprised a smaller proportion. Data on acceptability from the perspective of the health care team implementing the tool, as well as level of burden and additional support and resources required to successfully implement care plans developed as a consequence, were rarely examined. To date, the RADPAC is the only identification tool which has been tested in a methodologically rigorous controlled trial. Despite being introduced within the context of a multi-component package that included GP education and training, no significant differences were found between the intervention and control group. The finding that a sub-group of identified patients reported more home deaths and fewer hospitalizations, and that trained GPs identified more palliative patients and delivered more palliative care, suggests utility and effectiveness warrants further examination. Organizations such as the European Association for Palliative Care Task Force have recommended the SPICT for use in HF populations (99), however, acknowledge further work is needed to validate this tool.

Most studies involved implementing tools without consideration of actions to be taken to address recognized needs. As part of this, a key challenge for needs-based approach is to determine the most appropriate methods for scoring unmet needs surveys and determining what constitutes a clinically significant change. Further, a lack of education and training for the providers involved was highlighted as an important limitation. For instance, in a Dutch study involving nurses implementing the NAT: PD-HF, nurses reported lacking the knowledge and training to address identified needs (61). In the case of the NAT: PD-HF and NAT: PD-ILD, these actions are largely based on clinical judgement, without clear criteria for referral. Evidence of effectiveness and cost-effectiveness for improving outcomes is also lacking.

Implications for Research, Practice and Policy

There is emerging evidence that palliative care is an effective approach for people diagnosed with HF and chronic respiratory conditions. Traditional palliative care approaches rely on prognosis and diagnosis as triggers for referral (102). However, the poor utility of available prognostic tools and the ambiguous relationship between prognosis and palliative care needs suggest that prognostication may not be an appropriate trigger (9, 26, 31, 99, 103). Implementing approaches confirmed as efficacious in one patient cohort, such as cancer, and translating them into practice with other non-malignant cohorts is insufficient given their unique burden and complexities (102). A needs-based approach offers a promising alternative, but the rigor of the approach must be established before such processes are accepted and widely implemented. The limited evidence for successful implementation and the psychometric shortcomings of existing tools, demonstrates the importance of psychometrically robust tools to progress the field. Further validation of tools that can reliably and repeatedly assess unmet needs across the broad range of palliative care domains, as well as identify changes in needs over time, is required. The interpretation and utility of these tools with HF and chronic respiratory populations also requires further development of criteria defining clinical significance and clinically important changes in needs.

Identification of needs must also be supported by care processes and actions that are informed by best available evidence, align with needs and do not cause undue harm. Structured care processes (e.g., care bundles) potentially have numerous benefits for delivering good clinical care, while also facilitating measurement and feedback processes (104, 105). Studies quantifying the nature, severity and trajectory of unmet needs for HF and chronic respiratory conditions can inform the selection of care processes with which to intervene. Generalist and specialist providers should receive targeted education and training to ensure they are equipped with the skills to: recognize palliative care needs; appropriately communicate this with patients; and provide appropriate care (102). Promoting earlier identification of palliative care needs and appropriate care planning, tailored to medical conditions, has the potential to achieve hospital avoidance, death in place of choice, better symptom control and less family distress. Improvements in planning and clinical care can also potentially reduce the distress experienced by health professionals in this field.

Study Limitations

A strength of this review include the systematic literature search that encompassed a wide range of broad search terms and multiple databases. However, gray literature, dissertations or policy documents were not included, as while this literature contributes important information, it

is not peer-reviewed. Publications were also restricted to English language, which may have resulted in some studies being missed.

CONCLUSION

The impetus to develop and implement tools for palliative care is reflected in the increasing number of needs assessment tools being developed and tested with HF and chronic respiratory disease populations. However, further evidence of psychometric quality is needed, particularly test-retest reliability, predictive validity, responsiveness, and clinical utility of these tools. Further, relying on "needs" as the recommended criterion must be supported by a systematic approach that incorporates structured care processes; improved community awareness of the potential benefits offered by palliative care; and education and training for providers across care settings. Rigorous evaluation to determine the impact of adopting a systematic needs-based approach for HF and chronic respiratory disease on the physical and psychosocial outcomes of patients and carers, as well as the economic costs and benefits to the healthcare system, is required.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

AW: conceptualization. AW, KF, and BH: screening of articles and data extraction (methodology). AW, BH, KF, and KC: analysis, interpretation, and writing (original draft preparation). All authors contributed to the final version of the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2022.878428/full#supplementary-material

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REVIEW
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Modification of Cardiovascular Drugs in Advanced Heart Failure: A Narrative Review

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Advanced heart failure (HF) is a complex entity with a clinical course difficult to predict. However, most patients have a poor prognosis. This document addresses the modification of cardiovascular drugs in patients with advanced HF that are not candidates to heart transplantation or ventricular assist device and are in need of palliative care. The adjustment of cardiovascular drugs is frequently needed in these patients. The shift in emphasis from life-prolonging to symptomatic treatments should be a progressive one. We establish a series of recommendations with the aim of adjusting drugs in these patients, in order to adapt treatment to the needs and wishes of each patient. This is frequently a difficult process for patients and professionals, as drug discontinuing needs to balance treatment benefit with the psychological adaption to having a terminal illness. We encourage the use of validated assessment tools to assess prognosis and to use this information to take clinical decisions regarding drug withdrawal and therapeutic changes. The golden rule is to stop drugs that are harmful or non-essential and to continue the ones that provide symptomatic improvement.

Keywords: advanced heart failure, palliative care, cardiovascular drugs, drug withdrawal, prognosis, end of life

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INTRODUCTION

According to the World Health Organization Global Atlas of Palliative Care at the End of Life there are already more adults in need of palliative care due to cardiovascular conditions than to cancer[1] and population aging will probably increase this tendency (1), making essential to include palliative approach in many routine cardiology consultations. Disabling symptoms are common in patients with cardiovascular disease, particularly in those with advanced heart failure (HF). The current Heart Failure Association-European Society of Cardiology criteria for defining advanced HF include severe and persistent symptoms (functional class III or IV), severe cardiac dysfunction, recent (in the last 12 months) episodes of congestion requiring high-dose intravenous diuretics, low output requiring inotropes or vasoactive drugs or malignant arrhythmias, and severe impairment of exercise capacity (2).

Deprescribing is a growing problem in modern medicine, which has been dominated by treatments focused on treating specific disease entities rather than treating patients with a global approach. Evidence-based medicine is mainly based on clinical trials results which included carefully selected patients with a specific disease entity. Patients with comorbidities, advanced age

[1] https://www.who.int/nmh/Global_Atlas_of_Palliative_Care.pdf

or disability are frequently excluded from the randomized trials. This is very relevant in HF, as mean age in HF patients is about 80 years and comorbidities are the rule. Guidelines for dealing with specific conditions as HF, mostly built on the results of clinical trials, rarely focus on the problem of multimorbidity and polypharmacy and the need to assess drugs interactions used for multiple indications. Previous authors have suggested that this is the case in HF, as current guidelines for diagnosis and treatment do not fit with clinical complexity (3). HF is rarely an isolated condition and in most cases occurs together with diseases of the cardiovascular system, such as arterial hypertension, ischemic heart disease, valvular disease, or atrial fibrillation; metabolic diseases such as diabetes or gout; respiratory disorders such as chronic obstructive pulmonary disease; chronic kidney disease; or liver failure. As a result, a patient with advanced HF is frequently treated by several specialists, each of whom treats "their" disease, leading to polypharmacy and common side effects and drug interactions (4).

In this context, reconsidering drugs use in the last phase of life seems obvious but, as this strategy is inadequately described in guidelines, protocol procedures for deprescribing are rarely launched. Patients with advanced HF often take multiple medications that may not have beneficial effects in view of their limited life expectancy and changing organ function. The potential interactions between cardiovascular drugs and palliative symptoms relievers should also be considered. On the other hand, stopping all cardiovascular medications is frequently a mistake as some improve symptoms and should be maintained while tolerated. In any case, decisions about the discontinuation of preventive medicines for individuals approaching the end of life are increasingly complicated, by the lack of clear deprescribing guidelines for these medicines (5). However, most data suggest that deprescribing should be more frequent, for instance, the five most common classes of medications prescribed near the end of life are antihypertensives, broncholytic drugs/bronchodilators, laxatives, antidepressants, and gastric protection agents (6).

Limiting polypharmacy decreases the risk of adverse effects, medical errors, associated cost and harmful drug interactions. Moreover, the time lag to benefit from the use of many cardiovascular drugs is frequently longer than the life expectancy of patients with advanced HF that are not candidates to heart transplantation or ventricular assist device. In these patients, frequently there is a need to modify, and even to discontinue, cardiovascular drugs. The decision to discontinue some drugs like lipid-lowering products is rather straightforward. In other cases, like antithrombotic therapy and specific HF drugs, the medication should be stopped in some patients but not in others. For instance, discontinuation of some HF drugs may provoke exacerbation of symptoms and should be considered only in the last weeks of life. In this revision, we address the modification of cardiovascular drugs in patients with advanced HF who are not candidates to life-prolonging therapies. We encourage the use of validated assessment tools to assess prognosis and to use this information to take clinical decisions regarding drug withdrawal and therapeutic changes. Physiotherapy and rehabilitation should also be recommended for all HF patients, as they may prevent or diminish pain and fatigue. In addition, the psychological effects of exercise cannot be forgotten.

PALLIATIVE EFFECTS OF CARDIOVASCULAR DRUGS

Dyspnea is a common complaint and even during hospital admission, breathlessness is frequently under-diagnosed and under-treated (7). Moreover, about a quarter of patients admitted with HF persist with severe dyspnea at discharge and HF patients present worse quality of life than patients with respiratory diseases (8). Diuretics are the basis for treatment of dyspnea and are used for pulmonary decongestion. The route of administration and dosages should be consistent with the clinical situation and degree of congestion, with close monitoring of the patient's response. In ambulatory patients with advanced HF, an alternative may be to administer subcutaneous furosemide (9). Oxygen therapy is also important to relive dyspnea, particularly in hypoxemic patients. Vasodilators can also be used as support in the treatment of dyspnea but can cause symptomatic hypotension or worsening of the renal function. The use of drugs to improve breathlessness should be complemented with other simple and effective measures, such as fresh air (breezes or fans) directed toward the patient's face. In addition, in case of refractory breathlessness, pharmacologic interventions are mandatory, and opioids play a key role in this setting. We need to remember that morphine has cardiovascular effects due mainly to its vasodilatory properties and effects related to anticipated anxiolysis. However, although morphine does not seem to increase the risk of short-term death in patients with acute advanced HF, the risk of long-term death and invasive ventilation might be increased (10).

Leg pain and discomfort related to edema can be frequently observed in patients with right ventricular HF or tricuspid valve insufficiency and might be exacerbated by HF-related liver cirrhosis and hypoalbuminemia. Loop diuretics and aldosterone antagonists are useful, although an equilibrium between their benefits and the risk related to hypovolemia or, in the case of loop-diuretics, hypokaliemia should be scrutinized. Also, diuretic resistance despite escalating doses of a loop diuretic to a ceiling level (80 mg of furosemide once or twice daily or greater in those with reduced glomerular filtration rate) is common in these patients. The use of local leg compression can also be considered (11). On the other hand, aldosterone antagonists may lead to hyperkaliemia or renal failure.

Fatigue is also common in patients with advanced HF and might be their main symptom. Ambulatory inotropes are an option in some patients that is increasingly offered as a palliative therapy. Although there remains a profound lack of data and guidance on the effect of palliative inotropes on quality of life, limited available data suggest that inotrope therapy improves functional class and does not impact survival (12). Levosimendan has shown some advantages: for instance, its effects are sustained after the initial infusion, it can be used in patients treated with beta-blockers, and it does not increase oxygen requirements (13).

PROGNOSIS ASSESSMENT

The use of HF risk scores is recommended to avoid the frequent overoptimistic subjective appreciation of prognosis (14). Physicians are inaccurate in their expected life predictions for terminally ill patients and the error is systematically optimistic, thus affecting the quality of care given to patients near the end of life. None of the contemporary risk scores shows a clear superiority over the others (15). Barcelona Bio-Heart Failure (BCN-Bio-HF) calculator provides the best discrimination and overall performance but tends to overestimate the risk. Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC-HF) has the best calibration, and Seattle Heart Failure Model (SHFM) and PARADIGM Risk of Events and Death in the Contemporary Treatment of Heart Failure (PREDICT-HF) tend to underestimate the risk. All these prognostic risk calculators are available and have been critically reviewed, although prognostication on an individual basis remains challenging. An uncertainty in prognosis prediction is almost inherent to advanced HF and should be explained to the patient and the family. Such previous explanation helps patients and relatives to better understand therapy re-adjustment that, as we will see in the next paragraph, might include restarting withdrawn drugs.

MEDICATION REVIEW AND DRUG-DISEASE INTERACTIONS

A full medication review of all patients with advanced HF should be undertaken with a view to rationalizing medications with questionable benefit in the face of limited prognosis. Target groups of medication to consider deprescribing would usually include statins, but also drugs with long-term effects prescribed for comorbid conditions such as vitamins, bisphosphonates and proton pump inhibitors. Drug-disease interactions are common for patients with advanced HF due to changes in pharmacokinetics as a result of impaired renal function, reduced hepatic metabolism, and gut edema.

CARDIOVASCULAR DRUGS DISCONTINUATION AND RE-ADJUSTMENT OF THERAPY

Reconsidering drugs in the last phase of life should be done more frequently, even more the case of advanced HF, as these patients frequently improve and deteriorate, sometimes unexpectedly. If patients improve, they may need new cardiovascular drugs and, in these cases, the withdrawing will be of palliative care drugs (for instance, opioids after dyspnea improvement). This re-adjustment of therapy might also include restarting or increasing previously reduced doses of cardiovascular drugs (16).

Drug deprescribing should be a proactive, patient-centered approach that should include a frequent assessment of goals of care, values, preferences and life expectancy. Patients may be reticent to the withdrawal of previously indicated therapies. Therefore, professionals need to motivate change by emphasizing the benefit of withdrawing some drugs, like the reduction in the number of pills per day or the prevention of side effects. In addition, deprescribing should not be associated to a reduction in medical care and should focus on realistic treatment goals mainly aimed quality of life improvement.

Transition of the goals of care toward improving comfort and focusing on alleviating symptoms requires a continuous communication with patients and their families. The validity of former indications for their use, after setting new goals, should be evaluated. Treatments relevant for symptom management (or prevention) should be continued unless relevant side effects appear. On the other hand, cardiovascular drugs prescribed for conditions that are becoming no longer relevant should be considered for withdrawal. Therapies causing adverse effects and most preventive drugs, especially those with a long delay in showing their benefits should be stopped. The simple message would be to maintain drugs that reduce the burden of symptoms (while recording these symptoms) and to reconsider drugs used to treat or prevent (chronic) illnesses (**Figure 1**). Therefore, routinely stopping cardiovascular drugs when starting palliative care is inappropriate, as many drugs are important for symptoms control.

ANTICIPATORY PRESCRIBING AND DEPRESCRIBING

Maintaining patient and family autonomy, preparing them for sudden unpredictable situations and providing the means for self-care are essential elements for successful care of patients with advanced HF. Anticipatory prescribing tries to prepare for future situations by doing prescriptions of drugs that might be needed in emergencies in the future. Making those drugs accessible at home with clear instructions for their use, can empower patients and caregivers in self-management until professional care is available. In a similar way, clear indications as when to withdraw a drug might help patient that are at home to stop using drugs that are no longer useful or that have become unnecessary.

TRIGGERS FOR DRUG ADJUSTMENT AND BAD NEWS DELIVERY

Drug adjustment and deprescribing should be a gradual process initiated as HF progresses. Prognostic tools, symptom assessment tools, and events as hospitalization might be an excuse to start conversations about the goals of care, and the need to readjust drug therapy. Other triggers to initiate this conversation might be uncontrolled symptoms, recurrent HF exacerbation, progressive frailty, patient and/or caregiver concerns. The moment when a do-not-resuscitate order protocol is decided might also be a good opportunity to initiate this talk (17). However, do-not-resuscitate orders, also known as do-not-attempt-resuscitation are frequently implemented in a very advanced situation, so drug adjustment should be ideally done weeks or months before (18, 19).

Table 1 describes the six-step protocol for delivering bad news SPIKES. Although originally described for cancer patients (20) it is perfectly applicable to initiate a conversation regarding

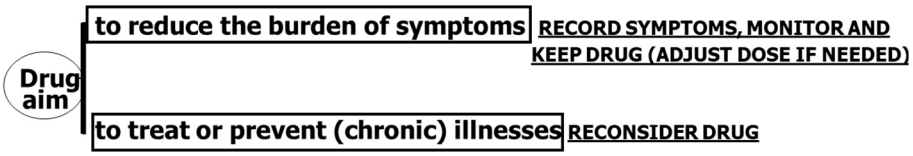

FIGURE 1 | Decision tree algorithm regarding the adjustment of cardiovascular drugs in patients with advanced heart failure.

TABLE 1 | A six-step protocol for delivering bad news.

Setting
• Privacy
• Involve significant others
• Sit down
• Look attentive and calm
• Adopt listening mode
Perception
• Before you tell, ask
• Assess the gap between the patient's expectations and the actual medical situation
Invitation
• Do not assume that all patients want to know all
• Ask about preferences regarding information
Knowledge
• Give a warning that bad news is coming
• Give the information in small chunks
• Use clear language
Empathy
• Acknowledge and address the patient's emotions
• Let them know that showing emotion is normal
Strategy and summary
• Ensure that the patient understands the information
• Summarize the information and give an opportunity for the patient to voice concerns

Please note the mnemonic acronym SPIKES [Sobanski et al., (16)].

TABLE 2 | Most common adjustment described in the literature of cardiovascular drugs in patients with advanced heart failure in need of palliative care.

	Recommendation	When to reduce dose or withdraw
Diuretics	Keep unless clear reason to stop	Hypovolemia, hyponatriemia, dehydration, hypotonia
Beta-blockers	Consider gradual dose reduction, risk of reflex tachyarrhythmias	Fatigue, hypotension, bradycardia
ACE inhibitor, ARB, Sacubitril/valsartan, MRA	Keep, consider dose reduction	Hypotension, renal failure, hyperkaliemia
SGLT2 inhibitors	Keep	Renal failure
Ivabradinine	Keep	Bradycardia
Inotropics	Keep if symptomatic benefit and if facilitates dying at home.	Withdraw in the last hours and in those without symptomatic benefit
Statins	Withdraw	Almost always
Antiplatelets	Withdraw unless recent PCI	Almost always
Anticoagulation	Withdraw unless high risk of stroke	Bleeding

(1) All decisions should be done on individual bases; (2) drugs with long-term effects as statins, aspirin, antihypertensives (and sometimes betablockers) usually should be stopped; (3) Cessation of medications will need sensitive explanation as patients may have been informed that these are lifelong therapies;(4) if severe deterioration and when swallowing becomes difficult: keep only drugs that maintain comfort, as subcutaneous options.
ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium–glucose co-transporter 2; PCI: percutaneous coronary intervention.

deprescribing and other palliative care issues in advanced HF (21). The setting is very important and patient privacy should be respected but, at the same time, it is essential to involve significant others unless the patient is opposed to their presence. Asking patients about their expectations and preferences regarding information before delivering it is also needed. A realistic approach of those expectations will help patients to accept drug adjustment, as will the use of clear language and the progressive presentation of the expected prognosis. Empathy helps to develop a meaningful relationship with the patient and summarizing the information with the specific therapeutic changes that will be performed gives patients and families the opportunity to voice concerns and ask questions.

COMMON CARDIOVASCULAR DRUGS ADJUSTMENTS

Table 2 shows the most common adjustment of cardiovascular drugs in patients with advanced HF. Drugs that produce symptoms relief, as diuretics, should be kept unless relevant side effects appear. Drugs with long-term effects should be withdrawn. In some cases, the decision is not straightforward, and specific patient characteristics like renal function and blood pressure might influence the decision to continue or withdraw, for instance with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonists, and sodium–glucose co-transporter 2. Beta-blockers might prevent tachycardia and/or angina, but they can also produce symptomatic hypotension or fatigue. As we have stated previously, inotropics may provide symptomatic benefit and can facilitate dying at home and avoid rehospitalizations but should be withdrawn in patients approaching the last days/hours and in those without symptomatic benefit. Finally, hypotonia is common in patients approaching the end of life, and might be aggravated by drugs that decease blood pressure. Drug reduction or even withdrawal should be evaluated, particularly in the case

TABLE 3 | Authors recommendation regarding factors to consider when withdrawing cardiovascular therapies.

- **Assess benefit-burden rate:** Knowing the time to benefit helps treatment decisions
- **Dialogue:** Goals might change. Making short-term goals usually helps
- **Metabolism:** Pharmacokinetics, bioavailability, and pharmacodynamics frequently change significantly in advanced HF
- **Individualize:** Consider specific needs, problems, and previous treatments
- **Renal function:** Little evidence to support HF drugs in patients with severe chronic kidney disease
- **Adverse effects:** the number of drugs is associated with an increased likelihood of adverse reactions
- **Total cost:** Resource allocation is also a legitimate reason to withdraw non-essential treatments
- **Implantable cardioverter defibrillator (ICD):** Consider turning off defibrillation function in ICD carriers
- **Other:** Emotional, psychological, and cultural effects of withdrawing drugs
- **Natural history/prognosis:** Use of specific heart failure prognostic indexes is recommended

Please note the mnemonic acronym ADMIRATION.
HF, heart failure.

of therapies that do not influence symptoms or trajectory of HF, as calcium channel blockers or nitrates.

FACTORS TO CONSIDER WHEN WITHDRAWING CARDIOVASCULAR THERAPIES

There are several factors to consider before withdrawing cardiovascular therapies. We have created the mnemonic acronym ADMIRATION that facilitates a correct therapy adjustment (**Table 3**). It is mandatory to assess the benefit-burden rate as knowing the expected time to benefit is essential in the decision making process as most patients with advanced HF will not leave enough time as to see profit from some drugs (22). A truthful empathic dialogue with the patient to establish specific goals helps the patient and the family to understand the need to modify the current treatment. Drug pharmacokinetics and pharmacodynamics frequently change dramatically in patients with advanced HF, for instance due to gut edema, liver dysfunction, and renal insufficiency. We should always consider specific patient needs, and baseline treatment before drug adjustment, with special attention to polypharmacy as the number of drugs is associated with an increased likelihood of adverse reactions. Resource allocation is also a reason to stop treatments that are not harmful but that might already be non-essential. Finally, in patients with implantable cardioverter defibrillators, the possibility of turning off defibrillation function should be covered (23). The goal is avoidance of suffering caused by high voltage therapies, so antitachycardia and antibradycardia pacing, and resynchronization therapy, that do not produce pain and improve symptoms should be kept.

DRUGS AS CAUSE OF FATIGUE AND OTHER SYMPTOMS

The phenomenon of incapacitating chronic fatigue is very common in patients with advanced HF. Although this symptom is mainly related with low cardiac output and reduced blood flow through the muscles and brain, multi-organ failure might also play role, including chronic kidney disease, liver failure, and adrenal insufficiency. Regarding drugs, diuretics and beta-blockers or their side effects, such as hyponatremia (24) or circulatory centralization, may also exacerbate fatigue. Especially in very frail people or those approaching end of live, thirst stimulus can be strongly reduced, with an increasing risk of dehydration. Depression is common in this group of patients and may be slightly aggravated by beta-blockers, although recent data do not support a clear association between beta-blocker therapy and depression (25). Beta-blockers may also exacerbate the freezing phenomenon of the limbs as a result of vasoconstrictive influence on microcirculation, a property mainly exhibited by beta-blockers devoid of vasodilatory properties.

Another factor contributing to significant weakness and aggravating the feeling of fatigue is anemia, which may be a consequence of bleeding resulting from the use of antiplatelet or anticoagulant drugs. Bleeding frequently causes worsening HF and rehospitalization (26). Moreover, these drugs are frequently prescribed with proton pump inhibitors. Proton pump inhibitors may increase the risk of cardiovascular events and might increase the risk of Clostridium difficile infection (27, 28).

WITHDRAWING LIFE-SUSTAINING DRUGS

The concept of life-sustaining drugs is not straightforward, although in some patients with advanced HF the decision to stop inotropes might be associated with death in a short period of time. Ethical commitments can make it hard for doctors to consider withdrawing life-sustaining drugs even when the patient, or their family, do not want treatment to be continued (29). Unfortunately, physicians and families often just do not know advanced HF patients' wishes and expectations. A written attestation from the patient and a formal record of drug might improve decision-making regarding drug withdrawal. Withdrawing life-sustaining drugs has clinical aspects but also ethical, legal, cultural, religious, and financial aspects that might also influence this decisions. Before taking the decision, it is essential to understand whether the treatment is providing a benefit to the patient. The term medical futility, although widely used, has recently been deemed misleading and calls have been made for it to be reserved for drugs that have no possibility of working (30). "Potentially inappropriate" are now being used for drugs that have at least some chance of still benefiting the patient, but clinicians believe that competing scientific and ethical considerations justify not to provide them.

FUTURE TRENDS

HF prevalence and health loss burden are constantly increasing, especially in the elderly. We need to redesign healthcare access, infrastructure and therapies including a multidisciplinary approach that includes palliative care of patients with advanced HF (31). New tools like telemedicine and artificial intelligence might help in the early detection of symptomatic needs but always with a personalized HF patient-centered approach (32). Despite greater adoption of a palliative approach in the terminal admission over the last decade, a significant proportion of patients with HF keep their usual medical treatment and receive palliative care late, just prior to death (31). An earlier recognition of HF terminal phase, to facilitate a correct modification of cardiovascular drugs and provision of an appropriate palliative approach remains a challenge. The involvement of patients and their care providers is essential to this adjustment of medical treatment. Patients with advanced HF have a high mortality and large healthcare utilization. Programs of integrated care for have been shown to be effective (33) and to increase treatment adjustments and the proportion of HF patients who died in non-acute care settings. More proactive, individualized palliative care referral of advanced HF patients to specialized palliative care should be implemented, particularly in the case of difficult and challenging scenarios.

In this manuscript, we have tried to present the challenges associated with cardiovascular drugs and life sustaining withdrawing. The readers should be aware that specific aspects of clinical practice and law may vary in different countries. Also, although we have focused in deprescribing, the decision not to start a drug is quite similar.

CONCLUSIONS

The adjustment of cardiovascular drugs is frequently needed in patients with advanced HF. The shift in emphasis from life-prolonging to symptomatic treatments should be a gradual one. This is frequently a difficult process for patients and professionals, as drug discontinuing needs to balance treatment benefit with the psychological adaption to having a terminal illness. The golden rule is to stop drugs that are harmful or non-essential and to continue the ones that provide symptomatic improvement. In complex cases, specialized palliative care consultation in the deprescribing process might be needed.

AUTHOR CONTRIBUTIONS

MM-S prepared the first draft of the manuscript. TG improved the manuscript with relevant content. Both authors contributed to the article and approved the submitted version.

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Unmet Needs in Patients With Heart Failure: The Importance of Palliative Care in a Heart Failure Clinic

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Background: There are increasing calls to establish heart failure (HF) clinics due to their effectiveness in the interdisciplinary management of people living with HF. However, although a recommendation exists for palliative care (PC) providers to be part of the interdisciplinary team, few of the established HF clinics include them in their teams. Therefore, in this qualitative study, we aimed to understand the unmet PC needs of patients with HF attending an already established HF clinic.

Methods: Secondary qualitative analysis of structured interviews undertaken within a larger study to validate the German version of the Needs Assessment Tool: Progressive Disease—Heart Failure (NAT: PD-HF). The NAT: PD-HF is a tool that aims to assess unmet needs in patients with HF. The interviews took place between January and March 2020 with patients from the ambulatory HF Clinic of a University Hospital in Switzerland. For this analysis, we transcribed and thematically analyzed the longest and most content-rich interviews until we reached data saturation at 31 participants. The interviews lasted 31 min on average (24–48 min).

Results: Participants ($n = 31$) had a median age of 64 years (IQR 56–77), the majority had reduced ejection fraction, were men, and were classified as having a New York Heart Association functional class II. Participants were in general satisfied with the treatment and information received at the HF clinic. However, they reported several unmet needs. We therefore identified three ambivalences as main themes: (I) "feeling well-informed but missing essential discussions", (II) "although feeling mostly satisfied with the care, remaining with unmet care needs", and (III) "fearing a referral to palliative care but acknowledging its importance".

Conclusion: Although patients who are receiving multidisciplinary management in ambulatory HF clinics are generally satisfied with the care received, they remain with unmet needs. These unmet needs, such as the need for advance care planning or

the need for timely and tactful end-of-life discussions, can be fulfilled by PC providers. Including personnel trained in PC as part of the multidisciplinary team could help to address patients' needs, thus improving the quality of care and the quality of life of people living with HF.

Keywords: heart failure, palliative care, patient-centered care, qualitative study, multidisciplinary team, quality of care/care delivery

INTRODUCTION

For several decades, evidence has shown that patients with heart failure (HF) not only have palliative care (PC) needs comparable to patients with cancer but often for a significantly longer period of time (1). However, in most countries, access to PC for patients with HF is still suboptimal and gaps between PC needs and PC delivery within this patient population are substantial (1, 2). In the 2019 European atlas of PC services (3), only eight European countries reported to have cardiology services that provided PC: the Czech Republic, Denmark, Ireland, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. The atlas also identified that collaboration between cardiology services and PC specialists occurs only occasionally (3).

Due to the complex needs of patients with HF, HF clinics, consisting of a multidisciplinary team that includes cardiologists, HF-trained nurses, internists, nutritionists, psychologists, physiotherapists, and social workers, are being established across the world to improve patient's HF management (4). According to evidence from observational studies and clinical trials, HF clinics are effective in reducing hospitalizations and all-cause mortality when compared to usual care (5–7). However, while these clinics are widely available in countries such as Norway and Italy, the current number of HF centers in other countries may not be sufficient to ensure a comprehensive evaluation according to current standards and recommendations (3).

Therefore, more HF clinics and multidisciplinary HF programs will need to be created in the future. Consequently, understanding the PC needs of patients seen in HF clinics, as well as the potential role for PC specialists or of PC-trained staff as part of these teams is crucial. Thus, we conducted this study to understand the unmet PC needs of patients with HF attending an already established HF clinic in a tertiary university teaching hospital in Switzerland.

MATERIALS AND METHODS

Study Design

This is a secondary qualitative analysis of structured interviews undertaken within a larger study (8) to validate the German version of the Needs Assessment Tool: Progressive Disease—Heart Failure (NAT: PD-HF). After obtaining ethical approval (#2018-02175) for this analysis, we transcribed and thematically analyzed the longest interviews, as they were the most content-rich because participants engaged in deeper discussions with the interviewer. Before transcription, we heard all interviews and noticed that the shortest ones did not allow for a comprehensive understanding of participants' experience of symptoms and of their unmet needs and therefore decided that not all could be analyzed in the depth that thematic analysis requires. We then included interviews until we reached data saturation, that is, the point at which the inclusion of additional interviews would have not added substantial new information to the analysis and the resulting themes and subthemes (9). Of the 70 interviews undertaken for the validation study, we reached data saturation at 31 interviews. The interviews included in this study lasted 31 min in average (range: 24–48 min).

Setting

The interviews took place between January and March 2020 with patients from the ambulatory HF clinic of the Inselspital, the University Hospital of Bern, Switzerland.

The HF clinic was created in the 1990s in the context of heart transplantation. Currently, it receives around 2,800 consultations per year and offers multidisciplinary care including cardiologists, HFnurses, cardiac rehabilitation, and cardiopsychology. The frequency of consultations depends on the stage and progression of the disease. Some patients may have consultations every month, every 3 months or even annually as in the case of transplant patients. Although the cardiopsychology service is open to all patients, a cardiopsychological assessment is routine and mandatory only before transplantation. As a means of information, brochures with different information related to HF are available for all patients. There are brochures with general recommendations on lifestyle, others explain what HF is, etc. There are no brochures with information on palliative care.

The Needs Assessment Tool: Progressive Disease-Heart Failure

The NAT: PD-HF (10) is a tool that aims to assess unmet needs in patients with HF and their informal caregivers. The tool was created to be filled out by a health care professional and evaluates different types of needs, including physical, psychological, social, and spiritual needs. Additionally, the NAT: PD-HF assesses information needs including need for information about disease prognosis, treatment options, advance directives, health support services, financial or legal issues, and social or emotional issues (**Supplementary Material 1**). The tool consists of four parts: (1) priority referral for further assessment, (2) patient well-being, (3) ability of the informal caregiver or family to care for the patient, and (4) caregiver well-being. For each question, the health care professional undertaking the assessment together with the patient selects the level of concern: (1) none, (2) some/potential, (3) significant.

Participants and Study Procedure

Patients were eligible to participate if they were adults (≥18 years old), able to communicate fluently in German and had a follow-up appointment at the HF clinic after having had at least one previous consultation at the clinic before. No stage or severity of HF was preselected as inclusion criteria, to ensure a complete and representative spectrum of patients at different stages of the disease. Patients who met the inclusion criteria were invited to participate via mail. For those who were interested, we arranged an appointment with a study member immediately before or after their scheduled consultation at the HF clinic. In the invitation package that was mailed to patients, we mentioned that the project aimed to evaluate the performance of a questionnaire to assess the needs of patients with HF and to improve the quality of care delivered to this population. We assessed patients' cognitive ability by asking them three questions about the study after explaining its purpose and the contents of the consent form and we excluded participants with poor comprehension capacity. Following participant consent, the interviews were conducted in Swiss German by JG, a 6th year female medical student. The interview addressed potential unmet needs of patients with HF and their family treated in an ambulant HF clinic. The interviews often focused on the care from the HF clinic but the experiences reported by the patients were not restricted to this care setting. All interviews covered the same questions and explored the areas in the same order as in the tool (refer to **Supplementary Material 1** for a copy of the tool used to guide the interviews). In addition, when necessary, the interviewer went deeper into some of the issues and needs reported by the patients in order to select the level of concern, which may help explain the variation in the length of the interviews. For the qualitative analysis, a Swiss German linguist specialized in English language and literature, translated and fully transcribed all interviews to English from voice recordings.

Data Analysis

We analyzed the interview transcripts via thematic analysis following Braun and Clarke (11), using NVivo software (12). VGJ, a female physician who was completing a PhD on PC in HF at the time of the study, performed all analyses with support from SCZ, a female psychologist with expertise in qualitative methods and PC research. VGJ and SCZ coded independently one of the interviews and compared all initial codes, to fine-tune the coding process. The coding comparison was made to ensure that VGJ was noticing all meaningful instances to be coded and to show the differences between semantic and latent coding, so that all subsequent interviews were coded in a similar way. At all times during the coding phase, SCZ and VGJ held discussions about how to code specific segments of data, when VGJ raised questions. Subsequently, and after familiarizing herself with all the interviews by reading and rereading the interview transcripts, VJG inductively assigned initial codes to all other interviews by staying close to the data and by keeping an audit trail with detailed notes about her assumptions and perceptions of initial thematic contents. The initial codes were either semantic or latent, meaning that at times portions of data were coded by explicitly describing what the participants stated (semantic coding), while the latent codes involved labeling the data with interpretations of underlying contents in participants' statements. Neither types of codes were given more priority than others in subsequent stages of analyses, though there were more semantic than latent codes across the dataset. In a second step, each of the codes was categorized under greater thematic categories, which were constantly defined and refined to fit the themes to the whole corpus of data. This process involved merging similar codes, renaming other codes, as well as establishing a hierarchy within the codes so as to promote some as themes and other as subthemes, always taking into account the different views expressed by participants across all interviews. Similarly, candidate themes and subthemes were then closely observed and reorganized to determine how well they represented the aspects discussed in all interviews, as well as cases which were less common across the dataset. In the last stage, VGJ and SCZ reviewed and agreed on the final themes via the same process of constant comparison and making final decisions about which themes allowed for the most comprehensive understanding of participants' accounts. At this stage, we also selected the most representative participant quotes to illustrate the themes and subthemes. We conducted, analyzed and report the study results according to the Consolidated Criteria for Reporting Qualitative Studies (COREQ) guidelines (13). In reporting the results, instead of presenting frequencies, we use terms such as "most" and "some," as suggested by Braun and Clarke (12).

RESULTS

Participants

The majority ($n = 26$) of the 31 participants were men. Participants had a median age of 64 years (IQR 56–77) and the majority had reduced ejection fraction and were classified as having a New York Heart Association functional class II. Twelve participants (39%) had an implantable cardioverter defibrillator, six (19%) had a ventricular assist device, and five (16%) were listed for a heart transplant (refer to **Table 1**). The distribution of clinical and sociodemographic characteristics were similar to those of the whole study population that participated in the validation study of the German version of the NAT: PD-HF). Even the proportion of women in our secondary analysis was equally low to the proportion of women in the original cohort (**Supplementary Material 2**). During the recruitment process, no patients were excluded due to poor comprehension capacity.

Themes

Participants were in general satisfied with the treatment and information received at the ambulatory HF clinic, however, upon further questioning, they would often report several unmet needs. We therefore identified three ambivalences as main themes: (I) "feeling well-informed but missing essential discussions," (II) "although feeling mostly satisfied with care, remaining with unmet care needs," and (III) "fearing a referral to palliative care but acknowledging its importance."

TABLE 1 | Characteristics of the patients included in the study ($n = 31$).

Characteristics	*n* (%) or median (IQR)
Sex	
Women	5 (16%)
Men	26 (84%)
Age	64 (56–77)
LVEF (%)	30 (20–50)
LVEF category	
HFrEF	18 (58%)
HFmrEF	8 (26%)
HFpEF	5 (16%)
NYHA functional class	
I	8 (26%)
II	14 (45%)
III	9 (29%)
ICD	12 (39%)
VAD	6 (19%)
Heart transplant list	5 (16%)
COPD	6 (19%)
T2DM	9 (29%)
CAD	13 (42%)
CKD	17 (55%)

IQR, interquartile rate; LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; NYHA, New York Heart Association; ICD, implantable cardioverter defibrillator; VAD, ventricular assist device; COPD, chronic obstructive pulmonary disease; T2DM, type 2 diabetes mellitus; CAD, coronary artery disease; CKD, chronic kidney disease.

Feeling Well-Informed but Missing Essential Discussions

The majority of participants reported very often that they felt well-informed. Yet, as the assessment tool guiding the interviews covered different topics, several unaddressed issues surfaced during the interviews. Within this theme, we identified four subthemes: (a) *Feeling well-informed about their diagnosis, treatment options, medication and medical support*, (b) *Lacking information about advance directives, prognosis or about concurrent palliative care*, (c) *Being confronted with end-of-life discussions in an untimely and tactless manner*, and (d) *Preferring other communication channels.*

a. *Feeling well-informed about their diagnosis, treatment options, medication and medical support:* The majority of patients considered that they had a good knowledge about their diagnosis of HF and the course of the disease. However, none of the patients elaborated on what they know about their disease or its course. When asked whether they would like to receive more information from the health care professionals on any of those aspects, none of them felt in need of more information and mentioned that if they needed it, they knew they could ask their cardiologist or said they could look for this information from other reliable sources. Participants also knew details about different treatment possibilities, mainly about medications or the option to have a cardiac device implanted. Some of the participants mentioned that although they did not know in detail how each of the medications worked specifically, they felt well-informed about the correct way of taking them.

> *Interviewer: Would you need more information about your heart disease, next steps or treatment options?*
>
> *Participant: Not really. I'm well-informed, I also know about the course of my heart disease. [...] The doctors here at (hospital) always told me you could still do this or that. And then you can still decide on your own whether you want it or not. (P26), male, 81 years old, NYHA III.*

b. *Lacking information about advance directives, prognosis or about concurrent palliative care*: Despite believing they had a good knowledge of their disease, when it came to its prognosis, some patients mentioned they lacked prognostic information and felt that the physicians at the HF clinic often avoided this topic. Other participants felt that they needed to obtain more concrete information about how to fill an advance directive or about non-curative options. Others, more than needing information on how to fill out an advance directive, wanted pragmatic help completing it. When asked if they had ever been referred to PC, none of the participants had been referred to PC in the past, which also brought about their complete lack of understanding of PC concepts and about concurrent PC. We observed this unfamiliarity at three levels: some participants were unfamiliar with the term PC, others said they had never received it because they were 'not at that stage' or because they still had curative therapeutic options available to them, and finally, because some thought that PC was only for patients with cancer and did not know it was available for patients with HF. Although some patients reported that "they were not at that stage", they did not specify when they would consider themselves in need of palliative care.

> *(obtaining information about) the prognosis is difficult. I tried to ask today. The doctors avoid it of course, that's clear.* (P46, male, 79 years old, NYHA II).

c. *Being confronted with end-of-life discussions in an untimely and tactless manner*: Some patients mentioned that when being hospitalized for an acute decompensation, they felt confronted when physicians discussed end-of-life issues with them in the intensive care unit or in another inpatient setting, perceiving these conversations as untimely and tactless. Participants did not seem in fear of the end-of-life discussions *per se* but felt that having them during an acute crisis was not appropriate. In many cases, these were the first instances when participants were confronted with end-of-life discussions while the physicians seemed to be in urgency to find out what to do or not to do should the patient be dying during their shift. One participant said that while he prefers direct conversations to having information withheld from him by health care staff or his family, he found the conversation while he was in the ICU to be crude and "*hated it.*" For another

participant, this conversation came late at night during the hospitalization leaving her shocked and scared of falling asleep for fear of dying in her sleep. They did not elaborate on how they would like these discussions to go or when they would have preferred to have had such discussions.

> *So, I was up there in intensive care. And then they said very clearly: "what do you want us to do? It could turn out this or that way, how far should we go?" That was brutal, I thought, "hey, you could word that a bit differently", I thought that was like a shock, that whole story.* (P12, men, 53 years old, NYHA II).

d. *Preferring other communication channels:* When discussing different information needs, such as treatment options, health support services, or emotional support, many patients mentioned receiving leaflets or brochures covering these and many other topics. Although they received these brochures and felt that these contained relevant information, the majority of participants had strong preferences for having additional, more personalized and interactive communication channels with the treating team. They mentioned that having a pile of brochures was not of real help, and that they perceived brochures and leaflets as tactless and impersonal. In addition, some reported that certain information they encountered when reading the brochures at home caused them anxiety or confusion and that they often had to wait for answers from their cardiologist during a later in-person consultation, which could still have been months away.

> *I would not want to be overwhelmed with material, without me doing anything about it. [...] in the hospital back then, those 3 days, you have—everything went quite quickly, you got that brochure, that booklet and then a woman came into the room, pretty much gave the quick run-through: Like this, this, this, here's the material, have a nice day. There I would wish that the person that's doing that would take a bit more time. Maybe more of the interpersonal, too, not just following a set pattern. That way you can probably reach a patient better and then, yes. (P32, male, 52 years, NYHA I).*

Although Feeling Mostly Satisfied With Care, Remaining With Unmet Care Needs

Several patients had a general feeling of being well-supported in the HF clinic and felt well-cared for by the HF team. However, some participants reported dissatisfaction with the care they received, including lack of support mainly in other hospital settings when they had a HF decompensation or at other crisis points. Within this theme, we identified four subthemes: (a) *Trusting the ambulatory heart failure team and having a general feeling of being well-supported*, (b) *Feeling alone and without support*, 3) *Feeling unheard when voicing specific symptoms*, and (c) *Lacking continuity of care.*

a. *Trusting the ambulatory heart failure team and having a general feeling of being well supported*: We found that patients had a general feeling of being well-supported in the HF clinic and that they acknowledged the benefit they derived from the support of the different areas of expertise covered by the clinic and the staff members. For example, the support of the psychologist was seen as important not only for addressing non-physical symptoms, but also in their role as a mediator between the physician and the patient.

> *They (the doctors) were always transparent with me, they always showed me where I'm at and because of that I have never experienced anything negative but always positive. And it was always clear to me how it would go on, what we are doing as a next step, so from that side I've always had great support up to now. I can't complain at all, that's probably why I'm sitting here, because of this support. I've profited a lot. And I can only say positive things, I can only give praise. [...] I was always really happy with the work of (name) and Dr. (name). From both sides I always received all the information. Additionally, I get this psychological support. When something was unclear on the somatic side, I could also talk to the psychologist, then she was also a mediator between patient and doctors. And that always worked really well, that was really great work. (P43, female, 50 years old, NYHA II).*

b. *Feeling alone and without support*: At specific times during the illness trajectory, some participants felt that they needed more support and mentioned feeling alone. For example, two patients reported feeling lonely and hopeless after discharge. Another participant mentioned feeling a lack of support in the process with the ventricular assist device both before implantation due to lack of information and discussions, and after implantation, in the process of adapting to living with the device. For another participant there was a need for religious support while being hospitalized, and for another one, the need for emotional support after an intense suffocation event. Finally, another participant felt unsupported when, after an acute event, he was referred to a cardiac rehabilitation clinic even though he still felt very weak physically and mentally. Situations like these made the participants feel vulnerable and without a key contact person who could offer support during those times.

> *It was also—You had to wait for the pacemaker for 3 months, right? And then I always felt like those 3 months, they're waiting to see if you survive or not. [...]Yes, yes, it was about that because the device I have is quite expensive and then they wanted to see if "that dude will even make it" [laughs]. And "if he makes it, you can give him the pacemaker" right? And otherwise, the money is thrown out the window, kind of like that. Then I have to say, yes, that gets to you, that gets to you! Although, it does make sense, I have to say. Why should you install an expensive device if he doesn't make it anyways? But for the individual it's hard to take and you're left alone with that. You're just sent home, now [wait and] see. (P8, male, 61 years old, NYHA II).*

c. *Feeling unheard when voicing specific symptoms*: Some patients referred feeling unheard when voicing specific symptoms or needs, particularly when these were not caused by the disease itself, but were secondary to treatments for the disease. This was the case for example, when participants reported having back pain due to the weight of the ventricular assist device

or when they found it cumbersome to carry out day-to-day activities with these devices. Other participants sought support for symptoms such as nausea, and often reported receiving no specific treatments for these. This often led them to feelings of disappointment or despair as they expected that these symptoms and concerns should have also been addressed in the HF clinic.

> *I of course have back pain. I always have to carry around these devices. No one is interested in that here. The (hospital name) doesn't give a [coughs] about this. Did you hear that? Little machine? That would be something that I thought would be important to have support with that—(P21, female, 57 years old, NYHA II).*

d. *Lacking continuity of care*: The consultations in the HF clinic were often performed by different physicians. For some of the patients it was uncomfortable to have a new physician at each follow-up consultation because they felt there was no time to develop a relationship with the physician.

> *What takes some getting used to is that there's always someone new, that there is not one (person)- Here, again, it was someone different who did the consultation hour. [...] It's pretty interesting, you get to meet different people all the time, but you don't actually get to know them, it's so quick. (P32, male, 52 years old, NYHA I).*

Fearing a Referral to Palliative Care but Acknowledging Its Importance

We identified that patients feared PC referrals because they associated these referrals with death or with "when there was nothing else to be done." However, while the term could generate some discomfort, participants were still able to understand the value of such an approach and seemed open to receiving PC later, especially after a brief explanation of the interviewer about what concurrent and early PC is. We identified three subthemes under this theme: (1) *associating palliative care with end of life and loss of hope,* (2) *acknowledging the importance of palliative care*, and (3) *explaining concurrent palliative care has the potential for positive impact.*

a. *Associating palliative care with end of life and loss of hope*: The majority of the patients associated PC with care at the end of life or thought of it as a last resort for when there were no more curative therapies to try. For some of the participants, this negative perception of PC stemmed from previous experiences with family members or acquaintances. For example, one patient associated PC with when his father with cancer was in the terminal phase. Another patient recalled hearing the term when during a hospitalization, the doctors told another patient he shared the room with, that they could no longer offer him curative therapies and therefore would move him to the PC ward. Many were thus misinformed about PC and therefore a referral to PC was associated with dying and death.

> *I've heard of it, it's just the last thing, when there's nothing, no rescue, so to say. (P45, male, 71 years old, NYHA II).*

b. *Acknowledging the importance of palliative care*: We found that several participants despite giving a negative connotation to PC, also associated it with symptom relief, particularly for the treatment of pain or for maintaining quality of life. One participant said that she was aware of the benefits of PC but because of the connotation it has, she felt that if referred to PC, it would have a negative psychological impact for her.

> *And it's certainly a good thing and when there's nothing else, it's certainly better than doing all kinds of stuff, with medication for and against it and the third one so that it can be tolerated and so on. And at some point you might have to say "no, that was it." (P50, male, 81 years old, NYHA III).*

c. *Explaining concurrent palliative care has the potential for positive impact:* After a brief explanation of the definition of concurrent and early PC, almost all participants thought the concept was interesting and expressed a desire to know more about it, as they could understand that it was not about dying, but about living with the disease. One of the participants associated it with psycho-cardiology, and another one thought that the option should be supported more within HF. Only one participant was the exception to this, as despite understanding what concurrent PC is, he reported not being interested in receiving this type of care.

> *I can imagine, the way you described it now, that this could make sense. Or that this would have potential to build on, as a form of support. Not in view of dying but more for living. (P56, male, 77 years old, NYHA II).*

DISCUSSION

Key Findings

Overall, participants were satisfied with the information and care received at the ambulatory HF clinic. However, even though the majority of the patients in our study were not at an advanced stage of their illness according to the NYHA classification, they still presented with several unmet needs. Most of these corresponded to a lack of anticipatory care planning including a lack of discussion about concurrent PC, prognosis, advance directives, and the end of life. In addition, some patients reported receiving little attention after verbalizing symptoms that had a high impact on their quality of life and perceived a lack of support during or after acute events or at other crises points, leading them to feel unheard and alone. Finally, we identified that patients had a negative perception of the term "palliative care" and therefore feared a PC referral. Nonetheless, after a brief explanation about what concurrent and early PC involves, they were eager to know more about it and were more open to it.

Clinical Implications

Systematic Screening of Unmet Needs

Participants were well-informed about the medical management of their disease because that is the routine focus of their consultations. However, possibly because there is no systematic screening of unmet needs, participants remained unaware that their unmet needs were potentially relevant to their HF

care, and only upon questioning of potential specific unmet needs, they voiced how those aspects were lacking discussion. Similarly, a systematic review assessing whether end-of-life care discussions were being held with patients with HF found that the great majority of patients had not discussed their prognosis, cardiopulmonary resuscitation or other life-sustaining interventions, or plans for future care with their healthcare professionals (14). Patients can thus remain under the false impression that anything that is important to their treatment would have been covered by the cardiologist, when in reality something important to them was missing in the consultation. Therefore, a systematic screening of unmet needs carried out in each HF clinic with a tool or questionnaire developed for this purpose (15, 16) could help introduce these topics as part of the routine within HF clinics and could help identify and meet patient and family needs at a more meaningful time than is usually done at present.

There might not be enough time to assess unmet needs of patients and their caregivers within the typical 10–15 min follow-up visit with the cardiologist and there are not enough PC specialists to assess the needs of all patients in the HF clinics. However, PC specialists are not necessary for routine needs screening. One solution could be the presence of a person with PC training (a HF nurse or general practitioner) in each HF clinic who periodically examines the needs of patients and, if necessary, treats them or refers them to a specialist, as appropriate. Similar models have been implemented for the identification of needs for the delivery of PC in the ambulatory management of patients with HF (17, 18). Finally, referrals to general or specialized PC do not mean that all efforts to treat patients in a comprehensive manner are delegated to the person providing PC. All other members of the multidisciplinary team should treat patients with a palliative lens across the disease trajectory (19). Therefore, cardiologists and other HF staff could benefit from training in fundamental palliative skills for patients with HF including basic management of both physical and emotional symptoms, discussions about treatment goals, and referral to specialized PC (20, 21).

Anticipatory Care Planning in the Ambulatory Setting

Despite their satisfaction with the ambulatory HF clinic and its multidisciplinary approach, the lack of discussion about prognosis and future treatments led patients to have negative care experiences in other care settings, particularly during hospitalizations. In the absence of end-of-life or advance directives discussions while the patient's condition is stable, patients were not prepared for a decision making process when there was an acute cardiac decompensation. They were suddenly confronted with these types of discussions without any preparation, which often generated additional and preventable trauma. The fact that participants were dissatisfied with the way end-of-life discussions were approached is not because they are not open to such discussions. Therefore, training in anticipatory care planning for cardiologists and other members of the HF clinic team is essential to delivering high quality care (22). Likewise, following communication guides such as the about serious illness conversations might be useful for physicians to support the patient in decision making (23). Quality care must be focused not only on the setting in which the service is provided, in this case the ambulatory setting, but must also proactively prepare for the care that the patient will receive throughout the continuum of care, including other settings such as the inpatient setting.

It is common practice in hospitals that patients hospitalized for exacerbation of their illness who are not clearly terminal are asked how to proceed in case of arrest (whether to receive CPR or not). Knowing that this is standard practice in settings such as the emergency department or the ICU, it is appropriate that in outpatient management this is discussed in advance. These discussions can occur with the general practitioner as well as with the cardiologist and/or with other staff in the HF clinic. It is important to emphasize here that anticipatory care planning, the process of discussing future care strategies, is not limited to patients with a short life expectancy or with advanced HF and recommended to begin early (19). Therefore, even in HF clinics, where NYHA II patients predominate, these discussions are essential. While discussing future care strategies in the ambulatory setting, including end-of-life care, can pave the way for when advanced measures are discussed in other settings, it is equally important to make an effort in other settings to improve the way these conversations are held.

Normalizing the Term "Palliative Care" via It's Concurrent Use With Life-Prolonging Therapies

We identified a negative connotation of the term "palliative care", which has been reported before in other studies among patients with cancer (24) and also with HF (25). The negative connotation of the term can provoke distress in patients with HF and their families. While we saw that explaining the concept of early and concurrent PC has a potential positive impact, if PC is only offered or discussed at the end of life, patients, families, and the community will continue to associate it with this last phase of life. Although the negative connotation of the term is a barrier to receiving it (26), health care personnel should make an effort to promote it and offering it concurrently with life-prolonging therapies, and in an early manner. This may also start at the level of the cardiology teams, as they have also been found to have misconceptions of the term which is often associated with a lack of referrals and suboptimal collaboration between PC and cardiology teams (27, 28).

Strengths and Limitations

To our knowledge, this is the first study to elicit patient experiences exclusively from a HF clinic. We highlight two strengths of our study, which are: (1) we focused on the needs of patients from their own perspectives following a structured guide for assessing needs in patients with HF; (2) participant inclusion criteria were broad, including a representative population of the HF clinic.

Although the data was collected with patients from the same HF clinic, the results of this study can be extrapolated to similar contexts, taking into consideration the aspects of our setting and

of our participant sample. Specifically, it is known that as the NYHA class increases, patients are at greater risk of frequent hospitalizations (29), depression (30), and poorer quality of life (31, 32). Therefore, it is likely that the PC needs we identified become even more relevant with increasing NYHA (33). Since the majority of participants in our study where classify as NYHA II, our study could not identify the needs of patients with more advanced HF stages and thus assess the potential role of a PC provider in HF clinics in people at advanced stages. However, the low proportion of patients classified as NYHA IV is common in ambulatory HF clinics (5, 33, 34), either because good pharmacological and non-pharmacological management keeps the functional class under control or because patients classified as NYHA IV despite optimal treatment are in other types of programs such as the transplant list program. Therefore, a lack of patients with a NYHA IV class should not hinder the transferability of our results to other ambulatory HF clinics.

The participants included in this qualitative study are a subsample of the patients included in the validation study of the German NAT: PD-HF (8). Since patients participated on a voluntary basis, patients who had negative experiences or felt that something was missing in their care may have been more inclined to participate in the study. The effect of self-selection bias can be circumvented by enhancing trustworthiness and rigor in the conduct, analysis and reporting of the study findings by following the established procedures that we have engaged with and reported at the different research phases (35). In addition, with our findings we are not suggesting that unmet PC needs are found in all HF patients, but that they can present in some of them and that careful screening by trained personnel can help with their identification.

As this is a secondary analysis of data collected from a structured interview, the main limitation of this study is the lack of depth of some of the interviews, which prevented a deeper understanding of the implications of the unmet needs of patients with HF or of their preferences for meeting those needs. However, a major advantage of the structured approach to interviewing is that all topics were addressed in all interviews uniformly, allowing us to be certain of the types of needs that were met or unmet in this patient population.

While this study focused on understanding the unmet needs of patients with heart failure from their own perspective, having the perspective of the family and caregivers would have added depth to certain themes or subthemes and helped put certain needs in context.

Today, women continue to be underrepresented in cardiology studies (36). The underrepresentation of women may affect the transferability of our results since women with HF are usually older than men with HF, have more comorbidities (and therefore more symptoms) such as kidney disease, diabetes, and hypertension (37, 38), and have more often HF with preserved ejection fraction. Although various types of drugs have been shown to improve symptoms in patients with reduced ejection fraction, little or no effectiveness has been found in patients with preserved ejection fraction (39, 40). Therefore, the latter might have different types of needs than patients with reduced ejection fraction. Additionally, as the primary caregiver is usually the partner and women outlive men, women tend to have fewer informal caregivers and require more support (41). Although in our study women were slightly more likely to accept participation than men (**Supplementary Material 3**), due to the low representation of female patients in the HF clinic at our institution we did not achieve adequate representation of women in our study.

CONCLUSION

Although patients who are receiving multidisciplinary management in ambulatory HF clinics are generally satisfied with the care received, they remain with unmet needs. These unmet needs, such as the need for advance care planning or the need for timely and tactful end-of-life discussions, can be fulfilled by PC providers. Though patient perceptions of PC may be a challenge, including personnel trained in PC as part of the multidisciplinary team to apply tools or questionnaires to systematically assess unmet needs, could help to address these needs, thus improving both the quality of care and the quality of life of people living with HF.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by BASEC-Swissethics. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

NL and JG collected the data. VG-J and SZ performed the analysis, drafted the manuscript, and responsible for the overall content of the manuscript. MM contributed to the analysis of results. MM, NL, JG, LH, and SE did a critical revision of the manuscript. All authors discussed the results and commented on the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2022.866794/full#supplementary-material

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Inpatient Specialist Palliative Care in Patients With Left Ventricular Assist Devices (LVAD): A Retrospective Case Series

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Background: Repeat hospitalizations, complications, and psychosocial burdens are common in patients with left ventricular assist devices (LVAD). Specialist palliative care (sPC) involvement supports patients during decision-making until end-of-life. In the United States, guidelines recommend early specialist palliative care (esPC) involvement prior to implantation. Yet, data about sPC and esPC involvement in Europe are scarce.

Materials and Methods: This is a retrospective descriptive study of deceased LVAD patients who had received sPC during their LVAD-related admissions to two university hospitals in Duesseldorf, Germany and Basel, Switzerland from 2010 to 2021. The main objectives were to assess: To which extent have LVAD patients received sPC, how early is sPC involved? What are the characteristics of those, how did sPC take place and what are key challenges in end-of-life care?

Results: In total, 288 patients were implanted with a LVAD, including 31 who received sPC (11%). Twenty-two deceased LVAD patients (19 male) with sPC were included. Mean patient age at the time of implantation was 67 (range 49–79) years. Thirteen patients (59%) received LVAD as destination therapy, eight patients (36%) were implanted as bridge to transplantation (BTT), and one as an emergency LVAD after cardiogenic shock (5%). None of the eight BTT patients received a heart transplantation before dying. Most (n = 13) patients lived with their family and mean Eastern Cooperative Oncology Group (ECOG) performance status was three. Mean time between LVAD implantation and first sPC contact was 1.71 years, with a range of first sPC contact from 49 days prior to implantation to more than 6 years after. Two patients received

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esPC before implantation. In Duesseldorf, mean time between first sPC contact and in-hospital death was 10.2 (1–42) days. In Basel, patients died 16 (0.7–44) months after first sPC contact, only one died on the external sPC unit. Based on thorough examination of two case reports, we describe key challenges of sPC in LVAD patients including the necessity for sPC expertise, ethical and communicative issues as well as the available resources in this setting.

Conclusion: Despite unequivocal recommendations for sPC in LVAD patients, the integration of sPC for these patients is yet not well established.

Keywords: heart assist devices, left ventricular assist devices, heart failure, palliative care, end of life care, quality of life, cardiac surgery

INTRODUCTION

Heart failure remains one of the leading causes of death worldwide (1, 2). Despite optimized pharmacological treatment and heart transplantation (HTX), implantation of mechanical circulatory support (MCS) often presents the last therapeutic option (3). In 2011, 355 HTX were performed and 693 MCS were implanted in Germany, compared to 340 HTX and 843 MCS in 2020 (4). Left ventricular assist devices (LVAD) are the most commonly used MCS option (4). The implantation of a LVAD can be based on different intentions. In bridge to transplant (BTT) patients, the LVAD provides hemodynamic support until possible HTX. Destination therapy (DT) is intended for patients for whom HTX is not an option. Both concepts, BTT and DT, prolong survival and enhance the quality of life (5). However, patients experience enormous physical and psychosocial distress and often suffer from LVAD-related complications, such as bleeding, driveline infection, or pump thrombosis, which lead to re-hospitalization (5). Data from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) report an overall LVAD 1-year mortality of 20% and a 2-year mortality of 70% (6). The dying process can be complicated and discussions about deactivation of a LVAD can be challenging and burdensome for patients, families, and health care teams (7). Knowledge about optimal end-of-life care in LVAD patients is scarce (7).

Palliative Care (PC) is defined by the World Health Organization (WHO) as "an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness [. . .]" (8). While all medical professions and disciplines provide general PC, specialist PC (sPC) is provided by a multi-professional sPC team (e.g., physicians and nurses with specialized education, psychologists and social workers) to in- and outpatients (9). Besides improving symptom control, the integration of sPC has been shown to be beneficial concerning shared decision making, defining and documenting end-of-life wishes (advanced care planning), and reducing distress of patients and relatives along their care pathway (9). Despite the fact that LVAD therapy is challenging for patients and their families (10), integration of sPC remains low (11) and European data on sPC involvement in the care for patients with LVAD are scarce (12, 13). Nevertheless, the European Society of Cardiology (ESC) generally recommends a palliative care consultation in all patients in the advanced stages of heart failure and for those considered for MCS or HTX before such interventions as a matter of protocol (3). The European Association of Palliative Care endorses in an expert position statement a needs assessment approach and to evaluate for sPC need during the regular heart failure visits (14). In the United States (U.S.), the issue of sPC in MCS was already addressed in 2010 by a clinical competence statement of a special task force (15). Mandatory sPC involvement in the DT-LVAD process is recommended since 2013 (16). The American Heart Association (AHA) guidelines also support the integration of sPC even *before* LVAD implantation (17). Since the publication of these recommendations in 2013, the involvement of sPC in the care of patients with LVAD has increased in BTT and DT (11, 18). A retrospective analysis in the U.S. from 2006 to 2014 showed an overall rate of 4% of LVAD patients received sPC and highlighted a significant increase of sPC involvement in 2014 to 7.2% (11). Nonetheless, to date there is no standardized sPC integration algorithm for LVAD patients (12, 19). Woodburn et al. developed a routine for sPC involvement in the DT-LVAD process before implantation and observed benefits for patients, caregivers, and clinicians (19). Therefore, sPC should not only be involved in end-of-life care, but also before the last year of life (20). Early integration of sPC (esPC) before LVAD implantation, in particular, could improve shared decision-making. However, availability of esPC is not yet widespread. Studies focusing on the need for sPC in BTT patients are rare (18). In addition to studies that evaluate these needs, the timing and format of sPC involvement in LVAD patients and investigations on the *status quo* in different countries are needed.

In our retrospective, descriptive study, we collected data from two university hospitals (Germany and Switzerland) to further explore the integration of sPC in deceased LVAD patients. Our main aims were to: (1) assess the extent to which LVAD patients received sPC, (2) determine how early an sPC is involved in the care trajectory, (3) identify the characteristics of patients who

Abbreviations: LVAD, left ventricular assist devices; BTT, bridge to transplant; DT, destination therapy; MCS, mechanical circulatory support; HTX, heart transplantation; sPC, specialist palliative care; esPC, early specialist palliative care; ECOG, Eastern Cooperative Oncology Group; ESC, European Society of Cardiology; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; AHA, American Heart Association; WHO, World Health Organization; DNR/DNI, do not resuscitate/do not intubate; IMC/ICU, intermediate care/intensive care unit.

received sPC, (4) assess where sPC took place, and (5) identify the key challenges in end-of-life care.

MATERIALS AND METHODS

This study was performed after approval of the local ethics committee of the Medical Faculty of Heinrich-Heine-University Duesseldorf, Germany (Study-Nr.: 2021-1600). An additional ethical approval by the Ethics Committee of Northwestern- and Central Switzerland was not required (Req-2021-01368). We followed the Enhancing the QUAlity and Transparency Of health Research (EQUATOR) network guidelines for retrospective observational studies (here: STROBE) (21). All deceased adult patients who underwent BTT or DT LVAD implantation since 2010 were included. Also, the possible inclusion of sPC before LVAD implantation was studied. We defined integration of sPC before LVAD implantation as early sPC (esPC). Of the patients who had received sPC, only the subgroup of deceased patients was studied due to better comparability. Patients with other MCS, an already explanted LVAD and patients aged < 18 years were excluded. In Duesseldorf, no written informed consent was required for participation due to the retrospective and anonymized nature of this study, because patients already provide it with the treatment contract. In Basel, some LVAD patients refused general research consent and were therefore not included in our study. Medical records from the two institutions were electronically explored for the following information: Number of implants in total, number of LVAD patients receiving sPC and number of deaths this latter group of patients. Assessable patient characteristics included sex, age, Eastern Cooperative Oncology Group (ECOG), LVAD concept and LVAD device, date of the LVAD implantation, date and place of first sPC contact, and date and place of death. Data were organized and analyzed in Microsoft Excel 2020 (version 16.42, Microsoft Corp., Redmond, WA, United States) using descriptive statistics. Figures were created using MATLAB (2021b, MathWorks Inc., Natick, MA, United States).

Specialist Palliative Care Setting

Duesseldorf and Basel have long established sPC services. sPC involvement consists of patients' contact to sPC nurses, to an sPC physician, and if needed to other sPC team members (e.g., psychological and social support, physiotherapy, creative therapy, and/or spiritual care). Both sPC teams have regular multiprofessional discussions about each patient's needs and treatment goals. Patient visits take place in-hospital as consultation services on cardiothoracic surgery wards, intermediate care units (IMC), or intensive care units (ICU). Both centers also offer out-patient services. Patients may also be transferred to an sPC unit. In Duesseldorf, the sPC unit is in-house. In Basel, it is external with services provided by the Palliative Care Center Hildegard, Basel. The University Hospital Basel shares a close cooperation with this nearby facility. Both Duesseldorf and Basel offer esPC before LVAD implantation, sPC in LVAD is initiated by an interdisciplinary consensus of the participating clinicians as well as the patient and his next of kin.

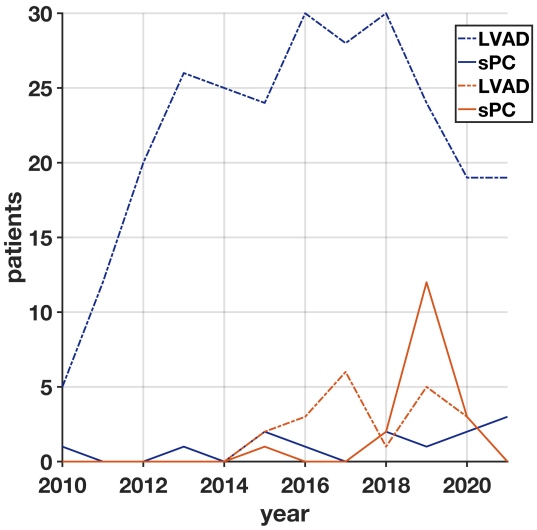

FIGURE 1 | Number of all patients (with research agreement) who had a left ventricular assist device (LVAD) implanted from 2010 until 2021 in Duesseldorf (blue, *n* = 262) and Basel (orange, *n* = 20) and number of LVAD patients having their first specialist Palliative Care (sPC)-contact in each year in Duesseldorf (blue, *n* = 13) and Basel (orange, *n* = 18).

RESULTS

Left Ventricular Assist Devices Implantations, Rate of Specialist Palliative Care Involvement and Deceased Patients

From 2010 to 2021, 262 patients underwent LVAD implantation at the University Hospital Duesseldorf, Germany and 26 at the University Hospital Basel, Switzerland. In Basel, 20 of these patients had provided a research agreement upon hospital admission. While 13 patients (5%) in Duesseldorf received sPC until December 2021, 18 patients (90%) in Basel received sPC during the same period. In Duesseldorf, 12 of 13 patients (92%) who had received sPC during their LVAD course had died. In Basel, ten of 18 (55%) of sPC patients died. Despite growing numbers of LVAD implantations in recent years (**Figure 1**), the proportion of LVAD patients receiving sPC in Duesseldorf remains low. In Basel, the cooperation between the LVAD and sPC teams has resulted in an increase of LVAD-sPC patients in 2018, but routine esPC was not realized in all patients. A total of 22 deceased LVAD patients who received sPC were included in the further analyses.

Patient Characteristics

The deceased LVAD-sPC patients were primarily male (86%, *n* = 19), their mean age was 67 (range 49–79) years. In 73%, the diagnosis leading to LVAD implantation was ischemic cardiomyopathy (*n* = 16), whereas six patients (27%) suffered from dilated cardiomyopathy. At the time of first sPC contact, 13 patients lived with their family, four on their own, and two in

TABLE 1 | Patient characteristics (n = 22).

		All patients (n = 22)	Duesseldorf (n = 12)	Basel (n = 10)
Age (years), median (range)		67 (49–79)	65 (49–77)	69 (54–79)
Sex, *n* (%)	Male	19 (86.4)	11 (91.6)	8 (80)
	Female	3 (13.6)	1 (8.3)	2 (20)
LVAD concept, *n* (%)	BTT	8 (36.4)	7 (58.3)	1 (10)
	DT	13 (59.0)	4 (33.3)	9 (90)
	Emergency	1 (4.5)	1 (8.3)	0 (0)
LVAD device, *n* (%)	HeartWare®	16 (72.7)	7 (58.3)	9 (90)
	HeartMate III®	5 (22.7)	4 (33.3)	1 (10)
	HeartMate II®	1 (4.5)	1 (8.3)	0 (0)
ECOG, *n* (%)	0	0 (0)	0 (0)	0 (0)
	1	4 (18.1)	0 (0)	4 (40)
	2	3 (13.6)	0 (0)	3 (30)
	3	3 (13.6)	2 (16.6)	1 (10)
	4	11 (50)	9 (75)	2 (20)
	Missing	1 (4.5)	1 (8.3)	0 (0)
Place of living, *n* (%)	Alone	4 (18.1)	2 (16.6)	2 (20)
	Family	13 (59.0)	6 (50)	7 (70)
	Care home	2 (9)	1 (8.3)	1 (10)
	Other	3 (13.6)	3 (25)	0 (0)

LVAD, left ventricular assist devices; BTT, bridge to transplant; DT, destination therapy; ECOG, Eastern Cooperative Oncology Group (performance status assessment score).

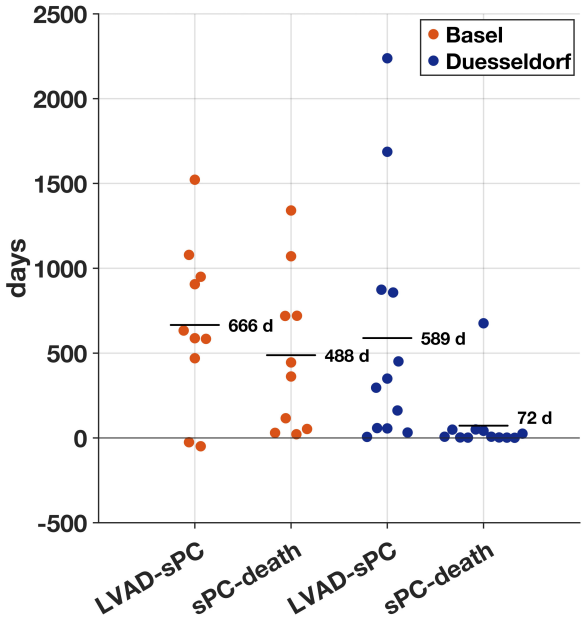

FIGURE 2 | Time in days between left ventricular assist device (LVAD) implantation and first specialist Palliative Care (sPC)-contact (LVAD-sPC) and first sPC-contact until death (sPC-death) in Basel (orange, n = 10) and Duesseldorf (blue, n = 12). Horizontal lines represent mean duration in days.

nursing homes. Data about the place of living was not available for three patients. Mean ECOG performance status was three. In total, eleven patients (50%) had an ECOG status of four, marking a completely disabled patient who cannot carry on any selfcare and is confined to bed or chair. In Duesseldorf, none of the patients had an ECOG status of one or two, whereas in Basel 70% of the patients were able to carry out light work (ECOG 1) or selfcare (ECOG 2). In total, eight LVAD patients were originally considered for HTX (BTT). None of these patients were transplanted before death. Of the remaining 22 patients, 13 were implanted as DT (59%), and one was an emergency LVAD after cardiogenic shock (5%). Demographic and clinical characteristics are shown in **Table 1**.

Specialist Palliative Care Involvement in Left Ventricular Assist Devices

Mean time between LVAD implantation and first sPC contact was 20.5 (−1.6 to 74.6) months (1.6 years in Duesseldorf and 1.8 years in Basel) (**Figure 2**). In Duesseldorf, all of the first sPC contacts took place on the IMC (n = 6) or ICU (n = 6), whereas in Basel the cardiothoracic surgery ward (n = 7) or the out-patient-clinic (n = 3) were places of first sPC contact. In Basel, two patients received esPC consultation 25- and 49-days prior to LVAD implantation, whereas in Duesseldorf esPC did not take place at all. In Duesseldorf, nine patients died in hospital, between one and 42 days after the first sPC contact (mean 10.2 days). All of these patients died of cardiovascular causes or LVAD complications (pump thrombosis: 2; infection of the driveline/LVAD: 2; bleeding: 2; cardiopulmonary failure: 2; hypoxic brain damage: 1). Three of these nine patients (33%) died on the ICU, five patients (55%) on the IMC, and one patient on a regular ward (11%). Three patients died out of hospital, the first patient at 49 days, the second (dependent on 24-h-intensive-care service at home) at 50 days, and the third 676 days after hospital discharge. In Basel, mean time between first sPC contact and death was 16 (0.7–44) months. The two esPC patients died 50 and 1,341 days after implantation. Five patients died on the cardiothoracic surgery ward, four on the ICU, and one patient on the external sPC unit (see "Case Report" below). In Duesseldorf, two patients were on the waiting list to be transferred to the sPC unit but died before admission. Survival time from first sPC contact is depicted in **Figure 3** using the Kaplan-Meier method. Median survival in Basel and Duesseldorf was 404 and 7 days, respectively (log-rank test: $p < 0.01$).

The review of reasons or inquiries that led to sPC involvement as documented on the sPC requests revealed several aspects: discussion of goals of treatment, evaluating change to a palliative therapy approach, wish to die, burden and enhanced stress levels of caregivers and next of kin, early integration of sPC, and prolonged ICU stay.

Regarding the content and implementation of sPC consultations in LVAD patients, our data show sPC involvement in the following: assessment and management of symptom burden, psychological support of the patient and his or her next of kin, provision of spiritual care, support from social workers, exploring end-of-life wishes, advance care planning

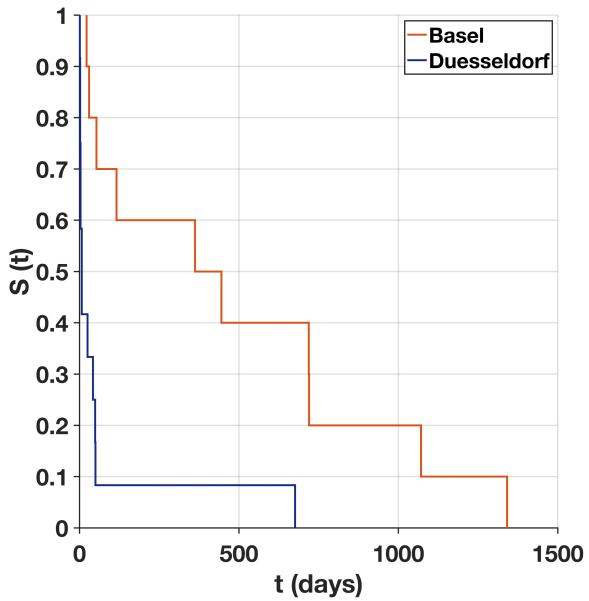

FIGURE 3 | Survival rate (S) over time (t) of first specialist Palliative Care (sPC) contact to death in days as estimated according to the Kaplan-Meier method for Basel (orange, $n = 10$) and Duesseldorf (blue, $n = 12$). Median survival in Basel 404 days, in Duesseldorf seven days (log-rank test: $p < 0.01$).

TABLE 2 | Patient characteristics of Case report 1 and 2.

	Case report 1	Case report 2
Age (years)	58	72
Sex	Male	Male
Diagnosis	ICM	DCM
LVAD-concepts	BTT	DT
Place of first sPC contact	IMC	Outpatient clinic
LVAD until sPC contact (years)	6.13	2.96
sPC contact until death (days)	3	362
Place of death	IMC	sPC unit
Context	Late sPC involvement in the LVAD process	LVAD deactivation

ICM, ischemic cardiomyopathy; DCM, dilatative cardiomyopathy; LVAD, left ventricular assist devices; BTT, bridge to transplant; DT, destination therapy; sPC, specialist Palliative Care; IMC, Intermediate Care Unit.

including advance directives and power of attorneys, and discharge planning. Data on the frequency and intensity of sPC contacts differ between study sites. In Duesseldorf, patients had sPC contact only during their index hospital stay and had a median time of direct sPC contact of 330 (270–1,500) min with incomplete data in three medical records. In Basel, patients had contact to the outpatient sPC clinic ($n = 4$) as well as during their inpatient stays. Data about the duration of each sPC contact are unavailable.

The following two case reports describe the course of two of the LVAD patients receiving sPC who died (**Table 2**). All identifying data have been removed and certain demographic data changed to protect privacy according to requirement of the local ethics committees.

Case Report 1: Example of Late Integration of Specialist Palliative Care

A 58-year-old man with ischemic cardiomyopathy and multiple comorbidities had a HeartMate II® LVAD implanted as a BTT 6 years ago. Before admittance to the hospital, the patient lived at home with his partner. Due to incurable Hodgkin-lymphoma, the patient was removed from the HTX waiting list 3 years ago. The patient was admitted to hospital because of LVAD thrombosis. He experienced new-onset headache due to a stroke. Replacement of the LVAD was discussed interdisciplinary. However, this option was abandoned after consideration of the patient's life expectancy. During thrombolytic therapy, intracranial hemorrhage occurred, and the therapy had to be discontinued. After cessation of the thrombolytic therapy, LVAD-thrombosis progressed, and the patient developed sepsis. Given the situation, an interdisciplinary family conference involving the patient, his next of kin, cardiothoracic surgeons, and intensivists led to a decision to focus on comfort care and to integrate sPC. Consultation by the sPC team was requested by the treating physicians and a do not resuscitate/do not intubate (DNR/DNI) order was established. The sPC physician evaluated the patient to be imminently dying, assessed symptom control and spoke to the patient, the next of kin and the IMC clinicians. Together, they decided to initiate intravenous morphine via continuous application (100 mg morphine/50 ml 0.9% saline) with a rate of 2 mg/h due to persistent pain and stopped all other oral medication that did not provide symptom control. The patient was already used to opioids with a pain-treatment medication of ibuprofen, fentanyl 50 µg/h via a transdermal patch and requested his breakthrough pain medication fentanyl 100 µg buccal tablets three to four times a day. In case of fear or agitation, additional medication with midazolam was recommended by the sPC team. The patient was then pain free and fully orientated in communication. In the course of the following day the patient refused to eat and drank very little. After 3 days of increasing LVAD failure due to the progressing thrombosis and constant contact to the sPC physician and the sPC nursing team, the patient became more confused, but could still walk some steps and was not in pain. As he became agitated during the night due to reappeared pain and progressing dyspnea, intravenous morphine application was increased to 3 mg/h. After about an hour, the patient passed away next to his partner on IMC unit.

Case Report 2: End-of-Life Care and Deactivation of Left Ventricular Assist Devices on the External Specialist Palliative Care Unit

A 72-year-old man with ischemic cardiomyopathy, acute on chronic renal failure, and other comorbidities had a LVAD implanted as DT 4 years prior to admission. His first contact to

the sPC outpatient-clinic was 3 years after implantation. Over time, the patient became severely impaired and led a bed-to-chair-existence due to weakness and dyspnea on exertion. He had been admitted to the university hospital due to deterioration of his general health condition weeks ago. During hospitalization, the patient suffered from hypoxia and *de facto* cardiac arrest due to unplanned disconnection of the LVAD batteries, performed by the patient himself. It remained unclear, whether this disconnection was performed consciously with suicidal intention or occurred accidentally. The patient was transferred to the ICU, regained cognition, ability to judge his situation, and was able to communicate. The sPC team was called for consultations. The patient reported physical distress due to breathlessness, fatigue, and severe anxiety due to worries about the future ("how can I go on like this"). Symptom control was established by the sPC team. In numerous round-table discussions over 2 weeks with the patient, his wife, and members from different disciplines, a shared decision-making process took place. At that time, the patient did not wish deactivation of the LVAD or escalation of other medical therapy, suicidal thoughts were denied. At that point, symptom-controlling measures were begun to promote wellbeing. The patient was then transferred to the external sPC unit. Before transferal, in collaboration with the cardio-technician who had been responsible for the patient for years, the sPC team was trained to manage and monitor the LVAD device.

In the sPC unit, the patient presented with anxiety, dyspnea, episodes of restlessness and delirium as well as neuropathic pain due to postherpetic neuralgia. Symptom control was established by the sPC team. Pain and dyspnea could be relieved with opioid therapy (hydromorphone 2 mg/day subcutaneous) in conjunction with non-opioids (dipyrone) and gabapentin. Also, the patient was treated with intravenous midazolam with a maximum of 8 mg/h during the night and 1 mg/h during the day due to anxiety and restlessness. The neurologic situation fluctuated, with intermittent phases of restlessness and disorientation. When the patient was awake and oriented, he often expressed a strong wish to die. His overall and neurologic situation declined further. After a multiprofessional meeting with the consulting ethicist, the wife, and the cardiology team, the decision to deactivate the LVAD under increased doses of opioids and benzodiazepines was made. The sPC physician inactivated the LVAD after being instructed by the perfusionist with intravenous propofol in standby for fast and deep sedation, whether this would have been necessary. The patient died within half an hour without signs of dyspnea, anxiety or other distress with his wife and the PC physician at his side.

Overall, the team of the sPC unit faced several challenges. The nursing team needed training and information about how to deal with the LVAD technically and about characteristics of the dying process of patients with an LVAD. Due to the unavailability of cardio-technicians or cardiology support during out-of-office hours in the sPC unit (not located on the university hospital campus), anxieties of the sPC nurses concerning the care of a patient with a LVAD device had to be addressed proactively and could be relieved.

DISCUSSION

In this study, we aimed to portray the current situation of sPC integration in LVAD patients in two German-speaking university hospitals. Notable findings of our investigation are as follows: (1) Consistent with the literature from the U.S. (11), we found that utilization of sPC in patients with LVAD generally remains low, with a strong discrepancy between centers. (2) Our data support the involvement of sPC in both DT and BTT patients. For DT patient, U.S. guidelines already recommend sPC prior to implantation. However, BTT patients can also benefit from sPC, for example when they experience a change of their treatment goal (HTX no longer intended) or even earlier. (3) The presented case reports show possible benefits of comprehensive and early sPC involvement, however, they also report challenges.

A retrospective analysis in the U.S. from 2006 to 2014 showed a 4% overall rate of sPC involvement in LVAD patients (11). Since the implementation of the U.S. guideline recommendation for sPC in DT-LVAD patients, this rate has significantly increased (11). In their retrospective study including 89 patients, Nakagawa et al. showed a significant increase with around 80% of BTT and DT patients receiving sPC in the last month of life (18). Although PC consultation prior to MCS implantation or HTX is suggested in the European guidelines in general, in a position manuscript published by the ESC, the situations "before LVAD implantation or transplant referral" are described as possible trigger for sPC, not as a mandatory recommendation as it is in the U.S. (22). In our study, sPC involvement occurred late in the LVAD process. Especially in Duesseldorf, it mostly occurred shortly before death. In Germany, the guideline for the treatment of chronic heart failure recommends an early and proactive screening of PC needs in patients with heart failure by the family doctor (23). Several potential reasons for the underutilization of sPC in heart failure have been identified. Many family doctors and cardiologists report lacking time for these conversations during primary care (24). Often, these clinicians refuse to talk to patients about their poor prognosis, and barriers exist among doctors to use the word "palliative" when talking to a patient (24). Also, the unpredictable disease trajectory of heart failure can promote a rather reactive use of sPC, most often during the latest phase of life (24). Crimmings et al. describe this current situation in the treatment of heart failure as a "death-denying culture" (24). Currently, a prospective, controlled multicenter study to explore the efficacy and cost-effectiveness of interdisciplinary sPC in symptomatic heart failure is in progress (25). Our study showed that despite the increasing trend of LVAD implantations at the two university hospitals, the integration of sPC in the care for LVAD patients is yet not well established. This discrepancy is highlighted by the 31 patients (11%) cared for with integration of sPC support among the 288 total LVAD implantations. Moreover, the disparity between the two centers, with only 5% of LVAD patients in Duesseldorf receiving sPC and 90% sPC involvement in Basel is revealing. Greater sPC involvement in Basel (especially after 2018) contributes to center-specific differences that make it difficult to compare the two cohorts and might partially explain

a significantly longer survival after sPC involvement in Basel (**Figure 3**). Also, LVAD expertise in Basel is rather new (since 2014) and was established when there was already an awareness of sPC need in LVAD patients in the literature and international guidelines. Therefore, a closer collaboration between the LVAD and sPC teams exists, especially since 2018. In Duesseldorf, sPC is only involved when cardiac surgeons contact the sPC teams or when patients are being discussed on the weekly sPC team visit on the ICU. This present study might increase the awareness of members of the heart-teams to include sPC at an early stage in the LVAD trajectory.

Numerous positive predictors for sPC integration like DNR status, female sex, and metastatic cancer have been identified (11). Men receive LVAD three times more often than women (26). In this study, most patients were men, which reflects the existing gender gap in LVAD treatment (26). It may be that women have a clearer idea about their end-of-life wishes and are more likely to refuse LVAD therapy. Women might be more afraid of the burden for their caregivers and prefer to have a quiet and peaceful end-of-life period without an alarming LVAD device. Comorbidities such as metastatic cancer, psychiatric diseases or other serious comorbidities have not been investigated in this present study. However, these might influence the need of sPC in LVAD patients as they also affect the prognosis. Until admission to the hospital that resulted in sPC involvement, most patients (77%) lived with their family or alone. Their mean ECOG was three, which indicates that patients were only capable of limited selfcare. In Basel, where sPC involvement is more prevalent, 70% of patients had an ECOG status of one or two, indicating a fully active or mildly restricted patient. A proactive and earlier sPC involvement before LVAD implantation or the onset of complications leading to hospital admission may support advance care planning when patients still live in their familiar surroundings. The definition of trigger criteria for sPC might help to increase the rate of sPC integration in LVAD according to each patient's needs.

Interestingly, most publications and the U.S. guidelines only focus on sPC in DT-LVAD patients (16, 19, 27). But in fact, the end-of-life issues of BTT und DT patients do not seem to differ significantly in terms of place of death, DNR orders, hospice enrollment, and PC during the last month of life (18). Our study shows that BTT patients might also have a need for sPC, since all eight presented LVAD BTT patients died without receiving HTX. When BTT patients experience a change of treatment goal (as presented in "Case Report 1" section), sPC can provide support especially during this phase.

Overall, our study shows late sPC involvement in the LVAD process. In Duesseldorf, the average time between first sPC contact and in-hospital death was around 10 days. During this rather short period, establishing a trusting relationship between the sPC team and the patient and their next of kin may be difficult. The AHA guidelines recommend starting sPC before implantation. In the context of cancer, early integration of palliative care has been shown to significantly prolong life and improve quality of life in a landmark study (28), while recent meta-analyses of cancer and non-cancer populations show no negative impact of esPC on survival (29, 30). Despite the cooperation between LVAD and sPC teams in Basel, only two patients had already received esPC before LVAD implantation, but in this center, the average time between first sPC contact and death was rather long compared to Duesseldorf. More data are needed to analyze the impact of esPC on the circumstances of death. Most patients (81%) died in hospital, mainly on the ICU or IMC ward, with just one dying on an sPC unit and three dying at home after hospital discharge. This finding may illustrate the fact that even despite esPC involvement, it is difficult to enable patients and their next of kin to die in their preferred place of death, which is known to be at home for most patients (31). Yet, earlier studies have found that significantly fewer LVAD patients die on the ICU after sPC involvement (18, 32).

The two case reports presented here demonstrate possible end-of-life scenarios as well as characteristics and challenges of sPC involvement. Concerning case report 1, the question occurs, why the patient was not presented to sPC earlier (e.g., when BTT changed to DT due to the non-curable comorbidity or even earlier, since BTT and DT patients experience similar distress and symptoms) (18). When LVAD thrombosis occurred in Case Report 1, the therapeutic focus still lay on life-sustaining intensive care therapy. Only after thrombolysis failed and sepsis occurred, end-of-life care and sPC integration was considered. As mentioned earlier, this sPC concept is rather reactive and suggests little anticipation of possible end-of-life scenarios and lack of screening for the patients' PC needs. Therefore, esPC could help here to reduce such barriers. A standardized esPC concept in DT offers multiple benefits such as increased quality of life of patients, more advanced care planning, and enhanced satisfaction among clinicians (19). Case report 2 demonstrates that earlier involvement of the sPC team helped with shared decision making, supported the relatives, and facilitated establishment of a further integrated care pathway to allow treatment of the patient and his family concerning to their needs and wishes on a sPC unit. It was possible to show that management of the patient, his symptoms and his family may be performed on a continued pathway on a sPC unit. Yet, a necessary prerequisite for this involved intensive teaching of the external sPC team and close collaboration with cardio-technicians and cardiologists, which may not be available outside the cardiology center. Besides the required technical expertise, also ethical issues may arise during LVAD care, especially at end-of-life. On the one hand, an ongoing LVAD as a life sustaining technology might prolong natural dying and sPC team members might explore moral distress which is also observed in intensive care clinicians who care for MCS patients (33). On the other hand, LVAD deactivation may present an emotional situation for next of kin and all team members. An interdisciplinary and multiprofessional checklist that outlines different steps required for LVAD deactivation might help in these situations (34). In both centers, the sPC teams work as an interdisciplinary team. Thus, experts from different medical disciplines are included, e.g., from anesthesiology, psychosomatic medicine and oncology. The teams are multiprofessional and comprise doctors, nurses, psychologists, physical therapists, social workers, clerics and volunteers. Also included are other therapists for

music therapy or animal assisted therapy. The team meets daily for a morning conference and monthly for supervision. Good communication between the team members and good integration of the different professions are considered crucial for a sustainable team. Each first patient contact starts with an assessment of symptoms by a sPC physician and a nurse, the patient's history regarding the medical and personal background and the patient's wishes and goals. Further patient contacts depend on the patient's and the next of kin needs, which includes psychosocial support as well as physiotherapy or spiritual care. With routine implementation of sPC in an LVAD program, ideally there should be a 24/7 on-call support from the primary treating heart-team.

Study Limitations

This is the first retrospective and descriptive study about sPC in LVAD patients in the German-speaking area. Limitations of this study are a limited number of patients as well as the fact that included patients were not compared to those who did not receive sPC. Therefore, we cannot observe an impact of sPC or esPC on, for example, the place or circumstances of death.

Another major limitation of our study is a possible selection bias resulting from the method of clinical database research. Only patients that ultimately received sPC and died in the process were included. Unfortunately, no information could be gathered about patients for whom sPC might have been discussed but ultimately was not provided. Also, data was collected from just two university hospitals in German-speaking countries and not from elsewhere in Europe. More data from other hospitals is needed to get a clear overview of the sPC situation in LVAD patients. In addition, the routine documentation process by each hospital's sPC team is different. Therefore, a standardized and comparable assessment could not be provided. Both centers routinely use the ECOG to assess a patient's performance status. This parameter was originally established in cancer patients and is not commonly used in heart failure patients. An analysis using parameters specific for heart failure patients seems more reasonable. However, cardiology-specific scores as the New York Heart Association (NYHA)-Classification have been shown to poorly discriminate between clinically important functional performance states in people with advanced heart failure (35). Additionally, other established physical performance tests in heart failure, such as the Six Minute Walking Test and the Timed Up and Go Test (36) focus primarily on functional activity rather than everyday-life performance as the ECOG does. The use of the Kansas City Cardiomyopathy Questionnaire (KCCQ) could also help in further studies to evaluate the health status (37). However, none of these parameters inform about uncovered needs that could require the involvement of sPC and therefore do not present suitable triggers to initiate sPC. The European Association for Palliative Care recommends sPC needs assessments in regular heart failure visits and advises to examine for "distressing symptoms, existential distress, recurrent heart failure exacerbation and progressive frailty or caregiver concerns" (14). Future studies are needed to identify specific triggers for standardized sPC in LVAD patients. Most obviously, as this is a retrospective real-world study, a control group is lacking. Although, case numbers are low and only two centers were involved, the observation of relatively large differences (e.g., in the time of sPC involvement) make the comparison between the two centers an interesting first step to study sPC involvement of LVAD patients. Due to the lack of generalizability with only two centers, certainly these differences have to be seen as site - rather than country - specific. To date, few sPC teams and very few sPC units or hospices are able to care for patients with LVAD. Therefore, this real-world pilot data may provide useful information for institutions planning to establish an sPC program for LVAD patients.

CONCLUSION

In conclusion, although the rates of LVAD implantations have been growing in the last decade, the integration of sPC in the care for these patients is yet not well established. An increased awareness of the sPC need of LVAD patients has led to a proactive use of (e)sPC in one center. In general, sPC involvement still occurs relatively late in the LVAD process but has great potential for both BTT and DT patients. Our findings suggest that there remains a lack of sPC provision in LVAD patients in the German-speaking area, and further involvement of sPC should be pursued in the future.

DATA AVAILABILITY STATEMENT

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

This study involving human participants was reviewed and approved by Ethics Committee of the Medical Faculty of Heinrich-Heine-University Duesseldorf, Germany (Study-Nr.: 2021-1600). An additional ethical approval by the Ethics Committee of Northwestern- and Central Switzerland was not required (Req-2021-01368). Written informed consent for participation was not required for this study in accordance with the retrospective nature of this study.

AUTHOR CONTRIBUTIONS

TT: concept and design, data collection, data analysis and interpretation, statistics, writing of the manuscript, and software. DSa: writing of the manuscript, data analysis and interpretation, and critical revision of the manuscript. DSc, MSc, JS, and SM: concept and design,

supervision, and critical revision of the manuscript. PA: data collection, critical revision of the manuscript, supervision, and resources. OP: critical revision of the manuscript, supervision, and resources. SW: data collection, data analysis and interpretation, software, and critical revision of the manuscript. SE: concept and design, supervision, critical revision of the manuscript, and data analysis and interpretation. FE and MSi: critical revision of the manuscript, supervision, and funding. JG and MN: concept and design, writing of the manuscript, critical revision of the manuscript, and supervision. All authors contributed to the article and approved the submitted version.

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REVIEW
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Non-pharmacological Management in Palliative Care for Patients With Advanced COPD

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Chronic obstructive pulmonary disease (COPD) is a disabling condition associated with progressive airflow limitation and lung tissue damage; its main symptoms are breathlessness, fatigue, cough, and sputum production. In the advanced stage of the disease, these symptoms may severely impact on a person's physical and psychological functioning, with some also developing chronic respiratory failure, associated with blood gas abnormalities. Non-pharmacological interventions can improve quality of life and functioning in the management of people living with advanced COPD. This article will provide an overview of common non-pharmacological methods used in the symptomatic management of severe COPD, including: breathlessness and fatigue management strategies, anxiety management, pulmonary rehabilitation (PR) and physical activity (PA), neuromuscular electrical stimulation (NMES), airway clearance techniques (ACTs), nutrition and non-invasive ventilation (NIV). The importance of a holistic and multi-disciplinary approach to people living with COPD will be discussed.

Keywords: palliative care, non-pharmacological management, COPD, narrative review, physiotherapy

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of chronic morbidity and mortality worldwide (1). COPD leads to mucous hypersecretion (chronic bronchitis), tissue destruction (emphysema) and small airway chronic inflammation and fibrosis (bronchiolitis) as well as systemic inflammation (2, 3). The progressive nature of the disease leads to severe poorly reversible airflow obstruction despite optimal bronchodilation therapy. This results in increased airway resistance and compliance and in consequence to air trapping, hyperinflation and flattening of the diaphragm (2, 3). The changes in mechanics of breathing in COPD lead to increased effort of breathing and energy expenditure at rest (4, 5). Further consequence of advanced COPD may be gas exchange abnormalities causing chronic hypoxaemia or nocturnal hypercapnia. The impact of systemic inflammation on other systems in the body are becoming more evident in advance stages of COPD. These consequences may include cachexia, skeletal muscle atrophy, osteoporosis, increased risk of cardiovascular disease or neuropsychiatric disorders (3). With the progression of the disease, the more frequent and more severe acute exacerbations lead to an increased risk of hospitalisations and deterioration of the function (6).

Consequently, COPD causes persistent and progressive respiratory and non-respiratory disabling symptoms, such as breathlessness, fatigue, cough, and/or sputum production (7, 8). It is also common for people with COPD to experience anxiety and depression (9). These symptoms negatively affect individuals with COPD including their health-related quality of life, activities of daily living, physical activity, and sleep (10). It is crucial to evaluate not only the intensity of these symptoms but also their impact on daily functioning and participation in family and social life. Importantly, patients with COPD had a 2-fold increased risk of frailty (11–13), which can affect prognosis and management in advanced COPD. Therefore, people suffering from severe COPD require a holistic and multi-disciplinary approach that involves a variety of healthcare professionals, including physicians, nurses, physiotherapists, occupational therapists, psychologists, and social workers (14). Palliative care is a multidisciplinary approach which focuses on patient's symptom management and improvement in quality of life, therefore it has to be incorporated earlier into the management of COPD (15).

This article provides an overview of methods used in palliative care for the non-pharmacological management of symptomatic patients with severe COPD, including the management of breathlessness, fatigue and anxiety, pulmonary rehabilitation (PR), neuromuscular electrical stimulation (NMES), management of sputum clearance, nutrition and chronic respiratory failure (e.g., non-invasive ventilation).

BREATHLESSNESS MANAGEMENT MODEL IN PALLIATIVE CARE

Breathlessness is the most common symptom in severe COPD (16), its prevalence is greater in the end stage of COPD (17–19). There may be several factors that contribute to the sensation of breathlessness (20). Management of this symptom should be multifactorial, based on an assessment of the patient to identify any elements contributing to the subjective sensation of breathlessness. The 'Breathing, Thinking, Functioning' model used by the Cambridge Breathlessness Intervention Service (CBIS), has been developed by Spathis and colleagues (21, 22). The model presents three features of the vicious cycle of breathlessness: (1) inefficient breathing, (2) thinking (including anxiety and distress), and (3) reduced function leading to muscle deconditioning (22, 23). With this model, it is possible to create categories of interventions to reduce breathlessness (see **Figure 1**) (21). Additionally, this model emphasized the need to implement multifactorial strategies to manage breathlessness.

DAY-TO-DAY BREATHLESSNESS MANAGEMENT STRATEGIES

Breathlessness progresses with time, may intensify with advancement of the disease, and often negatively impacts on function (24). Individuals with advanced COPD will experience breathlessness on a regular basis. Their breathlessness may be triggered by exertion, for example during activities of daily living or a change in emotional state. Strategies to manage an acute onset of breathlessness may include positioning, breathing techniques, panic management, and desensitization (20).

Positioning to Relieve Breathlessness

The "leaning forward" position is frequently used in clinical practice for the management of breathlessness triggered by activities of daily living or during rehabilitation. The theory behind this technique proposes that fixing the shoulder girdle, reduces activity of both the scalenes and sternomastoid muscles whilst increasing both transdiaphragmatic pressure (via diaphragmatic recruitment) and thoraco-abdominal movements (25–29). Using the forward lean to improve efficiency of respiratory muscles and decrease work of breathing is thought to lead to quicker recovery from breathlessness.

Breathing Techniques

Although evidence supporting the effectiveness of breathing techniques varies, depending on the specific technique in question (30), their use is recommended to help breathless people gain better control of their breathing (31). Purse-lip breathing (PLB) technique has one of the strongest evidence-bases to support its use. The technique requires to inhale slowly through the nose and exhale through the mouth with the puckered lips, which alters respiratory mechanics (32). The increased resistance from half-opened lips on expiration physiologically generates an extrinsic positive end expiratory pressure (extrinsic PEEP), which decreases airway collapse by reducing the Bernoulli effect (33). This leads to decreased "air trapping" in patients with emphysema resulting in a reduction of hyperinflation.

Applying PLB lowers oxygen consumption, respiratory rate (RR) and reduces breathlessness in people with COPD (34). It shows to improve inspiratory capacity (IC) at rest (35) and reduced level dynamic hyperinflation during activity (36). PLB used on exercise shows to improve exercise tolerance (33, 37), reduce respiratory rate (RR) and improves recovery time in people with COPD (38).

Other breathing techniques, such as Breathing Control (BC), Blow as you go (BAYG) or Paced breathing, have less evidence to support their effectiveness, but some patients find them helpful in managing their breathlessness either on exercise or during recovery (39).

However, not all breathing techniques are beneficial for the management of breathlessness in severe COPD; diaphragmatic breathing may increase dyspnoea (40) by increasing chest wall asynchronicity (41, 42), leading to increase work of breathing. Another technique, slow deep breathing may predispose the diaphragm to fatigue (43). Therefore, clinical guidelines do not recommend use of either of these techniques for patients with advanced COPD (31).

Walking Aid

Walking aids may be used to help with management of breathlessness during ambulation and enable patients with severe COPD to stay active and independent. The rollator frames on exertion may reduce work of breathing by maintaining the lean forward position during activity (44). Evidence from a research study by Probst at al. (45) shows rollator frames can significantly

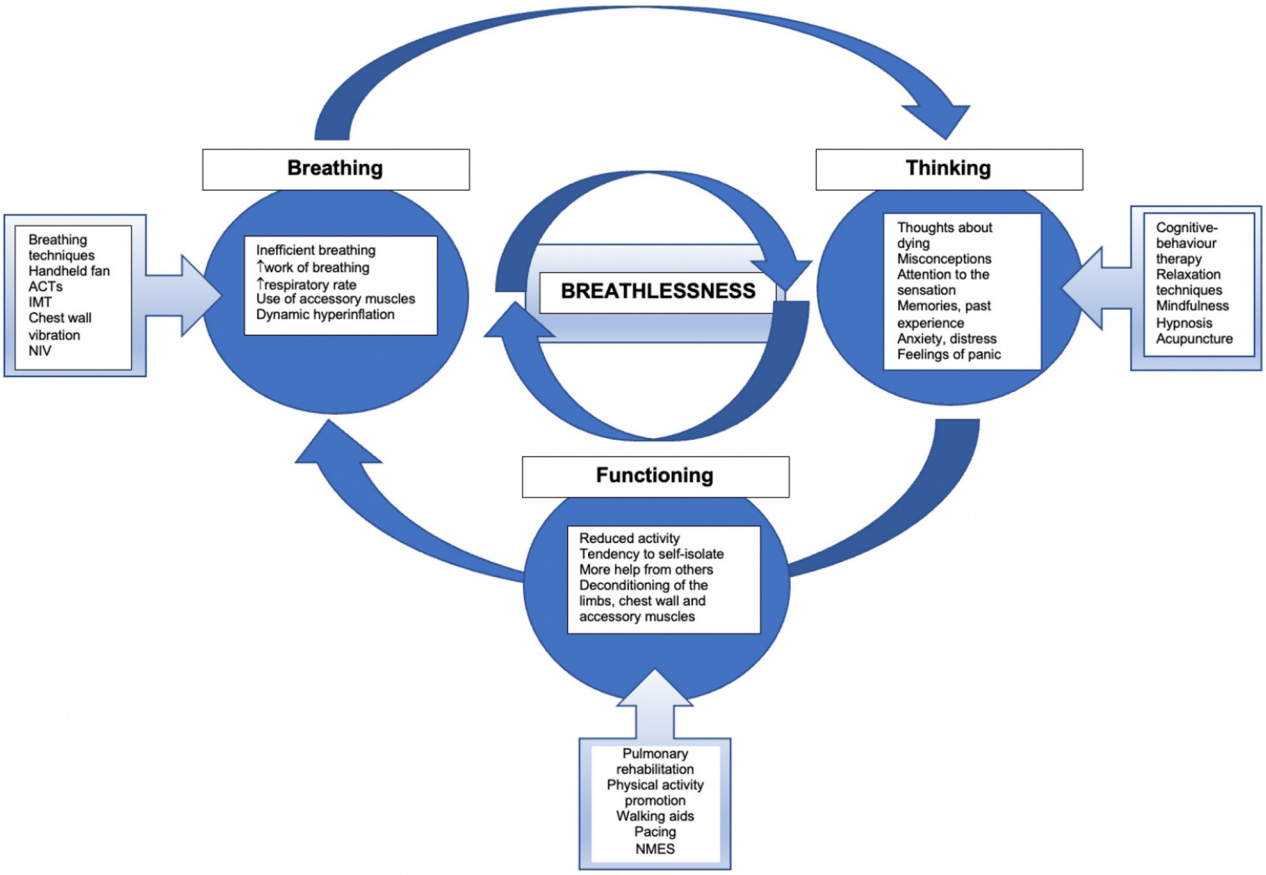

FIGURE 1 | The model of breathlessness and management approaches. Adopted from Spathis et al. (21).
ACTs, airway clearance techniques; IMT, inspiratory muscle training; NIV, non-invasive ventilation; NMES, neuromuscular electrical stimulation.

increase walking distance, whilst reducing exertional dyspnoea in patients with COPD. The effect on respiratory function was demonstrated with improvements in oxygen uptake, tidal volume and minute ventilation. Similarly, the use of gutter frames with elderly COPD patients have been shown to increase walking distance and reduce oxygen desaturation during ambulation (46).

Handheld Fan

The benefits of utilizing cool, flowing air on the facial skin for patients with COPD is has long been known, with many patients reporting having benefited (47). The mechanism of action is explained in part through stimulation of facial temperature receptors (48) and modulation of central perception of breathlessness (49). Although a systematic literature review from 2008 showed insufficient data to support the evidence for fans' effectiveness (50), the authors emphasized that more research is necessary on selecting and identifying those who might benefit from using handheld fans (51, 52). Subsequently a number of studies showed that a cool draft of air from a handheld fan directed to the face can be helpful in reducing the sensation of breathlessness in patients with advanced COPD (53–55). Moreover, there is data that suggests that using a handheld fan increases physical activity (56). Some authors indicate that future research should explore the relationship between handheld fan characteristics and relief of breathlessness (57). The authors researching handheld fans for breathlessness emphasize their acceptability to patients, relative inexpense, portability and ability to give patients more control; and recommended their use as part of palliative management to support patients' self-management and independence (53, 54, 58, 59).

LONG-TERM BREATHLESSNESS MANAGEMENT STRATEGIES

There are also some strategies to improve chronic breathlessness in the longer term. This includes exercise training or more comprehensive programmes such as pulmonary rehabilitation (PR) (60). Furthermore, in patients with COPD with dysfunctional breathing patterns, breathing retraining programmes may be considered. However, a systematic review by Holland et al. (30) demonstrated inconsistent evidence about improvement in breathlessness.

There is also evidence that Inspiratory Muscle Training (IMT) in moderate-to-severe COPD improves dyspnoea and quality of life (61, 62). A recent systematic review (63) presented

results from 23 studies, which all indicated that IMT training decreased dyspnoea. However, there were some indications that improvement was limited to patients with pre-existing respiratory muscle weakness.

FATIGUE MANAGEMENT STRATEGIES

The sensation of fatigue may be defined in various ways, including as tiredness (64), a lack of energy (65), exhaustion or weakness (2). The mechanism of subjective fatigue in COPD is complex and multidimensional (66, 67).

Exercise training alone or as a part of PR has been found beneficial in managing fatigue. A recent literature review demonstrated that any type of exercise could reduce fatigue (68). It has been also established that pulmonary rehabilitation reduces fatigue (60, 65), in particularly general, physical and reduce motivation (69).

One study investigated the effect of an 8-week progressive muscle relaxation programme on fatigue (70). It showed reduced fatigue and an improvement in sleep quality following the programme. There are some indications that sleep quality influences fatigue (71). Other fatigue management strategies reported by a qualitative study included pacing, protection, energy conservation, keeping active, resting or planning daily living and prioritizing (71, 72).

Energy conservation involves modifying an activity or the environment to decrease the level of energy required to complete a task. Pacing and energy conservation are also used for management of fatigue (73). A recent randomized controlled trial of a 2-week training programme involving energy conservation techniques (ECT) for COPD patients (74), demonstrated that after the programme there was lower level of desaturation and decrease in the metabolic equivalent of task (MET) while performing activities of daily living. Another observational study showed that ECT decreased heart rate, oxygen uptake, minute ventilation and dyspnoea. Although, ECT are recommended for management of fatigue in clinical practice, there is no evidence to demonstrate decrease of fatigue with this intervention.

ANXIETY MANAGEMENT

Feelings of anxiety are common in patients with advanced COPD (9). More intense breathlessness is associated with greater levels of anxiety (20). These symptoms negatively affect patients' physical functioning and increase their social isolation (75–78). Currently, we observe a growing number of studies addressing the issue of the use of non-pharmacological methods in the treatment of COPD patients affected by anxiety. The evaluated interventions included: relaxation (79, 80), hypnosis (81), cognitive behavioral therapy (82), and mindfulness (83). One study investigated also breathing techniques and found out them beneficial in managing anxiety (84). A recent systematic review, demonstrated significant, clinically relevant improvement in anxiety and depression following PR programme (85). Further research is needed to determine which interventions are the most effective and could be an efficacious add-on to standard PR programs or stand-alone treatment.

PULMONARY REHABILITATION AND PHYSICAL ACTIVITY

Pulmonary Rehabilitation (PR) is an important part of integrated care for patients with COPD. PR is a comprehensive programme which includes a variety of non-pharmacological interventions, exercise training and education (86). It has proved to be highly effective in management symptoms, improving QoL, physical and psychological functioning of patients with COPD (60, 85). In advance disease, people with COPD may experience frequent exacerbations and are at greater risk of frailty. Patients who complete PR after acute exacerbation would also have a lower risk of hospital readmission and mortality (87). Furthermore, COPD patients with frailty and risk of frailty showed benefit from PR, but they are more likely not to complete the programme (88).

Despite undisputable benefits from PR, in advanced stage of the disease, there may be number of barriers which could make attending programme difficult. The recent clinical report indicated that patients may struggle to complete post-exacerbation PR due to transport issues, advance disease, co-morbidities such as anxiety, poor motivation, and high fatigue (89). These patients are often fragile and may not always have the sufficient reserve to initiate the programme. It may be difficult for these patients to spend time outside home in late stage of disease, which may require effort and may create additional stress.

Nevertheless, the interventions aiming to reducing sedentary lifestyle and increase physical activity (PA) should still be considered. The evidence for different exercise-based PA-enhancing interventions is inconsistent. Behavioral change using tele-coaching or coaching, pedometers, applications, walking and home exercise programmes has been suggested to boost PA in patients with COPD (90, 91).

NEUROMUSCULAR ELECTRICAL STIMULATION

Impaired muscle function and decreased cross-sectional muscle mass are common features in people with severe COPD, which affect the respiratory and the skeletal muscles, especially of the lower limbs (92, 93). Patients with advanced COPD who are severely affected by muscle weakness, including those who are housebound, may benefit from Neuromuscular Electrical Stimulation (NMES) (94). NMES usually is applied to the quadriceps muscle and improves impaired muscle function and structure by increasing cross-sectional muscle mass, muscle force, endurance, and exercise tolerance as well as reducing dyspnoea (94–96). Moreover, some studies report that NMES promotes a reduction of the perceived sensation of dyspnea during exercise in patients with COPD (97). For people admitted to an intensive care or high dependency unit with an acute exacerbation of COPD, research suggests NMES combined with conventional exercise may reduce the time taken for patients to first sit out of bed (98).

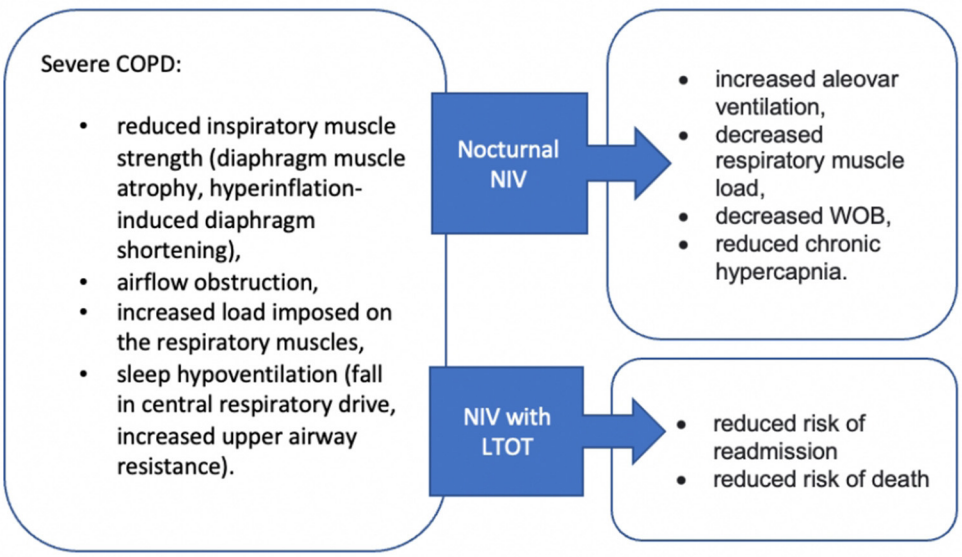

FIGURE 2 | Effectiveness of Non-invasive ventilation in patients with advanced COPD. NIV, non-invasive ventilation; WOB, work of breathing.

The effectiveness of NMES in adults with advanced COPD and other diseases was analyzed in two Cochrane Systematic Reviews (50, 98). The authors conclude that there is a high strength of evidence that NMES may be an effective treatment for muscle weakness in adults with advanced progressive disease.

AIRWAY CLEARANCE MANAGEMENT

For some COPD patients, cough and sputum may be a burden, especially during exacerbations. When the patient experiences difficulties with sputum expectoration, advice and support may be required. There are several airway clearance techniques (ACTs) recognized as effective methods (99, 100). Application of ACTs decreases breathlessness, lower need for ventilatory assistance and Positive Expiratory Pressure (PEP) devices improve sputum volume expectoration and decrease hospital length of stay for COPD patients admitted due to acute exacerbation (101, 102). In a recent review, significant improvements in the rate of exacerbation frequency at 6 months of ACTs use was demonstrated (100). Therefore, it would be important to review if sputum is cleared effectively and identify potential need for management with appropriate ACTs in COPD patients.

NUTRITION MANAGEMENT

Many people in advanced stages of COPD are underweight and may demonstrate sign of cachexia. Evidence suggests that 25–40% of all COPD patients have low body weight, 25% of patients have moderate to severe weight loss, and 35% of patients with extremely low fat-free mass (FFM) index (103). This has a negative effect on muscle mass and function and impacts exercise tolerance. Therefore, the European Respiratory Society (ERS) recommends that nutritional interventions should be considered as a single treatment or integrated with exercise training (104). Especially, patients with negative energy balance, may benefit from energy- and protein-enriched diet and the evidence suggests that nutritional supplementation promotes weight gain among patients with COPD (105). Furthermore, because exercise increases energy expenditure, it is suggested to assess the nutritional status of COPD patients before starting Pulmonary Rehabilitation (86). In patients with weight abnormalities, dietary counseling and food fortification or nutritional supplementation should be considered. Some authors suggest that smaller volumes of food may be more appropriate to optimize energy intake (106). Education and advice on nutrition are indicated as methods that bring a short-term effect on improving intake (106).

VENTILATORY SUPPORT

Due to the small airway disease and lung hyperinflation, the diaphragm muscle is flattened, which may lead to its atrophy and greater fatiguability in severe COPD (107). Sleep hypoventilation is also observed in some people in advanced COPD (108). These factors may lead to a development of the type 2 respiratory failure. Therefore, these patients may benefit from nocturnal non-invasive ventilation (NIV) to support their respiratory muscle. The American Thoracic Society (ATS) Clinical Practice Guidelines recommend the use of nocturnal NIV in addition to usual care for patients with chronic stable hypercapnic COPD (109). A systematic review on the use of NIV in severe stable COPD concluded that

TABLE 1 | Effectiveness of non-pharmacological interventions used in palliative care in COPD.

Intervention	Help to manage	Stength of evidence	Clinical practice recommendations
Pulmonary Rehabilitation	Breathlessness, fatigue, anxiety, improves exercise tolerance	+++ (60, 87, 114–116)	BTS/ACPRC guideline (31) ERS/ATS statement (86)
Positioning to relieve breathlessness	Breathlessness, anxiety	x	BTS/ACPRC guideline (31)
Breathing techniques	Breathlessness, anxiety	+++ PLB-Pursed-lip breathing (117, 118) x (BAYG- blow as you go, BC- breathing control, PC-paced breathing)	BTS/ACPRC guideline (31) Diaphragmatic breathing not recommended by BTS/ACPRC guidelines (31)
Respiratory muscle training	Breathlessness, Fatigue	+++ (119)	BTS/ACPRC guideline (31)
Breathing retraining	Breathlessness	++ (50)	-
Walking aid	Breathlessness	++ (45, 50)	Rollator frame and a gutter rollator frame are recommended by BTS/ACPRC guideline (31)
Handheld fan	breathlessness	+++ (52, 53, 55, 56)	-
Chest wall vibration	breathlessness	+++ (50)	May be difficult to use in practice.
Energy conservation techniques	fatigue	+ (74)	BTS/ACPRC guideline (31)
Airway clearance techniques	Breathlessness	-	ACBT, AD, OPEP are recommended (31, 120)
Relaxation	Breathlessness, Fatigue, Anxiety	x (79, 80)	BTS/ACPRC guideline (31)
Non-invasive ventilation	Breathlessness, Fatigue	+++ (110, 113)	BTS/ACPRC guideline (31) ATS clinical practice guideline (109)
Neuromuscular Electrical Stimulation	Breathlessness	+++ (50, 96, 121) x (95, 97)	(120)
Acupuncture		++ (50)	-

+++ Strong evidence (based meta-analysis, systematic reviews); ++ Moderate evidence (based on few RCT); + weak evidence (based on non-randomized studies); x not sufficient evidence to support effectiveness, BTS, British Thoracic Society; ATS, American Thoracic Society; ERS, European Respiratory Society; ACBT, Active Cycle of Breathing Techniques; AD, Autogenic Drainage; OPEP, Oscillatory Positive Expiratory Breathing.

bilevel non-invasive positive pressure ventilation may have an adjunctive role in the management of chronic respiratory failure through attenuation of compromised respiratory function and improvement in health-related outcomes (110). There is also evidence that long-term NIV added to home oxygen therapy reduces risk of readmission and death (111). **Figure 2** highlights the key benefits from NIV. Furthermore, it is important to consider the application of appropriate therapeutic pressures, which is the key factor guaranteeing clinical effectiveness for carbon dioxide level reduction (112). However, McEvoy et al. (113) emphasizes that whilst nocturnal NIV in stable oxygen-dependent patients with hypercapnic COPD may improve survival, this appears to be at the cost of worsening quality of life. Hence, it is important to take into consideration individual patient preferences and agree on the treatment plan collaboratively.

This article discussed several non-pharmacological interventions used to manage symptoms and clinical problems arising in the palliative care for patients with advanced COPD. The summary of these various interventions, their evidence and clinical practice recommendations are presented in **Table 1**.

CONCLUSION

For patients in the advance stage of COPD, whilst a ceiling effect in pharmacological treatment is often reached, there is a range of management strategies which could be used to improve

their quality of life, as it was presented it this article. There are several interventions suggested for relief of symptoms in clinical practice, but not all the methods have a strong evidence-base to support their effectiveness. However, palliative care does not always fit the Evidence-Based Medicine framework (122). Whereas breathlessness received the greatest attention and there is a wide body of evidence to support management of this symptom. Hence, there are specially designed services to address this problem. Other symptoms, such as fatigue, may be acknowledged, but there are not always specifically treated or may lack the complex management approach. This is potentially the reason why, the palliative care for COPD patients is often fragmented and interdisciplinary approach not always well-coordinated. The palliative care for patients with COPD should be a key part of the long-term management plan and a gold standard of care in advanced COPD. Therefore, there is a need for more research into management of symptoms other than breathlessness and development of more complex management programmes for palliative management in COPD.

AUTHOR CONTRIBUTIONS

Both authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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REVIEW
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Ethical and Legal Concerns Associated With Withdrawing Mechanical Circulatory Support: A U.S. Perspective

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Hundreds of thousands of Americans have advanced heart failure and experience severe symptoms (e. g., dyspnea) with minimal exertion or at rest despite optimal management. Although heart transplant is an effective treatment for advanced heart failure, the demand for organs far exceeds the supply. Another option for these patients is mechanical circulatory support (MCS) provided by devices such as the ventricular assist device and total artificial heart. MCS alleviates symptoms, prolongs life, and provides a "bridge to transplant" or a decision regarding future management such as "destination therapy," in which the patient receives lifelong MCS. However, a patient receiving MCS, or his/her surrogate decision-maker, may conclude ongoing MCS is burdensome and no longer consistent with the patient's healthcare-related values, goals, and preferences and, as a result, request withdrawal of MCS. Likewise, the patient's clinician and care team may conclude ongoing MCS is medically ineffective and recommend its withdrawal. These scenarios raise ethical and legal concerns. In the U.S., it is ethically and legally permissible to carry out an informed patient's or surrogate's request to withdraw any treatment including life-sustaining treatment (LST) if the intent is to remove a treatment perceived by the patient as burdensome and not to terminate intentionally the patient's life. Under these circumstances, death that follows withdrawal of the LST is due to the underlying disease and not a form of physician-assisted suicide or euthanasia. In this article, frequently encountered ethical and legal concerns regarding requests to withdraw MCS are reviewed: the ethical and legal permissibility of withholding or withdrawing LSTs from patients who no longer want such treatments; what to do if the clinician concludes ongoing LST will not result in achieving clinical goals (i.e., medically ineffective); responding to requests to withdraw LST; the features of patients who undergo withdrawal of MCS; the rationale for advance care planning in patients being considered for, or receiving, MCS; and other related topics. Notably, this article reflects a U.S. perspective.

Keywords: mechanical circulatory support, ventricular assist device, total artificial heart, extracorporeal membrane oxygenation, medical ethics, advance care planning, palliative care, end of life

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INTRODUCTION

Hundreds of thousands of Americans have advanced heart failure and experience severe symptoms (e.g., dyspnea) with minimal exertion or at rest despite optimal management (e.g., lifestyle changes, medications, devices, and surgery). The median time from the diagnosis of advanced heart failure to death is 12 months (1, 2). Diagnosing advanced heart failure is important as affected patients may be eligible for heart transplant and/or mechanical circulatory support (MCS), which alleviate symptoms and prolong life (1).

However, in the U.S., only about 3,000 hearts are transplanted each year and many heart transplant candidates die waiting for donor hearts (3). While on the waiting list, some heart transplant candidates receive MCS with a surgically implanted ventricular assist device (VAD), a scenario known as "bridge to transplant." A VAD, which is connected to a control system and an energy source outside of the body, pulls blood from the left ventricle and pumps it into the aorta. Patients with potentially reversible heart failure can be supported with a VAD while waiting for their hearts to regain function, a scenario known as "bridge to recovery." Some patients with permanent advanced heart failure who are not heart transplant candidates can be supported with a VAD indefinitely, a scenario known as "destination therapy" (4).

Similarly, some patients with heart failure may be eligible for MCS provided by a total artificial heart (TAH). Implantation of a TAH requires removal of most of the recipient's native heart. A pneumatically driven diaphragm directs blood through two mechanical ventricles; four mechanical valves ensure unidirectional blood flow. Drive lines connect the TAH to an air compressor outside of the body. The choice between VAD and TAH is determined by the patient's underlying pathophysiology. Indications TAH include severe biventricular heart failure, heart transplant graft failure, cardiac malignancy, infiltrative or restrictive cardiomyopathies, congenital heart disease, and others. TAH is used for "bridge to transplant" and "destination therapy" (5).

Extracorporeal membrane oxygenation (ECMO) is another form of MCS. With ECMO, blood is drained from the venous system and pumped through a semipermeable membrane allowing for oxygenation and removal of carbon dioxide. The blood is then reinfused into the venous system (venovenous ECMO) or the arterial system (venoarterial ECMO) depending on the patient's underlying pathophysiology. For example, patients with respiratory failure, but normal cardiac function, may receive venovenous ECMO; the patient's heart circulates ECMO-treated blood. Patients with cardiac or cardiopulmonary failure may be receive venoarterial ECMO; the ECMO pump circulates blood independent of the patient's underlying heart function. ECMO is usually provided in intensive care units. ECMO scenarios include "bridge to transplant" (heart and/or lung), "bridge to MCS" (e.g., VAD), "bridge to recovery," and "bridge to decision" for patients whose clinical situations are unclear (6).

The prevalence of Americans receiving MCS with VADs, TAHs, and ECMO is increasing. Also, these technologies are improving (e.g., size, ease of use, outcomes, etc.). Nonetheless, morbidity (e.g., infection, stroke, and multiorgan failure) and mortality in patients receiving MCS are substantial (7). A patient receiving MCS, or his/her surrogate decision-maker, may conclude the treatment is burdensome and no longer consistent with the patient's healthcare-related values, goals, and preferences and, as a result, request withdrawal of MCS. Likewise, the patient's clinician may conclude ongoing MCS as medically ineffective and recommend its withdrawal. These scenarios raise ethical and legal concerns.

In this article, the following frequently encountered ethical and legal concerns regarding requests to withdraw MCS are reviewed: the permissibility of withholding or withdrawing life-sustaining treatments (LSTs) including MCS from patients who no longer want such treatments; what to do if the clinician concludes ongoing LST will not result in achieving clinical goals (i.e., medically ineffective); responding to requests to withdraw LST including MCS; the features of patients who undergo withdrawal of MCS; the rationale for advance care planning in patients being considered for, or receiving, MCS; and other related topics. Notably, this article reflects a U.S. perspective.

ETHICAL AND LEGAL PRECEDENTS REGARDING WITHHOLDING AND WITHDRAWING LIFE-SUSTAINING TREATMENTS AND IMPLICATIONS FOR CLINICAL PRACTICE

Prima facie Principles of Ethics

Clinical ethics involves identifying, analyzing, and resolving moral problems that arise while caring for patients (8). Four *prima facie* principles encompass most ethical dilemmas encountered while caring for patients. *Beneficence* is the duty to act in the best interests of the patient. *Non-maleficence* is the duty to avoid harming patients (including not providing ineffective treatments). *Respect for patient autonomy* is the duty to respect the patient's rights to bodily integrity and self-determination. *Justice* is the duty to treat the patient fairly. Sometimes these principles conflict with each other. For example, contemplating a patient's request to withdrawal MCS may conflict with the clinician's desire to help, and avoid harming, the patient (8, 9).

Is It Ethically and Legally Permissible to Carry out a Patient's or a Surrogate's Requests to Withhold or Withdraw Life-Sustaining Treatment?

A life-sustaining treatment is one that prolongs life without which patient death would likely occur. There are many LSTs including mechanical ventilation, hemodialysis, artificial nutrition and hydration, MCS, and others. Ethically and legally, withholding and withdrawing treatment are equivalent (10,

Abbreviations: LST, life-sustaining treatment; MCS, mechanical circulatory support; VAD, ventricular assist device; TAH, total artificial heart; ECMO, extracorporeal membrane oxygenation; AD, advance directive.

11). Carrying out a request to withhold or withdraw any treatment, including LST, is predicated on informed consent and, specifically, informed refusal. The principle of respect for patient autonomy is the basis of informed consent and refusal. Patient autonomy is optimized when the patient understands his/her diagnosis and treatment options, including no treatment, and participates fully in decision-making regarding these options. The clinician is obligated to ensure the patient is informed regarding his/her diagnosis and treatment options. Components of informed consent and refusal include information (typically the amount of information a reasonable patient needs), patient voluntariness, and patient decisional capacity. Decisional capacity refers to the patient's ability to make healthcare-related decisions. Requirements for decisional capacity include being able to grasp pertinent information, understand the clinical situation at hand, rationally manipulate information, make a decision consistent with one's own healthcare-related values, goals, and preferences, and communicate a decision. The clinician should not presume decisional incapacity if the patient makes a decision contrary to the clinician's recommendation. Rather, capacity should be presumed. Nonetheless, evidence for capacity varies according to the complexity of the decision to be made; i.e., the more complex the decision to be made, the higher the level of capacity required to make it. Notably, in the U.S., "competence" is a legal term and determined by courts. Most patients who lose decisional capacity due to illness are not declared incompetent by courts. Rather, in these situations, clinicians determine decisional capacity. With rare exceptions (e.g., an emergency), the clinician should not treat the patient without informed consent. The patient has the right to accept a proposed treatment, proceed with another option, or refuse treatment altogether (10, 11).

In the U.S., codes of ethics are clear regarding the patient's right to make healthcare-related decisions. Not only does the patient have the right to refuse any treatment, he/she also has the right to refuse any ongoing previously consented treatment, including LST, if the patient concludes the burdens of the treatment outweigh the benefits and is inconsistent with his/her healthcare-related values, goals, and preferences. While the effectiveness of a treatment (e.g., based on clinical trials) is the purview of the clinician, the burdens and benefits of a treatment are the purview of the patient. Whatever the clinician's intent, commencing or continuing a treatment the patient does not want is battery. The clinician's duty is to ensure the patient's refusal of, or request to withdraw, a treatment is informed (10–13).

U.S. courts have consistently ruled that, based on rights to bodily integrity and self-determination, the patient has the right to make healthcare-related decisions including refusing LST before it is started and requesting its withdrawal after it is started. The precedents established by landmark U.S. court cases include: (a) the right to refuse, or request the withdrawal of, any treatment including LST; (b) there is no difference between withholding a treatment and withdrawing an ongoing treatment; (c) the patient refusing, or requesting the withdrawal of, LST need not be terminally ill; (d) carrying out an informed refusal of, or request to withdraw, LST is not a form of physician-assisted suicide or euthanasia; (e) death that follows carrying out an informed refusal of, or request to withdraw, LST is due to the underlying disease; (f) the patient without decisional capacity has the same rights through a surrogate decision-maker (see below); (g) no treatment has unique moral status in that the treatment must be started or, once started, must be continued; and (h) there is no right to physician-assisted suicide or euthanasia (10, 14–16). Parenthetically, consistent with the "rule of double effect," clinicians should provide treatment to alleviate suffering even if the treatment has the potential to hasten patient death. Doing so, if the intent is to relieve suffering, is ethical, legal, and not a form of physician-assisted suicide or euthanasia (17–20) (**Table 1**).

TABLE 1 | Precedents of landmark U.S. court cases regarding the permissibility of carrying out informed refusals of, or requests to withdraw, life-sustaining treat ments.

1. Patients have a right to bodily integrity and self-determination; imposing treatment on a patient who does not want the treatment is battery
2. There is no difference between withholding a treatment and withdrawing an ongoing treatment
3. A patient has the right to refuse, or request the withdrawal of, any treatment including life-sustaining treatment
   a. The patient need not be terminally ill
   b. The clinician's duty is to ensure that a refusal of, or request to withdraw, treatment is informed
   c. Carrying out an informed refusal, or request to withdraw, life-sustaining treatment is not a form of physician assisted suicide or euthanasia
   d. Death that follows carrying out an informed refusal, or request to withdraw, life-sustaining treatment is due to the underlying disease
4. A patient without decisional capacity has the same rights as a patient who has decisional capacity through a surrogate
5. No treatment, including life-sustaining treatment, has unique moral status in that the treatment must be started or, once started, it must be continued
6. There is no right to physician-assisted suicide and euthanasia
7. Clinicians should provide treatment to alleviate suffering even if the treatment might hasten a patient's death (rule of double effect); the clinician's intent determines whether the act is a form of physician-assisted suicide or euthanasia

Who Makes Healthcare-Related Decisions for the Patient When the Patient Cannot?

In the U.S., a court-appointed guardian makes medical decisions for the patient declared incompetent by the court. For the patient who lacks decisional capacity due to medical illness, clinicians must rely on a surrogate. If the patient has an advance directive (AD), and the AD identifies a surrogate, that person should make decisions for the patient (10, 11). An AD is a legal document completed by a patient that provides instructions for future care in the event the patient loses decisional capacity. In general, there are three types of ADs: health care power of attorney, living will, and combined ADs. In a health care power of attorney, the patient designates another person as his/her surrogate decision-maker. In a living will, the patient provides instructions for future care (e.g., LST) and circumstances (e.g., terminal illness). The patient can also indicate his/her healthcare-related values, goals, and preferences, what to do if pregnant, and organ donation. The combined AD has features of both a healthcare power of attorney and living will. Laws regarding ADs vary by U.S. state, but all 50

states regard the AD as an extension of the patient when he/she was fully autonomous (21).

The surrogate should make decisions based on the contents of the patient's AD. In addition, the clinician should adhere to the contents of the patient's AD, unless the instructions are unreasonable (e.g., impractical, illegal, etc.). There are benefits of having an AD. For example, a systematic review of 45 observational studies showed that patients who had ADs experienced reduced rate of hospitalization, reduced risk for dying in hospitals, reduced use of LSTs, and increased used of hospice and palliative care (22). Also, ADs coupled with advance care planning, may reduce moral distress among surrogates and clinicians when making difficult decisions by providing insights regarding the patient's healthcare-related values, goals, and preferences (i.e., what the patient would decide if he/she had decisional capacity).

Unfortunately, only about one-quarter of U.S. adults have ADs (21, 23). However, most U.S. states have laws which specify a hierarchy of surrogate decision-making for patients who lack decisional capacity and don't have ADs. Typically, a spouse, child, or other first-degree relative is the surrogate. Nonetheless, there is variability among U.S. states regarding these hierarchies (23).

When making decisions for the patient who lacks decisional capacity, the surrogate should adhere to the contents and instructions in the patient's AD, if extant. The surrogate should make decisions based on "substituted judgment"; i.e., based on the patient's, not the surrogate's, healthcare-related values, goals, and preferences. To optimize "substituted judgement," a useful question to ask the surrogate is, "If (the patient) could wake up for 15 minutes, understand [his/her] current medical situation completely, and then had to go back into it, what would [he/she] tell us to do? (24)" If the patient's healthcare-related values, goals, and preferences are unknown, the surrogate should base his/her decisions on the "best interests" of the patient (e.g., quality of life). In the rare instance in which the clinician and/or care team perceive the surrogate is not making decisions for the patient based on substituted judgment or best interests, meeting with the surrogate to explore these concerns and ethics consultation should be considered (11).

Notably, although no treatment has unique moral status, some U.S. states necessitate high levels of evidence of the patient's wishes regarding artificial hydration and nutrition (e.g., written documentation in an AD) before carrying out a surrogate's request for it to be withdrawn (10).

What Should Be Done if the Patient's Clinician Concludes Ongoing LST Will Not Result in Achieving Clinical Goals?

The American Medical Association Code of Ethics states, "Physicians are not ethically obligated to deliver care that, in their best professional judgment, will not have a reasonable chance of benefitting their patients" (11 p16). A clinician and his/her care team may conclude ongoing LST will not result in achieving clinical goals such as restoration of consciousness and discharge to home (i.e., medically ineffective). In these circumstances, the team should seek to understand the patient's healthcare-related values, goals, and preferences, obtain input from the surrogate if necessary, provide prognostic information, and take into account the intent of the LST, which the AMA declares "should not be to prolong the dying process without benefit to the patient…" (11 p18). The clinician and care team should consider the patient's cultural and religious beliefs and how these might affect decision-making regarding withdrawal of LST. Based on this information, the clinician and care team should recommend withdrawal of LST coupled with a shift to palliative care. This process can be facilitated by holding a multi-disciplinary care conference, which involves the patient (if able), surrogate, loved ones, clinicians, nurses, chaplain, and other care team members. Shared decision-making, consensus regarding withdrawal of LST, and clarifying goals of care should be emphasized. For some cases, ethics consultation can be helpful (10, 11).

Is Withdrawing Mechanical Circulatory Support a Form of Physician-Assisted Suicide or Euthanasia?

Clinicians may wonder whether withdrawing MCS is a form of physician-assisted suicide or euthanasia. However, carrying out an informed request to withdraw an unwanted LST such as MCS differs from physician-assisted suicide and euthanasia in important ways. First, when withdrawing an unwanted LST, the clinician's intent is to remove a treatment the patient or surrogate regards as non-beneficial, burdensome, and inconsistent with the patient's healthcare-related values, goals, and preferences—not to hasten the patient's death. In contrast, in physician-assisted suicide, the clinician's intent is to terminate the patient's life by providing a lethal prescription to be taken by the patient. In euthanasia, the clinician's intent is to terminate the patient's life by administering a lethal agent to the patient. Second, death that follows carrying out a patient's or surrogate's informed request to withdraw an unwanted LST is due to the patient's underlying disease and pathophysiology. In contrast, in physician-assisted suicide and euthanasia, death that follows taking, or being administered, a lethal prescription is due to the lethal prescription—a newly introduced pathology—not the underlying disease (4, 5, 10, 15–17, 20).

The U.S. Supreme Court has differentiated withholding and withdrawing LST from physician-assisted suicide and euthanasia. In *Vacco*, Chief Justice Rehnquist wrote,

> "The distinction comports with fundamental legal principles of causation and intent. First, when a patient refuses life-sustaining medical treatment, he dies from an underlying fatal disease or pathology; but if a patient ingests lethal medication prescribed by a physician, he is killed by that medication…our assumption of a right to refuse treatment was grounded not…on the proposition that patients have a…right to hasten death, but on well-established traditional rights to bodily integrity and freedom from unwarranted touching" (16).

While the U.S. Supreme Court has declared a constitutional right to refuse treatment, it has not declared a constitutional right

TABLE 2 | End of life interventions, causes of death, clinicians' intention of the interventions, and legality of the interventions in the U.S. From Olsen et al. (17).

	Withhold life-sustaining treatment	Withdraw life-sustaining treatment	Palliative analgesia and sedation	Physician-assisted suicide	Euthanasia
Cause of death	Underlying disease	Underlying disease	Underlying disease[a]	Intervention prescribed by the physician and used by the patient	Intervention administered by the physician
Intention of the intervention	Avoid burdensome intervention	Remove burdensome intervention	Relieve symptoms	Termination of the patient's life	Termination of the patient's life
Legality of the intervention?	Yes[b]	Yes[b]	Yes[c]	No[d]	No

[a] *Note the rule of double effect (18).*
[b] *Some U.S. states limit the power of surrogates to make decisions about life-sustaining treatments.*
[c] *Washington v. Glucksberg (19).*
[d] *Physician-assisted suicide is legal in several U.S. states.*

to physician-assisted suicide or euthanasia. Today, physician-assisted suicide is illegal in most U.S. states and euthanasia is illegal in all states (10, 17).

In summary, carrying out an informed patient's or surrogate's request to withdraw LST is ethically and legally permissible and not a form of physician-assisted suicide or euthanasia (**Table 2**). While, to the author's knowledge, no U.S. court case has involved a patient receiving MCS, given the results of prior ethical analyses involving MCS (4–6) and court decisions involving other LSTs, the same conclusion can be drawn about carrying out informed requests to withdraw MCS.

Is Mechanical Circulatory Support a Morally Unique Treatment?

Despite the permissibility of carrying out informed requests to withdraw other LSTs, MCS has features that may cause some clinicians to question the permissibility of carrying out requests to withdraw it. For example, some argue MCS once started should not be withdrawn as it is a treatment that is continuous and constitutive (i.e., provides a vital function the patient's body no longer provides). Also, death inevitably follows withdrawal of MCS. However, it is widely accepted that carrying out informed requests to withdraw other continuous and constitutive LSTs (e.g., mechanical ventilation, artificial nutrition and hydration, etc.) is ethically and legally permissible (4–6, 25).

Some clinicians may view MCS as a replacement treatment (i.e., the treatment becomes part of the body and assumes all functions of the diseased organ) and, hence, cannot be withdrawn. However, a genuine replacement treatment is one that is responsive to physiologic changes and independent of external control, maintenance, and energy sources. Examples of replacement treatments include bioprosthetic heart valves and organ transplants. Carrying out a request to remove these treatments would be invasive, harmful, introduce a new pathology (i.e., surgical wound) and, hence, unethical. In contrast, MCS does not have the features of a genuine replacement treatment. Also, withdrawing MCS is noninvasive and painless (4–6, 25).

Some clinicians may object to carrying out requests to withdraw MCS as doing so may acutely precipitate heart failure symptoms (e.g., dyspnea) and death may occur shortly thereafter. However, similar symptoms and death may occur shortly after withdrawal of other LSTs such as intravenous inotropic agents, intra-aortic balloon pump therapy, and mechanical ventilation—treatments that are commonly withdrawn in end of life situations. Hence, the possibility of acute symptoms and death shortly after withdrawal of MCS are not ethically relevant (4–6). Rather, the clinician and care team should inform the patient or surrogate regarding potential symptoms associated with withdrawal of MCS, the likely timing of death, and once withdrawal occurs, manage the dying process expectantly.

As mentioned previously, U.S. courts have not recognized any treatment as being morally unique (10). However, courts have not considered withdrawal of MCS. Nonetheless, MCS does not have features that make it a morally unique treatment.

What Are the Features of Patients Who Undergo Withdrawal of Mechanical Circulatory Support?

Three case series describing the features of patients who have undergone withdrawal of MCS have been reported by Mayo Clinic researchers. In a series of 68 patients who received VADs during 2003–2009, 26 had died, of which 14 requested, or surrogates requested, withdrawal of VAD support. All were receiving other LSTs. Eight patients died with multiorgan failure. For 12 patients, requests for withdrawal of VAD support were made by surrogates. For 11 patients, multidisciplinary care conferences were held before withdrawing VAD support. All died within a day of withdrawing of VAD support (4).

In a series of 47 patients who received TAHs during 2007–2015, 21 had died, of which 14 requested, or their surrogates requested, withdrawal of TAH support. All were receiving other LSTs. All died with multiorgan failure. For 13 patients, requests for withdrawal of TAH support were made by surrogates. For all 14 patients, multidisciplinary care conferences were held before withdrawing TAH support. All died within minutes of withdrawing TAH support (5).

In a series of 235 patients who received ECMO during 2010–2014, 118 had died. For 62 patients, requests for withdrawal of ECMO support were made. All were receiving other LSTs. Forty-six patients died with multiorgan failure. None of the patients had decisional capacity. For all patients, decisions to withdrawal

ECMO were jointly reached by surrogates and clinicians. All died within a day of withdrawing ECMO support (6).

Other series have had similar results (26, 27).

Notably, in these three series, many patients did not have ADs, and of those who did, their ADs did not mention the MCS technology.

ACTIONABLE RECOMMENDATIONS

Responding to Requests to Withdraw Mechanical Circulatory Support: Who Decides? By What Criteria? How Are Conflicts Resolved?

Obviously, intentionally withdrawing MCS from a patient without consent is wrong and a form of killing. Because physician-assisted suicide is illegal in most U.S. states and euthanasia is illegal in all U.S. states, the clinician's intent when withdrawing MCS must be to remove a treatment the patient or surrogate regard as non-beneficial, burdensome, and no longer consistent with the patient's healthcare-related values, goals, and preferences. The intent must not be to terminate the patient's life (17).

Pellegrino describes a 3-question approach to responding to requests to withdraw LST (28). The first question is, "Who decides?" In the U.S., ethically and legally, the patient has the authority to make healthcare-related decisions and this authority supersedes the clinician's authority. If the patient lacks decisional capacity, then the patient's AD and surrogate guide decision-making. The clinician's duty is to ensure that a request to withdraw LST is informed. In the 3 previously described case series, only a few patients had decisional capacity. Hence, for most patients, surrogates made decisions. Of the patients who had ADs, none of the ADs addressed MCS. Hence, surrogates had to rely on "substituted judgement" or "best interests" in making decisions. For nearly all patients, decisions to withdraw MCS were made after multidisciplinary care conferences.

The second question is, "By what criteria?" Answering this question requires assessment of the LST's clinical effectiveness, and its perceived benefits and burdens. The clinician determines treatment effectiveness, whereas the patient determines treatment benefits and burdens. In the 3 previously described series involving MCS, nearly all decisions to withdraw MCS were made during multidisciplinary care conferences. Ongoing MCS was perceived by clinicians and care teams as medically ineffective and by patients and usually surrogates as non-beneficial and burdensome. This scenario, in which MCS merely maintains circulation and a moribund state, has been described as "destination nowhere" (29). In the three previously described series, withdrawal of MCS was justified.

The third question is, "How are conflicts among decision-makers resolved and prevented?" When conflicts arise in the care of patients receiving MCS, care conferences involving the patient, surrogate, and multidisciplinary care teams, as well as palliative care and ethics consultation can be helpful in resolving them. All patients being considered for, or receiving, MCS should undergo advanced care planning, also known as "preparedness planning," including completion of an AD that addresses the MCS technology and its management at the end of life. Involving palliative medicine specialists in this process can be especially helpful. During these discussions, the circumstances surrounding permissibility of withdrawing MCS should be discussed including what to do if device failure, catastrophic complications, debilitative comorbid conditions (e.g., stroke), and inadequate quality of life occur (10, 11, 30–32). Such planning may prevent conflicts.

Processes for withdrawing specific MCS technologies—VAD, TAH, and ECMO support—are described elsewhere (33–37). Overall, withdrawal of MCS should be based on established palliative care principles and evidence-based best practices. The clinician should anticipate and manage symptoms that occur during the withdrawal process, involve palliative medicine specialists if necessary, and provide comfort to affected love ones.

What if a Clinician Conscientiously Objects to Withdrawing Mechanical Circulatory Support?

Some clinicians, despite the ethical and legal permissibility of carrying out informed requests to withdraw LST, may object to the practice. If acceding to such a request violates a clinician's conscience, then the clinician should arrange for a transfer of the patient's care to another accepting clinician. In the meantime, the patient should not be abandoned. Similarly, clinicians and other care team members (e.g., nurses) who conscientiously object to withdrawing MCS should not be compelled to do so (4–6, 10).

CONCLUSIONS

In the U.S., the prevalence of patients with advanced heart failure is increasing. Heart transplant is an effective treatment for patients with advanced heart failure. However, the demand for organs far exceeds the supply. In these patients, MCS alleviates symptoms, prolongs life, and "bridges" patients to transplant or a decision regarding future management such as "destination therapy" in which the patient receives lifelong MCS. However, the patient, or his/her surrogate, may determine that the burdens of ongoing MCS outweigh the benefits and is no longer consistent with the patient's healthcare-related values, goals, and preferences and, as a result, request withdrawal of MCS. Likewise, the patient's clinician and care team may conclude ongoing MCS is medically ineffective and recommend its withdrawal. In the U.S., it is ethically and legally permissible to carry out requests to withdraw LST made by an informed patient, or his/her surrogate, if the intent is to remove a burdensome treatment and not to terminate the patient's life. Under these circumstances, death that follows withdrawal of the LST is due to the underlying disease and not a form of physician-assisted or euthanasia. It is the clinician's duty to ensure that such requests are informed. These concepts also apply to withdrawal of MCS. Given the seriousness of his/her illness, the patient being considered for, or treated with, MCS should engage in advance care planning and document his/her healthcare-related values, goals, and preferences including end of life care and the management of the MCS device. Likewise, palliative care consultation should be considered for all such patients. When

carrying out a request to withdraw MCS, clinicians should anticipate and manage symptoms that occur, involve palliative medicine specialists if necessary, and provide comfort to affected love ones.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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IPF Respiratory Symptoms Management — Current Evidence

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Idiopathic pulmonary fibrosis (IPF) is a progressive, chronic disease of the lungs which is characterized by heavy symptom burden, especially in the last year of life. Despite recently established anti-fibrotic treatment IPF prognosis is one of the worst among interstitial lung diseases. In this review available evidence regarding pharmacological and non-pharmacological management of the main IPF symptoms, dyspnea and cough, is presented.

KEYWORDS

breathlessness, dyspnea, cough, idiopathic pulmonary fibrosis (IPF), non-invasive ventilation (NIV), high flow nasal cannula (HFNC), ambulatory oxygen therapy (AOT), non-invasive positive pressure ventilation (NIPPV)

Introduction

Idiopathic pulmonary fibrosis (IPF) is the most frequent idiopathic interstitial pneumonia and one of the most frequent interstitial lung diseases (ILD) (1). It is a chronic, progressive disease of the lungs which has a distinct pattern, both radiologically and pathologically, of usual interstitial pneumonia (2). Despite recently established anti-fibrotic treatment IPF prognosis is one of the worst among ILDs with a mean survival of 2.5–5.0 years. Its course is characterized by heavy symptom burden especially in the last year of life (3, 4). Symptomatic treatment is an important aspect of palliative care which also addresses spiritual, social and psychological needs. Unfortunately, patients with IPF, as with other chronic lung diseases, are not referred to palliative care centers nearly as often as cancer patients. Furthermore, their symptomatic treatment is withhold partly due to the fear of opioids (5). Planning palliative care for IPF patients can also be hindered by heterogeneous course of the disease—loss of lung function might be gradual, rapid or suddenly accelerates because of a life-threatening acute exacerbation (3). This unpredictability is probably one of the reasons why the majority of IPF patients die in a hospital, subjected to life-prolonging procedures (6, 7). On the other hand, referring the IPF patient to palliative care too early, when the disease is mild, might worsen quality of life in short term, probably due to a worsening of depression or anxiety (8). Nonetheless, there is evidence that palliative care, compared to usual care, might improve respiratory symptoms and quality of life in patients with advanced IPF (9, 10).

The aim of this review is to present current evidence on symptomatic treatment of dyspnea and cough in IPF patients.

Breathlessness—pathophysiology and treatment

Dyspnea in IPF results from both respiratory and circulatory limitations: reduced lung compliance, loss of lung volume, increased dead space ventilation, increased respiratory drive, gas exchange abnormalities and pulmonary hypertension (11). In turn, breathlessness treatment is a multifaceted process involving effective treatment of comorbidities, rehabilitation, pharmacological and oxygen treatment and non-invasive ventilation.

Non-pharmacological treatment

Rehabilitation

Exertional hypoxemia, along with skeletal muscle dysfunction, restrictive ventilatory impairment and cardiovascular limitation, i.e., reduction in stroke volume, are responsible for exercise limitation in ILDs (12, 13). Exercise intolerance, in turn, is associated with reduced quality of life and increased mortality (14).

Cochrane review of 16 studies on pulmonary rehabilitation of ILD patients showed that this intervention can improve dyspnea and health-related quality of life, 6 min walking test (6MWT) distance and cardiopulmonary exercise test parameters, i.e., peak workload, peak oxygen uptake and maximum ventilation. Furthermore, evidence showed that improvements in dyspnea and SGRQ Impact score were sustained at 6–12 months. Sustained improvement affected not only dyspnea but also exercise capacity and health-related quality of life up to 12 months since rehabilitation program (15). Whether increases in 6MWT distance and peak oxygen uptake, both of which are predictors of IPF mortality, translate into prognosis improvement is unknown (16).

The positive effect of pulmonary rehabilitation on ILD patients is probably a result of repetitive chest expansion and stretching of the thoracic muscles what, in turn, translates into improvement of tidal volume. Increase in tidal volume leads then to improvement of peak oxygen uptake (16). Furthermore, it is suggested that rehabilitation improves peripheral oxygen extraction (17).

Rehabilitation of ILD patients is frequently complicated by desaturation which is why clinical supervision is essential for its safety and effectiveness (18). It is advised that supplemental oxygen should be used to maintain $s_pO_2 \geq 85\%$ during exercise, if needed (18). To no surprise then, most of the studies (18 out of 21) included in the Cochrane review, were conducted in a supervised outpatient setting (15).

There is some conflicting evidence on time of referral to pulmonary rehabilitation for IPF patients. In studies by Kozu et al. and Holland et al. (19, 20) more advanced disease, i.e., lower mMRC score (20), lower forced vital capacity, greater exertional hypoxemia and higher right ventricular systolic pressure (19), predicted smaller improvement of 6MWT distance (20). It is worth underlining that such association was not evident for other than IPF ILD patients (19). On the other hand, study by Ryerson et al. showed that greater baseline 6MWT distance was associated with smaller 6MWT distance gain (21). It is author's view that the above should not discourage trial of pulmonary rehabilitation in advanced IPF patients.

Ambulatory and long term oxygen treatment

Exertional hypoxemia is one of the defining features of ILDs (12). Desaturation during 6MWT alone is an independent mortality and pulmonary hypertension risk factor (22–24). Furthermore, its severity in ILD is reported to be greater than in chronic obstructive pulmonary disease (COPD) (25). Nonetheless, studies failed to show unequivocal results of oxygen treatment in patients without significant hypoxemia at rest. Cochrane review of three crossover randomized controlled trials (RCT), performed in physiology laboratories, on 98 IPF patients altogether, failed to show any effect of short-term supplementary oxygen on exertional dyspnea (26). One of the studies showed increase in endurance time during constant load ergometry (27). None of them titrated oxygen to prevent desaturation, but used pre-determined fixed oxygen flow rate. Another systematic review, by Bell et al., incorporating 9 reports on short-term supplementary oxygen, showed similar results—no significant effect on dyspnea was detected while exercise capacity seemed to improve (28).

However, recently performed RCTs showed different results. A crossover RCT, by Dowman et al., on 11 patients with IPF, showed significant improvement of Borg dyspnea score and endurance time during cycle endurance test with oxygen supplementation where FiO2 (fraction of inspired oxygen) was set at 50%. It is noteworthy that Borg fatigue score did not improve (29). In another crossover RCT, on 20 fibrotic ILD patients, Schaeffer et al. showed that supplemental oxygen with FiO_2 equal 60%, increased endurance time, reduced dyspnea and leg discomfort ratings (30). The most recent crossover RCT, AmbOx, the only study yet asserting effect of ambulatory oxygen treatment (AOT) on quality of life of fibrotic ILD patients, reported improvement of total K-BILD (King's Brief ILD questionnaire) scores and its breathlessness, activity and chest symptoms subdomains. However, this subjective improvement did not translate into increase of physical activity measured by biaxial accelerometer. It is worth underlining that each of the 76 AmbOx participants had flow rate of oxygen titrated during screening visit 6MWT to maintain $s_pO_2 > 90\%$. Patients were then instructed to use their lightweight gas cylinders with the set flow during routine activities for 2×2 weeks (31). Authors reported that at the end of the trial 33% patients chose to discontinue oxygen treatment delivered *via* cylinders, however,

those who experienced most dyspnea reduction were the most likely to continue. Younger age was also significantly predictive regarding the decision to continue AOT (31).

In light of the above national societies suggest a trial of AOT in patients with significant exertional desaturation, if there is evidence of benefit (32–34). One should take into consideration challenges connected with using the oxygen devices, especially outside home.

National guidelines are more unequivocal when ILD patients develop chronic hypoxemia at rest. Long term oxygen therapy (LTOT) is recommended even though the evidence is lacking (32–34). No RCTs were performed in this indication but three retrospective studies of which two did not include control group and none assessed effect of LTOT on breathlessness (28). Nonetheless, guidelines authors extrapolate evidence on survival benefit from COPD trials (32–34).

High flow nasal cannula

Compared to conventional oxygen therapy high flow nasal cannula (HFNC) provides oxygen at higher FiO_2 (up to 100%) and at a higher flow, which matches patient's inspiratory demand and washes out CO_2 from pharyngeal dead-space. Reduction of ventilatory dead-space might in turn improve the ventilation-perfusion inequality. High flow, up to 60 l/min, also generates a small amount of positive expiratory pressure. Furthermore, heating and humidifying of the respiratory mixture might reduce the metabolic cost of breathing (35). Laboratory studies show that HFNC might reduce work of breathing not only in healthy volunteers or COPD patients but in IPF patients as well (36, 37).

HFNC effectiveness in treating breathlessness was assessed in a study by Hui et al. on 30 advanced cancer patients, whose dyspnea intensity was ranked $\geq$3/10 despite supplemental oxygen. Patients received 2-h HFNC and 2-h NIPPV (non-invasive positive pressure ventilation), i.e., BiPAP, in a random sequence, both with FiO_2 set at 100%. Dyspnea improved in both treatment arms, with no significant differences between, however, HFNC was better tolerated than BiPAP (38). Similar results were obtained by Koyauchi et al., who retrospectively assessed 84 ILD patients with do-not-intubate order and acute, hypoxic respiratory failure associated with ILD. Fifty-four patients used HFNC, 30—NIPPV. Temporary interruption of the therapy and discontinuation rates were significantly higher in the NIPPV group, whereas oral intake and ability to converse were significantly better in HFNC group. Three-day survival and in-hospital mortality did not differ significantly between the groups (39). Furthermore, HFNC compared to standard oxygen therapy seems to improve endurance time of IPF patients during constant-load exercise testing on cycloergometer in laboratory studies (40–42).

No studies so far have assessed domiciliary HFNC in ILD patients. However, recent two studies by Storgaard et al. in COPD patients with chronic hypoxemia show that HFNC used alongside LTOT might be of added benefit compared to LTOT alone (43, 44). In the first study, a RCT on 200 chronically hypoxemic COPD patients on LTOT, participants in HFNC group were instructed to use HFNC for 8 h daily, mainly during the night, as an add-on to LTOT, for at least 12 months. Seventeen percent of the participants discontinued HFNC. Thirty two percent used HFNC only during the day, 53% used it nightly, whereas the remaining 15% used HFNC both at night and day. Use of HFNC in conjunction with LTOT allowed for reduction of COPD acute exacerbation rate—which was the primary outcome. Furthermore, compared to LTOT alone, patients using HFNC additionally preserved their SGRQ score and 6MWT distance which dropped in the control group and reported significantly reduced mMRC score (43). Qualitative part of the study on 12 patients and 8 relatives showed that patients in the HFNC group found the device easy to use. Moreover, most patients reported that HFNC improved their sleep quality, despite the noise generated by the apparatus. In authors view this improvement was due to airway humidification and reduced work of breathing during sleep. Airway dryness, aggravated by LTOT, was reported by the patients as a significant reason for sleep interruption and awakening. Participants also reported a reduction in cough frequency (44).

Taking the above into consideration, HFNC seems as a viable option for oxygen delivery in IPF patients, although, high quality trials are needed.

Non-invasive ventilation

Respiratory exchange can be supported not only by conventional oxygen therapy or HFNC but also NIPPV. European Respiratory Society (ERS) and American Thoracic Society (ATS) guidelines suggest a trial of NIPPV in breathless patients in the setting of terminal condition (45). Available evidence encompasses two feasibility studies of RCT design in cancer patients (38, 46). Nava et al. randomized 200 end-stage cancer patients with solid tumors and acute respiratory failure to NIPPV (BiPAP) or oxygen. Only patients with PaO_2/FiO_2 ratio smaller than 250 were enrolled. Evident reversible causes of respiratory failure such as pulmonary edema were an exclusion factor. The study showed that NIPPV was significantly more effective in reducing dyspnea than conventional oxygen therapy but only in hypercapnic patients. Furthermore, 11% of NIPPV patients declined BiPAP due to poor tolerance (46). In a previously mentioned study, by Hui et al., NIPPV resulted in dyspnea reduction in cancer patients in a similar degree to HFNC, however it was significantly worse tolerated than HFNC (38).

The loss of lung compliance in IPF is associated with increased work of breathing and thus dyspnea. Offsetting the inspiratory burden by providing ventilation support could

help treat breathlessness in IPF (11, 46). This would be especially true for patients in advanced stages of IPF who may develop hypercapnia—a sign of failing respiratory muscles unable to sustain the imposed load (11, 47). Hypercapnia in IPF could also be a sign of concomitant pleuroparenchymal fibroelastosis (PPFE), characterized by fibrosis involving the visceral pleura and subpleural parenchymal fibroelastosis. The resulting extrapulmonary restriction can in turn produce hypoventilation and hypercapnia (48, 49). Unfortunately, there are no studies which would assess effect of NIPPV on breathlessness in IPF patients. Data on NIPPV in ILD are limited to retrospective studies analyzing its effectiveness in treating acute respiratory failure, especially as means to avoid endotracheal intubation (50).

Dyspnea treatment summary, regarding AOT/LTOT, HFNC, and NIPPV, is presented in Table 1.

Pharmacological treatment

Opioids

Pharmacological treatment of dyspnea mainly involves opioids which by acting upon their central and peripheral nervous system receptors can decrease anxiety, modulate central perception of dyspnea and reduce respiratory drive without significant changes in blood gases (51–55). Unfortunately, high quality RCTs of opioid effectiveness in treating ILD-related breathlessness are lacking. Available evidence includes retrospective, population based studies (4), open-label studies with oral opioids (56, 57) and RCTs with nebulized morphine (58–61). Only oral morphine studies showed its effectiveness in treating ILD-related dyspnea. However, one of them employed just a small group of 11 IPF patients (57), whereas the other studied a mixed group with a minority of ILD patients (n = 10; 12%). Nonetheless, guidelines do embrace oral morphine for IPF dyspnea treatment because of its proven effectiveness in chronic lung diseases in general (34). This recommendation is also backed up by data on opioid safety reported not only by retrospective (62) but also prospective studies (63).

Cough

In IPF cough is one of the most frequent symptoms reported by 50–80% of patients (64, 65). Though it is typically described as dry (66), more than half of patients might expectorate sputum (64). Furthermore, cough was found to be an independent predictor of disease progression (64). Chronic cough in IPF can weigh heavily on quality of life by interrupting sleep, limiting speech or by causing significant desaturation, musculoskeletal pain and urinary incontinence. It is to no surprise then that cough might limit social interactions (67).

Mechanism of chronic cough induced by IPF is not precisely understood. It is assumed that increased cough reflex sensitivity, which is in complex interplay with frequent IPF co-morbidities—gastroesophageal reflux disease and obstructive sleep apnea, is involved. This increased sensitivity might be a result of increased traction forces impacting the function of stretch receptors. Other possible mechanisms involve destruction of inhibitory nerves by fibrosis or upregulation of vagal sensory fibers (66, 67). A significant role of stretch receptors in pathogenesis of IPF cough seems to be confirmed by results of the study by Jones et al. (68). Authors found that IPF patients, compared with healthy non-smoking controls, were significantly more susceptible to induction of non-productive cough by mechanical percussion of the chest wall especially when percussor was applied to the posterior lung base (68). As pointed out by van Manen, this correlates with the clinical finding that vibration caused by talking or coughing starts a self-perpetuating cough cycle (67).

Taking the above into consideration, a trial of treatment of IPF cough with neuromodulator i.e., gabapentin, as in idiopathic chronic cough, is recommended (69). Its effectiveness in idiopathic chronic cough was assessed in a RCT on 62 patients, who experienced significant improvement of cough-specific quality of life after 8 weeks of treatment. However, 10 patients, 31% of the gabapentin group, reported side effects with nausea and fatigue as the most common (70). Speech therapy, especially combined with pregabalin is also recommended (66, 69). If the above fails, guidelines suggest a trial of opioids (69). Nonetheless, this recommendation is based only on one RCT, of small-dose, slow-releasing morphine in 27 patients with idiopathic chronic cough (71).

Two other drugs have been trialed in IPF cough and showed efficiency. In a crossover RCT by Horton et al., thalidomide, a potent immunomodulatory drug, significantly improved cough-related quality of life in 20 patients with IPF during 12 weeks of treatment. However, 77% of patients reported side-effects: constipation, dizziness, malaise, anorexia and asymptomatic bradycardia (72). In light of these results thalidomide was not recommended by CHEST Expert Cough Panel experts in treatment of cough in IPF. Small size of the study population, side effects, prescription barriers and cost were among factors influencing this decision (69). In a crossover RCT by Birring et al., a novel formulation of sodium cromoglicate delivered by mesh nebulizer reduced cough frequency but did not improve cough-specific quality of life or cough severity in 24 IPF patients after 2 weeks of treatment (73).

Conclusions

Evidence for different interventions in symptomatic treatment of IPF patients is lacking. Consequently, IPF guidelines often base their recommendations on trials

TABLE 1 Types of oxygen therapy and ventilatory support and their potential in treating breathlessness in IPF patients.

	Mechanism of action	Evidence	Disadvantages
AOT LTOT	- Improvement in neuro-mechanical uncoupling (74) - Lower neural respiratory drive (74) - Stimulation of upper airway receptors by gas flow (55) - Improved cardiovascular function and pulmonary hemodynamics (75) - Delayed lactate accumulation (76)	**In patients with ILD and exertional hypoxemia:** - Improvement of total K-BILD score and its subdomains i.e., breathlessness, activity and chest symptoms during routine activities of daily living (31) - Increase in cycle endurance time (28, 29) - Increase in CPET peak work capacity (28) - Increase in CPET peak oxygen uptake (28) - Reduction of Borg dyspnea score at the end of cycle exercise test and at the iso-time (29, 30) - Improved leg muscle oxygenation and reduction of fatigue (77) **Dyspnea was not assessed in LTOT studies in ILD patients** (28)	**Portable oxygen systems** • expensive, • may be hard to carry and difficult to use, • deliver limited amount of oxygen, • attract unwanted attention when used outside home **Stationary oxygen systems** • Risk of tripping over the tubing • Fire and burning hazard • Activity limited to the immediate surroundings of the oxygen system
HFNC	- Pharyngeal dead space washout (35) - Reduction of work of breathing (36, 37) - Matching patient's high inspiratory demand (35) - EPAP generation (up to 7.4 cm H_2O) (78) - Lung compliance increase (35) - Upper airway resistance reduction (35) - Reduction of metabolic work associated with gas conditioning i.e., warming and humidifying (35) - Improvement of mucocilliary clearance (35)	Direct evidence i.e., based on studies involving ILD patients: - Increase in cycle endurance time (40–42) Indirect evidence: - Improvement of dyspnea in advanced cancer patients compared to oxygen therapy (38) - Improvement of dyspnea when used alongside LTOT in COPD patients compared to LTOT alone (43)	• Expensive • Only for stationary use • Requires high flow O2 source/sources (79) • Generates fair degree of noise (44)
NIPPV	- EPAP effects (80): *Lung compliance increase *Alveolar recruitment *Upper airway resistance reduction - IPAP effects (80): *Unloading of respiratory muscles *Tidal volume increase	*Indirect evidence:* - Improvement of dyspnea in advanced cancer patients compared to oxygen therapy (38), especially those with hypercapnic respiratory failure (46)	• Most expensive solution among discussed • Less comfortable than HFNC (38) • Doesn't allow for food intake and impedes speaking • Risk of face ulcerations secondary to tight-fitting masks • Patient might need help putting on the mask

6MWT, six-minute walking test; AOT, ambulatory oxygen therapy; CPET, cardiopulmonary exercise testing; EPAP, expiratory positive airway pressure; HFNC, high glow nasal cannulae; ILD, interstitial lung disease; IPAP, inspiratory positive airway pressure; IPF, idiopathic pulmonary fibrosis; K-BILD, King's Brief ILD questionnaire; LTOT, long term oxygen treatment; NIPPV, non-invasive positive pressure ventilation.

conducted in other chronic lung diseases. High quality trials are needed to verify efficiency of guidelines-compliant pharmacological treatment of cough and breathlessness in IPF patients. Positive results of AOT, NIPPV, and HFNC in treatment of breathlessness in other lung diseases should encourage similar studies in IPF patients as well.

Author contributions

PJ wrote the first draft of the manuscript. All authors contributed to conception of the review. All authors contributed to manuscript revision, read, and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Palliative care provision for people living with heart failure: The Geneva model

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As life expectancy rises and the survival rate after acute cardiovascular events improves, the number of people living and dying with chronic heart failure is increasing. People suffering from chronic ischemic and non-ischemic heart disease may experience a significant limitation of their quality of life which can be addressed by palliative care. Although international guidelines recommend the implementation of integrated palliative care for patients with heart failure, models of care are scarce and are often limited to patients at the end of life. In this paper, we describe the implementation of a model designed to improve the early integration of palliative care for patients with heart failure. This model has enabled patients to access palliative care when they normally would not have and given them the opportunity to plan their care in line with their values and preferences. However, the effectiveness of this interdisciplinary model of care on patients' quality of life and symptom burden still requires evaluation.

KEYWORDS

palliative care, heart failure, left ventricular assist device (LVAD), quality of life, symptom management

Introduction

As life expectancy increases and the survival rate after acute cardiovascular events improves, the number of people living and dying with serious health-related suffering is growing and this tendency is expected to increase, especially in people aged 70 and over (1). People suffering from chronic heart diseases, whether ischemic or non-ischemic, have been shown to experience a substantial symptom burden and a decrease in quality of life (QoL) that is equal to or even more pronounced than that of patients suffering from cancer (2).

Palliative care (PC) is an approach that aims to improve the QoL of patients with life-limiting diseases, through the thorough assessment and treatment of pain and other symptoms whether physical, psychological, social or spiritual (3). In 2019, the United Nations recognized PC as an essential health care service to be included in the Universal Health Coverage. PC should therefore be integrated in a continuum of care and be available for all people requiring it. Improving QoL has been identified as being as important in public health as prevention, cure and prolonging life (4).

Heart failure (HF) was clearly identified as one of the conditions causing severe health-related suffering that could benefit from PC interventions (4). Many cardiology and PC societies recommend integrating PC in the care of patients living with HF with the aim of improving quality of life (5–9). Some of them clearly specify that this integration should take place regardless of the stage of the disease, which is aligned with the opinion of patients and their relatives who would prefer if PC was offered early in the course of their illness (5, 9, 10). Despite this knowledge, patients living with HF still have limited access to PC, which, despite recommendations, is provided very late in the disease trajectory, for a short period of time, generally in the days preceding death (11). However, this tendency seems to be improving in recent years (12).

Several models for the integration of PC into the care of patients with HF have been suggested, mainly in relation to HF-related hospitalizations (13–15). These models are all designed based on prognosis rather than on the existence of unaddressed needs and therefore only include patients who have a high, short-term, risk of dying. Although early integration of PC is now recommended by both the European Society of Cardiology (ESC) and the European Association for Palliative Care (EAPC) position papers and guidelines for patients with chronic HF, models for the early integration of PC in HF outpatients are surprisingly scarce (9, 16, 17).

At this stage, many questions remain regarding the most effective way to implement PC provision for people living with HF, such as how to identify patients who could benefit from it, when to begin implementing PC into their usual care and how to best assess their needs (18, 19).

Access to PC is mainly dependent on policy, funding, center-based expertise and local resources (20). Models of integration of PC for patients with HF need to be adapted in order to be appropriate to the setting, population and health care system in which it is provided. This paper presents the concept of an integrated PC service for patients with HF in a tertiary HF center based at the Geneva University Hospitals in Switzerland.

Context

The Geneva University Hospitals (HUG) include eight public hospitals in the canton of Geneva and two clinics, making it the biggest university hospital conglomerate in Switzerland with a total of 13,557 employees for 2,109 beds (21). In 2020, 280,000 patients were hospitalized at the HUG and a total of 1,074,645 out-patient consultations were conducted (21). The HUG are recognized on a national and international level for their expertise in several disciplines including cardiovascular diseases, and collaborate actively with the World Health Organization (21).

In 2017, the Division of Cardiology of the HUG created a HF unit which is mainly dedicated to the ambulatory care of patients with advanced HF, of patients with left ventricular assist devices (LVAD) and of transplant patients. The main objective of the unit is to offer specialized care to these patients in order to avoid unnecessary hospitalizations and increase survival rate, to evaluate the need for and discuss advanced HF therapies and to improve patients' quality of life. In 2021, 4,005 consultations (2,267 nurse-led consultations and 1,738 medical consultations) were conducted in approximately 400 HF or transplant patients.

The HUG provides patients with a network of specialized PC. The Division of Palliative Medicine includes three acute PC units with a total of 36 beds, two mobile PC teams, one working in the acute care and rehabilitation hospitals and one in the geriatric and psychiatric hospitals. A mobile PC team provides care to patients living in the community, either at home or in nursing homes. An outpatient PC consultation opened in 2019 where an average of 202 patients per year have been assessed and followed. In 2021, 2,626 patients, aged 16 to 103, have benefited from specialized PC at the HUG.

Implementing palliative care for patients with heart failure

In 2018, we initiated an interdisciplinary working group including a PC physician, a PC nurse, a cardiologist and three cardiology nurses. The aim of this group was to improve PC provision for patients suffering from HF by implement PC interventions at all stages of the patient's trajectory. Based on national and international recommendations, we define three PC interventions, that could easily be implemented (9, 16, 22, 23):

1. Creating an interdisciplinary consultation for patients with advanced HF.
2. Implementing a routine PC consultation for all patients undergoing evaluation for a LVAD or a heart transplant.
3. Training sessions for the cardiology team in order to provide them with the skills necessary to perform symptom evaluation and initiate advance care planning.

The idea underpinning each of these interventions was to provide early integrated PC for patients suffering from HF, since we had acknowledged the fact that PC was often implemented too late in the disease.

An important aspect of our care model was to ensure that patients were still followed primarily by their cardiologist, as continuity of care is a core component of good quality care and of patient satisfaction with care (10).

Interdisciplinary consultations

Patients are initially identified by HF physicians or nurses, based on a screening of PC needs, concerning mainly symptom burden, complex psycho-social circumstances or the identification of potentially divergent goals of care between patient and healthcare professionals. This evaluation is currently based on a narrative review as no validated tool currently exists in French for the evaluation of PC needs in patients with HF.

After a patient has been identified, an initial consultation is conducted by a PC physician and a cardiologist either together or back-to-back depending on the physicians' availability. This consultation is aimed at presenting the scope of PC, conducting a thorough evaluation of symptoms and psycho-social concerns and evaluating the patient's knowledge of disease, values and willingness to discuss advance care planning. If the primary consultation cannot be conducted by the cardiology and the PC physicians simultaneously, one of the cardiology nurses will generally accompany the patient to the first PC consultation in order to complement the information provided by the PC specialist and later communicate important elements of the discussion to the cardiology team. This consultation is then transcribed in a report that is included in the patient's electronic medical record and forwarded to the patient's cardiologist, general practitioner, home care service and any other professionals involved in the patient's care.

After the first consultation, patients are offered PC follow-up consultations, conducted by a PC physician, at a frequency adapted to suit the patient's needs and symptoms. During these follow up consultations, all patients are assessed for symptom burden, psychological, social and spiritual needs and offered the possibility of discussing advance care planning and document its conclusions (e.g., in the form of advance directives). Referral to a social assistant or home care services can be organized if required. Psychological support is provided by psychologists and psychiatrists from the ambulatory psychiatry division of the HUG. Spiritual issues, frequently independent or beyond religious concerns, are generally assessed during the first PC consultation. Spiritual assistance can be provided by one of the chaplains working with the HUG, if they do not already have support from their community chaplain. Symptoms are assessed by the Edmonton Symptom Assessment System (ESAS) (24). This validated tool allows patients to rate intensity of nine common symptoms in PC, such as pain, breathlessness, anxiety and drowsiness on a scale of 0 (none) to 10 (severest). If breathlessness is reported, patients are asked to complete the Dyspnea-12 questionnaire. This tool was developed and validated in many cardiopulmonary diseases, including HF, for breathlessness assessment based on physical and affective components (25–27). This evaluation helps inform the need for non-pharmacological (e.g., cardiovascular rehabilitation) and/or pharmacological (e.g., opioids) interventions to alleviate breathlessness and complementary approaches such as hypnosis or sophrology to improve general well-being and crisis management. Social needs are assessed through discussion and patients are referred to appropriate services as required. All patients are offered the possibility to rediscuss advance care planning throughout the PC follow-up triggered by the progression of symptoms and needs and encouraged to name a healthcare surrogate. Follow-up consultations mainly focus on the patient's needs, but always include a comprehensive symptom assessment.

Pre-LVAD and -transplant palliative care consultation

Heart transplantation remains the best treatment option offered to patients with advanced HF. However, only a small number of eligible patients undergo heart transplantation and alternative options should be discussed early on in the process.

As of 2020, all patients electively hospitalized for a five-day pre-transplant or pre-LVAD workup, either as destination therapy or as a bridge to transplant, were systematically scheduled for a PC consultation. The PC consultation is planned in the patient's agenda, alongside other consultations such as radiological exams, pulmonary evaluation and psychological assessment. The consultation is conducted by a senior PC physician. The main topics addressed are the aims of PC and advance care planning. Patient's lived experience of the disease as well as hopes and fears regarding the planned intervention, its results and the life thereafter are discussed, and information about advance directives and a healthcare surrogate are given. Depending on the patient's needs, follow-up ambulatory PC consultations can be offered. Since October 2020, 11 patients have undergone a PC evaluation before a LVAD implantation or heart transplant. No patient refused the PC consultation. One patient left the hospital early and did not complete the work-up, including PC assessment.

Training sessions

Healthcare providers' lack of knowledge about PC has been found to be one of the main barriers to providing quality PC to patients with HF (28). The PC team therefore started by providing knowledge about the definition and aim of PC through a series of presentations/coaching sessions given to the interprofessional HF team. A PC specialist nurse then conducted individual training sessions with the cardiology nurses on how to evaluate symptom burden and initiate advance care planning with patients.

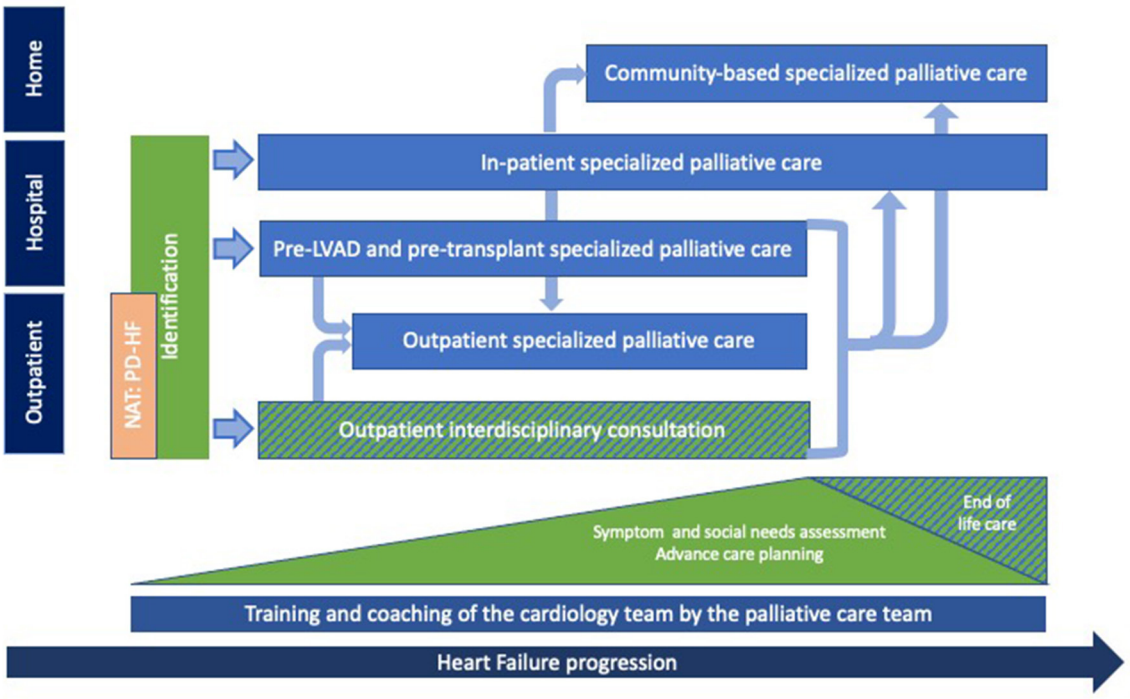

FIGURE 1
Palliative care provision for patients with heart failure: The Geneva model. PC provided by the palliative care team (light blue) for patients with HF according to setting and disease progression. Identification of eligible patients and provision of general palliative care, mainly symptom assessment, social needs evaluation and discussions about advance care planning, are provided throughout the disease trajectory by the interprofessional cardiology team (green). End of life care is provided by the cardiology and the PC team. Training and coaching sessions of the interprofessional cardiology team are conducted continuously by the PC team (dark blue). The NAT: PD-HF (orange) is currently being integrated to our model and should allow for an earlier access to PC provision for patients with HF. PC, palliative care; HF, heart failure.

TABLE 1 Numbers of HF patients having benefited from a consultation with a PC physician per year since October 2020, outside specialized PC units.

Year	Inhospital	Ambulatory	Pre-transplant
2020	25	0	3
2021	40	5	6
2022 (January–March)	7	9	3

The Geneva model

International recommendations suggest integrating PC at every stage of the HF trajectory, in a flexible, adaptable way (9, 16). Based on the development of the previously listed interventions, we designed a model of care for the integration of PC for patients with HF according to care setting (e.g., in hospital, in out-patient consultations or in the community) and disease progression (Figure 1). Integration of specialized PC is done after identification of PC triggers by cardiologists/HF nurses in the outpatient or in-patient setting. Depending on the patient's situation, specialized PC is then either introduced during hospitalization for acute HF, at a pre-LVAD or pre-transplantation consultation or during an interdisciplinary outpatient consultation. After this first contact, specialized PC can continue to be provided, according to the setting, as an interdisciplinary consultation, as a specialized PC outpatient consultation, as a specialized PC in-patient consultation or as a home-based specialized PC consultation.

Certain elements of general PC are now being carried out by the cardiology team such as assessing symptoms, social needs and initiating advance care planning discussions. The palliative care team simultaneously provides support by providing members of the cardiology team with presentations on palliative symptom assessment/management and coaching sessions on how to initiate advance care discussions with patients and their families. With the aim of maintaining continuity of care, end of life care is provided by the cardiology and PC team, as required.

Since the beginning of this collaboration in October 2020, the number of PC consultations for patients with HF has been increasing in all settings, whether for ambulatory or pre-transplant patients (Table 1). In the out-patient setting, patients

benefited from an average 1.5 consultations (range-1–4) that lasted from 30 min to an hour and a half, depending on the patient's needs. All of them were offered the possibility of discussing advance care planning. More than half of all patients completed advance directives following the PC consultation.

Discussion

Chronic ischemic and non-ischemic heart diseases are amongst the leading health conditions driving the global burden of serious health-related suffering in the world, and the number of affected individuals is expected to increase in the near future (1). Finding ways to support people throughout a chronic disease trajectory even when improvement of the underlying condition can be expected, as in patients awaiting transplantation, should be a health priority. Despite the fact that integration of PC for patients with HF was shown to improve QoL and patient satisfaction, it is still underprovided (29).

In 2017, Rogers et al. evaluated an interdisciplinary PC intervention in addition to evidence-based HF care (14). This intervention showed a significant benefit to the patients' QoL, anxiety, depression and spiritual well-being compared to usual care alone (14). The core components of the intervention which were symptom management and identifying goals of care were the same as in our intervention. However, the study only included patients with a high risk of 6-month mortality, therefore late in the disease.

A recent systematic review and meta-analysis conducted on PC interventions for patients with HF identified 15 studies, only two of which involved outpatients (29). Rabow et al. (30) compared HF patients followed by a general medicine outpatient clinic (usual care) with HF patients benefiting from usual care and PC team consultations. This study showed improvement in patient outcomes such as dyspnea, anxiety and spiritual well-being. In the second study, Evangelista et al. examined the effects of an outpatient PC consultation on symptom burden and QoL in patients with symptomatic HF (17). In this study, patients were recruited in an inpatient setting during an acute HF exacerbation and given an appointment for a PC consultation on the same day as their next outpatient cardiology consultation. Outcomes were evaluated 3 months after that single PC consultation and showed an improvement of symptom burden, depression and QoL compared to the usual care group. Although this study involved the PC and the HF teams, consultations were conducted separately and there were no elements of collaboration between the two teams. It can be hypothesized that a close collaboration between the PC and the HF team may further improve patient-reported outcomes by the early implementation of PC in the disease trajectory and the early collaborative discussions concerning goals of care. This may also, as in cancer patients, reduce the number of futile or harmful interventions at the end of life (31, 32).

Although many models of care for the integration of PC for patients with HF have been suggested it seems important to adapt these models to the local setting, resources and needs (29). Furthermore, it seems important to work together and offer interdisciplinary support in a collaborative manner as opposed to separate PC consultations (30). Evidence shows that patients with HF may have unfavorable impressions of PC (33). Patients value continuity of care and trust their cardiologist, who has often followed them for many years, to provide them with the best, most appropriate care. The integration of PC as an element of comprehensive cardiological care, as provided in our model, assures that the interprofessional cardiological team remains in charge of HF patients' care throughout the disease trajectory.

One of the aims of our interdisciplinary collaboration was to provide healthcare professionals working at the HF unit with the knowledge and tools to identify patients who could benefit from PC. This is a unique feature of our model that focuses on empowering healthcare professionals who may not be initially at ease with PC in providing what is now recognized as good practice for patients with HF (34). This element may be particularly relevant in settings that may have limited resources in specialist PC. As the number of patients in need of PC is constantly increasing, there is an urgent requirement for non-PC specialists to be able to provide general PC. Currently, our model has focused on training nurses and physicians. Other members of the interprofessional cardiology team such as healthcare workers and physiotherapists working with patients during cardiovascular rehabilitation should also be involved in the collaboration so as to create a global culture of care centered on maintaining HF patients' QoL.

Members of the PC teams have also benefited from this interdisciplinary collaboration. Indeed, it has provided the PC team with important knowledge on the needs and trajectory of patients with non-oncological diseases such as HF. It has also offered valuable insight on the management of this population's expectations, in particular regarding the prospect of life-prolonging therapies (e.g., LVAD implantation) in the context of a life-limiting disease.

One of the remaining questions is when and who should receive PC (14, 19, 33). As with oncology patients, it has been suggested that HF patients be referred based on a high risk of dying, poorly controlled symptoms and psychosocial-spiritual distress, hospitalization and discharge or end-of-life transition (18). However, this approach often led to PC being offered very late in the disease course and being reactive as opposed to pro-active. Referring HF patients to PC when they are unwell, does not leave much place for anticipation and contributes to the erroneous perception that PC is only provided to people whose health is deteriorating and prognosis obviously bad. Changing the pattern of care from referral to PC after exhaustion of cardiological treatments, to involving PC into the care, as the needs emerge, eliminates the main barriers among health care providers (who do not need to give up their patients to the

PC team) and patients (who do not need to be considered as imminently dying) and allows to focus on QoL during the entire disease journey and not only during the dying phase.

There are currently no French-validated tools for the identification of HF patients who could benefit from PC. The Needs Assessment Tool: Progressive Disease - Heart Failure (NAT: PD-HF) was first developed nearly 10 years ago to identify and inform the management of physical and psycho-social issues experienced by patients suffering from chronic HF (35). It is a tool that is completed in <5 min and can guide physicians when assessing the PC needs of patients with HF and their relatives and help to identify those requiring specialist PC care. The German translation and validation has recently been published by our colleagues in the German-speaking region of Switzerland and we are now collaborating with them on the validation of the French translation (36). We believe implementing the NAT: PD-HF may help increase the number of HF patients receiving PC, based on their needs.

Future prospects

The idea behind our concept is to provide person-centered care focused on improving the QoL of people living with cardiovascular diseases, particularly HF, during the entire course of their diseases, based on their needs and independent of treatment options and prognosis. More than a single intervention, we have developed a close collaboration between the cardiology and PC teams. Regular interaction has also brought the opportunity to work on streamlining certain procedures such as designing protocols in anticipation of dealing with the end-of-life and death of patients with implanted LVAD or an implantable cardioverter-defibrillator. As LVAD is a relatively recent therapy, there is little evidence or information about the process and a protocol that included contextual information was needed in order to help the physicians who would have to care for these patients (37–39). Indeed, the inactivation of mechanical circulatory support is emotionally challenging and bears ethical dilemmas for most healthcare professionals, patients and their relatives.

We are currently finalizing a guideline to help healthcare professionals care for patients implemented with a LVAD at the end of their life. This guideline includes a presentation of the HEARTMATE 3^{TM}, to whom it is destined, main complications, required maintenance and care (40). The guideline describes the step-by-step procedure to inactivate the LVAD including discussions that should be held with the patient and his caregivers and how to guide the patient and his/her family through the process. A pocket guide has also been conceived for physicians on how to inactivate the LVAD alarms. Once completed, this guideline will have to be reviewed by the healthcare professionals involved in the procedure, mainly cardiologists, cardiology technicians, intensive care and internal medicine specialists and the PC team.

Limitations

Our model of care was based on needs identified by healthcare professionals, mainly physicians and nurses, working with HF patients. We acknowledge the fact that our model could have benefited from the input of patients and caregivers. This could be done through focus groups in order to refine the process.

We acknowledge the subjectivity underlying the referral of HF patients to the PC team in our model. This is due to the absence of a validated instrument in French to identify HF patients who could benefit from specialized PC. In order to address this, we are actively working on the French validation of the NAT: PD-HF.

Although it was not the aim of this paper, we recognize that our model has yet to be tested for its effectiveness in improving patients' QoL and symptom burden as well as its impact on healthcare resource utilization. We plan to study these different aspects in the near future.

Furthermore, we are aware that this model was constructed following a needs assessment conducted in the specific HF unit of a tertiary high-income country and may not be appliable to other settings. However, the specialized PC team is small with only one physician currently conducting outpatient consultations. As mentioned previously, PC should be provided by every healthcare professional involved in the care provided to HF patients and not only by a specialist PC team. This model does not therefore require a broad range of PC specialists.

We are also aware that the success of any collaboration is dependent on the motivation of all parties involved, especially the discipline leaders. Healthcare professionals working with HF patients have many pre-conceived ideas about PC and often mistake PC for imminent end-of-life care. We are extremely privileged to be working with health care professionals that recognize the potential benefits of a collaboration between the cardiology and PC teams for patients suffering from HF and acknowledge the fact that this may be a limiting factor to the integration of PC for HF patients in many other settings.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Comprehensive care for people living with heart failure and chronic obstructive pulmonary disease—Integration of palliative care with disease-specific care: From guidelines to practice

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Heart failure (HF) and chronic obstructive pulmonary disease (COPD) are the leading global epidemiological, clinical, social, and economic burden. Due to similar risk factors and overlapping pathophysiological pathways, the coexistence of these two diseases is common. People with severe COPD and advanced chronic HF (CHF) develop similar symptoms that aggravate if evoking mechanisms overlap. The coexistence of COPD and CHF limits the quality of life (QoL) and worsens symptom burden and mortality, more than if only one of them is present. Both conditions progress despite optimal, guidelines directed treatment, frequently exacerbate, and have a similar or worse prognosis in comparison with many malignant diseases. Palliative care (PC) is effective in QoL improvement of people with CHF and COPD and may be a valuable addition to standard treatment. The current guidelines for the management of HF and COPD emphasize the importance of early integration of PC parallel to disease-modifying therapies in people with advanced forms of both conditions. The number of patients with HF and COPD requiring PC is high and will grow in future decades necessitating further attention to research and knowledge translation in this field of practice. Care pathways for

people living with concomitant HF and COPD have not been published so far. It can be hypothesized that overlapping of symptoms and similarity in disease trajectories allow to draw a model of care which will address symptoms and problems caused by either condition.

KEYWORDS

heart failure, chronic heart failure, chronic obstructive pulmonary disease, palliative care, advanced care planning

Introduction

Cardiovascular diseases (CVD) and respiratory diseases are the leading causes of morbidity and mortality in developed countries (1, 2). Among them, chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are regarded as the most common. Both diseases may cause serious clinical, social, and economic burden (1, 2). Heart failure (HF) affects up to 4% of the global population, and the number of new cases is constantly rising (1–3). The causes of this phenomenon are associated mostly with aging of the society and, paradoxically, with the improved survival in HF and acute coronary syndromes being one of common causes of HF (1). COPD is currently the third leading cause of death worldwide (2, 4). As smoking, which is a major risk factor for the development of COPD, as well as for coronary artery disease, is still widespread in the population, particularly of low and moderate incomes, an upward trend in the number of new cases of COPD is still predicted (2, 4). CHF and COPD having similar risk factors coexist in about 30% (range 9–52%) (2, 5, 6). If CHF and COPD coexist, the function of many organs and systems is affected more profoundly, the symptoms overlap, the quality of life (QoL) is limited more seriously, and the mortality risk is higher, particularly in the elderly (1, 2, 7). CHF increases mortality risk in people with COPD and CVD being the most common cause of death among this population, but the influence of COPD on all-cause mortality in the HF has not been proven so far (8, 9). The management of people living with CHF and COPD needs to address similar problems and symptoms and to prevent recurrence of exacerbations of these diseases (1, 5, 6). The guidelines recommend implementation of disease-specific management for HF and COPD even in the most advanced stages of disease. Interestingly, most of them recommend care provided by multidisciplinary team, including palliative care (PC), if needed (1–3, 10, 11).

Palliative care is an active, holistic approach that focuses on improvement of QoL of people living with life-threatening diseases that relieve health-related suffering (12, 13). Nowadays, it is dedicated to all suffering from a disease that does not fully respond to disease-specific management. It should be provided alongside the whole trajectory of living with the disease, regardless of diagnosis, prognosis, and risk of death (1–3, 10, 14–16). The core principle of PC is facilitating effective collaboration between the ill person, her or his family, and healthcare professionals from all disciplines and specialties involved in the care with the goal to empower the person living with a disease to achieve best possible QoL, according to personal values, to strengthen autonomy, and to secure maintaining dignity (17). PC acknowledges the relatives, often being informal caregivers, as subjects who need (PC) support, with the goal to maintain their QoL and facilitate their ability to care (11, 18). PC goes beyond alleviation of symptoms and perceives addressing psychological, spiritual, and social needs as integral aspects of care (1–3, 10, 14–16). Many scientific societies recommend that PC should be integrated in the care for people living with CHF and COPD as soon as the needs emerge. (1–3, 10, 14–16).

Triggers for the implementation of palliative care for people living with advanced chronic heart failure and severe chronic obstructive pulmonary disease

The current guidelines recommend PC as a key component of multidisciplinary approach to people living with CHF and COPD, which should be applied based on needs, along with disease-specific management, regardless of the stage of these diseases and the expected survival (1–3, 11). Needs should be assessed as often as it is necessary, for example, in the case of significant changes in the course of the underlying disease, in general health, or in factors related to the person or his family, optimally using validates tools (1–3) (**Table 1**). The Needs Assessment Tool: Progressive Disease (NAT:PD) has been validated in cancer, HF, and interstitial lung disease and recently has been proposed as applicable in any progressive disease (19). It contains prompts to assess the needs and wellbeing of the ill person, the ability to care of relatives, and their wellbeing. The last prompt is dedicated to the consideration who will address existing needs (3, 20). Alternatively, other available validated

scales assessing the presence and the severity of symptoms can be used to recognize indication for PC involvement (1–3). The most widely used tools are Numeric Rating Scale (NRS) and Edmonton Symptom Assessment Scale (ESAS) being in fact a list of NRS for nine most common and one self-determined symptoms, the Integrated Palliative Care Outcome Scale (IPOS) (3).

The involvement of PC in care for people with heart and/or lung disease is less common than with cancer (18, 21, 22). The EPICTER study has shown that only 15% of patients hospitalized with advanced HF (23% of all HF hospitalizations) receive PC, but mostly only those with symptomatic cancer (as concomitant disease) in the last hours of life, after standard therapy has been exhausted (21, 23). The main causes for late PC involvement are depicted in **Table 2** (3, 22–25). After the needs have been assessed, PC can be implemented stepwise. This process is presented below, with particular emphasis on the interdisciplinary approach in this group of patients (**Figure 1**).

Although PC for those sub-populations exists, there is a lack of guidelines for the PC management of people living with COPD and coexisting CHF. This manuscript merges the available general and specific for either condition PC.

Main clinical problems in people living with heart failure and chronic obstructive pulmonary disease

The disease-specific management should be continuously optimized according to current guidelines, even in the most advanced stages of the disease and in people receiving care with the main focus on symptom relief. The applicability of this treatment and adjustment of treatment goals, according to given situation, is mandatory (1–3) (**Figure 2**). It should be emphasized that patients with COPD and CHF present many similar symptoms and experience many common problems that may overlap, constituting a therapeutic challenge for cardiologists and pneumologists (1–3, 5, 6) (**Figure 3**).

The symptomatic management of most common symptoms experienced by people with advanced CHF and severe COPD is discussed below.

Breathlessness

Breathlessness is ubiquitously present in people living with CHF or COPD, beginning from very early stages of disease till the phase of dying. Disease-specific treatment alleviates it, but does not eliminate it completely, especially in advanced disease, when it is present all the time, despite optimal cardiological or pneumological management (1–3). The term "breathlessness" is commonly used to call the difficulties in breathing; however, people experiencing it use several descriptors to express their experience (e.g., tightness in the chest, air hunger, shortness of breath, shallow respiration, breathlessness, difficulty in breathing, heavy breathing, and feeling lack of air). It is regarded that this plurality of names describes the plurality of pathophysiological processes evoking breathlessness (1–3). Even if the factors causing breathlessness in heart and lung disease differ in less advanced stages, as the diseases progress, they increasingly overlap or even become common (1–3, 14, 26) (**Figure 4**).

The first step in alleviating breathlessness is optimization of treatment of the underlying disease or concomitant disease that can additionally aggravate it (like pneumonia, hydrothorax, or anemia). For many years, the intensification of β-blocker therapy in patients with HF and coexisting COPD has been controversial. Nevertheless, according to the current ESC and GOLD guidelines, these patients should be treated for HF in the same way as patients without COPD, including optimization of β-blocker treatment. Recent studies showed that β-blockers, particularly cardioselective ones, are safe in the treatment of COPD patients, reduce all-cause mortality, and might contribute to the reduction of COPD-related hospitalizations (27–29). On the contrary, long-acting anticholinergics and β_2-agonists needed for COPD can evoke tachycardia, undesired in CHF. Optimization of treatment of each disease requires close monitoring of the function of the other one (30).

Improvement of the burden caused by breathlessness requires implementation of non-pharmacological management which may be especially successful if the breathlessness is of moderate severity (14, 26). In COPD, dyspnea exceeding point 2 on mMRC scale is an indication for general and pulmonary rehabilitation. In alleviation of chronic breathlessness training, the breathing technique adapted to the needs and possibilities of physical activity, cooling the face with a hand-hold fan directed at the triangle between mouth, nose, and cheeks, spraying a cold water on this area, psychological support, and education of patients and their relatives are considered as potentially helpful (1–3, 14, 26, 31). In COPD neuromuscular electrical stimulation and chest wall vibration, stimulation of mucus removal can be tried (2, 26). Oxygen can improve breathlessness in the majority of patients with COPD, sometimes even without documented hypoxemia, and in some patients with HF, predominately those with hypoxia (1–3).

The pharmacological, palliative treatment of chronic, refractory dyspnea is based on low doses of opioids (i.e., significantly lower, as used for pain management), mainly morphine. They have been studied predominantly in COPD and in cancer. Their efficacy and safety in HF are still not well-proven; however, they are recommended in cardiological guidelines (1–3, 14, 26, 32, 33). Morphine significantly alleviates breathlessness in about 50% of treated patients. The most commonly suggested initial dose is 10 mg/day p.o. that, if

TABLE 1 The most important changes in the course of HF and COPD initiating the assessment of PC needs; based on: (1–3, 8, 11, 13, 132).

HF	COPD
• *De novo* HF with severe symptoms refractory to treatment • Symptoms of advanced CHF (NYHA IV) • Qualification for CIEDs • Qualification for TAVI • Eligibility for valve replacement surgery • Qualified for HTX or MCS	• *De novo* COPD with severe symptoms refractory to treatment • Symptoms of advanced COPD (category D, bronchial obturation GOLD 3/4, mMRC grade 3/4) • Eligibility for lung transplantation • Initiation of long-term oxygen therapy • Initiation of home non-invasive ventilation
• Progressive worsening of CHF and COPD with severe symptoms refractory to treatment • Care dependence and poor self-management • Frequent, recurrent exacerbations of CHF and/or COPD • Cachexia • Inability to attend cardiopulmonary rehabilitation • Survived cardiopulmonary resuscitation • Eligibility for heart and lung transplantation	

CIEDs, cardiovascular electrical devices; COPD, chronic heart failure; GOLD, global initiative for chronic obstructive lung disease; HF, heart failure; HTX, heart transplantation; MCS, mechanical cardiac support; MRC, medical research council; NYHA, New York heart association; TAVI, transcatheter aortic valve replacement.

TABLE 2 The most common causes of insufficient PC involvement in people living with COPD and CHF; based on (3, 16, 20–23).

Cause	Solution proposal
• Uncertain prognosis of COPD and CHF	• Collaboration in a multidisciplinary cardiopulmonary team to optimize standard care and choose the optimal time to start PC • Implementing of needs based model of triggering PC involvement
• Underestimation of the PC needs	• Regular assessment of the PC's needs using available scales, both in primary and secondary care
• Person's fear of talking about PC and end of life	• Improving awareness on PC principles in the society • Providing the patient with psychological, spiritual and social support in the scope adjusted to the needs based model of PC provision
• Insufficient physician's communication skills on end-of-life related topics	• Training in clinical communication skills in non-PC specialists
• Incorrect perception of the PC as a solely care for the dying, lack of PC education	• Palliative care education and training programs for healthcare professionals
• Insufficient cooperation between PC specialists and other healthcare providers	• Meetings in a multidisciplinary group, including cardiologists, pneumonologists and PC specialists aimed at implementing an integrated PC

CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; PC, palliative care.

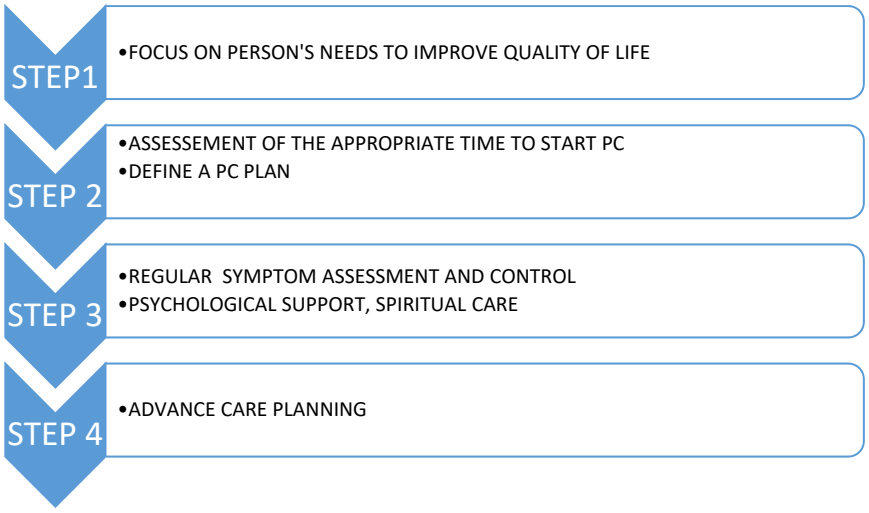

FIGURE 1
Steps in PC in people living with CHF and COPD; based on (1–3). CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease.

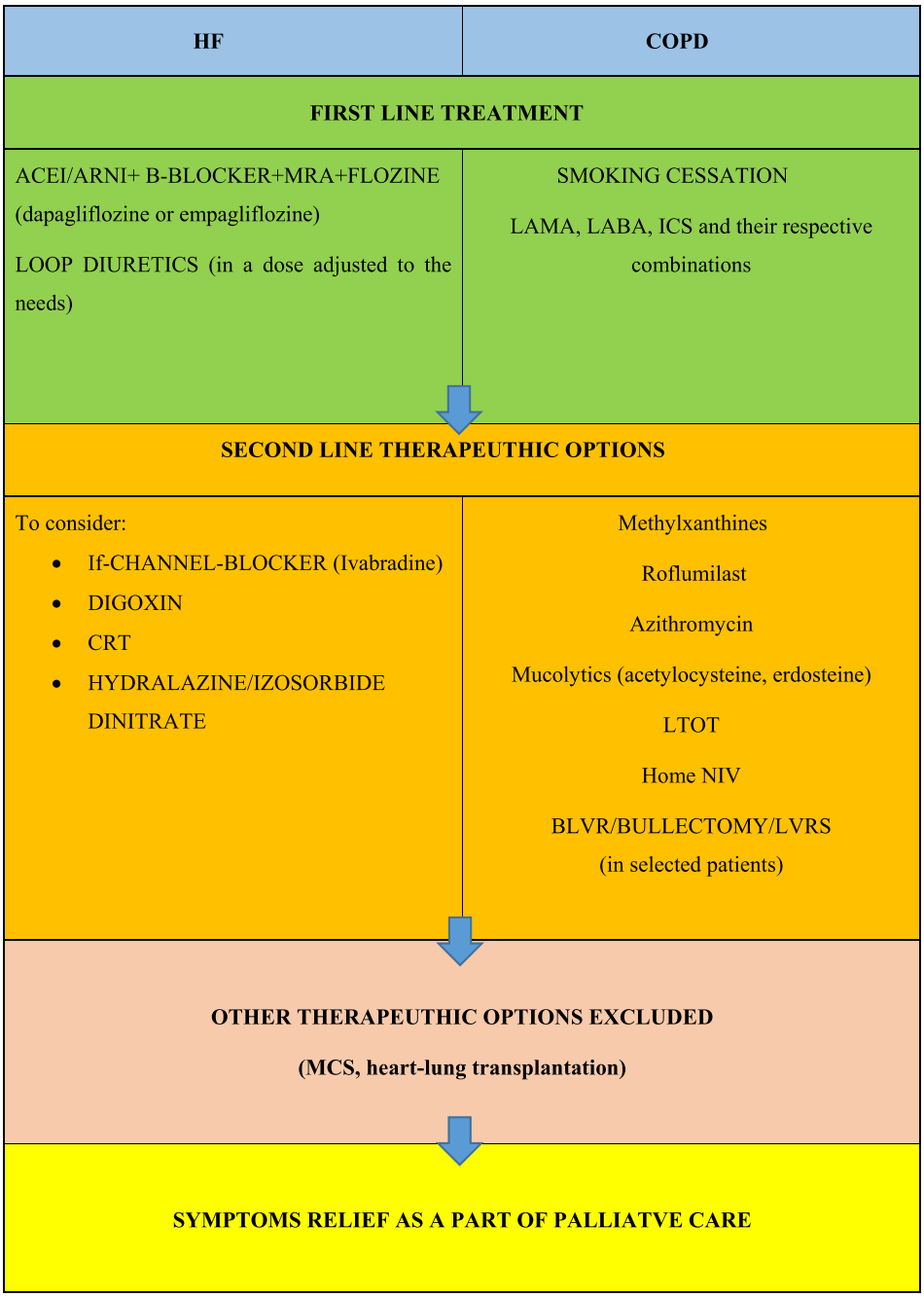

FIGURE 2
Principles of optimizing the treatment of the underlying disease in people living with COPD and HF; based on (1–3). ACE, angiotensin converting enzyme inhibitor; ARNI, angiotensin receptor neprilysin inhibitor; BLVR, bronchoscopic lung volume reduction; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronisation therapy; CS, corticosteroids; HF, heart failure; ICS, inhaled glucocorticoids; LABA, long acting B_2 agonist; LAMA, long acting muscarinic antagonist; LTOT, long term oxygen therapy; LVRS, lung volume reduction surgery; MCS, mechanical cardiac support; MRA, mineralocorticoid receptor antagonist; NIV, non-invasive ventilation; PDE-4, phosphodiesterase-4; SABA, short acting β agonist.

needed, can be up titrated gradually by 10 mg/day steps, every 7–10 days, to maximal 30 mg/day. Some experts recommend starting with much lower dose, what can be reasonable in elderly, cachectic, fragile, affected with comorbidities, with organ insufficiency (3, 34). The side effects, seen sometimes even with low doses of opioids, include constipation, usually transient nausea and vomiting, sedation/drowsiness, and addiction (1–3, 26). The most feared is respiratory depression that can be

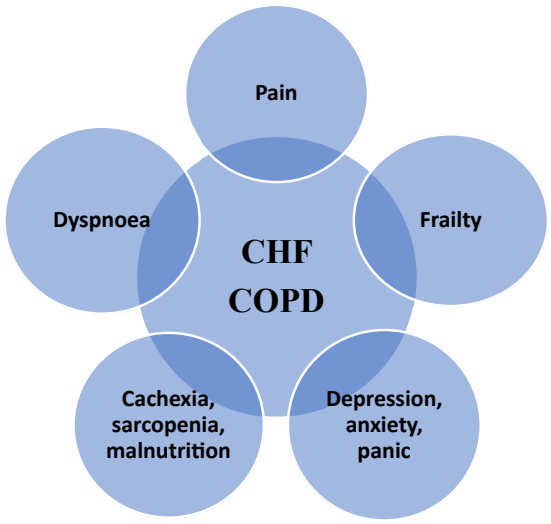

FIGURE 3
The most common clinical problems overlapping in CHD and COPD; adapted from (1–3). PC, palliative care.

successfully prevented by proper dose titration and meticulous monitoring of symptoms and side effects as well as changes in clinical status and co-medication. The fear of opioid side effects (respiratory depression and addiction) together with lack of skills in their prescribing by non-palliative medical specialties is the most frequent cause of undertreatment of breathlessness (33). Benzodiazepines are commonly used for breathlessness alleviation, despite the lack of proven benefits and known harms of side effects. High doses can cause drowsiness and somnolence, especially in the elderly. The risk of addiction should not be neglected. Myorelaxant properties can impair respiratory muscle function and increase the risk of falls (1–3). Benzodiazepines may be considered as second- or third-line treatment of acute dyspnea in case of ineffectiveness of other therapeutic options, particularly in the presence of severe anxiety or in the dying (1–3). Mirtazapine is waking growing interest as a therapeutic option for people suffering for refractory breathlessness, especially those with concomitant anxiety, but randomized trials are underway (35).

Pain

Pain is as common in people living with CHF and COPD as in people living with cancer, but its intensity is lower (36). That is why non-pharmacological management and non-opioids are more often sufficient, as in people with cancer. If the pain is severe, the addition of opioids should be considered. The non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated in people with HF, unless in very selected situation, the antiphlogistic effect is indispensable, as additionally to general sided effects (like gastrointestinal bleeding), they increase the risk of HF-related hospitalizations, renal function worsening, major atherothrombotic events, and death (1–3). The only exception among NSAIDs is acetylsalicylic acid (ASA), used at a dose of 75–100 mg/day as secondary prophylaxis in atherosclerosis (i.e., coronary artery disease). There are not known specific contraindications for their use in people with COPD, but administration of NSAIDs, including ASA, has been shown to increase risk of new atrial fibrillation or bleeding (37, 38). The randomized ENABLE-CHF-PC trial has shown that PC telehealth significantly improves pain intensity and its interference with daily life, but not QoL or mood (39).

Sarcopenia and cachexia

Sarcopenia is a metabolic syndrome characterized by muscle loss, leading to diminished muscle strength, and performance, resulting in reduced mobility (40, 41). If sarcopenia is accompanied by unintended loss of more than 5% edema-free body weight within 12 months, cachexia should be diagnosed. Both conditions are seen in people living with advanced chronic diseases, with a prevalence 5–15% in advanced COPD and HF. The prevalence of sarcopenia, due to lack of universal clinical criteria, is more difficult to ascertain. Some authors suggest that it can affect 27% patients with COPD, with the prevalence growing with the advancement of the disease (42, 43). Among those living with HF, the prevalence of sarcopenia is 20% higher than in the age-matched healthy probands (44). It is associated with adverse outcomes, including falls, dysfunction, weakness, and death (42, 45). The most important factors leading to sarcopenia and cachexia are inadequate protein intake, malabsorption due to gut edema and hypoperfusion, metabolic imbalance, and physical inactivity (46, 47).

Nutritional screening should be performed in each patient with CHF and COPD using on of established tools: Nutritional Risk Screening 2002 (NRS 2002), Subjective Global Assessment (SGA), Mini Nutritional Assessment (MNA), Malnutrition Universal Screening Tool (MUST), Short Nutritional Assessment Questionnaire (SNAQ), for cachexia and SARC-F, SARC-calF test, and Mini Sarcopenia Risk Assessment (MSRA) for sarcopenia (48–55). Monitoring of weight is not a sensitive screening method as fluid retention can mask the loss of dry body weight and malnutrition. Useful for muscle function assessment is the handgrip strength measurement (56). Alternatively, body composition analysis (BIA), dual-energy X-ray absorptiometry (DXA), or muscle ultrasound may be used (47). BIA is a safe, reliable, inexpensive, and widely available tool (57). The main limitation of BIA and DXA in PC CHF/COPD patients is body water accumulation which may negatively affect the results (58).

Aerobic exercise and dietary interventions are suggested to prevent sarcopenia/cachexia, but there are no large studies

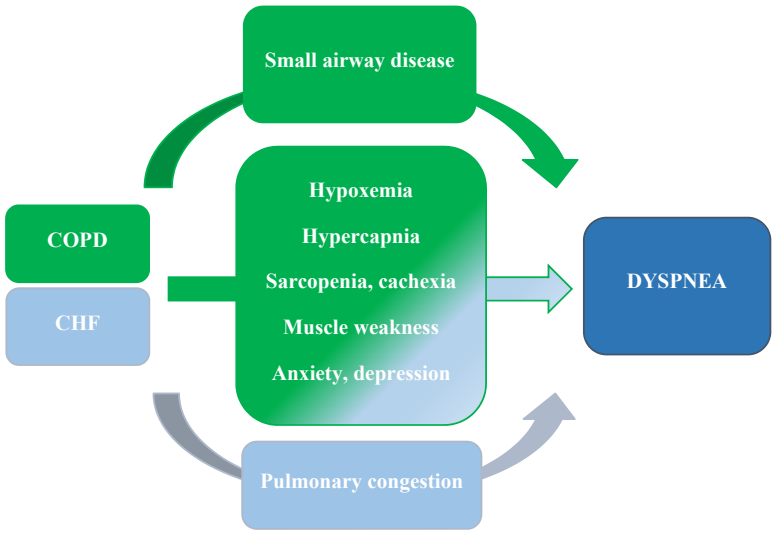

FIGURE 4
The major causes of dyspnea in people living with COPD and CHF coexistence; based on (1–3, 30).

in people with advanced CHF and COPD. The hypercaloric and hyperproteic supplementation of Dietary Approaches to Stop Hypertension (DASH) or Mediterranean diets are recommended, but this has not been evaluated in randomized studies (47). Participation in rehabilitation programs lead to improvements in exercise capacity and QoL (59).

Exacerbations

Acute exacerbations of COPD (AECOPD) and acute decompensations of CHF (ADCHF) are the common cause of (re-)hospitalizations (1, 2). Nearly 20% of COPD patients and about 25% of CHF patients are re-hospitalized within 1 month (1, 2, 18, 24, 60). Each ADCHF and AECOPD are a potential life-threatening condition and significantly increase the risk of all-cause mortality and re-hospitalization (1, 2). Undoubtedly, the optimization of guidelines directed management for COPD and CHF is crucial for the prevention of disease exacerbations (1, 2). Preliminary reports suggest that PC provided as an element of holistic approach may also additionally contribute to reduction of the rate of exacerbation-related readmissions (21, 24, 61–65).

Exercise rehabilitation

Exercise rehabilitation is an essential part of the multidisciplinary approach to people with HF and COPD recommended by ESC guidelines to all patients with HF and by GOLD experts to all patients with COPD who are able to undertake it (1, 2, 66). In population with HF, the rehabilitation improves physical capacity and QoL and reduces the frequency of HF-related hospitalizations (1, 2, 66–68). HF is a cause of only 15% of referral for cardiac rehabilitation, and as high proportion as 20% of patients with HF terminate the rehabilitation programs prematurely (69). Pulmonary rehabilitation, particularly involving aerobic exercises, increases physical capacity, reduces the feeling of dyspnea and fatigue, and significantly improves the QoL in people living with COPD (2, 14, 26, 70, 71). In patients with coexistence of CHF and COPD, exercise rehabilitation is especially needed, because in this group the decrease in cardiopulmonary capacity has a particularly negative impact on physical capacity, the severity of the dominant symptoms (particularly breathlessness), and the QoL (72, 73). The limitation of physical capacity cachexia and sarcopenia resulting in skeletal muscle dysfunction exaggerates breathlessness and fatigue in people with CHF and COPD (1, 2, 66). Exercise rehabilitation improves function of peripheral muscles, physical condition, symptoms of depression, and anxiety in people living with HF and COPD (14, 74, 75). Aerobic exercises or endurance training, inspiratory muscle training, or neuromuscular electrical stimulation (NMES) of lower limb muscles are especially recommended (76). The coexistence of COPD and CHF does not limit benefit of exercise rehabilitation (77). Exercise rehabilitation should be thus considered in all patients with HF and COPD, including severe forms of these diseases (1, 2, 66).

The rehabilitation can be part of an integrated PC in patients with COPD and CHF. Maddocks et al. and Reticker et al. suggest that PC and pulmonary rehabilitation have common goals (14, 78). The choice of the type, intensity, and duration of training should be tailored individually, with emphasis on the patient's general condition and capabilities,

the severity of the underlying disease, and the coexistence of comorbidities. Even in patients with severe HF and COPD, supervised exercise rehabilitation allows for individualization of training while maintaining a high level of safety (1, 2, 66). Telerehabilitation offers remote supervision of rehabilitation specialists (26, 79). Bernocchi et al. showed that with 4-month home telerehabilitation, the improvement with the distance in 6-min walk test (6MWT), the severity of dyspnea, the physical activity, and QoL can be achieved (80). Unfortunately, despite the clear benefits of simultaneous cardiac rehabilitation and pulmonary rehabilitation in COPD and CHF patients, implementation of cardiopulmonary rehabilitation in the form of integration of both programs is still challenging (81, 82).

Psychiatric disorders

Diagnosing of depression in people living with advanced disease can be quite challenging, as anxiety, fatigue, loss of appetite, or insomnia can be caused by diminished physical capacity and mood disorder. Using Patient Health Questionnaire-9 (PHQ-9) can facilitate timely and proper recognition of this comorbidity (83).

Depression is common and affects up to 40% of people living with CHF and/or COPD (84, 85). Depression favors unhealthy living still, smoking, diminished activity, and weight gain (84). It exerts negative impact on the QoL and adherence to treatment and increases the risk of hospitalization and death, including suicides (85–88). For those reason, it is suggested to assess people affected by HF for depression and treat them if required (3). Adequate statements with COPD have not been published so far, but it can be hypothesized that the approach should be similar. The management should consist of non-pharmacological (cognitive behavioral therapy (CBT) and aerobic exercise) and pharmacological interventions (89, 90). Selective serotonin reuptake inhibitors (SSRI) and mirtazapine are considered the first choice (35). Sertraline and escitalopram have been shown to be safe in people with HF and sertraline gave promising results in COPD (91, 92). Citalopram can cause QTc prolongation, especially in higher doses and in older patients, that is why it should be prescribed with caution. SSRIs can cause hyponatremia in the mechanism of syndrome of inappropriate antidiuretic hormone secretion, especially when combined with thiazide diuretics. SSRIs co-administrated with ASA and/or clopidogrel increase the risk of bleeding. Fluvoxamine and fluoxetine increase the concertation of warfarin, but decrease the metabolism of clopidogrel to its active metabolite.

Bupropion, noradrenaline and dopamine reuptake inhibitor (NDRI), is an effective and safe antidepressant registered for smoking cessation, which is particularly significant in COPD patients. Importantly, bupropion is a substrate for CYP2D6 similarly to clopidogrel and can decrease digoxin level; therefore, serum concentration monitoring is required. Most SSRIs, duloxetine, and bupropion inhibit CYP2D6 causing increased exposure of beta-blockers, and their dose reduction might be required. Mirtazapine has an interaction of unknown mechanism with warfarin causing increased risk of bleeding (93). Mirtazapine can also cause somnolence and weight gain which in some cases, however, can be beneficial. Medications used in COPD like beta-agonists used with SSRIs, mirtazapine, and trazodone can induce QT prolongation. Muscarinic antagonists can increase the risk of delirium and symptoms like dry mouth, constipation, and urinary retention which can be also caused by mirtazapine and trazodone (94). SSRI and NDRI—like venlafaxine and duloxetine—can cause hypertension and prolong QT interval. Tricyclic antidepressants and monoamine oxidase inhibitors are contraindicated in HF due to effect on blood pressure and QT prolongation, trazodone although trazodone is useful as a hypnotic agent not causing addiction should not be used in patients with ventricular arrhythmias (84, 93). A good strategy is to "start low, go slow" considering decreased drug metabolism. A new antidepressant strategy is ketamine—NMDA antagonist which turned out to be effective, rapid-acting add-on treatment in resistant depression (TRD). Its intranasal enantiomer es-ketamine has been recently approved by the FDA as an add-on treatment in TRD. Cardiac safety of add-on es-ketamine was evaluated in 1700 patients with TRD (95). Other experimental treatment used in depression and existential distress in patients with life-threatening disease is psilocybin-assisted psychotherapy. An RCT found reduction in the level of depression, suicidal ideation, and hopelessness after single dose of 0.3 mg/kg psilocybin administered in conjunction with psychotherapy (96). The results of recent Omega-3 Supplementation for Co-Morbid Depression and Heart Failure Treatment (OCEAN) trial revealed that high dose omega-3 was associated with improvement in cognitive depressive symptoms, social functioning, and 6MWT in depressed patients with HF (97).

Anxiety

General anxiety disorder and panic disorder are common, especially in COPD patients and in patients with implantable cardioverter defibrillator (ICD) (85, 98). The Hospital Anxiety and Depression Scale (HADS) is a good tool to screen hospitalized patients for anxiety and depression (99, 100). In COPD patients, CBT is recommended as an effective non-pharmacological treatment for anxiety (101). Pharmacotherapy, apart from SSRIs, which are the first-line treatment for anxiety disorders, includes also buspirone (93). BDZ is generally not recommended in elderly and patients with HF due to risk of falls and delirium (102, 103). Alprazolam—short acting benzodiazepine, has an interaction with amiodarone which inhibits its metabolism through CYP3A4 and can cause enhanced alprazolam effects (93).

Insomnia is common and requires efforts to remediate the underlying cause if it is possible. When pharmacotherapy is needed, antidepressants and melatonin can be considered.

Delirium

Delirium is an acute neuro-psychiatric condition caused by global brain dysfunction reaching prevalence up to 40% in palliative setting. The hallmark of delirium is disturbance in attention and awareness (104). Typically, delirium has acute onset and fluctuating course. Delirium is often underdiagnosed or misdiagnosed. A useful screening tool recommended by National Institute for Health and Care Excellence (NICE) is Confusion Assessment Method (CAM) (105, 106). Etiology of delirium is multifactorial, but most common triggering factors are infection, substance withdrawal, electrolyte disturbance, hypoxia, dehydration, anemia, hypo/hyperglycemia, organ dysfunctions, neurological diseases, and medications. Delirium correlates with increased mortality, morbidity, longer hospitalization, and higher costs of treatment. It increases the risk of falls and significantly disturbs the process of communication with the person (107). According to NICE guideline, prevention strategies like avoiding unnecessary catheterization, optimizing sleep conditions, encouraging physical activity, avoiding sensory deprivation (glasses, hearing aids), and using clock and calendar for orientation can be very effective (105). There are data on melatonin as an effective and safe preventing therapy in older patients undergoing surgical procedures (108).

The main goal in treatment should be identifying and cessation of the source of delirium. About 50% cases of delirium in palliative patients can be reversed with good communication at the end of person's life (107, 109). No medication is registered for delirium treatment, but if the person is distressed or considered risk to themselves or others, low dose and short-term haloperidol or olanzapine can be considered (105, 110).

Spiritual care

Spirituality is the dynamic dimension of human life that relates to the way persons experience, express and/or seek meaning, purpose, and transcendence, and the way they connect to the moment, to self, to others, to nature, to the significant, and/or the sacred (111).

Living with progressive disease confronts people with spiritual issues, that is, why spiritual care is integral part of PC. It supports people in coping with existential questions. As the spirituality, especially in West-European countries goes beyond religiously, spiritual care needs to be provided by, in addition to chaplains and pastoral care workers, all healthcare professionals offering their therapeutic presence. This kind of care is based on relations between the patient, caring team, and patients' close ones (3). Evidence shows that spiritual counseling improves QoL in patients with HF (112). Spiritual peace along with healthy lifestyle has been shown to predict 5-year mortality better than functional status and comorbidity in people with HF (113).

Advance care planning

Advance care planning (ACP) is a process of preparedness for the decision-making for the future, whereby individuals identify their goals and preferences concerning future care and treatment as well as discuss these goals and preferences with healthcare providers and family (114). It is aimed to ensure medical care the person receives, especially at the end of life, aligns with their preferences (115). During ACP process, the person is invited to reflect her or his personal values and goals, and based on this, to try to foresee what from applicable treatment and care options could be concordant with those values and goals in future, usually in the hypothetical end-of-life situation (116). Open and honest clinical communication helps to get realistic insight in current disease-related situation, the risk of progression, and chances for improvement in case of treatment success but as well for deterioration in case it fails (117, 118). The ACP decisions should be recorded and revised or update if appropriate (119). The outcome of the ACP process can be just being prepared for the moment of decision-making, writing advance directives (AD), sharing the conclusions with family (i.e., advance statement) without preparing any formal document, or asking the treating physician to prepare orders for life-sustaining therapies (Physician Orders for Life-Sustaining Therapies, POLST) (120). The AD can summarize the treatment or care options expected or unwished and/or indicate formal representative who will make medical decisions (surrogate) for the case the person loses decision-making capacity. The appropriate form of expression own will in given country is matter of local law and local traditions (121–123).

The ACP process in people living with HF and COPD should, additionally to general topics like hospital admission, or tube feeding, address disease-specific issues like ventilation, modification of cardiovascular implantable electronic devices (CIEDs), and/or mechanical circulatory support (124). The decision how to proceed with ventricular assist device (VAD) in case of serious advance events like refractory sepsis, cerebral bleeding, or cerebrovascular embolic insult is especially challenging, as most of affected people lose their decision-making capacity in such situations (125).

People with cardiovascular and pulmonary diseases prefer the early initiation of ACP conversations, that is, at the time of diagnosis and at transition points in the follow-up (126, 127). In practice, healthcare providers often initiate ACP process at the advanced stage of illness only (128, 129).

Composition of palliative care team

For the adequate provision of specialized PC services, a qualified multidisciplinary team is required (130). The core team consists of physicians and nurses with specialized training, whereas psychologists, physiotherapists, social workers, and spiritual care workers constitute the extended, multiprofessional PC team. Other important contributors include psychologists, office workers, bereavement counselors, wound management and lymphedema specialists, occupational, art and speech therapists, dietitians, pharmacists, complementary therapists, trainers, and librarians (131). To ensure cohesive continuity of care, all involved including the person living with a disease and her or his family need to create a network (130, 132). Trained volunteers are important members of the therapeutic team, supporting services provided by professionals (133). Close cooperation of cardiology and/or pulmonology team, certified PC nurse, and physician assure achievement of better QoL and symptom relieve in people living with HF and COPD (134, 135).

Organization of palliative care

Every person with needs has a right to get access to PC and pain as well as other symptom relief. To realize this, governments should facilitate integration of PC in healthcare systems and healthcare insurances need to reimburse the service (136, 137). PC can be provided on two levels: PC approach (called as well generic PC) and specialist PC (13). In case of PC approach, all healthcare professionals used to be engaged in the management of the person living with a disease implement basic PC principles in the care they usually provide, in a place the person has been cared for so far (e.g., general hospitals, cardiology or pulmonology units, outpatients clinics, and nursing homes). The specialist PC is provided by healthcare professionals having special training, provision of PC is their main business, this level of care should be provided to people with complex needs, or PC approach has appeared as not enough sufficient. Specialist PC should optimally be served by multiprofessional team, but acceptable can be engagement of physician and nurse with PC expertise cooperating with such a team (138). In many countries, there are also hospital PC support teams, providing an advisory service to hospital staff (139).

Modification of cardiovascular implantable electronic devices activity at the end of life

Growing number of people living with CHF, also those with coexisting COPD, had received one of CIEDs, which, when the end-of-life approaches, can require a special attention to prevent device related suffering and/or providing futile therapies. The family of CIEDs includes antibradycardia pacemakers, cardiac resynchronization therapy (CRT) pacemakers, ICDs, or combination of them (CRT + ICD = CRT-D). They are originally implanted to improve the QoL (antibradycardia pacing and CRT) and/or prevent sudden cardiac death (ICD and CRT-D). Pursuing the main goal of healthcare—assuring the best possible QoL, during the whole life, even its last phase–dying, requires adjustment of all ongoing therapies, including the electrotherapies provided by CIEDs. Modification of CIEDs activities is aimed to prevent unneeded suffering caused by under- or over-treatment. Keeping active the whole devices or their functions that prevent, in unnoticeable for the patient way, bradycardia- or pauses-related symptoms or improve the synchrony of heart contraction, has from a medical perspective never to be questioned. On the contrary, the high voltage antitachycardia therapies (cardioversion/defibrillation), usually painful, and in the dying phase (when the death is not consequence of tachyarrhythmia) futile, should be considered as medically not indicated and discontinued (after receiving patient's consent). Low-voltage antitachycardia pacing, even if adequate and unnoticeable, can prolog the dying, as terminating of tachycardia, even if potentially lethal, cannot save the life of person dying for otherwise end-stage disease (not for arrhythmia). When impending of the death can be anticipated, the sense of device activity must be evaluated and discussed with affected person. If the death cannot be avoided, and the potential arrhythmia is not the cause, but the mode of deaths, terminating it should be considered as prolonging dying, and not saving life (140–142). The deactivation of shocking function should be performed at the end of life, but the communication on this should happen much earlier, optimally even before implantation of CIED. Decision on modification of CIED activity should be integral part of advance care planning (141, 143). Communicating this is regarded by many clinicians as more challenging than withdrawal from other life-sustaining therapies (144). Clinicians should be educated that ICD deactivation is not a form of euthanasia and their decision should be supported by healthcare provider organizations with policies of management of devices with an option of planned device inactivation (140).

Conclusion

Chronic heart failure and COPD are common, often coexist, and cause similar symptoms that cannot be completely alleviated with optimal guidelines driven disease-specific treatment, especially in advanced stages. The persistent symptoms caused by either condition limit the QoL and are a cause of suffering that can potentially be addressed by PC. The PC should be understood as additional layer of care, provided additionally to the disease-specific treatment, but not its alternative, that should be applied always when

the needs emerge, independent of expected length of life/risk of dying. In people affected by HF and COPD, the close cooperation between cardiologists, pneumonologists, palliative medicine specialists, general practitioners, and other specialists, if necessary, is crucial. If the needs are complex or have not been efficiently addressed by multidisciplinary team, the involvement of specialized PC team should be considered.

Author contributions

AK, MB, PS, AW, IP, LP, PJ, and EJ wrote sections of the manuscript. All authors contributed to conception and design of the study, manuscript revision, read, and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A training programme for medical students in providing spiritual care to people with advanced diseases and their loved ones: A case study from the Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland

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Purpose: This article presents the first programme on spiritual care particularly for people with advanced life-limiting illness including heart failure, lung disease or cancer for medical students in Poland implemented at the Collegium Medicum in Bydgoszcz of the Nicolaus Copernicus University in Toruń.

Methods and materials: Several steps were identified for the development of the first programme on spirituality for medical students at the Collegium Medicum in Bydgoszcz including preliminary work on the content of the programme, agreement on key concepts, terms, and definitions; consultations with teachers and review of the literature.

Results: The first Polish spiritual curriculum for medical students was implemented. The spirituality curriculum will potentially contribute to better care for the people with advanced illnesses such as heart failure, chronic lung disease or cancer and improve the quality of relationships between professionals and patients.

Conclusion: The article presents the content of the program, the expected learning objectives and ascribed teaching methods, along with the preliminary evaluation made by students.

KEYWORDS

spiritual care, spiritual curriculum, education on spirituality in medicine, medical students, spiritual needs of people with advanced illness

Introduction

Caring for people with advanced illnesses such as heart failure, chronic lung disease or cancer is a significant challenge for healthcare professionals. Diagnosing patients' needs, preparing treatment plans, and providing support require a deep engagement. The resolution of complex clinical situations may be predicated on the relationship that develops between a professional and a person in need of help. That relationship between a healthcare professional and a patient is particularly challenged through the situation of illness, suffering, or death, which requires intimate knowledge regarding the life history. By promoting an holistic approach to patient care, where one is focused on whole-person caregiving as opposed to a single organ that is failing, the breadth of knowledge of medicine and medical protocols may prove to be insufficient (1). The wider impact of this life-changing event also needs to be considered. Medicine is a field in which the influence of personal, emotional, and spiritual aspects on the course of illness and/or patients' recovery and emotional balance is prominent. Enhanced spiritual care has a favorable effect on survival (2), demonstrates better coping with disease (3), patient satisfaction with treatment and care (4), compliance with treatment (5), greater well—being and quality of life (6–10) as well as reduced anxiety and depression (11–15). Patients are also more able to cope with their disease and have more positive attitude despite their difficult health situation (3, 15). The relationship with quality of life, coping with the disease, and spiritual support received confirm that spirituality is an essential part of human life and patient care (1, 16, 17). Looking at patients holistically sets new standards of treatment, care and support, necessitating healthcare professionals to learn interpersonal skills which include the ability to care for patients' spiritual needs and understand, where possible, their existential quest (18). Such an approach enforces changes in medical curricula to ensure that students receive substantive learning in relation to whole person care. This article presents the first such programme as a curriculum for medical students in Poland. It discusses the development of the "Spirituality in Medicine" programme and its successful implementation at the Collegium Medicum in Bydgoszcz of the Nicolaus Copernicus University in Toruń.

Methods

The "Spirituality in Medicine" Programme supported by the Polish Association for Spiritual Care in Medicine (PASCiM), was launched in 2017 and several focus areas were identified (Figure 1).

Preliminary work on the content of the programme, agreement on key concepts, terms, and definitions

A curriculum capable of meeting the needs of professionals should ideally be founded on a well-defined concept. It was therefore necessary to develop a common definition of spirituality, covering the sphere of human religious experience and practice, existential search and other significant values in human life. Adopting such a construct offered medical students an opportunity to examine the deepest layers of what it means to be human, areas which can provide strength but may also cause a personal struggle. Through this approach it was proposed that it would be easier for them to realize that their patients can suffer not only physically but also spiritually; consequently they are in need of spiritual care and support, which should be an integral part of the treatment process (19).

Two definitions of spirituality were used for the development of the assumptions and plan for the programme. The first was the definition proposed by the European Association for Palliative Care (EAPC) Task Force in 2011 (revised in 2020), who consider "spirituality is the dynamic dimension of human life that relates to the way persons (individual and community) experience, express and/or seek meaning, purpose and transcendence, and the way they connect to the moment, to self, to others, to nature, to the significant and/or the sacred" (revised definition from 2011) (20). The second definition was developed by PASCiM which defines spirituality as a dimension of human life that relates to transcendence and other existentially important values (21, 22). Based on the EAPC approach to spirituality, PASCiM similarly recognizes three dimensions of spiritual experience which include: religiousness of a person, especially his/her relationship with God, personal beliefs, and religious practices, as well as community interaction; existential quest, especially with regard to the meaning of life, suffering, and death, issues of own dignity, personhood, a sense of individual freedom and responsibility, hope and despair, reconciliation and forgiveness, love and joy; values by which a person lives, especially with regard to oneself and others, work, nature, art and culture, ethical and moral choices, and life itself (20–22). These definitions provided the basis for planning the program.

Consultations with international teachers of spirituality in medicine

Another factor that made a significant contribution to the programme's final shape was extensive consultations with

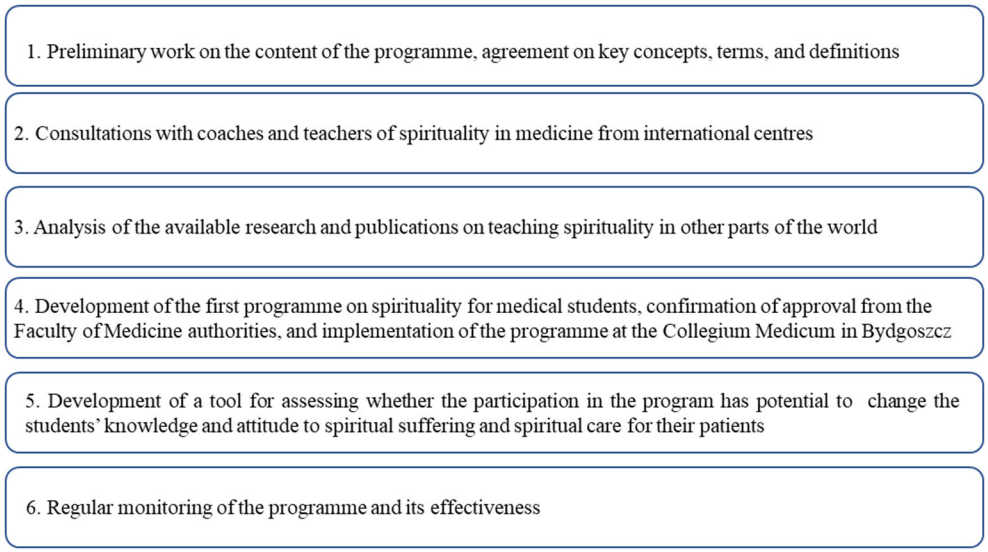

FIGURE 1
Key areas of development of the "Spirituality in Medicine" programme.

international experts in the teaching of spirituality in medicine. Contribution to the development of the curriculum included visits to the University, engagement in workshops and seminars, teaching of medical students and evaluation of content as a basis for the development of a new curriculum. Such exposure to current international examples of spiritual care education enabled a better understanding of which elements and tools were potentially transferable to the Polish context and ensured parity with current international standards.

Analysis of the available research and publications on teaching spirituality

A review of existing international programmes was conducted (23–27). This included an in-depth analysis of the course curricula and teaching methods to underpin the proposed programme. Consequently, ideas were chosen that were not only in line with the adopted definitions but also in compliance with the highest available global standards of spirituality teaching.

Development and implementation of the first programme on spirituality for medical students

The proposed programme as a compulsory course for medical students was approved by the Faculty of Medicine of the Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, and introduced for the first time during the 2018/2019 academic year. It envisaged work with students throughout the subsequent years of studies (i.e., from 2nd to 5th year, a total of 48 teaching hours) (Table 1). In the years 2019/2020 and 2020/2021, the entire programme was implemented over a course of 22 teaching hours for the second-year students. However, from the academic year 2021/2022 it is now taught during the 2nd and 5th years of medical studies (the latter as a part of palliative medicine module) reflecting a change in the general strategy of University. As a result, these developments have created the unique opportunity to monitor and compare the efficacy of different approaches to teaching spirituality to medical students regarding the question if it is better to teach spirituality every year or just at the beginning and at the end of medical studies.

Development of a tool for assessing whether the participation in the program changes the students' knowledge and attitude to spiritual suffering and spiritual care for their patients

It was crucial to assess not only the knowledge of spirituality as acquired by medical students, but also the impact of teaching spirituality on the improvement of their skills and sensitivity in this area, therefore enhancing the students' competences as future doctors. Students were asked to fill in a questionnaire before and after their participation in the programme on spirituality. This structured and standardized psychometric tool

TABLE 1 An outline of the obligatory programme of education in spirituality for medical students at the Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń.

Form	2nd year ($n = 189$)	3rd year ($n = 177$)	4th year ($n = 177$)	5th year ($n = 175$)
Program implemented in 2018/2019				
	Introduction to spirituality in medicine. Basic spiritual care provided by doctors. Specialist spiritual care. Total pain, spiritual pain and suffering. Compassion in clinical practice. Communication and own pathway to be a doctor.	Mindful presence or spirituality in clinical practice. Diagnosing spiritual needs. Non–violent communication.	Helping family to say goodbye to loved one who is dying alone in hospital from COVID-19. Spiritual care for the patient with COVID-19. Spiritual care from the perspective of psychologist. Cooperation with the chaplain. Dignity Therapy. How doctor can support his/her patient.	Developing hospital program on spiritual care. Helping find meaning. Communication about spirituality.
Lectures	4	4	-	-
Seminars	4	4	8	4
Workshops	4	4	4	8
Program implemented in 2019/2020 and 2020/2021				
Form	2nd year (in 2019/2020: $n = 266$; in 2020/2021: $n = 263$) Introduction to spirituality in medicine. Basic spiritual care provided by doctors and specialist spiritual care. Hospital programs dedicated to spiritual care. Diagnosing spiritual needs. Dealing with hope. Compassion in clinical practice or spiritual care in clinical practice. Clinical case—spiritual care in psychiatry. Dignity Therapy. Non–violent communication.			
Lectures	10			
Seminars	6			
Workshops	6			
Program implemented since 2021/2022				
Form	2nd year(as "Spiritual care") ($n = 216$) Introduction to spirituality in medicine. Basic spiritual care provided by doctors. Hospital programs dedicated to spiritual care. Healing in medicine. Diagnosing spiritual needs. Compassion in clinical practice. Communication about spirituality. Cooperation with healthcare chaplain.		5th year (spiritual care as the part of palliative medicine module) Interventions for spiritual distress: dignity therapy and helping find meaning. Communication about spirituality. Mindful presence	
Lectures	4		-	
Seminars	-		6	
Workshops	6		6	

n, number of students participating in the programme.

Spiritual Support Scale (SpSup) Scale have been described elsewhere (28).

Regular monitoring of the program and its effectiveness

In addition to the SpSup Scale, two other tools have been applied to evaluate the classes:

1. A questionnaire for the evaluation of the program at the end of their course, consisting of three open questions (what was the most useful? what was the least useful? what do I propose to change or include?).
2. Qualitative interviews conducted with a sample of students' of each class by open invitation. Interviews were conducted at the end of the course, were anonymous and voluntary. Participants were asked to consider the following five questions:

- What do you think about the spirituality classes in which you participated?
- What is the meaning of the spirituality classes to you as a future doctor as well as in your own life?
- What advantages and disadvantages could you see in the spirituality program (what subjects were not discussed enough and which ones should be excluded)?
- In what way has the spirituality curriculum changed your view on spirituality?
- Is this sphere important to you in own life and your work with people who are ill? In what way?

The interviews lasted about 30–45 min and were recorded with the agreement of the participants.

Results

The overarching aim of our "Spirituality in Medicine" program was to provide medical students with knowledge about spirituality (as defined above) and improve their competences in this area. The subjects taught during the classes as well as the expected learning outcomes correspond to the following objectives:

- To learn about spirituality as defined in the program and how to refer this knowledge to one's own experiences, beliefs, and values;
- To learn about compassion in the context of spiritual care as a key aspect of interpersonal skills;
- To gain competence in diagnosing patients' spiritual needs and suffering;
- To learn how to provide help and spiritual support corresponding to the spiritual needs reported by patients (e.g., non-aggressive communication, interpersonal communication, mindful listening);
- To learn the necessary methods, techniques, and research tools to diagnose patients' spiritual needs and suffering;
- To learn about possible therapeutic methods that can be used when providing spiritual care to patients;
- To be able to cooperate—as a physician—with a chaplain;
- To learn how to help patients examine their lives, find a meaning and leave a spiritual legacy (e.g., elements of dignity therapy) (29).

Table 1 provides a general outline of the program, highlighting in particular:

- The academic year for which a given module was intended;
- Topics to be discussed during the classes;
- The expected learning outcomes.

In our classes, all students of each year participated in mandatory lectures and workshops (Table 1).

Regardless of the number of teaching hours allocated to this subject, we wanted students to have the opportunity to gain similar knowledge and skills in core aspects of spiritual care and spirituality. The amount of material covered varied depending on the time available for the respective thematic block.

In order to achieve the intended aims and objectives and ensure expected learning outcomes, a number of teaching methods were proposed and have since been implemented during the classes. The most important of these are thematic lectures, as well as seminars and workshops.

Other techniques employed during the classes were as follows.

- **Excerpts from films, case studies, stories** - Using various aids related to topics covered during the classes to apply the newly acquired knowledge and skills to concrete examples.
- **Role play, psychodrama** - To practice new skills.
- **Students sharing their own experiences** - In order to analyse their own emotions and experiences and thus better understand themselves while also highlighting possible reactions as well as the spiritual needs, suffering, and experiences of patients.
- **Interactive discussion** - Addressing problems faced during the classes after watching a film or studying a case.
- **Students' own work based on case study presentation** - Writing papers focused on the specific case study, including proposed spiritual interventions and techniques to be implemented.
- **Students sharing their experiences from practice** - Based on direct contacts with patient.

The initial analyses of the interviews show that our classes were initially approached with reserve and reluctance. At the beginning, some students thought that the main aim of the programme was to "convert" them or "discuss religion". They had doubts about whether it really should be part of "a doctor's work". However, as the course progressed, they started to appreciate the variety of topics covered. With time they changed their minds and evaluated the course positively. Interviewees clearly expressed their appreciation for the newly acquired skills. They also found valuable that the classes presented them with different methods of diagnosing spiritual needs or suffering, conducting an intervention, and providing support.

The interviews with students participating in the classes indicate that students particularly enjoyed working on case studies and discussions based on films that dealt with the topics taught during the classes. Indeed, there was a belief that most of the issues covered during the course would prove useful in their future work, particularly in the case of students who plan to work with chronic disease patients.

Although we invited all students, who participated in the classes, only 5 agreed to be interviewed. However, qualitative research samples are usually small and sufficient data saturation was achieved with this number of interviews (30).

Discussion

This is the first compulsory spiritual care programme offered in a medical school in Poland. Teaching future physicians how to engage with spiritual care is essential for the development of whole person care medicine (19, 23, 26). Physicians are not only "technically-competent" specialists in the specific branches of medicine, but compassionate persons accompanying other persons who are suffering, searching for the meaning, real hope, forgiveness, or closeness to God and/or other people (23).

How physicians builds the relationship with patients depends on a blend of professional knowledge, communication, compassionate presence and understanding of the experience of illness and suffering. To enable this, medical curricula should be directed toward improvement of skills and competences needed to address spiritual care (31), the aim of this first spiritual care in medicine program in Poland.

The aims and objectives of our program cited earlier are similar to those defined for the educational programs introduced at medical universities in United States, South America, United Kingdom and some other European countries (24–27, 31–39). These different spirituality curricula are generally focused on improving the student mindfulness, compassion and empathy, careful listening and communication on what is integral to the person, what he/she believes in, and hopes for. These also frame the starting point for the Polish curriculum (24, 26, 40).

Programs concentrating on improving the ability to perform spiritual care are usually based on case discussions, real patient history taking or self-reflective journaling (27). These complement the structured clinical knowledge achieved in a medical degree and are an important component of holistic mastery in clinical medicine. Thus, education on spirituality should be at least partially included during the clinical years of studying medicine. As we monitor the efficacy of teaching spirituality to medical students, we hope in the near future to assess whether it is better to teach spirituality every year, only at the beginning or just at the beginning and at the end of medical studies.

A recent systematic review of international medical school and residency program curricula that address spiritual care pointed also to some other core content not included in our current curriculum, such as chaplain shadowing, OSCE (Objective Structured Clinical Examination), simulated patients or spirituality dinners (27).

To date, the program on spirituality in medicine as a curriculum is provided only in one medical university in Poland. Future analysis of its effects on students' attitude and practice would help to determine the relevance of such education.

Conclusions

Working with patients, particularly those with advanced illnesses such as heart failure, chronic lung disease or cancer at the end of life, reveals how patients develop an intrinsic curiosity in their life situation, show interest in their medical and human needs, and seek compassion. Patient wish to derive some meaning to their experience. They seek answers and have a need to talk about that experience, even if difficult or challenging for them.

The proposed programme of teaching spirituality to future doctors is the first educational project of this type in Poland. It is our hope that this new curriculum will equip future doctors to respond sensitively and appropriately to the complex questions raised by illness, frailty and death.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of the Collegium Medicum in Bydgoszcz of Nicolaus Copernicus University in Toruń, Poland (KB 736/2018). In accordance with the local legislation and institutional requirements, written informed consent was not required for the anonymous survey among students.

Author contributions

MF-K and MK contributed to the creation and development of the program along to the process of its implementation and monitoring. PL and RG contributed to the preliminary work on the content of the program. MF-K was responsible for the critical analysis of the literature on teaching spirituality in other parts of the world and for drafting the first version of the manuscript. MK was a coordinator of the program in the University. All authors were involved in critical analysis, interpretation of the study results, and preparation of the final version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Regular, low-dose methadone for reducing breathlessness in people experiencing or at risk of neurotoxic effects from morphine: A single-center case series

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Breathlessness is a common symptom suffered by people living with advanced malignant and non-malignant diseases, one which significantly limits their quality of life. If it emerges at minimal exertion, despite the maximal, guidelines-directed, disease-specific therapies, it should be considered persistent and obliges clinicians to prescribe symptomatic, non-pharmacological, and pharmacological treatment to alleviate it. Opioids are recommended for the symptomatic treatment of persistent breathlessness, with morphine most extensively studied for this indication. It is extensively metabolized in the liver into water-soluble 3- and 6-glucuronides, excreted by the kidneys. In the case of advanced renal failure, the glucuronides accumulate, mainly responsible for toxicity 3-glucuronides. Some people, predominantly those with advanced renal failure, develop neurotoxic effects after chronic morphine, even when prescribed at a very low dose. A single-center case series of consecutive patients experiencing neurotoxic effects after long-term, low-dose morphine or at risk of such effects were transferred to methadone to avoid the accumulation of neurotoxic metabolites. Over the course of 4.5 years, 26 patients have been treated with methadone in the median dose of 3.0 mg/24 h p.o., for persisting breathlessness. Sixteen of them had been treated previously with an opioid (usually morphine) at the median dose of 7.0 mg/24 h (morphine oral daily dose equivalent). They were transferred to methadone, with the median dose of 3.0 mg/24 h orally (methadone oral daily dose equivalent), and the median morphine-to-methadone dose ratio was 2.5:1. All patients experienced a meaningful improvement in breathlessness intensity after methadone, by a median of 5 points (range 1–8) on the 0–10 numerical rating scale (NRS) in the whole group, and by 2 points (range 0–8) in those pretreated with

other opioids, mainly morphine. Low-dose methadone can be considered an efficient alternative to morphine for reducing breathlessness in people experiencing neurotoxic effects or at risk of developing them following treatment with morphine.

KEYWORDS

breathlessness, opioids, palliative management, heart failure, morphine, methadone

Introduction

Breathlessness is a common symptom in advanced malignant and non-malignant life-limiting illnesses. It affects up to 98% of people living with advanced chronic obstructive pulmonary disease (COPD), 88% of those living with advanced heart failure (HF), and 77% of people with advanced cancer (1, 2). In HF, it is so ubiquitous that is considered its hallmark symptom (2, 3). The threshold of exercise evoking breathlessness decreases in parallel to the severity of HF. In the most advanced stages, breathlessness is present with minimal exertion (like speaking, eating, or toileting) or even at rest. It is depicted in the most used classification of staging HF, the New York Heart Association (NYHA) classification. Similarly in COPD, breathlessness is one of the main factors determining its progression accordingly to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification (4, 5).

When recognizing new or worsening breathlessness, actively seeking condition(s) that evoke or worsen, it is mandatory (6). Reversible conditions need to be sought actively and treated as effectively as possible. If severe breathlessness persists despite optimal treatment of all underlying conditions, symptomatic non-pharmacological and pharmacological management should be considered (7, 8).

Opioids are the recommended pharmacological therapy for the symptomatic reduction of persisting breathlessness in cancer (9), COPD (10), and HF (3, 11). Morphine is the most studied opioid; hydromorphone, diamorphine, codeine, fentanyl, and buprenorphine have been studied much less frequently for the symptomatic reduction of breathlessness. Fear of potential side effects of opioids (non-respiratory: drowsiness, sedation, impaired cognition, nausea, constipation, immunosuppression, and suppression of testosterone) and respiratory effects (respiratory depression and respiratory failure) limit their prescription, even if they are clinically indicated. Most participants in controlled clinical trials have been prescribed sustained-release morphine. Persisting breathlessness is a registered indication in Australia for sustained-release morphine commencing at 10 mg/24 h with the ability to titrate this by 10 mg/24 h weekly up to a maximum 30 mg/24 h. In most countries, the lowest possible sustained-release morphine dose is 20 mg/24 h (12–14).

The limitation in prescribing morphine is the risk of accumulation, primarily its neurotoxic metabolite [morphine-3-glucuronide (M3G)] in the case of renal insufficiency (15, 16). Regular morphine should be used more cautiously if the glomerular filtration rate is very low (17, 18). Hydromorphone, commonly suggested as an alternative to morphine in this situation, undergoes similar metabolism to morphine [to hydromorphone-3-glucuronide (H3G)], which can accumulate in severe renal impairment, encountering the same risk of neurotoxicity as M3G, and thus should be used with increased caution (16, 17, 19). The risk of neurotoxicity from opioids in people with advanced conditions is probably more common than identified, as impaired renal function is commonly seen in people with advanced disease, especially in advanced HF (20, 21). For this reason, clinicians prescribing opioids should be aware of the possibility of neurotoxic side effects, even if the doses are low. Fentanyl is sometimes suggested for breathlessness management, but the effect of transmucosal fentanyl is very short (about 1 h), making it unsuitable for the management of chronic breathlessness. In this consecutive case series, a bedside decision was made to prescribe methadone for those patients suffering from chronic breathlessness.

Methadone, in the case of renal failure, also accumulates but does not have neurotoxic metabolites, so reduction of doses (to 50–75%), prolonging the intervals between doses, and careful monitoring of effects should be sufficient to prevent overdose (22). Methadone can be prescribed by oral, sublingual, intravenous, subcutaneous, intramuscular, or rectal routes. In people who cannot swallow, sublingual methadone can be especially useful, with a quick onset of action (23).

The aim of this consecutive case series was to describe the effect of methadone on persisting breathlessness in people experiencing unacceptable side effects, or at risk, from other opioids mainly morphine.

Methods

This article presents a retrospective analysis of medical records of consecutive patients hospitalized in a single palliative care unit in a district hospital in Switzerland, who experienced neurotoxic effects after small doses of morphine

prescribed for breathlessness management, due to severe renal failure (stage 4 or 5 according to Kidney Disease Improving Global Outcomes (KDIGO) classification) or at risk of such effects. After the indications for symptomatic breathlessness management had been verified, all other opioids were discontinued (if a patient was not opioid naïve), and the intensity of breathlessness was regularly assessed. Patients who were able to take medicines orally received 1 mg methadone s.l., and then twice daily if needed. If the patient experienced a satisfactory reduction in breathlessness, the planned dose was delayed or omitted. If needed, an additional dose was allowed at least 3 h after the last methadone dose. After 3–4 days, the total daily dose was calculated, based on the mean daily dose in the previous 48 h, and usually prescribed every 12 h.

Results

From September 2017 to February 2022, 26 consecutive patients were included (14 women and 12 men), median age of 73.5 years (range 55–94). Eighteen patients had cancer, seven had advanced chronic obstructive pulmonary disease (COPD) with a median GOLD score of 3 (of whom four also had cancer), two people predominantly had heart failure, and two people had amyotrophic lateral sclerosis (ALS). Fifteen people used oxygen therapy through nasal prongs (median 2 L/min), with a median pulse oximetry of 94%, generating similar measures to patients not on oxygen (94%). Patients with ALS were treated with non-invasive positive pressure ventilation (servo-ventilation), one during the night hours only, the other progressively until continuous ventilation was required in the time directly preceding her death. The median glomerular filtration rate (GFR) in the whole group was 61 ml/min/1.73 m^2 body surface area (BSA), but in 5 people the GFR was under 30 ml/min/1.73 m^2 BSA (range 16–27). The detailed patient characteristics are depicted in **Supplementary Table 1**.

All patients were informed that methadone treatment for the symptomatic reduction of persisting breathlessness is not standard therapy. All agreed to try this approach; however, one person [ultimately the person with the longest period of opioid treatment (550 days)] was originally hesitant to start taking opioids, as she did not consider herself as dying. Eighteen patients died during hospitalization, one was discharged and seen in an ambulatory capacity (this person, under supervision of the general practitioner, gradually lowered the dose and finally discontinued methadone after 550 days of treatment, due to the improvement of exercise tolerance after breathlessness had been alleviated), and seven patients were discharged from the palliative care unit alive and not followed up as the study was a retrospective analysis of medical records, not a clinical study.

Breathlessness assessment

The breathless burden was assessed using the modified Medical Research Council (mMRC) classification and the intensity using a 0–10 Numerical Rating Scale (NRS). Before starting the opioids, the breathlessness median grade was 4 according to mMRC (range 2–4; two people with grade 2; nine with grade 3, and 14 with grade 4), the median intensity was 8 NRS (range 5–10). One person experiencing breathlessness at rest was unable to describe its intensity and in the records of another person, mMRC and NRS assessments were missing with only the narrative information about the improvement of breathlessness documented.

Sixteen of the 26 people had already been on an opioid for persisting breathlessness: (morphine—14 people, morphine then oxycodone—1 person, and hydromorphone—1 person).

All included in this analysis reported improvements under methadone in breathlessness—by mMRC grade median from 4 (range 2–4) to median 3 (range 2–4), and the median difference was 1 (range 0–3). NRS scores shifted from a median 8 (range 5–10) to 3 (range 2–7), with a median difference of 5 (range 1–8) vs. pretreatment.

After starting methadone (9 people methadone was prescribed *de novo* and 1 person received only one rescue dose of morphine and was perceived as opioid naive), the median mMRC grade was 3 (range 2–4) in the whole population, 2 (range 2–4) in those who had been pretreated with another opioid, and 3 (range 3–4) in those who were put directly on methadone. The median NRS when prescribed methadone was 3 (range 1–6) in all groups.

The median time on methadone was 21 days (range 3–550).

Two to three days after starting methadone, two people reported breathlessness at rest (mMRC grade 4), 11—mMRC grade 3, and 10—mMRC grade 2. For one patient, breathlessness was not experienced at rest, but more detailed grading was not possible as he was completely bedbound, and in the case of two others, only descriptive data were available from the notes.

Dosing of opioids

The median dose when pre-treated with opioids expressed as morphine oral daily dose equivalent was 7 mg/(range 2.5–23). The median steady-state methadone oral daily dose was 3 mg (range 0.5–9.5). The median dose ratio between morphine and methadone after reaching stable improvement (72 h after final dose adjustment) was 2.5 (interquartile range 1.9–4, and data of one patient transferred from a very high-dose hydromorphone prescribed predominantly for pain management, calculated as morphine oral daily dose equivalence 180 mg has been omitted from all calculations).

Illustrative cases

Patient #1 developed hallucinations and drowsiness that lasted about 36 h after a single dose of 5 mg intermediate-release (IR) oxycodone. The breathlessness alleviation was shorter than the duration of hallucination (about18–24 h). After hospital admission, oral oxycodone was rotated to morphine and administered subcutaneously in a syringe driver starting with 5 mg/24 h without any neurotoxic effects but with some improvement in breathlessness. The dose needed to be escalated gradually to 10 mg s.c./24 h. With this dose, drowsiness (but not hallucinations) became evident. The patient was rotated to an i.v. infusion of methadone, and the dose was gradually titrated to 5 mg/24 h (calculated as 6 mg methadone oral daily dose equivalent) with significant improvement of consciousness and satisfactory breathlessness improvement. To optimize symptom control, the dose was gradually increased to 8 mg i.v. (oral dose equivalence 9.5 mg) without causing relevant sedation or hallucinations.

Patient #6 with breathlessness caused by alveolar hypoventilation secondary to ALS had occasionally tried in the past to use 1 mg intermediate-release morphine orally up to maximum of 3 times per day. It always changed the character of breathlessness at rest from air hunger to qualitatively very different thoracic and neck rigidity disturbing breathing, being a little less distressing than the original breathlessness. Starting 1 mg methadone, once daily orally, alleviated the breathlessness successfully without causing the unpleasant effect of muscle stiffness. The effect remained stable for several months. Occasionally, the patient requested a pause in the administration of methadone, to make sure its continuation was still needed. Breathlessness relapsed every time within 2–3 days and settled as methadone was restarted. This pattern lasted for several months until death.

Patient #8 had oxygen-dependent, severe COPD with persisting breathlessness, which was well-controlled for 7 months on morphine 8 mg/24 h (oral IR solution—2 mg every 6 h). The person developed hallucinations (the cause of an emergency room presentation) likely caused by morphine metabolites accumulation secondary to acute renal failure. After rehydration and discontinuation of morphine, the hallucinations disappeared, but breathlessness reappeared after 18–24 h. Because the breathlessness reappeared before the normalization of renal function and the patient declined continued morphine (due to the experience of the hallucinations), oral methadone was commenced (1 mg every 12 h) providing good relief from breathlessness, with the benefit lasting more than 10 months at that dose. With methadone, the patient was able to gradually increase her exercise capacity while still relying on around-the-clock oxygen therapy and walking aids.

Patient #20 with lung cancer and a malignant pleural effusion treated with drainage reported increasing tiredness preventing dose escalation after starting morphine IR 2 mg every 6 h. Breathlessness NRS scores had dropped from 7 to 4. The introduction of 2 mg methadone per day (escalated to 3 mg) generated quantitative and qualitative improvements in breathlessness. Two weeks after methadone was introduced, hospital admission was required due to the worsening of breathlessness and deterioration of the general condition. He died 1 week after breathlessness alleviation was reached with a methadone dose escalation to 10 mg.

Discussion

Breathlessness is a common symptom in people living with advanced diseases, both in malignant and non-malignant life-limiting illnesses. If it remains severe despite optimal disease-specific treatment, it should be considered "persisting" and oblige clinicians to initiate symptomatic management, consisting of non-pharmacological interventions and pharmacological treatment mainly by regular, low-dose opioids, particularly morphine (9, 12, 14). Morphine is extensively and rapidly metabolized in the liver, especially after oral administration, to morphine-6-glucuronide (M6G) considered as main metabolite responsible for pharmacologically desired effects, and M3G perceived as probably responsible for adverse, neurotoxic effects. M3G is more likely to accumulate in severe renal failure. For this reason, opioids that do not have potentially harmful metabolites that can be used in this population are relevant. In this consecutive case series of 26 patients who experienced or were at risk of neurotoxicity from other opioids, all were successfully treated with methadone in a single Swiss center over a 4.5-year course.

All treated patients experienced clinically meaningful improvements in breathlessness intensity after methadone administration by a median of 5 (range 1–8) in the whole group in comparison to pretreatment (change from median 8 to median 3 points) on the NRS. Those who were pretreated with another opioid experienced further reductions in breathlessness in comparison to change after morphine by a median of 2 (range 0–8; from median to median 2.5) points on the NRS. The median improvement of breathlessness after morphine in comparison to pretreatment was 3 points on the NRS (range 0–7 points). According to mMRC after starting methadone, the median improvement reached 1 point (range 0–3) for methadone vs. pre-treatment in the whole group, 1 point (range 0–2) vs. pretreatment in those directly commenced on methadone, and further reductions in breathlessness in comparison to change under morphine by 1 point (range 0–2). The current study outlines the improvement of breathlessness after methadone even in people who had experienced symptomatic benefits from a previous opioid (10, 12, 14). The absorption of methadone

from oral mucosa allowed convenient administration of single drops, even in unconscious patients. No one reported neurotoxic effects. One person required a dose reduction to 0.5 mg methadone daily due to slight sedation.

The median methadone oral daily dose equivalence needed for stable symptom management was 3 mg (range 0.5–9.5). For those who were previously treated with other opioids (n = 16), mainly morphine, the median morphine oral daily dose equivalence was 7 mg. The median of the dose ratio between morphine and methadone was 2.5:1 (interquartile range 1.9–4), a little less than described by other authors (24). It can be hypothesized that patients in our study were treated with a little higher than equipotent dose of opioids. Despite this, they reported better management of breathlessness from methadone, both quantitatively and qualitatively, including a few patients who ceased taking morphine and commenced course methadone. That could mean slightly different receptor affinities of opioids are targeted.

Limitations

This is a retrospective record analysis of patients treated in a single center. All non-randomized and non-blinded studies bear considerable risks of bias, and any causative relationship of pharmacological interventions with clinical outcomes needs to be interpreted with caution.

Conclusion

Low-dose methadone can be considered as an alternative to other opioids, for breathlessness management, in those who experience neurotoxic effects after other opioids, or those at risk of such effects (due to *severe* renal failure), although this hypothesis requires further exploration. Variations in its half-life make it more challenging to titrate, and this needs to be done on a case-by-case basis. Further studies are needed to verify these preliminary findings.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

PS chaired the Palliative Care Department, where the case series has been recruited. The design of the retrospective analysis, a draft of the manuscript, presentation of data, and interpretation of data have been developed by both authors. Both authors agreed the final version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.925787/full#supplementary-material

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Spirituality in people with advanced chronic obstructive pulmonary disease – challenge for more effective interventions, support, and healthcare education: Mini-review

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More recently there has been a growing interest in spirituality in medicine, especially in the field of palliative care, oncology, intensive care, and cardiology. However, according to literature, it seems to be a limited number of researches on how healthcare professionals should provide spiritual care (SC) for people with non-malignant lung diseases and what kind of education for them enables them to do it efficiently. This mini-review aims to provide an overview of current knowledge of an area of spirituality and SC for people with advanced chronic obstructive pulmonary disease, including spiritual well-being and religious/spiritual coping, their relations with the quality of life and symptom burden, exercise capacity and daily functioning, mental health, or medication adherence. It also analyses the use of interventions to meet patients' spiritual needs and patients' expectations regarding SC provided by professional careers. Based on the literature authors try to show the fields that should be improved and proposed future research directions.

KEYWORDS

spirituality, religiosity, spiritual well-being, religious/spiritual coping, interventions, chronic obstructive pulmonary disease, COPD

Introduction

One of the dimensions of growing significance in modern medicine is a holistic approach to patient care with the recognition of the central place of spirituality in a person's life (1, 2).

According to European Association for Palliative Care (EAPC) and Polish Association for Spiritual Care in Medicine (PASCiM), spirituality is multidimensional and includes religiousness of a person, existential quests, and value-based considerations (3–5). The evidence shows a favorable impact of higher level of religiosity/spirituality or greater spiritual well-being (SWB) on survival (6), coping with disease (7), patient's satisfaction with treatment and care (8), less depression (9), lower anxiety (10), or better resilience (11). Thus, besides palliative care, spiritual care (SC) has started to be recognized as an integral part of care especially for people with cancer (12), heart failure (13), or admitted to an intensive care unit (14). Much less is known about spirituality in patients with advanced chronic lung diseases even though they usually suffer from breathlessness, cough, fatigue, fears of suffocation, numerous social limitations, anxiety, and depression every day (15, 16).

The purpose of this mini-review is to provide a comprehensive analysis of the current knowledge on the role of spirituality in people with advanced chronic obstructive pulmonary disease (COPD) and to propose future research directions and potential role of SC for these patients.

Spiritual well-being of individuals with COPD

Spiritual well-being of individuals with COPD has been evaluated in a number of studies (17–24) (**Table 1**). It was found to be similarly low among people with COPD and with inoperable lung cancer (18). SWB was higher in patients with mild airflow limitation, experiencing fewer COPD exacerbations and black individuals, and lower in those with more symptom burden, physical impairment and poor mental health as well as current smokers (18, 20, 21, 24). Also patients with advanced pulmonary diseases (50% with COPD) on a waiting list for a lung transplantation presented a higher SWB as compared to patients not considered for a lung transplant (22). In COPD patients with a moderate level of SWB, the religious component was shown to have more significant contribution than the existential one (17). In a longitudinal study, SWB remained relatively stable over time (median 15 months) in people with advanced congestive heart failure (CHF) and COPD (18).

Religious/spiritual coping in patients with COPD

Chronic obstructive pulmonary disease patients mostly use positive religious coping (RC), such as seeking God's love and care, looking for control through a partnership with God, benevolent religious reappraisal, and asking forgiveness for sins (19, 24–28). However, they also use negative RC such as questioning God's love and punishing God's reappraisal more often than healthy individuals (19, 25, 26). Some factors such as sex or nationality and culture are important. Women were shown to present a higher positive RC than men (27). Dutch patients who reported at least a little faith in God or a spiritual power employ positive RC more often than non-believers (19). However, Brazilians applied more positive and less negative RC as compared to Dutch patients (29). Praying, support within the religious community, church attendence, sign of the cross, and icons of saints were helpful in coping with the burden of the disease among the Greek (30) and more than half of Polish COPD patients (31). Also religious/spiritual ceremonies give patients some hope and a sense of meaning while dealing with an illness. Those who are regular churchgoers ask for God's help and try to find spiritual support and a church is a safe place for them (30).

More than a half of Polish patients believed that God had a plan for their lives and would not allow illness without a reason (31). Some patients with COPD experience also guilt because of smoking before illness and to deal with it use different strategies such as active or passive acceptance (32). Some had to face helplessness (33). Both emotions exert the impact on patients' daily life and coping with an illness. Self-blame appeared to intensify feelings of helplessness and passive resignation, as well as poor self-management (33). For patients who focused on faith in God, church and family provided a more positive effect and existed alongside helplessness. They did not experience self-blame but they articulated strongly held beliefs in God, the Church and family and repeatedly reported those to be the most important things that helped them live with their illness (33).

Spiritual well-being and quality of life of COPD patients

A number of studies demonstrated positive associations between SWB and quality of life (QoL) and more varied outcomes relating to associations between religiosity and QoL in COPD patients (17–19, 22, 24, 29, 34). A high sense of spirituality was shown to correlate with lower stress and higher QoL (34). Total SWB measured by FACIT-Sp-12 was positively associated with emotional function and mastery evaluated by Chronic Respiratory Disease Questionnaire (CRQ), while two SWB domains: meaning and peace with total scores of CRQ (24). Faith domain of SWB of FACIT-Sp-12 and

religiosity measured with a Duke Religion Index (DUREL) was not associated with QoL in this study (24). Similar results were reported by other authors (22), while according to others, faith subscale of FACIT-Sp score positively correlated with the scores of Multidimensional Index of Life Quality (MILQ) (18). Also increased religiosity measured with the three components of DUREL (organizational religiosity, ORA; non-organizational religiosity, NORA; and intrinsic religiosity, IR) was associated with a better QoL of COPD patients (29). Individuals having at least a little faith in God had a higher QoL compared to individuals with beliefs in a spiritual power only (19). Individuals with higher SWB as well as religious well-being reported higher satisfaction with the treatment, one of health-related QOL domains measured using the Seattle Obstructive Lung Disease Questionnaire (SOLDQ) (17). QoL of COPD patients was also shown to be associated with strategies of coping with the disease. Higher negative RC was correlated with worse QoL (19, 24, 29), while positive RC associated with a better QoL of COPD patients (29). Furthermore, positive RC positively and negative RC inversely correlated with patients' satisfaction with life (28).

Spiritual well-being and symptom burden in COPD patients

The relationship between spirituality and RC and symptom burden in COPD patients were investigated in a number of publications (18, 20–22, 24–27, 34). SWB and its "peace" domain measured using FACIT-Sp-12 were demonstrated to be negatively correlated with symptom distress/burden measured using the Memorial Symptom Assessment Scale-Global Distress or the COPD Assessment Test (CAT) (18, 21, 24). Although not all (34), some studies show a negative association between SWB and religiosity and dyspnea (20, 24, 35). Patients who experience more breathlessness assessed by the modified Medical Research Council (mMRC $\geq$ 2) presented lower levels of SWB (20). A higher score on the "peace" domain of FACIT-Sp-12 was negatively associated with breathlessness (total, affective, and physical components) measured by Dyspnoea-12. The total score of FACIT-Sp-12 was inversely correlated with the affective component of dyspnea. A higher level of the total and affective component of dyspnea was also demonstrated in individuals presenting more negative RC (24).

Higher SWB was also associated with less anxiety and depression in COPD individuals (24, 36). Total scores of FACIT-Sp-12 as well as "peace" and "meaning" domains were negatively correlated with anxiety (24). Moreover, total scores and scores for all three domains of FACIT-Sp-12 ("peace," "meaning," and "faith") as well as IR were negatively associated with depression (24). Also, individuals who utilize more negative RC showed more anxiety (24) and depressive symptoms (24, 26, 27).

TABLE 1 Benefits and impacts of spirituality among patients with COPD according to the literature.

Main findings
Spiritual well-being
SWB is comparably low in people with advanced COPD and inoperable lung cancer (20).
SWB is lower in COPD patients with higher symptom burden, poor mental state, with more disease exacerbations and in current smokers (18, 20, 21, 24).
SWB is higher in individuals waiting for a lung transplantation (22).
Religious/spiritual coping in disease
COPD patients mostly use positive RC, such as seeking God's love and care and asking forgiveness for sins. They, however, employ negative RC, such as questioning God's love and punishing God reappraisal, more often than healthy individuals (19, 24–28).
Spiritual well-being and quality of life
High sense of spirituality correlates with lower stress and higher QoL (34).
Higher negative RC correlate with worse QoL, while positive RC are associated with a better QoL (19, 24, 29).
Spiritual well-being and symptom burden
SWB negatively correlates with symptom distress/burden (18, 21, 24)
Patients who present a higher level spirituality and SWB may experience less dyspnea, fewer symptoms of anxiety and depression (20, 24, 35).
Individuals who utilize more negative RC show more dyspnea, anxiety and depressive symptoms (24, 26, 27).
Spirituality, exercise capacity, daily functioning and pulmonary function
Patients with higher SWB show better resilience, self-management and medication adherence (21, 23)
Interventions to improve spiritual well-being
At hospital daily visits of chaplains may decrease anxiety, shorten length of hospital stay and increase satisfaction with quality of care (40). At home clergy-laity support is related to the benefit to patients' mental health (41).
Pulmonary rehabilitation (PR) promotes improvement in anxiety, depression, dyspnea, exercise capacity and QoL. It increases ORA, positive RC and decreases negative RC (37).
Dignity Therapy may have positive impact on well-being of patients with advanced COPD with a short life prognosis. It may help them to identify and meet their spiritual needs (42)
Patients' expectations regarding spiritual care provided by professional carers
Almost all and almost half of patients who declare to have or not to have religious and spiritual beliefs, respectively, agree that physicians should ask patients about their beliefs when they become gravely ill (43). Physicians rarely discuss spiritual/religious issues with their patients even at their end-of-life (47). Two thirds of patients state that their trust in a physician would increase if he/she asked them about spiritual matters (43)

QOL, quality of life; SWB, spiritual well-being; ORA, organizational religiosity; RC, religious coping.

Interpreting the lung disease as punishment from God was the strongest predictor of trait anxiety, depression, and psychosocial disability (25).

Spirituality and faith have been shown to prevent depression, suicidal thoughts, and improve hope and dignity (15). Religious beliefs and spiritual activities were associated with less severe illness and fewer prior psychiatric problems (35). People with CHF and chronic pulmonary disease who prayed or studied the Bible daily or more often were less likely to report prior psychiatric problems (35).

Spirituality, exercise capacity, daily functioning, and pulmonary function of COPD patients

Associations between levels of spiritual and religious well-being, RC and physical capacity of COPD patients have so far been understudied (17, 18, 22, 24, 27, 29, 37). Religious activities and intrinsic religious attitudes were inversely related to the severity of the medical illness, physical disability, or perceived shortness of breath, while religious activities (especially religious attendance) were associated with greater social support (35). Physical impairment measured with the Sickness Impact Profile (SIP) in patients with COPD and CHF negatively correlated with SWB (18). A higher score on "peace" domain of FACIT-Sp-12 was found to be associated with a better exercise capacity measured using the 6-min walk test (6MWT) in individuals waiting for lung transplantation (22). The distance covered in 6MWT was strongly inversely associated with negative RC in individuals with moderate and severe COPD (27). Other publications presented negative or no associations between spirituality/religiosity and patients' functioning (17, 24, 29). For example, Silva et al. found negative correlation between religious well-being assessed as a component of SWB and physical functioning in a sample of COPD patients with severely compromised physical function (17). Of note, no association between physical function and the total score of SWB and the score of its existential component was found in this study. Also, increased religiosity and increased positive RC were shown to be associated with shorter distance covered (6MWT) in COPD patients from Brazil and the Netherlands (29).

Importantly, in a study by Chen et al., the authors found positive correlations between SWB and resilience as well as four dimensions of patients' self-management (symptom management, daily life management, emotion management, and self-efficacy) (23). COPD patients with higher SWB showed better medication adherence (21).

Only a few studies explored relationships between spirituality and pulmonary function with varied outcomes (21, 22, 29). For example, SWB was positively associated with FEV1/FVC values (21) and NORA (DUREL) was negatively associated with forced expiratory volume in the first second (FEV1) (29). The latter result seems to reflect the fact that patients with more advanced disease turn to religion and spirituality.

Interventions to improve spiritual well-being of patients with COPD

Spiritual care is provided by healthcare providers (basic SC) who address spiritual concerns and cooperate with trained chaplains (specialist SC) who especially deal with unmet spiritual needs or spiritual distress of the patients. Apart from the referral to a chaplain as the best proven spiritual intervention, several others focused on finding a meaning of life, supporting dignity, or helping to review own life have been shown to be effective, especially for people at their end-of-life (38, 39).

However, the literature search indicated very few studies regarding interventions aiming at improving specifically COPD patients' spiritual functioning. Daily visits from chaplains in patients with COPD resulted in a significant decrease in anxiety compared to the non-visited controls and to a shorter length of hospital stay and satisfaction with the quality of care (40). In the case of home care, visits from clergy or other members of a patient religious community were significantly and inversely related to depression among seriously ill patients including people with advanced COPD (41). Patients who were visited often by clergy and laity reported significantly fewer symptoms of depression than those visited only a little.

Following pulmonary rehabilitation increase in positive RC and ORA, and a decrease in negative RC was observed in a non-randomized controlled trial (37). Pulmonary rehabilitation promoted improvement in anxiety, depression and depressive symptom severity, exercise capacity, dyspnea, and QoL. As already mentioned, changes in ORA and positive RC positively correlated with increases in patients' exercise capacity (measured as 6MWT) and negatively with CAT, which reflected better QoL (37).

Dignity therapy (DT) has been shown to have a positive impact on the well-being of the patients with advanced COPD with a short life prognosis (42). Such interventions well received by patients may help them in recognizing and fulfilling their spiritual needs in the last phase of their life.

COPD patients' expectations regarding spiritual care provided by professional carers

Studies show that patients with chronic diseases wish to talk to doctors about spiritual issues. This may, however, vary in different populations (19, 43–45). Almost all (94%) ambulatory patients visiting a pulmonary faculty office (no specific diagnoses presented) who declared to have religious and spiritual beliefs and 45% of those not declaring religious and spiritual beliefs agreed that physicians should ask patients about their beliefs if they become gravely ill (43). Approximately 45% percent of participants declared religious or spiritual beliefs that would influence their medical decisions in a severe disease. Approximately 66% stated that their trust in a physician would increase if he/she asked about spiritual matters (43). However, among newly diagnosed individuals with severe chronic lung diseases none of the participants wanted to discuss religious and spiritual issues with a professional and few recalled to have had such a need in the past (19).

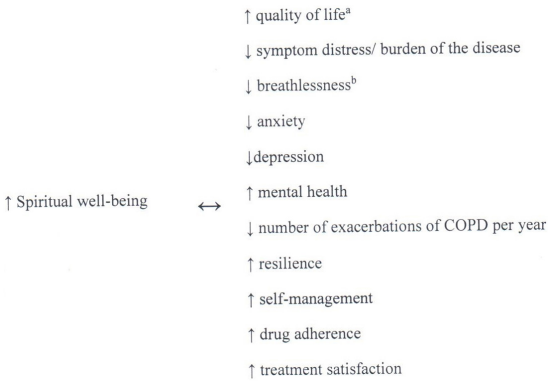

FIGURE 1
Associations between spiritual well-being and clinical outcomes (17–24, 29, 34). Non-casual-relationships can be proved on the base of studies identified. [a]no association in patients with COPD in a study by Hasegawa et al. (20). [b]no association in a study by Delgado et al. (34).

Asking about spiritual and religious beliefs was one of four issues which physicians rarely discussed during communication about end-of-life care. Approximately 82.6% of oxygen-dependent COPD patients reported not having been asked about religious and spiritual beliefs (46). In a survey among Polish pulmonologists, about 16% respondents talk on spiritual/religious needs to their patients with advanced COPD routinely (always or often) contrary to almost 29% never discussing those issues (47).

Discussion

This mini-review provides an analysis of the important role of SWB and RC of people with advanced COPD. It also discusses what has been proven, and what still needs to be researched, on the relations between SWB and QoL, symptom burden, resilience, self-management, satisfaction with the treatment and with own life, physical functioning and mental health, or medication adherence (**Figure 1**).

Unfortunately, despite increasing evidence on the importance of patient spirituality, still very little is known about the efficacy of SC and the interventions directed to meet the patient spiritual needs. Much more has been proven in many other fields of medicine. For example, in intensive care, the chaplain activities (48) have been examined in detail including evidence of higher family members' satisfaction with SC if a pastor or spiritual advisor was involved within 24 h of patient death (49), or the association of chaplaincy services with significantly lower rates of hospital intensive care units deaths and higher rates of hospice enrollment (50). In case of hospitalized COPD patients, daily visits of chaplains exerted a positive impact on anxiety, length of hospital stay, and satisfaction with the quality of care (40). However, as these patients usually spend much more time suffering from symptom burden and many limitations not in hospital but at their homes, the preliminary observation that clergy-laity support is related to the benefit to their mental health, gives an argument for involving SC into integrated care for people with COPD (41). Taking into account, the widely accepted recommendation on pulmonary rehabilitation for COPD patients, its potential influence on ORA and positive RC is very promising and should be further studied (37). Besides the preliminary observations on the role of chaplaincy, pulmonary rehabilitation, and DT; the latter shown to be helpful in fulfilling the spiritual needs of patients with COPD at the end of their life (42), there is a lack of research on other interventions. The recommendation of respiratory societies could help to change this situation, as it seems to be the case in other branches of medicine. Taking into account the negative impact of the spiritual crisis on patients coping with cancer, its physical symptoms, and its treatment, National Comprehensive Cancer Network presented to clinicians some standards of care, based on multidisciplinary team and cooperation with a certified chaplain (12). American Society of Clinical Oncology gave a strong recommendation for clinicians to explore how a patient's culture, religion, or spiritual belief system affects their end-of-life decision making or care preferences along with the strategies on communication, using standardized tool to assess a patient's spiritual or religious beliefs and in case of spiritual distress – cooperation with a medically trained chaplain (51). In case of the adult cancer patient at the end of life, European Society for Medical Oncology recommended routine assessment of spiritual distress, using compassionate listening, some specifically proven interventions and referral to a trained chaplain or SC professional (38). American College of Critical Care Medicine even recommended that healthcare provider pray with the patient who requested it if a clinician felt comfortable with it, as a part of holistic intensive care (52). Similar guidelines, as mentioned above, published by respiratory societies could promote more efficient approach for clinicians to the spiritual needs of people with advanced COPD. Our mini-review also revealed the great need of improving the education of healthcare professionals on SC. On the one hand, many COPD patients wish to talk to doctors about spiritual issues (43). On the other hand, a huge minority of doctors do it as a routine approach (47). However, education how to provide SC especially for people at the end of life is not only about communication, using diagnostic tools or implementing specific interventions, which, by the way, are mandatory components of SC. According to the European Association for Palliative Care, the first recommendation for the training of clinicians caring for people at the end of life is the development of the reflective capacity of staff to consider the importance of spiritual dimensions in their own lives (3). Only by learning

how to care about ourselves, will we be able to care for other people including supporting them spiritually.

Conclusion and future directions

Spirituality and SWB of people with advanced COPD are related with their QoL, symptom burden, resilience, self-management, satisfaction with the treatment and with their own life, physical functioning and mental health, or medication adherence. However, there are some emerging challenges such as proving the efficacy of interventions aimed at meeting patients' spiritual needs, preparation of respiratory societies' guidelines on SC, and the implementation of optimal education for healthcare professionals caring for people with advanced COPD.

Author contributions

AK-L developed the concept and structure and wrote the first draft of the manuscript. MF-K and MK contributed to the writing of the manuscript. All authors reviewed and approved the final manuscript.

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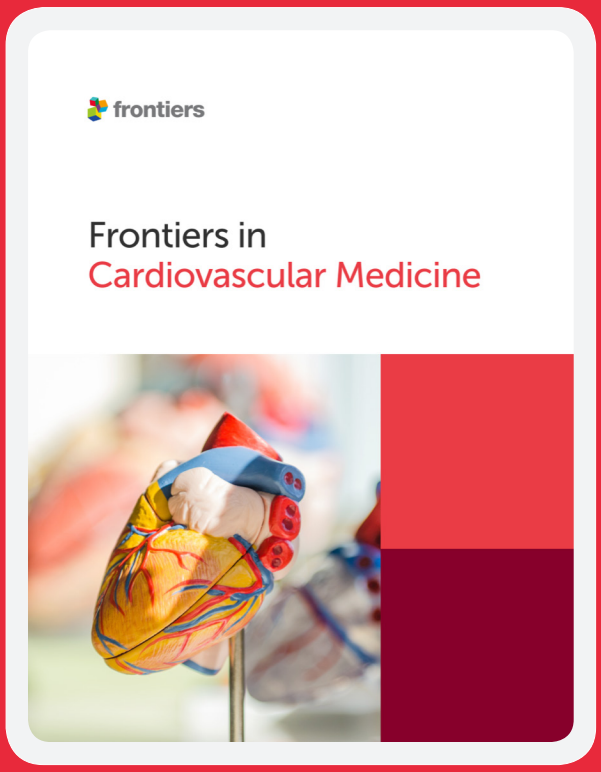

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