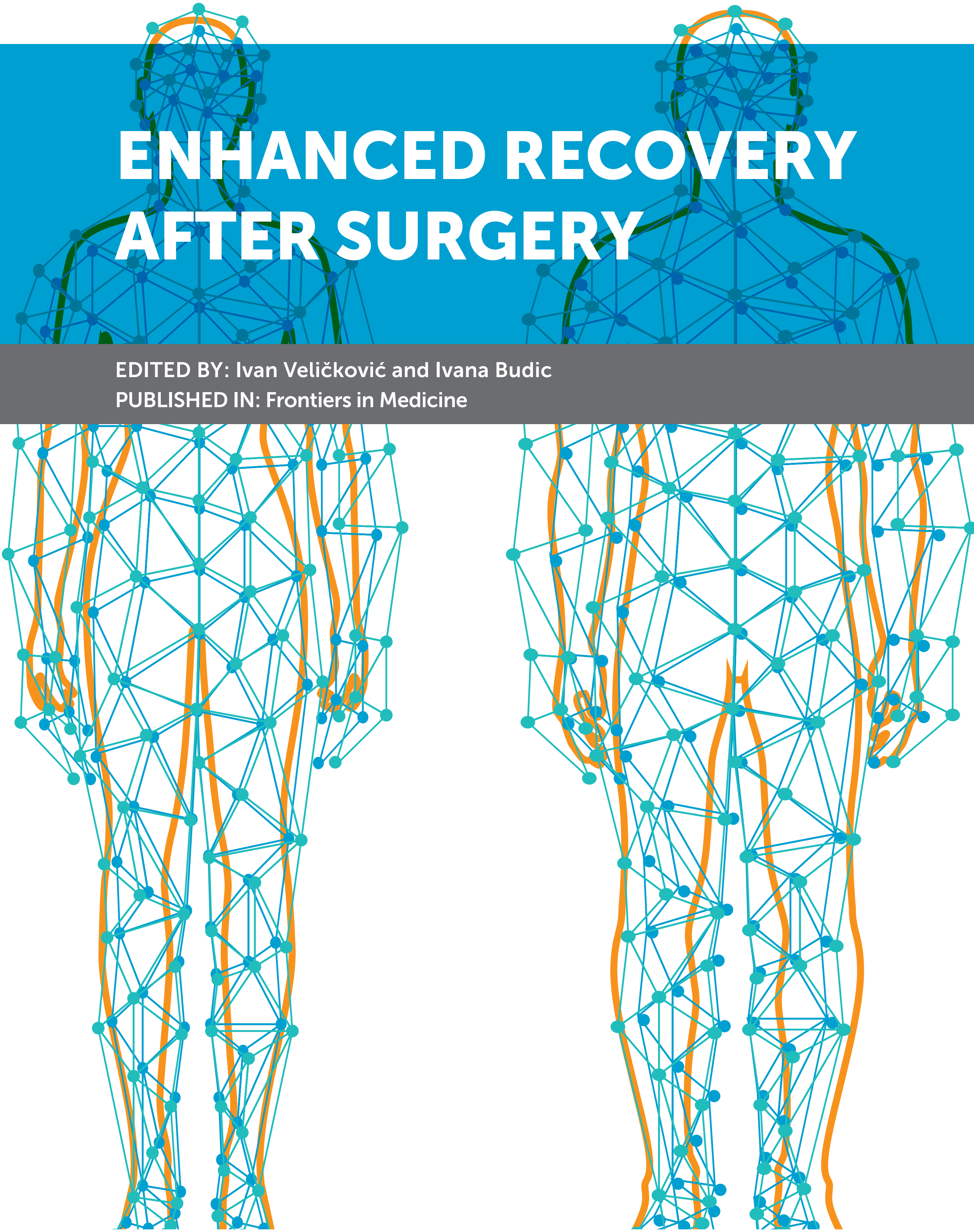
ENHANCED RECOVERY AFTER SURGERY



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ENHANCED RECOVERY AFTER SURGERY

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Table of Contents

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EDITORIAL
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Editorial: Enhanced Recovery After Surgery

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Keywords: enhanced recovery, protocols, surgery, anesthesia, intensive care

Editorial on the Research Topic

Enhanced Recovery After Surgery

Enhanced Recovery After Surgery (ERAS) is a multidisciplinary approach to the care of surgical patient. ERAS protocols are multimodal perioperative care pathways designed to achieve early recovery after surgical procedures by maintaining preoperative organ function and reducing the profound stress response following surgery (1). ERAS started mainly with colorectal surgery but has been shown to improve outcomes in almost all major surgical specialties (2). ERAS process implementation involves a team consisting of surgeons, anesthesiologists, nutritionists, nurses, and other staff from services who are involved in patient care. In the past few years, several different centers have focused on ERAS programs resulting in many protocols that are now available with multiple elements to be considered (3). Despite the evidence of improved postoperative outcomes and recovery (4–7), ERAS implementation is slow and varies between different hospitals.

The overall goal of this research topic is to examine ERAS protocols and their implementation in different settings. The issue contains a series of review articles as well as original research articles.

Recent studies suggest that ERAS protocol can be successfully applied in vascular surgery. In a narrative review article, Stojanovic et al. present the evidence that application of ERAS program reduces the length of hospital stay, decreases the surgical, and non-surgical complications in the postoperative period, and improves the overall outcome in patients undergoing vascular surgery. Having reviewed recent literature, Dinic et al. highlight potential procedures and techniques that might be incorporated into the ERAS program after thoracic surgery. Golic et al. conducted a retrospective analysis of nine cases of patients who developed flail chest following blunt trauma, and were treated with early osteo-fixation of the chest wall and postoperative epidural analgesia. The authors concluded that surgical stabilization and epidural analgesia reduced ventilator support, shortened intensive care unit stay, and reduced medical costs. Vukovic and Dinic analyzed the components of ERAS protocols in urologic surgery. They concluded that there are still very few guidelines for ERAS protocols in urology and emphasize the importance of preoperative medical optimization, epidural analgesia, and nutritional management.

The idea of incorporating ERAS protocols in surgical intensive care unit (SICU) setting has great potential for promoting enhance recovery of SICU patients. Jovanović et al. comprehensively explain the role of sedation, analgesia, early oral intake, and early mobilization as integrative parts of SICU ERAS concept implementation.

Simić et al. in their review focus on the importance of postoperative analgesia in children. The authors describe the utility of continuous peripheral blocks (CPNB) for complete and prolonged postoperative analgesia of pediatric patients.

Sivevski et al. provide an in-depth review of the available data from the literature as well as evidence-based recommendations considering the concept of low dose spinal anesthesia for

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patients undergoing gynecological surgery. An interesting result of the study is that there was no respiratory depression in geriatric patients receiving 100 μg of spinal morphine. This study also highlights the hemodynamic stability of elderly patients who received low-doses of intrathecal bupivacaine in combination with opioids.

Pujic et al. developed a survey tool of 22 questions with multiple choice answers that was sent by email to all hospitals in Serbia (4 university teaching hospitals and 45 general hospitals) that provide obstetric services. The questionnaire asked whether ERAS protocols had been formally adopted for surgical patients and about their use in patients undergoing cesarean delivery (CD). Responses were obtained from 46 of 49 hospitals (3 university and 43 general hospitals; a 94% response rate). ERAS protocols were in use in 11 of 46 (24%) of surveyed hospitals and 63% of the time the responsibility for patients counseling was shared between the obstetrician and anesthesiologist. However, even ERAS hospitals reported a higher number of discharges after 3 days compared to surveys of UK hospitals where the majority of women are discharged within 2 days of their CD.

Quadratus lumborum block (QLB) is a new form of the abdominal wall block which is relatively easily performed thanks to clear ultrasound anatomic markers. QLB is safe and has found its place in multimodal postoperative pain therapy in patients undergoing abdominal surgery, gynecological and obstetric procedures, and orthopedic interventions on hips, whether interventions are performed in general or spinal anesthesia, both in adults and in children. Akerman et al. conclude that improved early oral intake and early mobilization can be more easily achieved with good pain control hereof QLB has a great potential in this area of ERAS.

In summary, this issue discusses particular aspects of ERAS protocols and an anesthesiologist's role in preoperative, intraoperative, and postoperative strategies for different surgical interventions and in different patient groups.

AUTHOR CONTRIBUTIONS

IB and IV have made a substantial contribution to the work and approved the final version of the manuscript to be published.

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MINI REVIEW
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Enhanced Recovery in Surgical Intensive Care: A Review

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Patients are admitted to the surgical intensive care (SICU) unit after emergency and elective surgery. After elective surgery, for further support, or to manage coexisting comorbidities. The implementation of the ERAS (Enhanced recovery after surgery) protocols in surgery should decrease the need for ICU beds, but there will always be unpredicted complications after surgery. These will require individual management. What we can do for our surgical patients in ICU to further enhance their recovery? To promote early enhanced recovery in surgical intensive care—SICU, three areas need to be addressed, sedation, analgesia, and delirium. Tools for measurement and protocols for management in these three areas should be developed to ensure best practice in each SICU. The fourth important area is Nutrition. Preoperative screening and post-operative measurement of the state of nutrition also need to be developed in the SICU. The fifth important area is early mobilization. ERAS protocols encourage early mobilization of the critically ill patients, even if on mechanical ventilation. Early mobilization is possible and should be implemented by special multidisciplinary ICU team. All team members must be familiar with protocols to be able to implement them in their field of expertise. Personal and professional attitudes are critical for implementation. In the core of all our efforts should be the patient and his well-being.

Keywords: ERAS protocol, surgical intensive care unit, recovery, perioperative care, early mobilization

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INTRODUCTION

History of Enhanced Recovery Concept

Enhanced recovery concept was first introduced by Henrik Kehlet in 1990's. As a colorectal surgeon he developed the idea of "fast tracking" in major abdominal surgery, in order to promote faster recovery, and diminish complication after surgery.

Factors that limit early recovery include pain, post-operative paralytic ileus and different organ system dysfunctions. The traditional approach in use for decades, utilize only unimodal solutions for these problems (1–3).

For enhanced recovery, a multimodal, evidence - based approach is proposed.

Implementation of this innovative concept was facilitated by the simultaneous development of new regional anesthesia techniques for pain control, and minimally invasive laparoscopic techniques in abdominal surgery.

In 2010, ERAS (Enhanced recovery after surgery) Society was formed as a nonprofit, academic, international multidisciplinary society and has played an important role in helping to provide guidelines, educational meetings, and other support (www.erassociety.org) (2–4). The mission of the ERAS Society is to develop peri-operative care and improve recovery through research, education, audit and implementation of evidence-based practice.

To the present day 9 ERAS Society guidelines are available: for colonic surgery, pancreaticoduodenestomy, elective rectal/pelvic surgery, radical cystectomy, liver, bariatric, head and neck cancer surgery, gastrectomy and breast surgery (3). Modified ERAS guidelines exist for gynecology, thoracic, vascular, pediatric, urologic, orthopedic, esophagectomy, and colorectal liver metastasis surgery.

As authors, we are not aware of the existence of ERAS protocols specific for surgical intensive care, and although all existing ERAS protocols have an influence on patients being admitted in surgical intensive care unit, we think that more can be done, to further enhance recovery of these patients.

EARLY RECOVERY PROTOCOLS AS CONCEPT IN SURGICAL INTENSIVE CARE

Patients are admitted to the intensive care unit after emergency or elective surgery. In case of admission after elective surgery, for further support to manage coexisting comorbidities.

ERAS protocols in surgery starts in the preoperative period, and potential need for post-operative ICU admission should be discussed with the patient preoperatively.

Surgical Intensive Care Unit

As JL Vincent highlighted, a neglect of recovery is one of the ten big mistakes in intensive care medicine (5). Everyday battle for patient survival draws attention from recovery and period after leaving the intensive care unit.

In theory, the implementation of the ERAS protocols in surgery should decrease the need for ICU beds, but will always be unpredicted complications after surgery, which will be managed individually.

The next question is what can be done for our surgical patients in SICU to enhance their recovery?

The Role of Sedation and Analgesia in Enhanced Recovery After Surgery in the Intensive Care Unit

Sedation and analgesia are an integral part of care for critically ill, but sometimes with low priority, as care for other organ systems, as cardiac, pulmonary, or renal system are more acutely in focus. Only a small percentage of SICU patients need prolonged deep sedation. In the most cases the objective is for the patient to remain calm, cooperative and comfortable. The concept of "e CASH" (**e**arly **C**omfort using **A**nalgesia, minimal **S**edatives and maximal **H**uman care) is being introduced to guide clinicians (5–7).

Using this concept strategies for sedation and analgesia in SICU can be provided.

Analgesia

All critically ill adult patients in medical, surgical, and trauma ICUs typically experience pain. Providing analgesia should be a priority, on humanitarian grounds, and in keeping with the ERAS concept.

Essential for early mobilization, multimodal approach to pain should be implemented (8).

As stated in recent guidelines "Multimodal analgesia or balanced analgesia is approach that involves the use of more than one method or modality of controlling pain. These modalities may operate through different mechanisms or at different sites (i.e., peripheral vs. central actions). One example of multimodal analgesia is the use of various combinations of opioids and local anesthetics to manage post-operative pain" (9).

Pain management is the mainstay of treatment and precondition for other treatment options such as early mobilization where multimodal approach to pain should be implemented (8).

Pain should be measured in order to regularly reevaluate and optimize treatment.

There are many tools for measuring the pain in critically ill patient (Critical Car**e Pain Observation Tool or BPS**—Behavioral Pain Scale) which can be used, or modified for local conditions (10).

Sedation and Delirium

Sedation is integral part of care in SICU to relieve discomfort and unnecessary suffering. Over sedation on the other hand is not beneficial and only a small percentage of patient need profound sedation and immobilization (5, 6). Benzodiazepines in the sedation of SICU patients should be avoided, and non-sedative drugs use such as propofol or dexmedetomidine should be encouraged (8).

Delirium is a common problem in some SICU patients affecting outcome in terms of prolonged ICU stay, persistent cognitive decline, reintubation, and worse overall outcome. Delirium is frequent in the medical and surgical Intensive Care Units (ICUs) with prevalence rates ranging from 32.3 to 77% and the incidence rates varying from 45 to 87% (11–14).

Currently there is a study recruiting patients "UNDERPIN-ICU" consisting of standardized protocols focusing on several modifiable risk factors for delirium, including cognitive impairment, sleep deprivation, immobility and visual and hearing impairment. The future results and maybe some implementation of the protocol remains to be seen (15).

In preventing delirium in ICU, there is a great potential in involving family members in activities that constantly serve as an orientation, cognitive or sensitive stimulus to the patients (16).

Abbreviations: RAS, Enhanced Recovery After surgery; ICU, intensive care unit; SICU, surgical intensive care unit; e CASH, early Comfort using Analgesia, minimal Sedatives and maximal Human care; ICU PAD, intensive care unit pain agitation delirium, ESPEN, European Society for Enteral and Parenteral Nutrition; A.S.P.E.N, American Society for Enteral and Parenteral Nutrition; ESICM, European Society of Intensive Care Medicine; BW, body weight ICUAW, intensive care unit-acquired weakness; ABCDEF bundle, Assess, Prevent, and Manage Pain, Both Spontaneous Awakening Trials and Spontaneous Breathing Trials, Choice of Sedation, Delirium: Assess, Prevent and Manage Early Mobility and Exercise, Family Engagement and Empowerment.

Patient-Centered Care

The patient should be in the center of all our efforts. Patient well-being and needs are our priority. Counseling, emotional support, and humanistic approach should be implemented in our everyday work. Many non-pharmacological modalities can be employed in sleep promotion and as alternative means of communication (5–7).

There are recent Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit (8), that should be used according to local organization of the health care system.

The 2013 PAD guidelines (**P**ain **A**gitation **D**elirium) have been incorporated into the ICU PAD Care Bundle, with corresponding metrics developed to facilitate implementation. The bundle emphasizes an integrated approach to assessing, treating and preventing significant pain, over or under sedation, and delirium in critically ill patients (8, 12).

To promote early enhanced recovery in SICU, we should provide protocols for sedation and analgesia in the SICU (or develop local ones), implement tools for assessing the patient level of sedation and pain, develop and implement prevention and treatment strategies for post-operative delirium. The best practice will be to develop and implement care bundles for sedation, analgesia and post-operative delirium in each SICU.

THE ROLE OF NUTRITION IN ENHANCED RECOVERY AFTER SURGERY IN THE INTENSIVE CARE UNIT

Early Nutrition in SICU

Patients undergoing surgery are subjected to a catabolic state through activation of the inflammatory response and the release of stress hormones—cortisol, catecholamine, and glucagon. The stress hormones and inflammatory cytokines exert catabolic effects by depleting liver glycogen stores and causing lipolysis and proteolysis of fat and muscle protein stores. Additionally, surgery naturally induces a state of insulin resistance or decreased insulin sensitivity, with breakdown of lean body mass. This has been associated with increased morbidity, increased mortality, and increased length of hospital stay (17, 18).

Providing nutrition and correcting existing nutritional deficiencies is one of the mainstays in all surgical ERAS protocols. Nutrition support in SICU is also of high importance and interconnected with other elements of care. Nutritional support provides optimal wound healing and prevent loss of lean body mass. Prolonged period of fasting causes breakdown of the gastrointestinal tract barrier function, atrophy of endothelial *microvilli* and decrease of gut lymphoid tissue. This process increases infection and development of sepsis (17, 18).

At the present moment, there are two guidelines: one from ESPEN (European Society for Enteral and Parenteral Nutrition) and one from A.S.P.E.N (American Society for Enteral and Parenteral Nutrition). Both guidelines support the idea of early start with enteral nutrition in critically ill patients. The only contraindications for early enteral nutrition are the conditions of uncontrolled shock and high doses of vasoactive drugs, life threatening hypoxia, hypercapnia, acidosis, or bowel ischemia (19, 20).

The most recent guidelines developed by ESICM (European Society of Intensive Care Medicine) Working group on Gastrointestinal Function within the Metabolism, Endocrinology and Nutrition made 23 recommendations for early enteral nutrition in critically ill patient. Early enteral nutrition is recommended in cases of concomitant usage of neuromuscular blockade, therapeutic hypothermia, extracorporeal membrane oxygenation, prone positioning, for patients with traumatic brain injury, patients with stroke, spinal cord injury, severe acute pancreatitis, after gastrointestinal surgery, after abdominal aortic surgery, abdominal trauma after confirmed/restored gastrointestinal tract, diarrhea (21).

Apart from above mentioned contraindications, delayed enteral nutrition is considered in cases of high output intestinal fistulas, progressing intraabdominal hypertension, abdominal compartment syndrome, acute upper gastrointestinal bleeding, and life threatening metabolic derangements (20, 21).

The Amount of Protein in Critically Ill

The exact amount of protein required in critically ill patient is still a matter of the debate among nutritionists involved in ICU. For the first 12 days in the ICU, an average ICU patient worldwide receives 1,034 kcal/day and 0.6 g/kg/protein (22).

After the first phase of the critical illness ("ebb phase") the patient enters the recovery phase, total protein, and calorie delivery needs to increase significantly. The total recommended protein intake of 1,2 g/kg/BW /day should increase to 1.5–2 g/kg/BW/day (23, 24).

There is scientific evidence that adequate protein intake leads to better patient functional recovery and quality of life after ICU discharge (22–24).

To enhance further recovery of surgical critically ill patient, implementation of existing protocols should be a high priority. As for pain, agitation, and delirium, screening (measuring) for malnutrition is also very important, and should start preoperatively. Care bundles for early nutritional interventions and implementation of nutritional protocols should be developed by multidisciplinary ICU teams.

THE ROLE OF EARLY MOBILIZATION IN ENHANCED RECOVERY AFTER SURGERY IN THE INTENSIVE CARE UNIT

Bed rest was first introduced as a medical treatment in the Nineteenth-century to promote recovery, and remains unchanged even today in many hospitals. Critically ill patients are often seen as too sick to be involved in some form of rehabilitation treatment. The rehab programs are frequently perceived as potentially harmful and could cause injury (24).

Immobilization has many deleterious effects on a critically ill patient significantly on the musculoskeletal, cardiovascular, respiratory, and cognitive systems (25, 26).

TABLE 1 | Summary of recommendations for ERAS in SICU.

1.Pain agitation delirium	1.a Pain treatment is precondition for other treatment options 1.b Implement existing protocols for sedation and analgesia in the SICU (or develop local ones) 1.c Implement tools for assessing the patient level of sedation and pain. 1.d Implement prevention and treatment strategies for postoperative delirium. 1.e Development and implementation of CARE BUNDLES for sedation, analgesia and postoperative delirium in each SICU. **Guidelines:** Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* (2013) 41:263–306.
2.Nutrition	2.a. Care bundles for early nutritional interventions and implementation of nutritional protocols should be developed by multidisciplinary ICU teams. **Guidelines:** 2016 Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient. *JPEN* (2016) 40(2): 159 –211.
3.Early mobilization	3.a ERAS protocols encourage early mobilization of the patients. 3.b Early mobilization is possible and should be implemented by special multidisciplinary ICU team. **Guidelines:** Physiotherapy for adult patients with critical illness: recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients. *Intensive Care Med* (2008) 34:1188–1199.
4.Logistic issues	4.a. All team members must be familiar with protocols in order to implement them in their field of expertise. 4.b Implementation will require an organizational modifications in the preoperative anesthesia visit, preoperative preparation, intraoperative pain management or fluid management, modifications in postoperative care **Guidelines**:www.erassociety.org

The development of intensive care unit-acquired weakness (ICUAW) is a longstanding problem in treatment of the critically ill patients and associated with a prolonged duration of mechanical ventilation, delayed rehabilitation, protracted ICU stay, and an increased risk for morbidity and mortality. The cause of ICUAW is multifactorial. There is no specific targeted treatment for prevention of ICUAW. Immobility and bed rest contribute to ICUAW and should be stopped as early as possible (27–29).

Mobilization and physiotherapy for mechanically ventilated patients is an even bigger challenge for health care workers in SICU. Only a small percentage of mechanically ventilated patients are regularly mobilized (<9%) (30, 31).

Prolonged (unnecessary) immobilization during hospitalization in SICU is still a frequent issue. There is mounting evidence that early physical activity and early mobilization are safe and effective. Despite this evidence implementation of this practice is still too low. All efforts aimed to promote this practice of early mobilization and rehabilitation will promote enhanced recovery in those patients (32–34).

ERAS protocols encourage early mobilization of the patients. Early mobilization is possible and should be implemented by special multidisciplinary ICU team.

CHALLENGES IN THE IMPLEMENTATION OF ENHANCED RECOVERY AFTER SURGERY IN THE INTENSIVE CARE UNIT

It has been more than 15 years from implementation of the first ERAS protocols and global and widespread implementation is yet to occur. It differs greatly among hospitals in different regions of the globe. There are many problems divided into two major categories: one category are caregivers and patients, and the other category are logistic issues (34).

Health Care Providers and Patients

The Health Care Providers

Implementing ERAS concept is more than making protocols. As mentioned above, there are vast scientific data from already existing ERAS protocols. Implementing them requires a multidisciplinary team of surgeons, anesthesiologists, nurses and other team members (nutritionist, physiotherapist, etc.). All team members must be familiar with protocols in order to implement them in their field of expertise. Personal and professional attitudes are critical for implementation. Sometimes enhanced recovery pathways may seem counterintuitive and contradict previous knowledge. For example, early nutrition and early mobilization, because bed rest and nil by mouth was the cornerstone of patient care for decades. All departments need some dedicated physician to promote the idea of enhanced recovery, but sometimes there is a "power play" among different professions over which profession should lead the program (35–37).

The Patient

As stated previously, in the core of our efforts should be the patient and his well-being.

Effective preoperative counseling is associated with improvements in post-operative recovery in terms of anxiety, faster return of bowel function and improved analgesia. Preoperative counseling is a very important component of the enhanced recovery protocol and should be done at all times. A realistic expectation and proper data are associated with more beneficial health outcomes. The informed patient is capable of making better decisions about their treatment (35, 37).

Logistic Issues

Organizational Issues

Analyzing enhanced recovery protocols, we come to the conclusion that some of them have more than 20 items.

Implementing all of them will require an organizational modifications in the preoperative anesthesia visit, preoperative preparation, intraoperative pain management or fluid management, modifications in post-operative care, which sometimes results in increased workload, it's time consuming or need additional training (37, 38).

Environmental Issues

Hospital environment has a positive impact on patient welfare. Specialized ICU, like geriatric ICU with a special features adjusted for geriatric patients, (e.g., single room), is the evidence that modern ICU gravitate to more "patient friendly" design. Enhanced recovery programs are sometimes perceived by health management as more expensive in terms of environmental and design alterations. Based on available data from the United States, ERAS programs lead to reductions in lengths of hospital stay that range from 0.7 to 2.7 days and substantial direct cost savings (39).

CONCLUSIONS AND FUTURE DIRECTIONS

The Society of Critical Care Medicine's ICU Liberation initiative aims to liberate patients from the harmful effects of pain, agitation, and delirium in the ICU. The Society of Critical Care Medicine introduced the concept of ABCDEF bundle for intensive care: **A**ssess, Prevent, and Manage Pain, **B**oth Spontaneous Awakening Trials and Spontaneous Breathing Trials, **C**hoice of Sedation, **D**elirium: Assess, Prevent and Manage **E**arly Mobility and Exercise, **F**amily Engagement and Empowerment. This concept and detailed care bundles can be found on the website www.iculiberation.org for details.

Future directions for the improvement and enhancement of the patient recovery in SICU is in development and implementation of specific care bundles (are being) carried out by SICU multidisciplinary teams. We can utilize existing ones or prepare and modify local ones.

Quality guidelines do already exist (8, 12, 19, 20, 33), therefore implementation in everyday practice is the key for impact and enhancement of the patients recovery in SICU. More emphasis on pain treatment, as well as treatment of delirium and agitation, early nutritional screening and interventions, early mobilization of critically ill patients, family member involvement and paradigm shift in our mentality as an ICU team members, is necessary for change to happen.

Summary recommendations for ERAS in SICU are in **Table 1**.

LIMITATATIONS OF THE REVIEW

One of the main limitations of this study is that these are recommendations for ERAS protocols in other settings, but there is not scientific data yet to show if they can be translated effectively into another (SICU) setting. This idea of incorporating ERAS protocols in SICU setting have great potential for future scientific research.

Second limitation pertains to the data we already have and that are proposed here to be used in SICU, such as existing protocols for assessment or management of sedation, analgesia, delirium, nutrition and early mobilization. Each and every item mentioned here is subject to some criticism in the present literature. For the present time, while waiting for further scientific refinement, those guidelines are the best scientific knowledge that we have. By using them we give structure and solid scientific background to our everyday work in SICU and their implementation can lead to optimization of various aspects of SICU practices.

AUTHOR CONTRIBUTIONS

GJ: conceptualization, investigation, literature review, visualization, and made a final version of manuscript, language supervision. DJ: conceptualization, literature review, writing the manuscript. ML-S: conceptualization, literature review, writing the manuscript, supervision.

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Epidural Analgesia With Surgical Stabilization of Flail Chest Following Blunt Thoracic Trauma in Patients With Multiple Trauma

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Flail chest, often defined as the fracture of three or more ribs in two or more places, represents the most severe form of rib fractures. Conservative treatment, consisting of respiratory assistance with endotracheal intubation and mechanical ventilation (internal pneumatic stabilization) and pain control, are the current treatments of choice in the majority of patients with multiple rib fractures. However, the use of mechanical ventilation may create complications. In selected patients, operative fixation of fractured ribs within 72 h post injury may lead to better outcomes. We conducted a retrospective analysis of a series of nine cases of patients who developed flail chest after blunt trauma, and were treated with surgical osteofixation of the chest wall and postoperative epidural analgesia at the University Clinical Center of the Republic of Srpska during the period from January 2015. to December 2016. Two patients had trauma to the chest only, and the other patients had associated injuries to the head, abdomen, spine, and fractures of the pelvis and long bones. In the majority of patients (77.7%), surgical stabilization of the chest was performed on the second day following the injury, (mean, 2.33 days) and no later than 5 days after the injury. All patients received epidural analgesia with 0, 25% bupivacaine and 0, 01% morphine and intravenous multimodal analgesia, beginning 6 h after thoracotomy. The average length of ICU stay was 14.7 days (range 2–36), while the average number of days of mechanical ventilation was 8.1. The average duration of hospitalization was 25.4 days. Tracheotomy was performed in 33.3% of study patients. Mortality in the observed group was 44.4%. This study shows that surgical stabilization and epidural analgesia reduced ventilator support, shortened trauma intensive care unit stay, and reduced medical costs vs internal pneumatic stabilization.

Keywords: thoracic epidural analgesia, blunt thoracic trauma, multimodal analgesia, operative fixation of ribs, retrospective analysis

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INTRODUCTION

Traumatic flail chest is a potentially life threatening injury, often associated with prolonged mechanical ventilation and intensive care unit stay. Unfortunately, there is little literature describing the incidence of admission to the ICU following blunt trauma. In one small series of patients, Veysi et al. found that 37.5% of their blunt trauma population were admitted to the ICU and reported a mortality rate of 18.7%. Their mortality rate is similar to that in other published series (1). These patients often have multiple other injuries that complicate thoracic wall treatment options. Rib fractures occur in 10% of all trauma patients, and in approximately 30% of all patients with significant chest trauma, and are cause of significant morbidity (2, 3). Flail chest, generally defined as the fracture of three or more ribs in two or more places, represents the most severe form of rib fractures. Conservative therapies, consisting of respiratory assistance and pain control, are the current treatments for the majority of patients with multiple rib fractures; however, mechanical ventilation >3 weeks is often associated with several ventilation related complications. In patient with flail chest who are not treated surgically, pneumonia develops in 27 to 70% of cases and carries a mortality rate of 51%. Morbidity and mortality increase with age and the number of ribs that are fractured. Patients older than 45 years and with more than four rib fractures are at significantly greater risk for poorer outcomes compared to the average patient (4). In selected patients, operative fixation of fractured ribs within 72 h post injury may lead to better results (5). More randomized control trials are needed to further determine who may benefit from surgical fixation of rib fractures. Intravenous analgesia is often use for pain relief, but is associated with significant adverse effects. Epidural analgesia offers the advantage of superior analgesia with the absence of the adverse effects of parenteral narcotic.

Despite many reports of blunt chest trauma management, the impact of chest injury severity on the outcome of patients with multiple trauma has been rarely described. Significant differences in mortality and morbidity have been recently reported between different health care institutions.

Epidural analgesia provides superior pain relief compared to other analgesic techniques and improves the pulmonary function tests of injured patients. Its use has been associated with an increase in tidal volume, functional residual capacity (FRC), lung compliance, vital capacity and PaO2 with reductions in airway resistance and the paradoxical movement of flail chest wall segments (6).

MATERIALS AND METHODS

We conducted a retrospective analysis of nine cases of patients who developed flail chest following blunt trauma, and were treated with osteofixation of the chest wall and postoperative epidural analgesia at the University Clinical Center of the Republic of Srpska (UCC RS) in Banjaluka from January 2015 to December 2016. All patients received a thoracic computed tomography (CT) scan upon admission to assess the severity of thoracic trauma. Osteofixation was performed under general endotracheal anesthesia with postoperative epidural analgesia. Thoracic epidural analgesia was located to a site corresponding to the level of the rib fracture as that technique has demonstrated superior analgesia in patients with blunt thoracic trauma (5). A solution of 0, 25 % bupivacaine with 0, 01% morphine was delivered by continuous infusion. The surgical osteofixation involved a posterolateral thoracotomy with pleural exploration in order to simultaneously treat lesions of the parenchymal lung and bronchus, control intrathoracic hemorrhage, and remove intrapleural clot.

RESULTS

The analysis included nine patients. All patients were male, aged 34–76 years, mean age 50 years. Four patients (44.4%) were motor vehicle accident victims, while five patients (55.5%) were injured at work. All patients underwent a posterolateral thoracotomy with osteofixation of the chest wall using an osteosynthesis plate. All patients had contusions of the lung parenchyma, and four patients had pulmonary parenchyma lacerations. Two patients had trauma to the chest only.

All patients had fractures of at least four ribs (range 4–8) and one patient had a bilateral flail chest. Seven patients had other major non−chest injuries: one had fractured mandible, 3 had intra-abdominal injuries (1 patient had a liver laceration and 2 patients had a splenic rupture), 1 patient had an L3 compression fracture, and one patient had fractures of the pelvis and lower extremities. All patients were transfused with a minimum of two units of packed RBCs (440 ml) and two units of fresh frozen plasma (360 ml). All the patients received epidural analgesia with 0,25% bupivacaine and 0,01% morphine at a rate 5–10 ml/ h-1 to keep pain score at less than 5 (on a visual analog pain scale of 0–10). Intravenous multimodal analgesia with additional non-narcotic analgesics were started within 6 h after thoracotomy. In the majority of patients (77.7%), surgical stabilization of the chest was performed on the second day of the injury, on average within 2.33 days of the injury, and no later than 5 days after the admission. The average duration of hospitalization was 25.4 days. The average length of stay of patients in the ICU was 14.7 days (range 2–36), while the average number of days on mechanical ventilation was 8.1 (range 2–16). Tracheostomy was performed in 33.3% of study patients. The overall mortality in the observed group was 44.4%.

DISCUSSION

Recently there has been renewed interest in surgical stabilization of ribs fracture in patients with flail chest (5). However, conservative treatment is still preferred in most surgical centers. Nishiumi et al. reported on the treatment of anterior flail chest with internal pneumatic stabilization in 42 patients. Continuous positive pressure ventilation was needed for 12.5 days and mechanical ventilation for 15.6 days (7). The goal of operative chest wall stabilization is to shorten the period of mechanical ventilation and thus reduce complications from its use.

Only three randomized controlled trials have compared operative vs. nonoperative treatment of multiple rib fractures (5). Leinicke et al., in a systematic review and meta-analysis of studies totaling 538 patients with flail chest, showed that operative management of flail chest was associated with a shorter duration of mechanical ventilation [pooled reduction: −4.52

days; 95% confidence interval (CI): −5.54 to −3.50], shorter ICU length of stay (−3.40 days; 95% CI: −6.01 to −0.79), decreased hospital length of stay (−3.82 days; 95% CI: −7.12 to −0.54), and decreased mortality (pooled Relative Risk (RR): 0.44; 95% CI: 0.28–0.69). A reduction in pneumonia (RR:0.45; 95% CI: 0.30–0.69), and tracheostomy (RR:0.25; 95% CI: 0.13–0.47) were also noted (8). In our study the average number of days on mechanical ventilation was 8.1 days, similar to that reported in the above meta-analysis. In our series the average patient age was 50 years (range 34–76 years), higher than the average reported in other studies. Several studies have described increased morbidity and mortality in elderly patients with traumatic rib fractures, and the increased death rate of our study may be explained by this. An age of 45 years or greater and more than four rib fractures is associated with significantly poorer patient outcome (8). Mortality in patients over 65 years with rib fractures compared with a younger population is 20.1 vs. 11.4% (9). In one retrospective study which analyzed data from the US National Trauma Data Bank, Kent et al. reported that 56 % of the mortality in patients greater than 65 years with thoracic trauma was due to rib fractures and no other injuries (4).

Contusion of the lung parenchyma was present in all patients in our case series and is an independent risk factor for the development of respiratory dysfunction, pneumonia, and acute respiratory distress syndrome. Pneumonia and prolonged respiratory dysfunction occurs in the 25–30% of patients with blunt trauma to the chest (4). Alveolar capillaries are injured, which results in an accumulation of blood and other fluids within lung tissue and interfere with gas exchange and leading to hypoxemia. The consequences of pulmonary contusion include ventilation/perfusion mismatching, increased arterio-venous shunting and loss of compliance of lung parenchyma. These physiological consequences occur within few hours after injury and usually resolve in 7 days. In one study of 139 patients with blunt thoracic trauma and pulmonary contusion, Novakon et al. reported a mortality rate of 17% (9).

All patients in our series received postoperative epidural analgesia via a thoracic epidural catheter. In addition to epidural analgesia, all patients received intravenous multimodal analgesia beginning 6 hours after chest wall ostefixation. Our goal was to achieve a pain score of 5 or less on a visual analog scale pain, which would provide good analgesia. Neuraxial blockade offers superior analgesia to systemically administered medications, although small supplementation of opioids is often required. In patients with one or two rib fractures, treatment with a systemic NSAID and modest amounts of systemic opioids often provides sufficient analgesia. However, such analgesic techniques are often not sufficient to provide satisfactory pain relief in patients with a greater number of fractured ribs who require physiotherapy or to allow effective coughing. Thoracic epidural analgesia with a catheter sited at the mean dermatomal level of the broken ribs provides superior analgesia when measured by subjective pain scale and objective respiratory parameters. Despite better pain relief, a recent meta-analysis which compared thoracic epidural analgesia to intravenous opioid therapy showed no statistically significant difference in mortality, duration of mechanical ventilation, or length of stay in the ICU and hospital (6). There is increasing evidence that multimodal analgesia combined with regional analgesia techniques other than thoracic neuraxial blockade reduces the severity of acute pain after thoracic surgery with yet unknown impact on the incidence and severity of chronic thoracic pain. As an alternative to epidural analgesia, continuous intercostal nerve blockade with local anesthetic may be used in a large number of patients. Paravertebral blockade may provide analgesia similar to thoracic epidural in patients with thoracic trauma and may have with fewer side effects.

The selection of patients and the timing of surgical intervention play an important role in the success of surgical osteofixation. Surgical stabilization of rib fractures is currently used in less than 1% of patients with multiple rib fractures (8). In our case series 77.7% of surgical stabilizations were done on the second day following the injury. Early vs. later intervention may improve outcomes as inflammation and callus formation increase between 3 and 5 days after the injury may complicate management. Most authors recommend early operative treatment within 72 h of injury. Although the combination of osteofixation and continuous thoracic epidural analgesia may reduce mortality, our mortality rate was higher than that of other studies. This is most likely due to the older patients we treated (mean age, 50 years; range 34–76 years) all of whom had significant lung parenchymal injury and numerous other non-thoracic injuries. Our study's significance is limited by the small number of subjects.

CONCLUSION

Early surgical fixation of a flail chest followed by continuous thoracic epidural analgesia may reduce the duration of mechanical ventilation, its complications and shorten the length of ICU and hospital stay in patients with flail chest following blunt thoracic trauma. Good analgesia may help to improve a patient's respiratory mechanics and to avoid intubation of the trachea for ventilatory support in some patients. This may dramatically improve the course of recovery.

AUTHOR CONTRIBUTIONS

DG: Main author, idea of writing the analysis, coordinated writing of the text and translation in English; DS: Analysis of litherature, writing of introduction, discussion, some part of translatin in english; SP: Correction of the text, correction of english version; NK: Statistical analysis, analysis of English.

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MINI REVIEW
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Neuraxial Anesthesia in the Geriatric Patient

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Neuraxial anesthesia is recommended as a well-accepted option to minimize the perioperative side effects in the geriatric patients. The available data from the current researches have shifted the focus from the conventional approach to spinal anesthesia to the concept of low dose local anesthetic combined with opioids. What remains clear from all these studies is that hemodynamic stability is much better in patients who received low-doses of intrathecal bupivacaine in combination with opioids, which is possibly result of a potent synergistic nociceptive analgesic effect and their minimal potential effects on sympathetic pathways thus minimizing spinal hypotension. Spinal anesthesia with 5–10 mg of 0.5% heavy bupivacaine, fentanyl 20 mcg and 100 mcg of long-acting morphine added to the perioperative plan decreased the incidence of spinal hypotension and improved perioperative outcomes in the geriatric patients undergoing (low segment) surgical procedures. These findings may be of interest in the gynecologic geriatric surgery also in which area there are very few studies concerning the use of low-dose concept.

Keywords: geriatric (aging), neuraxial anesthesia, low-dose, opoids, hypotension

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INTRODUCTION

The European population is growing older. It is anticipated that in the next years more than 30% will be older than 65. Particularly fast growing sub-population is the one older than 85 (1). The anatomical and physiological changes of aging present challenge for the anesthetic and surgical management.

There is no ideal anesthetic for geriatric patients. More important than the choice of anesthetic technique is adequate pre-operative assessment and planning of appropriate monitoring. Together with tight control of the perioperative physiological parameters it will favor positive patient outcomes. The decrease of hospital stay in elderly patients undergoing surgery decreases the incidence of adverse events like reduction of both respiratory events and nosocomial infections, as well a less postoperative cognitive dysfunction (POCD) at 1 week in the postoperative period.

The physiological changes of aging have impact on neuraxial anesthesia techniques, both spinal and epidural. With advancing age, as a result of some anatomical irregularities (reduction in number of neurons, deterioration of myelin sheaths, sclerotic closure of the intervertebral foramens etc.) the level of analgesia increases after epidural administration of local anesthetics (LA) (2). With spinal anesthesia, the level of analgesia also increases after spinal administration of hyperbaric solutions (3).

CLINICAL RESEARCHES

There is no controlled trial that can demonstrate that either neuraxial or general anesthesia is clearly superior in terms of outcome in elderly patients. Cochrane systematic review of studies of hip surgeries in elderly, looked at 17 trials (2,567 patients) comparing general to neuraxial anesthesia. The review concluded that the long-term mortality was equal for both groups (4). However, neuraxial anesthesia remains a well-accepted option to: minimize the surgical stress (tachycardia and hypertension), reduce the pulmonary compromise (atelectasis, pneumonia, prolonged mechanical ventilation), thus showing superior postoperative pain control and reduction of perioperative opioids consumption, hence minimizing opioid side effects. Neuraxial anesthesia results in better peripheral vascular circulation and reduces total blood loss. Neuraxial anesthesia also reduces the incidence of POCD in the first postoperative week (4). In addition, neuraxial anesthesia favors early ambulation thus preventing deep venous thrombosis.

Results from the current research have shifted the focus from the conventional approach to spinal anesthesia (SA) to the concept of low dose LA combined with lipophilic opioids. The antinociceptive synergism between LA and intrathecal (IT) opioids is well known. This concept provides effective and superior analgesia and may prolong the duration and effectiveness of postoperative analgesia without associated motor blockade (5, 6). Most importantly, use of low dose of LA reduces the incidence of hemodynamic side effects in elderly (7). Carpenter at al. identified the high levels of sensory anesthesia and increasing age as two main risk factors for the development of spinal hypotension (8). In elderly, SA is associated with 25–69% incidence of hypotension (8). Decreased physiologic reserve and increased incidence of systemic disease, particularly cardiovascular disease, make the elderly population prone to long term complications even with brief episodes of uncorrected hypotension (9, 10).

Fentanyl is the most frequently used intrathecal lipophilic opioid and when administered in single dose of 10–30 mcg, it has a rapid onset (10–20 min) and short duration of action (4–6 h) with minimal cephalic spread. These properties minimize the risk of delayed respiratory depression and favor use of intrathecal fentanyl in ambulatory anesthesia where enhanced analgesia without prolonged hospital stay is important (11, 12).

Morphine is unsuitable for ambulatory surgery because of its slow onset time (30–60 min), dose-related duration of analgesia (13–33 h) and side-effect profile, particularly the delayed onset respiratory depression. Administration of up to 200 mcg of IT morphine with LA for peripheral vascular surgery in elderly patients (average age of 68) can be safely performed with minimal adverse respiratory risk (9). Two meta-analyses determined the incidence of respiratory depression in patients receiving low-dose (<0.2 and 0.2–0.3 mg) IT morphine to be 0–1.2% (13, 14). A retrospective audit of IT morphine in adult patients (409) where more than half the patients (57.2%) were aged 70 years or older and the doses of IT morphine used ranged from 0.1, 0.15, or 0.2 mg (22.9, 30.2, and 45.3%) only one patient, a 74 old-male with past history of cerebrovascular accident and epilepsy, developed respiratory depression (0.24%) (15).

Other researchers concluded that 100 mcg of morphine added to the spinal anesthetic (hip surgery) provided the most optimal balance between analgesia, pain relief and pruritus with acceptable risk of respiratory depression (16). There was no case of respiratory depression (Sat < 94%, RR < 8) or sedation score>2 in all of these studies. Therefore, we consider the risk of respiratory depression with 100 mcg of IT morphine added to low-dose mixture of LA plus fentanyl to be minimal and patients can leave the hospital the day after surgery. Also, the 100 mcg IT morphine could provide post-operative analgesia for the first 24 h, which is superior to the short-term fentanyl-analgesia in the immediate post-operative period.

Other studies with low dose bupivacaine and sufentanil showed similar results (17). Kumar et al reported hypotension in 44% in the conventional group (12.5 mg of 0.5% hyperbaric bupivacaine in a total 2.5 ml), and only 8% in the low-dose group, while Olofsson et al. treated 88% patients for hypotension in their conventional SA group (18, 19). The higher incidence of hypotension in these studies might be the different definition of hypotension. What remains clear from all these studies is that hemodynamic stability is much better in patients who received low-doses of intrathecal bupivacaine in combination with opioids, which is possibly result of a potent synergistic nociceptive analgesic effect and their minimal potential effects on sympathetic pathways thus minimizing spinal hypotension.

Besides lower incidence of hypotension, low-dose SA is characterized with less intense and shorter motor block, although the degree of motor block was not so important for this type of surgical procedure (17, 19). Nevertheless, the time in bed and ambulation was decreased, consequently reducing the incidence of potential postoperative complications. The post-operative pain was also at a satisfactory low level, while the percentage of side-effects minimal. Similar observations were found in other similar studies in the geriatric population (20, 21).

Elderly patients undergoing neuraxial anesthesia are at increased risk of hypothermia and shivering, which can lead to increased oxygen consumption, ventilation and cardiac output. There are studies showing that addition of fentanyl to low-dose bupivacaine decrease the incidence of shivering during spinal anesthesia in elderly patients (12, 18).

There are more options for adding adjuvants to LA in the SA. However, the opioids and α_2 adrenergic agonists are more commonly used as adjuvants in clinical practice. Dexmedetomidine, a selective α_2 adrenergic receptor agonist, has been shown to be a better adjuvant of LAs for neuraxial blocks although clonidine is the first clinically used intrathecal α_2-adrenoreceptor agonist.

Adding dexmedetomidine to LA in the SA is a relatively new area and there are almost no data on its use in an elderly population. In a systemic review and meta-analytic study dated from 2017, where researchers independently searched the PUBMED, EMBASE, Cochrane library and CBM for randomized controlled trials comparing the effects of dexmedetomidine and fentanyl as adjuvants to LAs for intrathecal injection (total of 639 patients from 9 studies), was reported that compared to fentanyl, dexmedetomidine as LA adjuvant in spinal anesthesia prolonged the duration of spinal anesthesia, improved postoperative analgesia, reduced the incidence of pruritus, and did not increase the incidence of hypotension and bradycardia (22).

There is no relevant evident data when comparing a dexmedetomidine with fentanyl-morphine combination as an adjuvant to LA in SA and especially applied in the elderly patients.

CONCLUSION

Current clinical evidence-based recommendations conclude that neuraxial opioid procedure must be one of the most important skills to master for the treatment of perioperative pain in the geriatric patients. This finding involves a broad type of surgical procedures that should benefit from the practice, ranging from minor (ambulatory) surgery to major procedures (23). Neuraxial anesthesia minimizes the risk of common postoperative side-effects seen with general anesthesia including POCD, fatigue, dizziness, pain, and gastrointestinal dysfunction while neuraxial opioids are safer and preferable to parenteral opioids.

A low-dose concept of SA, that consists of LA plus opioids, improved perioperative outcomes in the geriatric patients undergoing elective (low segment) surgery. A combination of intrathecal lipophilic and hydrophilic opioids, such as fentanyl and morphine added to a low dose LA, can improve and prolong perioperative analgesia in the first 24 h postoperatively. It is a simple and practical technique that decreases incidence of spinal hypotension, particularly undesirable in the elderly. The risk of respiratory depression is negligible when used in such a low dose settings. The SA with 5–10 mg 0.5% heavy bupivacaine mixed with fentanyl 20 mcg and morphine 100 mcg could be an acceptable choice in the growing segment of geriatric gynecological population also. There are very few studies concerning neuraxial low-dosage mixture in the geriatric gynecological surgery and more research must be done to confirm safety and efficacy of this concept.

AUTHOR CONTRIBUTIONS

AS, DK, EI, and AK declare that: (1) they made substantial contributions to the conception or design of the work; (2) they drafted the work and revised it; (3) they approve its publication; and (4) they agree to be held accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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A Survey of Enhanced Recovery After Surgery Protocols for Cesarean Delivery in Serbia

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Enhanced recovery after surgery (ERAS) protocols have been described for patients undergoing colon surgery. Similar protocols for cesarean delivery (CD) have been developed recently. CD is one of the most commonly performed surgical procedures, and adoption of ERAS protocols following CD might benefit patients and the health-care system. We aimed to determine which Serbian hospitals reported ERAS protocols, which elements of ERAS protocols were used in CD patients, and whether ERAS and non-ERAS hospitals differed. The survey was sent to all hospitals with obstetric services and 46 of 49 responded. The questionnaire asked whether ERAS protocols had been formally adopted for surgical patients and about their use in CD patients. Specific questions on elements described in other obstetric ERAS protocols for CD included preoperative patient preparation, type of anesthesia and temperature monitoring used for CD, maternal/neonatal contact, and time to discharge. ERAS protocols are used in 24% of surveyed hospitals, 84% admit the patient the day before elective CDs, 87% use a maternal bowel preparation morning on the day of CD, and 80% administer maternal deep venous thrombosis prophylaxis. Only 33% remove IV in the first postoperative day, and 89% of women do not eat solid food until the day following their CD. Neuraxial anesthesia is used in 46% of elective CDs in ERAS hospitals compared to 9% in non-ERAS hospitals ($P < 0.01$), and neuraxial narcotics for post CD analgesia are given more often in ERAS hospitals. Thirty-six percentage of ERAS patients are discharged within 3 days vs. none in the non-ERAS group. Few elements of ERAS protocols reported from other centers outside Serbia are employed in Serbian hospitals performing CD. Despite significant changes that have been made recently in CD care, enhanced recovery after CD could be significantly improved in Serbian hospitals.

Keywords: cesarean delivery, enhanced recovery, neuraxial anesthesia, length of stay, obstetric anesthesiology

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INTRODUCTION

The significance of enhanced recovery after surgery (ERAS) protocols has been well established in non-obstetric surgery patients and was described by Wilmore and Kehlet, 15 years ago (1). Soon after ERAS protocol successes in speeding patient recovery, decreasing times to discharge form the hospital and improving patient outcomes were described in colorectal surgery patients (2), successful application was reported in urological, breast, pancreatectomy, liver resection, and gynecologic surgery (3–9). The ERAS approach emphasizes optimization of the processes of patient care, so that enhanced patient recovery can occur without decreasing the quality of care or patient satisfaction.

ERAS aims to return the patient to normal life quickly. The increased efficiencies have been demonstrated to reduce waste of scarce resources (10) and thus reduce the overall cost of care. While significant variations in ERAS protocols exist both within and between surgical specialties (11), common elements often include effective patient education and acceptance, good perioperative hydration and nutrition, use of surgical techniques associated with fastest patient recovery, maintenance of perioperative patient normothermia, early removal of urinary catheters, adequate pain relief that promotes early ambulation and minimal use of perioperative opioids (which helps the return of bowel function quickly). The multidisciplinary approach requires commitment from the patient, as well as all of the persons involved in their perioperative care: surgeons, anesthesiologists, pain specialists, nursing staff, physical and occupational therapists, social services, and hospital administration. Successful ERAS protocol implementation involves the creation of a core team of anesthesiologists, obstetricians, specialist nurses, and hospital managers (12). The large number of elements that are required for implementation of an ERAS protocol often requires significant culture change in the health organization (12).

Background and Rationale

Enhanced recovery after surgery protocols have been developed for patients undergoing cesarean delivery (CD) in recent years. CD is one of the most commonly performed operations worldwide, its incidence is increasing, and elective CD accounts for an increasing proportion of those operations (13). Therefore, CD represents an increasing burden on national health-care systems. Recent guidelines of the UK National Institute for Health and Care Excellence suggest that a majority of women undergoing elective CD could be discharged on the day after delivery (14). Such early discharges are not associated with either increased patient morbidity or higher readmission rates than in women discharged later (15). One recent report suggested that many women would prefer to be discharged a day earlier than occurred following their delivery (16). The widespread adoption of ERAS protocols for CD was recently advocated by Lucas and Gough as a means for achieving these positive outcomes (17).

Reports describing the implementation of ERAS protocols for CD have been recently published (13, 16, 18–21). In addition to the ERAS elements used in non-obstetric surgeries, these reports often describe early skin-to-skin contact in theater between mother and neonate, infant temperature monitoring to prevent neonatal hypothermia, delayed cord clamping, and early breast-feeding after maternal breast-feeding education. Most of these reports are from the UK, and two survey reports from there note a growing consensus of the elements that ERAS for CD should contain (21, 22).

No reports describing ERAS protocols for CD from Eastern European or middle-income countries have been published, and the number of institutions that use them are unknown. Accordingly, we aimed to determine the use of ERAS protocols for CD in Serbia and to determine the differences in use of common ERAS elements between those institutions that report the use of ERAS protocols and those that do not.

MATERIALS AND METHODS

A survey tool of 22 questions with multiple choice answers was sent by email to all hospitals in Serbia (4 university teaching hospitals and 45 general hospitals), which provide obstetric services (**Table 1**). This survey was approved by Ethical Committee at the Clinical Center of Vojvodina. The questionnaire was completed by either the Chief of Obstetrics or Chief of Anesthesiology who had knowledge of all aspects of perioperative care within the institution, and only one questionnaire per institution was

TABLE 1 | Questionnaire.

INSTITUTION ____________________
SPECIALTY (around)
– Obstetrics
– Anesthesiology

QUESTIONAIRE

In this research are included all hospitals in Serbia (4 university and 45 general Hospitals). Please answer the following questions by around the letter in front of the right answer or you write your answer. Filled questionnaire return by e-mail to following addresses:

borislava60@yahoo.com
mkendrisic@yahoo.co.uk

According to your answers, we shall try to understand which of the "Fast track" surgery criteria (ERAS: enhanced recovery after surgery) are implemented in our hospitals and to make some guidelines for cesarean delivery (CD).

1. Is the ERAS protocol for better and faster recovery after cesarean section introduced to the parturients in your institution?
   A. Yes
   B. No
   C. Sometimes
   D. ________________

2. Who inform the parturients preoperative?
   A. Obstetrician who takes care during the pregnancy
   B. Obstetrician who perform CS
   C. Anesthesiologist in anesthesia clinic
   D. Anesthesiologist who perform anesthesia for CS
   E. __________________________

3. In your hospital is usual patient's admission prior CS?
   A. Evening before schedule surgery
   B. 24 h before
   C. In the morning, on the surgery day
   D. _____________________________

4. In your institution do you use bowel preparation before CS?
   A. Yes
   B. No
   C. Sometimes
   D. ________________

5. In your institution do you use antibiotics prophylaxis 30' before CS?
   A. Always
   B. Sometimes
   C. Never
   D. ________________

6. In your institution do you use DVT prophylaxis before or after CS?
   A. Always
   B. Sometimes
   C. Never
   D. ________________

(*Continued*)

TABLE 1 | Continued

7. What is the percentage of regional anesthesia (RA) for scheduled CS in your institution?
   A. <10%
   B. 10–29%
   C. 30–49%
   D. >50%
8. What is the percentage of RA for emergent CS in your institution?
   A. <10%
   B. 10–29%
   C. 30–49%
   D. >50%
9. Do you use opiates intrathecal for postoperative analgesia (morphine)?
   A. Always
   B. Sometimes
   C. Never
   D. ________________
10. Analgesia following CS is:
   A. IV
   B. IM
   C. combination (IV and IM)
   D. per oral
   E. ________________
11. How long parturients are on the IV infusion?
   A. < 24 h
   B. 24 h
   C. 48 h
   D. Depends of case
   E. ________________
12. When do you start with per oral liquids intake?
   A. Immediately postoperative
   B. Following 12 h
   C. Following 24 h
   D. Following 48 h
13. When do you start with per oral food intake?
   A. Following 12 h
   B. Following 24 h
   C. Following 48 h
   D. ________________
14. Do you use chewing gum following CS?
   A. Yes
   B. No
   C. Sometimes
15. When they start walking after CS?
   A. In the evening (On the day of CS)
   B. Tomorrow morning (following 24 h)
   C. Following 48 h
   D. ________________
16. When do you remove urinary catheter following CS?
   A. On the day of CS
   B. Tomorrow
   C. Following 48 h
   D. Depends of case
17. Do you use "skin to skin" contact on the operating table?
   A. Yes
   B. No
18. Do you use temperature checking intraoperative?
   A. Yes
   B. No

(*Continued*)

TABLE 1 | Continued

19. Do you use active warming during CS?
   A. Yes
   B. No
   C. Sometimes
20. Do you use medication to prevent chronic pain (gabapentin or pregabalin)?
   A. Yes
   B. No
   C. ________________
21. How many CS do you have at your hospital per year?
   A. <500
   B. 501–1,000
   C. >1,000
22. How long are parturients at the hospital following CS before discharge home?
   A. <3 days
   B. 4–6 days
   C. >6 days

returned. One of the authors (BP) followed up after distribution of the survey to answer all responder questions. The questionnaire asked for the presence of ERAS protocols for CD in the hospital, preoperative patient counseling of the elements within the protocol, time of admission to hospital and hospital stay, bowel preparation prior surgery, antibiotic prophylaxis prior to skin incision, prevention of deep venous thrombosis (DVT), percentage of neuraxial anesthesia (NA) for elective and emergency CD, use of intrathecal analgesia, medications for postoperative analgesia, oral intake after CD, use of chewing gum in the early postoperative period, duration of IV fluid therapy, urinary catheter removal, early mobilization of the parturient, skin-to-skin contact between mother and baby in the operating theater, monitoring of body temperature, and active maternal warming intraoperatively. Overall responses were recorded, and the responses between those hospitals with ERAS protocols in place were compared with those who did not report having them. Pearson' chi square test was used where appropriate for comparisons between groups in this prospective observational study (R version 3.3.3, R Core Team, R Foundation for Statistical Computing). Differences of $P \leq 0.05$ were considered significant.

RESULTS

Responses were obtained from 46 of 49 hospitals (3 university and 43 general hospitals; a 94% response rate). ERAS protocols were in use in 11 of 46 (24%) of surveyed hospitals and 63% of the time the responsibility for patients counseling was shared between the obstetrician and anesthesiologist (**Table 2**).

Survey Elements With Similar Responses Between ERAS and Non-ERAS Hospitals

Many surveyed items did not vary between institutions that reported ERAS use vs. those that did not. Surveyed hospitals reported admitting the patient the day before elective CD 84%

TABLE 2 | Survey items with similar responses from institutions with and without ERAS protocols.

Item	Overall	ERAS protocol	No ERAS protocol	*P* value
1. ERAS protocol is used	11 (24%)			
2. Who educates patient?				0.47
Obstetrician	9 (20%)	1 (9.1%)	8 (23%)	
Anesthesiologist	8 (17%)	3 (27%)	5 (14%)	
Either	29 (63%)	7 (64%)	22 (63%)	
3. When admitted for CD				0.17
Day before	37 (84%)	11 (100%)	26 (79%)	
Day of	7 (16%)	0	7 (21%)	
4. Bowel prep is used				0.35
Yes	39 (87%)	11 (100%)	28 (82%)	
No	4 (9%)	0	4 (9%)	
Sometimes	2 (4%)	0	2 (4%)	
5. Antibiotics 30 min before CD				0.08
Yes	21 (51%)	8 (73%)	13 (43%)	
No	5 (12%)	2 (18%)	3 (10%)	
Sometimes	15 (37%)	1 (9%)	14 (47%)	
6. DVT prophylaxis				0.29
Yes	37 (80%)	11 (100%)	26 (74%)	
No	1 (2%)	0	1 (3%)	
Sometimes	8 (17%)	0	8 (23%)	
7. Neuraxial narcotics for CD				0.09
Yes	4 (9%)	2 (18%)	2 (6%)	
No	25 (56%)	3 (27%)	22 (65%)	
Sometimes	16 (35%)	6 (55%)	10 (30%)	
8. Parenteral narcotics administration				0.56
IV	14 (36%)	2 (22%)	12 (40%)	
IM	1 (3%)	0	1 (3%)	
Both	24 (61%)	7 (78%)	17 (57%)	
9. When IV is removed				0.16
Immediately after CD	0	0	0	
<24 h after CD	13 (33%)	6 (55%)	7 (24%)	
24–48 h after CD	26 (65%)	5 (45%)	21 (72%)	
>48 h after CD	1 (2.5%)	0	1 (3%)	
10. When solid food is allowed				0.89
Immediately after CD	0	0	0	
12 h after CD	5 (11%)	1 (9%)	4 (12%)	
24 h after CD	20 (44%)	6 (55%)	14 (41%)	
48 h after CD	20 (44%)	4 (36%)	16 (47%)	
11. Chewing gum is used				0.15
Yes	0	0	0	
No	36 (86%)	10 (100%)	26 (74%)	
Sometimes	9 (20%)	0	9 (26%)	
12. Urinary catheter removed				0.44
Day of CD	2 (5%)	0	2 (6%)	
First post-operative day	26 (59%)	8 (73%)	18 (55%)	
Second post-operative day	11 (25%)	3 (27%)	8 (24%)	
Clinician judgment	5 (11%)	0	5 (15%)	
13. Skin to skin contact				0.09
Yes	22 (49%)	8 (73%)	14 (41%)	
No	23 (51%)	3 (27%)	20 (59%)	
14. Monitor maternal temp				0.32
Yes	5 (11%)	0	5 (14%)	
No	41 (89%)	11 (100%)	30 (86%)	
15. Active warming during CD				0.24
Yes	2 (4%)	0	2 (6%)	
No	34 (76%)	7 (64%)	27 (80%)	
Sometimes	9 (20%)	4 (36%)	5 (14%)	
16. Routinely give gabapentin				1.0
Yes	10 (22%)	2 (18%)	8 (23%)	
No	36 (78%)	9 (82%)	27 (77%)	

P values calculated using the Pearson Chi square test.
CD, cesarean delivery; NA, neuraxial anesthesia; h, hours; temp, temperature; admin, administration; DVT, deep venous thrombosis; min, minutes; ERAS, enhanced recovery after surgery.

of the time, use of maternal bowel preparation in the morning on the day of CD in 87% of patients, measures to prevent maternal DVT during the peri-partum period in 87% of mothers, administration of gabapentin approximately 22% of the time as an analgesic adjunct, with no differences between ERAS and non-ERAS groups.

Perioperative maternal temperature monitoring was reportedly used only 11% of the time and active warming of either IV fluids or other active measures was used less than 5% of the time; there were no differences between ERAS and non-ERAS groups. The maternal urinary catheter was nearly always retained until at least the first postoperative day and was removed in approximately a quarter of women on the second day, with removal in the rest after that. Only 5% of women had their IV removed within 24 h after delivery and 88% did not have solid food until the day following their CD. Among hospitals reporting ERAS use, 73% administered antibiotics within 30 min of a CD, compared to 43% in non-ERAS hospitals, and skin-to-skin contact during CD under NA occurred in 73% of ERAS institutions compared to less than 43% of non-ERAS hospitals, differences that nearly reach statistical significance. The use of neuraxial narcotics for postoperative analgesia is rare in Serbian hospitals, used 9% of the time overall, but 18% of ERAS protocol hospital reported using them vs. 6% of non-ERAS institutions, a difference that also nearly reached statistical significance.

Survey Elements With Differing Responses Between ERAS and Non-ERAS Hospitals

The use of NA for CD, time to ambulation, time to first PO fluids, and days to discharge varied between groups (**Table 3**). In the ERAS group, 46% of parturients received NA for elective CD and 36% were given NA for urgent CD over 50% of the time; only 9% of non-ERAS hospitals use NA for elective CD and 6% for urgent CD >50% of the time ($P < 0.01$ for both comparisons). PO fluid intake was allowed in 91% of patients in the ERAS group within 12 h of delivery, compared to 31% of the non-ERAS group ($P < 0.01$). Thirty-six percentage of ERAS group patients were discharged within 3 days of delivery, vs. none in the non-ERAS group, and no patient stayed after 6 days in the ERAS group compared to 20% in the non-ERAS group ($P < 0.01$). Hospitals in the ERAS group had significantly more deliveries and more patients walked on the day of their CD in the non-ERAS vs. the ERAS group.

TABLE 3 | Survey items with differing responses from institutions with and without ERAS protocols.

Item	Overall	ERAS protocol	No ERAS protocol	P value
1. NA for scheduled CD				<0.01
<10%	17 (39%)	1 (9%)	16 (49%)	
10–29%	13 (29%)	2 (18%)	11 (33%)	
30–49%	6 (14%)	3 (27%)	3 (9%)	
>50%	8 (18%)	5 (46%)	3 (9%)	
2. NA for urgent CD				<0.01
<10%	28 (62%)	2 (18%)	26 (77%)	
10–29%	8 (18%)	3 (27%)	5 (14%)	
30–49%	3 (7%)	2 (18%)	1 (3%)	
>50%	6 (13%)	4 (36%)	2 (6%)	
3. First ambulation				0.04
Day of CD	24 (53%)	3 (27%)	21 (62%)	
First post-operative day	20 (44%)	7 (64%)	13 (38%)	
Second post-operative day	1 (2%)	1 (9%)	0	
4. First PO fluids				<0.01
Immediately after CD	6 (13%)	2 (18%)	4 (11%)	
12 h after CD	15 (33%)	8 (73%)	7 (20%)	
24 h after CD	23 (50%)	1 (9%)	22 (63%)	
48 h after CD	2 (4%)	0	2 (6%)	
5. Number of deliveries				0.04
<500	28 (61%)	5 (46%)	23 (66%)	
501–1,000	12 (26%)	2 (18%)	10 (28%)	
>1,000	6 (13%)	4 (36%)	2 (6%)	
6. Days to discharge after CD				<0.01
<3 days	4 (9%)	4 (36%)	0	
3–6 days	35 (76%)	7 (64%)	28 (80%)	
>6 days	7 (15%)	0	7 (20%)	

P-values calculated using the Pearson Chi square test.
CD, cesarean delivery; NA, neuraxial anesthesia; h, hours; ERAS, enhanced recovery after surgery.

DISCUSSION

This is the first survey of ERAS use in obstetrics in a middle-income country. In Serbian hospitals, patients are not encouraged to eat solid food early after surgery, early mobilization is not encouraged, and a bowel preparation is mandatory in almost all hospitals. There is also a low percentage of NA for CD and a low rate of neuraxial narcotics use.

The low rate of skin-to-skin contact during CD may be due to a low rate of NA use and may interfere with successful breast feeding. Lack of successful breastfeeding is among those factors that have been associated with longer lengths of stay after CD in the UK (16).

A quarter of hospitals in Serbia reported having adopted ERAS protocols. A similar type survey conducted in the UK by Aluri and Wrench, showed that only 10 of 158 labor units in the UK were specifically following one (22). Despite this larger reported use, many elements in the ERAS protocols implemented elsewhere have not been routinely adopted by hospitals in Serbia. Most hospitals, both those with ERAS and those without ERAS, admit patients the night before elective CD, use a bowel preparation, do not allow oral intake up until a few hours before the procedure, do not routinely remove urinary catheters on the day of operation, do not monitor perioperative maternal temperature, and do not engage in active measures to avoid maternal hypothermia. These are practices that differ from hospitals outside Serbia that report using ERAS protocols. Although use of maternal temperature monitoring is routine in less than half of labor and delivery units in the UK, use of the other ERAS elements appears widespread among patients who undergo CD (21, 22).

In 2012, Abel et al. reported on a 2-month use of ERAS protocols for CD and compared two groups of 60 parturients who followed ERAS and non-ERAS pathways (19). Drinking in the recovery room was encouraged and patients were fed and mobilized early. The length of stay (LOS) decreased from 3.3 to 2.1 days, and the readmission rate was reduced from 8.3% to 3.3%. They showed that most of the patients in the ERAS group (97.8%) were satisfied and would recommend ERAS to others undergoing CD or would choose it for themselves in the future. We do not know if patient acceptance would be similar in Serbian mothers as we did not include measures of patient satisfaction in our survey.

Wrench et al. reported initiation of an ERAS for elective CD in 2012 and noted a decrease in LOS and patient satisfaction. Over 2 years, the maternal discharge rate on Day 1 increased from 1.6 to 25.2% (16). In Serbian hospitals, mothers are almost never discharged after CD on postoperative days 1 or 2, although many mothers express the desire to do so. Wrench et al. reported initiation of an ERAS for elective CD in 2012 and noted a decrease in LOS and patient satisfaction. Over 2 years, the maternal discharge rate on Day 1 increased from 1.6 to 25.2% (16). In Serbian hospitals, mothers are almost never discharged after CD on postoperative days 1 or 2, although many mothers express the desire to do so. One reason may be that the cost to the patient of in hospital care is low and patients may not feel an economic incentive to leave. Hospital administrators may also have little economic incentive to do so either. Finally, robust follow-up after patients are discharged may be necessary for patients discharged sooner after CD and the out of facility Serbian health-care system may not be able to assist parturients who are discharged home early.

We showed that Serbian hospitals that report ERAS use discharge patients home earlier than in non-ERAS groups. However, many ERAS hospitals reported a high number of discharges after 3 days compared to surveys of UK hospitals that show that a majority of women are eager go home and are discharged within 2 days of their CD. The elements of an ERAS program that are most associated with a greater chance for early discharge have not been determined. Although we showed that few elements of ERAS protocols reported elsewhere are routinely used in Serbian hospitals, adoption of an ERAS protocol lead to earlier patient discharges. We suggest that the adoption of an ERAS protocol leads to a greater effort on part of hospital staff and patients to achieve earlier maternal discharge, independent of the elements within the protocol. This change in organization and the re-setting of both staff and patient expectations may be the most important reason for reducing hospital stay, as has been suggested by others (12).

The lower rate of early ambulation in the ERAS group vs. the non-ERAS group may reflect the greater use of NA in the ERAS group. Practitioners in Serbia may discourage ambulation in patients for fear of post dural puncture headache (PDPH) after NA, despite substantial work that suggests that the rate of PDPH after NA is not influenced by patient activity.

The cost benefits of ERAS adoption for CD may be considerable. Pilkington et al. (16) reported a possible reduction of 200,000 euros in hospital expenses after implementation of ERAS protocol for CD in their hospital.

All patients may not be suitable candidates for ERAS. The factors suggesting which patients would benefit most from ERAS protocols have not been determined. However, Lucas and Gough suggested that a successful ERAS implementation for CD requires at a minimum good patient education, good in-hospital care, and good community out-of-hospital care for early discharged mothers and babies. Coates et al. showed how implementation of an ERAS program increased maternal satisfaction, primarily by increasing the number of earlier discharges (22). They also noted that a significant improvement in neonatal assessment and early determination of a neonate's status was essential for safe early discharge of both mother and child.

Our survey study has many limitations. As noted earlier, we did not survey for patient satisfaction, which would help in deciding if ERAS protocol introduction would be appropriate. We asked either the Chief of Obstetrics or Chief of Anesthesiology to complete the survey and there may be differences between groups of respondents, although follow-up to ensure understanding of the elements of the survey tool by author BP was rigorous and should have removed this bias. We did not ask the respondents about what barriers prevent the adoption of ERAS protocols, and thus using our data to affect change only identifies those elements for improvement, not how best to implement them. We asked many questions to help to describe perioperative CD care. This may have lead to our finding differences between ERAS and non-ERAS groups that may not be real. Finally, the elements of ERAS protocols which lead to improved maternal and neonatal outcomes have not been determined.

We found that hospitals that have adopted ERAS protocols discharge patients earlier than those that have not, although they do not use many of the elements reported from the UK. We simply do not know which elements are the most important. Patient education and institutional culture change may be the vital change needed. We suggest that setting the patient's expectation that they would be discharged home early and setting staff expectations for the same may be more important than other factors in determining time to discharge after CD; we cannot determine this from our study.

CONCLUSION

Enhanced recovery after surgery protocols are in use at some Serbian hospitals for surgical procedures (mostly colorectal procedures), and some report the use of some elements of ERAS protocols for have CD as well. The results showed uncommon use of antibiotic prophylaxis prior to skin incision but routine use of DVT prophylaxis, earlier oral intake, and earlier discharge from the hospital post CD compared to hospitals not reporting ERAS use. Successful ERAS protocol implementation for CD in Serbian hospitals will require the great efforts of a multidisciplinary medical staff team and the outside community.

AUTHOR CONTRIBUTIONS

BP, MK, MS, YS, and CB all made substantial contributions to the conceptual design of the work, in acquiring the data, and in its analysis. All helped draft the work and revised it critically. All the authors approved this copy for publication. All agreed to be accountable for all aspects of the work in ensuring its accuracy and integrity.

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REVIEW
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Enhanced Recovery After Surgery Protocols in Major Urologic Surgery

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The purpose of the review: The analysis of the components of enhanced recovery after surgery (ERAS) protocols in urologic surgery.

Recent findings: ERAS protocols has been studied for over 20 years in different surgical procedures, mostly in colorectal surgery. The concept of improving patient care and reducing postoperative complications was also applied to major urologic surgery and especially procedure of radical cystectomy. This procedure is technically challenging, due to a major surgical resection and high postoperative complication rate that may reach 65%. Several clinical pathways were introduced to improve perioperative course and reduce the length of hospital stay. These protocols differ from ERAS modalities in other surgeries. The reasons for this are longer operative time, increased risk of perioperative transfusion and infection, and urinary diversion achieved using transposed intestinal segments. Previous studies in this area analyzed the need for mechanical bowel preparation, postoperative nasogastric tube decompression, as well as the duration of urinary drainage. Furthermore, the attention has also been drawn to perioperative fluid optimization, pain management, and bowel function.

Summary: Notwithstanding partial resemblance between the pathways in major urologic surgery and other pelvic surgeries, there are still scarce guidelines for ERAS protocols in urology, which is why further studies should assess the importance of preoperative medical optimization, implementation of thoracic epidural anesthesia and analgesia, and perioperative nutritional management.

Keywords: urology, recovery, radical cystectomy, enhanced recovery after surgery, fast-track pathway

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INTRODUCTION

The new era in perioperative medicine, defined as enhanced recovery after surgery (ERAS) protocols, started with the increase of the importance of a multimodal approach to surgical patients. The most important aims of the multimodal approach are the improvement of patients' preoperative status and the perioperative maintenance of homeostasis, by minimizing stress response and inflammation. This new approach was first used in colorectal surgery (1) and then started spreading to all other types of surgeries (2–4).

There is an increased interest in ERAS protocols in urology. Radical cystectomy (RC) and radical prostatectomy (RP) are predominantly studied urologic procedures. These procedures have major surgical resection, increased risk of bleeding and perioperative transfusion, and in case of cystectomy, urinary diversion and high frequency of postoperative complications. Furthermore, patients undergoing major urologic surgery are usually the elderly, with cardiovascular and other comorbidities, anemia, possible infection, and malnutrition.

PREOPERATIVE PERIOD

The ERAS preoperative period consists of several important elements, which are described below.

Preadmission Counseling and Education

When it comes to ERAS guidelines, the initial phase of different surgeries is preadmission counseling (4–6). It has been determined that the reduction of anxiety by means of sharing details of admission, as well as surgical and anesthetic procedures, may improve pain control (7), early mobilization, and perioperative feeding and hence reduce postoperative complications (8, 9).

Even before first studies of ERAS in urology, Hobisch et al. (10) found out that 65–71% of the patients scheduled for different types of urinary diversion RC had received no information about various therapy options before being admitted to the Department of Urology. After admission, 78.8% of ileal conduit patients and 91.3% of neobladder RC patients were completely satisfied with the information given. Most of the studies from this period (10, 11) mainly examine the need to explain different types of RC urinary diversions to patients and the impact they will have on everyday care after hospitalization. The importance of preadmission counseling and patient education, along with a precise and detailed clarification of the immediate perioperative pathway was not emphasized. To the best of our knowledge, there are no specific studies dealing exclusively with preadmission counseling and education. This issue has so far been analyzed only as a part of the study of ERAS elements.

Dutton et al. (12) examined 165 patients undergoing open RC with urinary diversion implementing ERAS protocol. Patients in this study went through three stages of patient education and counseling. The first stage involved pre-referral by patient's family doctor, the second one was outpatient assessment by a nurse specialist, and the third one included preoperative patient education (both written and verbal) explaining ERAS, as well as stoma or neobladder care before hospital admission. The authors pointed out that the patients were informed at earliest opportunity. Taking everything into account, it can be concluded that the implementation of ERAS elements in this study was safe, coupled with early feeding of patients, early mobilization, and rapid discharge from hospital.

In the following years, more researchers (13, 14) have included preadmission counseling as an obligatory element of ERAS protocols in urology. In the prospective study of Pang et al. (14), preoperative counseling included detailed 30–40 min description of the treatment, provided by a surgeon, a nurse, a stoma therapist, and an anesthesiologist, if necessary. In this study, the patients were additionally preoperatively provided with an information booklet.

Matulewicz et al. (15) also suggested the use of multimedia tools (websites and videos) and intensive verbal and written counseling regarding the expectations and the goals of RC. The authors furthermore proposed the implementation of "Urostomy Education Scale" (16) as an important tool for patient education in patients with urostomy after RC. Moreover, within the systematic review (17), the importance of RC patients' participation in advocacy networks was also stressed, with the aim of improving perioperative care, both before and after surgery.

Preoperative Optimization

Preoperative optimization involves assessment and improvement of medical conditions, as well as the reduction of risks that affect perioperative homeostasis. The guidelines provided by the European Society of Anaesthesiology on preoperative evaluation (18) recommend different strategies that should be used for reducing perioperative risks.

Current or former smokers comprise 80% of RC patients (15). Preoperative smoking cessation might reduce the risk of pneumonia, mechanical ventilation longer than 48 h, and unplanned tracheal intubation. According to the study of Turan et al. (19), active smokers have higher rates of myocardial infarction, postoperative cardiac arrest and stroke, deep vein thrombosis, and sepsis. Systematic review (20), which included urological and genitourinary patients, revealed that intensive smoking cessation intervention with individual counseling and included pharmacotherapy, 4–8 weeks before surgery, reduced the risk of postoperative complications. Meta-analysis (21) of different surgical patients showed that quitting smoking 8 weeks before surgery has no negative impact on postoperative outcome. The guidelines for ERAS pathways in urology (6, 22) recommend smoking cessation 4–8 weeks before surgery.

Daily intake of more than two to three drinks decreases the immune response, prolongs bleeding time and increases endocrine stress response to surgery (23). More importantly, the preoperative 4-week-long abstinence from alcohol reduces exaggerated surgical stress response of alcohol abusers (24).

Perioperative Nutritional Therapy

It has been shown (25) that the patients undergoing RC are at risk of malnutrition due to advanced age and prolonged hospital stay with high frequency of postoperative complications. In addition, these patients already have some degree of inflammation as a part of malnutrition. In a retrospective cohort study of 538 patients with RC (26), nutritional deficiency measured by preoperative weight loss, body mass index and also serum albumin, strongly predicts a 90-day survival, as well as poor overall survival.

Therefore, nutritional risk screening before a surgical procedure (27) is a highly recommended screening tool for establishing a possible risk of malnutrition. When it comes to establishing perioperative nutritional status, dietician referral 1 day before RC, represents yet another step forward in this whole process, just as it was already shown in the study of Arumainayagam et al. (28).

Perioperative nutritional therapy should be initiated before surgery if the patient is at nutritional risk or has malnutrition (29). The indication for preoperative nutritional therapy also exists if there is a trend of less than 50% of recommended oral food intake for more than 7 days, or food abstinence for more than 5 days.

In a randomized trial of Hamilton-Reeves et al., cystectomy patients showed different immune response to surgery and late infection (30) if perioperatively fed with specialized immunonutrition in intervention group. In accordance with the guidelines (29), perioperative or at least postoperative administration of specific formula enriched with immunonutritents should be given to malnourished patients undergoing major cancer surgery. However, the potential role, specific type, and financial aspects of preoperative nutritional therapy in RC patients are yet unknown.

Bowel Preparation

The need for oral bowel preparation has been examined especially for ileum diversions of RC. Reduced bowel preparation in patients with mainly ileal conduit diversion of RC produced no detrimental effect on morbidity or mortality (28). In the study of Tabibi et al. (31), spillage was observed in all studied patients, in both bowel prepared ones and in those who had no preparation. The infection complications did not increase in the group without bowel preparation for cystectomy. In the randomized trial of Xu et al. (32), patients were randomized to a preoperative bowel preparation group and to another one with no preparation. It has been concluded that bowel preparation did not present any advantages in RC, neither with regard to patient recovery nor to complication occurrence.

The colorectal surgery meta-analysis (33) showed no clinical benefit from mechanical bowel preparation. This study also pointed out that inadequate bowel preparation with the presence of liquid content increases the risk of infections.

ERAS guidelines for RC (6) recommend that preoperative bowel preparation can be safely omitted.

Thromboembolic Prophylaxis

Patients undergoing RC and RP are considered to be high risk of venous thromboembolism (VTE) because of the cancer disease and the surgery procedure lasting more than 120 min (34). Novotny et al. (35) revealed about 5% incidence of clinically significant deep vein thrombosis in RC patients, while according to Vukina et al. (36) incidence in open RP is 1–5% and just 0.5% in robotic RP. Despite importance of prevention of VTE in major urologic surgery, variations in utilization of prevention treatment are demonstrated and criticized (37).

European guidelines on perioperative VTE prophylaxis for fast-track surgery (34) recommend the first dose of LMWH 12 h before the procedure or 6–8 h after the procedure. In case of a planned neuraxial anesthesia, postoperative administration might be a preferred option. Furthermore, according to Sachdeva et al. (38), adding graduated compression stockings or compressive stockings enables more effective thromboprophylaxis.

ERAS Society guidelines for rectal/pelvic surgery (5) recommend taking into consideration extended prophylaxis for 4 weeks in patients with the increased risk of VTE. These recommendations are in accordance with the American College of Chest Physician guideline (39) and refer to high risk patients with cancer.

Preoperative Fasting

It has been demonstrated (40) that long food and water abstinence produce stress and deteriorate surgical patient wellbeing. The European Society of Anaesthesiology fasting guidelines encourage patients to drink clear liquids (tea, coffee without milk and water) up to 2 h before the elective surgery. With the highest level of evidence, they recommend the prohibition of solid food 6 h before the elective operation. Patients with conditions such as gastro-esophageal reflux, obesity, diabetes, and pregnant women, who are not in labor, may have delayed gastric empting. More evidence is needed for fasting recommendations regarding these groups of patients.

In major urologic surgery, Rege et al. (41) reduced preoperative fasting period introducing clear liquids to 2 h before laparoscopic live kidney donor surgery in ERAS group of patients. They pointed out that the reduction of preoperative fasting period enhances patient's comfort, reduces thirst and anxiety, thus facilitating faster recovery. In their study, patients with ERAS perioperative pathway had shorter length of hospital stay. On the other hand, in some early fast-track studies (42) of patients undergoing laparoscopic RP, liquid drinks were allowed only until midnight of the preoperative day. The only difference between the conventional and the ERAS group of patients in this study was that the ERAS group of patients was allowed to have lunch and soup for dinner, whereas the patients in the conventional group were not allowed to consume any food whatsoever after breakfast on the day before the surgery. Even without this preoperative element of ERAS pathway, the authors observed shorter length of hospital stay in the ERAS group.

According to previous discrepancies more evidence is needed about impact of shortening of fasting before major urologic surgery procedures.

Preoperative Carbohydrate Loading

One of the main goals of ERAS protocols is the reduction of perioperative insulin resistance. Meta-analysis (43) of randomized controlled trials investigating preoperative oral carbohydrate treatment before elective surgery revealed significant reduction in the length of hospital stay of the patients receiving the treatment when compared with control groups. However, the authors pointed out that this was valid for patients undergoing major abdominal surgery, and they also emphasized that there was significant heterogenicity among different studies.

The extent of insulin resistance after surgery is proportional to the magnitude of the surgery (44) and blood loss (45). Both risk factors are present in RC (32) and other major urologic procedures. Several studies (40, 46, 47) of open RC conducted after the year 2010, used carbohydrate loading liquids 2 h before surgery with the aim of reducing postoperative insulin resistance. In the study of robotic-assisted laparoscopic cystectomy (48), 31 patients received carbohydrate loading at 6:00 p.m. the day before the surgery and at 5:00 a.m. on the day of the surgery. Patients within the study group showed significant differences in terms of mobilization within the room, the time to regular diet, and lower use of postoperative opioid analgesia. In other major urologic procedures, the reduction of insulin resistance was also found to be an important part of ERAS pathways. In the retrospective analysis (41) of patients undergoing laparoscopic live kidney donor surgery, preoperative carbohydrate loading liquids were used for ERAS pathway group. Further studies are needed to evaluate CHO loading for patients undergoing major urologic surgery.

Antimicrobial Prophylaxis

European Association of Urology guidelines (49) suggested optional use of antimicrobial prophylaxis in RP and nephrectomy, since there are no studies on this issue. In RC patients, prophylaxis for both aerobic and anaerobic pathogens is recommended. The combination of cefuroxime and aminopenicillin/betalaktamase inhibitor plus metronidazole is recommended. In case of prolonged operation or important morbidity factors, antimicrobial prophylaxis might be prolonged to <72 h.

Prolongation of antibiotic prophylaxis is not recommended if urinary drainage is left in place after surgery.

Prevention of Postoperative Nausea and Vomiting (PONV)

There is insufficient evidence regarding the incidence of PONV after urologic surgery. Shabsigh et al. (50) reported 29% of gastrointestinal complications from the overall number of complications, among which just 1.5% of patients were the ones with emesis. Nevertheless, PONV may intensify postoperative pain, wound dehiscence and hematoma and hence increase patient distress (51). With the aim of reducing the incidence of PONV, patient baseline risk should be assessed using validated score (52). Recommended risk scores are Apfel et al. (53) and Koivuranta et al. (54).

After establishing baseline risk, PONV is considered through all three parts of ERAS pathway, preoperative, intraoperative and postoperative. Prevention of PONV is accentuated especially in laparoscopic urologic surgery. In this way in the non-randomized retrospective analysis (43) of laparoscopic nephrectomy, antiemetics were started preoperatively with scopolamine patch, dexamethason and ondansetron were given intraoperatively and scopolamine and ondansetron postoperatively. For preoperative and postoperative phases, rescue antiemetics were also suggested. In conclusion, the rate of postoperative PONV was not analyzed albeit patients from intervention group had reduced length of hospitalization.

In the prospective randomized study (55) of RC patients, a guided intraoperative fluid therapy reduced the incidence of PONV (11 vs 3, $p < 0.01$ and 13 vs 1, $p < 0.0001$).

Yoo et al. (56) studied the incidence of PONV between group of patients with propofol total intravenous anesthesia (TIVA) and the group of patients with desflurane anesthesia for robot-assisted laparoscopic RP. The incidence of PONV was significantly lower in TIVA group both in post-anesthetic care unit and 1–6 h after the surgery.

INTRAOPERATIVE PERIOD

This section reviews several important components of the intraoperative period (**Table 1**).

Perioperative Analgesia

The use of neuraxial anesthesia in RC and in RP patients is widely applied as one of the crucial elements of fast-track pathways (42, 59, 60). The American Pain Society (61) points out the importance of using neuraxial anesthesia in major thoracic and abdominal surgery, especially in patients with cardiologic and pulmonary morbidity or in those at risk of postoperative ileus (POI).

The epidural provides different positive effects on the general perioperative status of patients. Several studies reveal decrease in mortality (61, 62) as well as decrease in the risk of cardiovascular and respiratory (63) events in abdominal surgery. In RP and in RC patients, the epidural is related with reduced intraoperative blood loss (64, 65), earlier recovery of gastrointestinal peristalsis (66), and postoperative pain control (64). Still, Doiron et al. (67) observed no difference in length of stay, 30- and 90-day readmission rate, nor any influence on 30-day mortality among cystectomy patients with or without perioperative epidural. This is consistent with other studies (68, 69) in which the epidural was compared with intravenous patient-controlled analgesia.

It is extremely important to determine the aspects of using epidural in major urologic surgeries in the future. The level of epidural insertion for different urologic procedures is not precisely defined. For example, in some studies (60, 66) authors used Th9–11 for RC patients; however, in the study of Autran et al. (69) Th11-L2 was used. In RP studies, Shir et al. (64) used L3–L5, but Hong et al. (65) used Th12-L2. ERAS guidelines for RC (6) strongly recommend the use of thoracic epidural for 72 h, by extrapolating results from rectal surgery.

There are, however, other ways of administering perioperative analgesia in urology, which showed promising results. For example, in the study of Dutton et al. (12), out of 165 cystectomy patients that entered an enhanced recovery pathway, 140 patients had rectus sheath catheter (RSC) analgesia (**Table 1**). The authors switched from regional anesthesia to RSC blocks because of their numerous benefits. The advantages of RSC blocks have previously been studied (70, 71), and they include highly successful placement, patient safety, the possibility to use in patients taking antiplatelet medications, as well as the reliability during postoperative care.

Intraoperative Fluid Therapy

The optimization of fluid therapy, as a part of fast-track pathways, aims at "zero balance," maintaining preoperative fluid composition and weight (72). According to Gupta and Gan (73), maintenance fluid therapy in adult patients during major abdominal surgery should be accomplished with 1–3 ml/kg/h.

Intraoperative fluid therapy in RC was studied in the prospective study of Pillai et al. (55). Patients were randomized to receive standard intraoperative or esophageal Doppler guided fluid therapy. The study demonstrated improvements in gastrointestinal function with significant reduction of ileus, PONV and also wound infection in the intervention group. The trial patients received significantly greater volumes of intravenous fluid during the first operative hour. Authors postulated that this was the underlying reason for avoidance of occult splanchnic hypoperfusion and lowering of postoperative complications. It was also pointed out that timing of fluid administration may be the goal for tissue perfusion, rather than volume. The major limitations of this study were small number of patients and inclusion just of ASA1 and ASA2 patients.

In another randomized trial (74), patients were allocated to receive low volume of fluid therapy (1–3 ml/kg/h) with preemptive

TABLE 1 | Summary of intraoperative elements from published trials of enhanced recovery after surgery (ERAS) protocols for RC.

Authors	Arumainayagam et al.	Mukhtar et al.	Dutton et al.	Smith et al.	Daneshmand et al.	Persson et al.	Pang et al.
Reference/(*n*)	(28)/(112)	(46)/(77)	(12)/(165)	(57)/(133)	(58)/(110)	(13)/(70)	(14)/(453)
Non-ERAS *n*/ERAS *n*	56/56	26/51	0/165	69/37 ERAS 1, 27 ERAS 2	0/110	39/31	60/393
Surgery type	Open RC	Open RC	Open RC	Open RC	Open RC	Open RC	Open and robotic RC (425/28 ptc.)
Ileal condui/Neobl./Con. cu.div.	47/9/0	48/3/0	131/34/0	133/0/0	35/70/5	52/18/0	368/25/0
Antibiotic prophylaxis	Not specified	Not specified	Single dose cefuroxime, metronidazole	Not specified	+ Continued for 24 h	+ (100% ptc.)	Coamoxiclav 24 h in men 48 h in women
Analgesic method, *n* (%)							
Epidural	+	+	+ 25 ptc.	– ERAS 1 – ERAS 2	–	+	–
RSC	–	–	+ 140 ptc.	+ ERAS 1 + ERAS 2	– Subfascial LA	–	+ (53% ptc.)
Other	–	–	–	–	iv. Acetaminophen	–	–
Avoiding of							
NGT	Not specified	+	+	+ ERAS 1 + ERAS 2	–	+	+ (84% ptc.)
Drains	–	+	–	–	–	+ (32% ptc.)	Consider omitting pelvic drain
Fluid/sodium management	Not specified	+	+ (GDFT)	+ ERAS 1, ERAS 2 (GDFT)	+ Monitored by SV and CVP	Not specified	+ (Limited fluid targeted to losses)
Intraoperative warming	Not specified	+	+	–	Not specified	+	+
Small incisions	Not specified	+	+	Change in surgical technique	Not specified	Not specified	+ (83% ptc.)
PONV prevention	Metoclopramide from day 1	+	Metoclopramide, omeprazole	Not specified	Not specified	+ (29% ptc.)	Antiemetics as needed
$MgSO_4$ replacement	–	–	–	Infusion in ERAS 2	–	–	–

RC, radical cystectomy; ptc., patients; Neobl., neobladder; Con.cu.div., continent cutaneous diversion; RSC, rectus sheath catheter; LA, local anesthetics; NGT, nasogastric tube; GDFT, goal directed fluid therapy; SV, stroke volume; CVP, central venous pressure; PONV, postoperative nausea and vomiting.

norepinephrine of 6 µg/kg/h intraoperatively. The intervention group had reduced complication rate and hospitalization time. Furthermore, in another study the authors (75) showed zero fluid balance and zero weight gain on the first postoperative day with the same intraoperative intervention.

In multivariate logistic regressions of Bazargani et al. (76), there was no significant link between higher intraoperative fluid intake and complications on the 30th and 90th days in 180 patients who underwent RC. It should be emphasized that this was ERAS pathway study for RC, *vice versa* to previously mentioned studies (55, 74). It was suggested that various measures of ERAS protocol attenuated possible negative effects of high fluid administration volumes. The controversy of fluid management in RC continues. Fluid restriction with possible silent or evident splanchnic ischemia and hypotension must be compared with fluid overload and interstitial and gut edema. Possible better monitoring of bowel perfusion and standardized protocols of intraoperative fluid administration in ERAS pathways in RC and other major urologic procedures is needed.

Preventing Intraoperative Hypothermia

The maintenance of normothermia during surgery prevents high oxygen consumption, wound infection, bleeding, and pain. China's national cross-sectional study (77) on 3,132 patients under general anesthesia showed increased ICU admissions and prolonged hospital stay in patients with intraoperative hypothermia.

The active warming strategies, such as the use of warm fluids and forced air warming (78), were more effective than passive warming in maintaining stable intraoperative hemodynamics and core temperature.

Surgery Type

Compared with open surgery (79), minimally invasive surgery enhances patients' recovery, due to less stress, and it also significantly lowers opioid requirements (80). According to systematic reviews (81, 82), the implementation of robotic RC has reduced blood loss and transfusion, inpatient narcotic requirements, time to regular diet, and length of hospital stay. In the prospective randomized study of Nix et al. (80), there was lower estimated blood loss and there were fewer narcotic requirements during robotic RC. Postoperative return of bowel function was more rapid in patients who underwent robotic RC. The authors believe that the probable reasons for the previously stated findings were lower degree of bowel manipulation, less fluid imbalance and lower overall opioid consumption. However, in addition to the benefits, it should also be stated that, according to some studies (79, 80), robotic cystectomy lasts significantly more and has similar rate of postoperative complications when compared with open RC.

Robot-assisted RP has gained popularity due to its benefits which are similar to those of robotic RC (56). Nevertheless, studies mainly investigate disease control and functional sequel. Maurice et al. (83) listed increased travel burden and limiting access to surgical care as disadvantages of RP. Further studies on the implementation of fast-track pathways in robotic prostatectomy are needed.

Studies of laparoscopic RC state different benefits. In the study (84) of 47 patients undergoing laparoscopic RC, before and after the implementation of the ERAS protocol, ERAS group had lower frequency of central vein catheter infection and paralytic ileus. Guan et al. (85) showed that patients with fast-track laparoscopic RC had shorter time to first flatus and regular diet, lower serum C-reactive protein and white blood count on the fifth and seventh day after surgery, as well as lower frequency of complications.

POSTOPERATIVE PERIOD

Several elements related to postoperative period are reviewed here.

Nasogastric Tube (NGT)

Early NGT removal was introduced in the study of Pruthi et al. (86) as a fast-track element for RC. The NGT was removed on the first day, and clear liquid was introduced on the second postoperative day. The main improvement was seen in postoperative morbidity. Park et al. (87) found out that early NGT removal after RC is not correlated with POI. In the prospective study (88), the authors examined the combination of metoclopramide and early nasogastric suction removal in RC patients and revealed reduction of postoperative atelectasis and earlier tolerance of solid food without complications, regarding bowel anastomosis. Retrospective analyses of RC patients (12) in the enhanced recovery program introduce "no routine NGT" as one step forward. The authors reserved the use of nasogastric suction only for patients with a POI. Outcomes of this study revealed no adverse effects on readmission and complications. It can be concluded that further studies will have objective to determine if the routine use of NGT in RC is necessary.

Postoperative Analgesia

Epidural analgesia given during the period of 2–3 days after surgery, preferably without opioids, provides more efficient analgesia, compared with patient-controlled analgesia (89) in colorectal surgery. As far as urologic surgery is concerned, according to the study of Hong et al. (65), postoperative pain scores were lower in patients with combined general and epidural anesthesia, compared with RP patients with general anesthesia only. The authors concluded that this may be important for the reduction of the incidence of postoperative chronic pelvic pain. In the prospective, randomized double-blinded study (90), it was shown that continuous epidural infusion of local anesthetics and sufentanil alone or combined produced adequate analgesia for RP and nephrectomy. The authors found out that ropivacaine, combined with sufentanil, was the most preferable combination because of low incidence of motor block.

As it was mentioned before, RSC analgesia (12) for RC and transverses abdominis plane block (91) in RP are getting attention as alternatives to neuraxial anesthesia for perioperative analgesia. The idea of combining motor blocks with oral paracetamol/non-steroidal anti-inflammatory drugs (91) may potentially eliminate opioids from postoperative analgesia.

Optimal postoperative analgesia for major urologic surgery includes different techniques and different drugs. The introduction of new minimally invasive surgical techniques implies the use of different modalities; therefore, the specific role of certain combinations of analgesia regimens needs to be investigated in future.

Prevention of POI

Postoperative ileus is a frequent gastrointestinal complication especially after RC. The incidence of POI in RC has been between 4 and 31% (13, 35). With the aim to define early postoperative morbidity after RC, Shabsig et al. (50) proposed the definition of ileus as "Inability to tolerate solid food by postoperative day five, the need to place NGT or the need to stop oral intake due to abdominal distension, nausea or emesis." Proposed mechanisms for POI after RC (92) are fluid overload, electrolyte shifts, bowel manipulation, and opioid use. It has been theorized that the presence of urine in the operative field during RC delays resumption of the bowel motility (47).

It has been shown (13) that patients guided with ERAS pathway have significant reduction in the average time of the first passage of stool compared with pre-ERAS group. The prevention of POI involves a sum of benefits of ERAS elements. These are epidural perioperative analgesia (66, 92), optimization of intraoperative fluid therapy (55), minimally invasive approach to surgery, early NGT removal with early oral intake (13), and early mobilization.

Other measures used with the aim of promoting bowel function and ileus prevention are chewing gum and using alvimopan. In the study of robotic RC (93), patients that chewed gum had shorter time to first flatus in comparison with the standard ones.

In a retrospective study of Hamilton et al. (94), the alvimopan group of patients undergoing RC had significantly shorter average time of resuming a regular diet (5.3 vs 4.1 days, $p < 0.01$).

Finally, regardless of the great importance of POI regarding postoperative morbidity in ERAS for RC, its significance in other major urologic surgeries is still to be evaluated.

Early Oral Intake and Postoperative Nutrition

The safety of early oral intake after bowel anastomosis was shown in several studies (95, 96). The guidelines for perioperative care in elective rectal/pelvic surgery recommend oral diet "*ad libitum*" 4 h after rectal surgery (5). Pruthi et al. (86) showed improvement in perioperative care in patients with RC by reducing time to clear liquid and regular diet. Early oral nutrition, as a part of multimodal approach (97), revealed reduced time to first flatus. Arumainayagam et al. (28) restarted clear fluids on the day of RC with other perioperative ERAS elements in 56 out of 112 patients. This study showed reduced total and postoperative hospital stay.

ESPEN guidelines for surgery (29) recommend that oral intake, including clear liquids, should be initiated within hours after surgery in most patients. ERAS society guidelines (6) for perioperative care after RC suggest that normal diet should be reestablished as soon as possible.

In the case of impaired oral or enteral tolerance for more than seven days, ESPEN guidelines (29) recommend adding parenteral nutrition. According to EPaNIC study (98) withholding of parenteral nutrition until day eighth appears to be superior strategy than early addition of parenteral nutrition. According to authors, early administration of parenteral nutrition suppresses autophagy thus preventing clearance of damaged cells and microorganisms. The study population was low severity critical care group of patients among which major surgical patients too. Moreover in the study of Roth et al. (99) in patients after RC with urinary diversion, immediate postoperative parenteral nutrition is associated with higher incidence of infection complications vs oral nutrition alone.

Early parenteral nutrition is beneficial in malnourished patients in whom oral or enteral nutrition is not feasible (29).

Early Mobilization

Prolonged bed rest causes respiratory, musculoskeletal, and neuropsychological changes (100).

Primary conditions that have to be fulfilled before patient mobilization are the following ones: the gaining of patient's motivation, postoperative pain relief, and the prevention of orthostatic intolerance (17). Furthermore, in the randomized study of Gatt et al. (101) on colonic surgery, the implementation of structured mobility plan with an active intervention of a physiotherapist resulted in longer period of time out of bed and in increased grip strength.

In the study of Pang et al. (14), the implementation of early mobilization of patients after RC along with other perioperative elements of the ERAS protocol reduces the length of hospital stay and the frequency of readmission. In this prospective study, on the first postoperative day, patients stayed out of bed for 6 h and walked 10–20 m, while on the second postoperative day they walked 100 m. Other authors (12, 13) also enlist early mobilization of patients into local ERAS protocol for cystectomy with similar results.

Early mobilization is emphasized in perioperative care of patients after RP as well. In the prospective randomized study of Gralla et al. (42), patients walked around their room and around the ward on the very day of the surgery. Patients from the conventional group were allowed only upright position on the same day.

Already defined as part of "proactive de-medicalization" (14), patient mobilization represents important prerequisite for stoma self-management and for the decrease in length of hospital stay.

Urinary Drainage

Urinary bladder drainage is a routine procedure in major and urologic surgery. Optimal duration of catheter drainage is 1 day after colonic resections (102) and after pelvic surgery in patients with low risk of urinary retention (5, 6). Catheter removal on the first postoperative day after thoracic and abdominal surgery reduces the incidence of urinary tract infections.

The time period of urinary drainage in radical RC patients is vaguely defined in scientific literature. According to the study of Mattei et al. (102), the stenting of ureteroileal anastomosis resulted in decreased postoperative upper urinary tract dilatation; it improved postoperative bowel function and also decreased metabolic acidosis. The consensus statement about the exact timing of the stent removal in ileal conduit patients varies from 5 to 14 days. The urinary catheter in orthotopic neobladder is left for, at least, 14 days (103) after surgery.

Bearing in mind insufficient evidence (6) analyzed so far, this particular field of ERAS protocol needs to be studied in the future.

CONCLUSION

Multimodal perioperative approach involves many evidence-based interventions with the aim of helping without doing any harm. Major urologic procedures, especially RC, represent a special challenge for future investigation in the ERAS era. Important fields for future investigation, regarding preoperative phase of surgery, are the following ones: the importance of nutritional therapy with the emphases on immune formulas, the omitting of preoperative bowel preparation, and the impact it will have on postoperative outcome, possible advantage of prolonged thromboprophylaxis regarding decreasing risk of VTE and further consideration of lowering insulin resistance. Intraoperative period studies will have to distinguish between the patients with possible risks of fluid overload and the need for guided fluid therapy and the patients who need special surgical techniques. New modalities of opioid sparing postoperative analgesia, the importance of implementing new drugs and special ERAS elements with the aim of preventing POI and the defining of optimal duration of urinary drainage, will be interesting issues to be studied in future, related with postoperative period in major urology. The main prerequisite for everything stated above is the increase of ERAS implementation in major urologic surgery.

AUTHOR CONTRIBUTIONS

NV conceived, designed, and wrote the manuscript. LD helped in analyzing the data.

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The Safety and Efficacy of the Continuous Peripheral Nerve Block in Postoperative Analgesia of Pediatric Patients

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Postoperative analgesia is imperative in the youngest patients. Pain, especially if experienced during childhood, has numerous adverse effects—from psychological, through complications of the underlying disease (prolonged treatment, hospital stay, and increased costs of the treatment) to an increase in the incidence of death due to the onset of the systemic inflammatory response. Peripheral blocks provide analgesia for 12–16 h, and are safer due to rare side effects that are easier to treat. The continuous peripheral block (CPNB) has been increasingly used in recent years for complete and prolonged analgesia of pediatric patients, as well as a part of multidisciplinary treatment of complex regional pain syndrome. It has been shown that outpatient CPNB reduces the need for parenteral administration of opioid analgetics. It has also been proved that this technique can be used in pediatric patients in home conditions. Safety of CPNB is based on the increasing use of ultrasound as well as on the introduction of single enantiomers local anesthetics (ropivacaine and levobupivacaine) in lower concentrations. It is possible to discharge patient home with catheter, but it is necessary to provide adequate education for staff, patients, and parents, as well as to have dedicated anesthesiology team. Postoperative period without major pain raises the morale of the child, parents. and medical staff.

Keywords: pediatric anesthesia, continuous peripheral nerve block, postoperative analgesia, pain management, perineural catheters

MINI REVIEW

The pain, according to the new definition, is a disturbing experience associated with existing or potential tissue damage, with a sensory, emotional, cognitive, and social component (1). Postoperative analgesia is imperative in the youngest patients. Pain, especially experienced during childhood, has numerous adverse effects—from psychological, through complications of the underlying disease (prolonged treatment, hospital stay and increased costs of the treatment) to an increase in the incidence of death due to the onset of the systemic inflammatory response (2). It is clear that all those who deal with child health care have a moral obligation to prevent and adequately cure their pain.

Regardless of immaturity, the child can feel pain since birth (3). The pain sensitivity is greater in younger children and so analgesia should be provided to them during, before and after the surgery since birth. Repetition of painful procedures determines the threshold for pain for the whole life (4). Inadequate treatment of acute pain is one of the important prerequisites for the development of chronic pain.

The goal of analgesia in the postoperative period is to reduce or eliminate pain with minimal additional harmful effects and overall treatment costs. Adequate postoperative analgesia, especially during the first 48 h, reduces the stress response of the organism to the surgical procedure, thereby affecting endocrine, metabolic, and inflammatory changes. This reduces the incidence of postoperative complications and improves the outcome of surgical treatment (4–8).

Single shot peripheral regional blocks provide analgesia for 12–16 h, almost the same length as central blocks (9). Peripheral blocks are safer due to rare side effects that are easier to treat and their use has increased significantly over the last two decades (10). The continuous peripheral block (CPNB) has been increasingly used in recent years for complete and prolonged analgesia of pediatric patients, as well as a part of multidisciplinary treatment of complex regional pain syndrome (CRPS) or epidermolysis bullosa (11).

It has been proven that outpatient CPNB reduces the need for parenteral administration of opioid analgesics (12). It has also been proven that this technique can be used in pediatric patients in home conditions (13, 14). Patients can be released home even with a residual motor block, after prescribed additional oral analgesic therapy and after they received verbal and written instructions regarding the use of CPNB and the identification of possible complications (muscle weakness, less feeling for hot or sharp objects…) (13). There is currently no publication on the wound catheter technique in pediatric patients (11).

There are still not enough prospective studies to confirm the efficacy and safety of CPNB technique and the existing studies have numerous limitations. Comparison of studies is difficult due to differences in the definition of side effects.

Safety of CPNB is based on the increasing use of ultrasound (US) as well as on the introduction of single enantiomers local anesthetics (LA) (ropivacaine and levobupivacaine) in lower concentrations. Originally, bupivacaine had a primacy, while today ropivacaine (0.1–0.2% by infusion, average 0.25 mg/kg/h) is mainly used because of its lower toxicity (9, 15, 16). This LA also provides a better differential block (sensory block without motor nerve paresis) (17). It can also be used for a patient controlled administration (0.2% ropivacaine 0.02 ml/kg/h, bolus 0.1 ml/kg, lockout interval 30 min) (18). The risk of LA toxicity to muscle tissue is increased in infants, so it is advised to use the lowest possible doses and concentrations of LA (11, 19).

However, if catheter efficiency is suspected in the immediate postoperative period, it is recommended to perform a test bolus dose of 3 ml of lidocaine 1.5% with epinephrine 1:200,000 (15). If tachicardia appears, the catheter is placed intravascularly.

Peripheral regional block in children has faster onset but short duration. In children under 1 year of age, nerve fibers are thinner, myelination is scarce, and Ranvier's nodes are closer. The volume of distribution is higher (20, 21), clearance is smaller (22), and the free drug fraction (unbounded for proteins) is higher (20) so the doses are almost the same as in adults. Cytochrome CYP1A2 on which ropivacaine is metabolized matures around the age of 4–7 years old, and CYP3A4/7 on which levobupivacaine is metabolized matures at the end of the first year (23).

Catheters are placed in sterile conditions with the help of a nerve stimulator (4.6%), ultrasound (30.2%), or a combination of these two techniques (62.9%) (15). Placement of perineural catheters under the control of US is becoming more and more frequent and has an increasingly wider use nowadays. In the study of Walker et al. (9), the ultrasound has advantages (in up to 90% of the cases depending on the type of block). Advantages of using US are reflected in the fact that it is possible to monitor the path of anatomical structures to achieve a safe orientation. The latest US devices allow visualization of the needle itself and in that way they ensure the best position of the needle in relation to the anatomical structures, reduce the risk of nerve injury and surrounding structures. US enables monitoring of the distribution of LA, preventing intravascular injection and optimizes the amount of LA which reduces the risk of toxic reactions. The catheter was usually placed under general anesthesia [in 92.9% of patients by Visoiu et al. (15) and in 98.9% of cases by Gurnaney et al. (12)].

Patient satisfaction is a very important indicator of the quality of treatment and higher pain control satisfaction score (PCSS) is an indicator of better patient care. Pediatric patients have expressed satisfaction with the popliteal CPNB (24). For the first time, Visoiu et al. evaluated pediatric patient satisfaction with analgesic therapy using PCSS and 91.4% of patients were very satisfied (8–10 out of 10) (15). They reported home PCSS for parents (9–10 out of 10) and for medical staff (9–10 out of 10). In Visoiu et al. study, more patients reported pain at home than during the Postoperative Ambulatory Care Unit (PACU) stays. Pain scores were lower in the PACU and on postoperative day 0 than on postoperative day 1 and the following days (15).

In a study by Visoiu M et al., 31.4% of patients did not have pain and did not receive any additional analgesics during their stay in PACU. After the release from the hospital, 25% of the patients did not have any pain at home, although 97% of patients received at least 1 dose of opioids (15). According to Dadure et al. about 60% of patients received at least 1 additional dose of oral analgesics (25). Study of Ganesh et al. showed that about 56% of children received opioid during the first eight postoperative days (13). The average time for the first dose of opioids in Gurnaney's study was 16 h (12). 60% of their patients needed an opioid within the first 8 h 40% of which received the opioid already in the recovery room (12). The incidence of patients needing opioid analgesia increased to about 74% by 48 h with about 26% of the patients not requiring any opioid analgesics (11). The reason for the frequent use of opioids could have been due to the preference of lower concentration and infusion rate of LA to avoid motor block (recommended 0.4 mg/kg/h maximum infusion rate for ropivacaine). Another reason could be that multiple nerves need to be blocked, to provide complete sensory block after certain procedures.

Continuous peripheral block does not exclude the additional use of opioids (13). In the PACU surgical analgesia is usually achieved by CPNB but some other pains (tourniquet) or reasons to be restless remains (anxiety, due to the absence of the parents, emergence delirium associated with sevoflurane, etc.). Postoperative use of opioids in home conditions is likely to occur because parents are advised to give the prescribed medication (as needed) to the children with low intensity pain or before going to sleep (15).

Perineural catheter technique is used in chronic pain. The management of patient with CRPS is integrated in a multidisciplinar approach associating pain management with physiotherapy treatment and psychological management. The keys to success are active physiotherapy treatment and restoration of normal limb movement to which CPNB may contribute. Recurrent CRPS remains a therapeutic challenge in pediatric patients. Dadure et al (11), reported that a 4-day CPNB after an initial Bier block is effective against intractable and recurrent CRPS in 13 children, leading to pain reduction, physiotherapy facilitation, and functional rehabilitation. In this study, all children were able to move about easily after the initial 24-h period and continued the treatment at home using infusion pumps.

Complications are rare and minor, mainly mechanical (accidental catheter withdrawal, dislodgement, or occlusion), and nausea and vomiting (11). So far, the largest study on the safety of perineural catheters use in children on over 2,000 set up catheters in children demonstrated a low degree of complication, which is correlated with the percentage of complications in the adult population (15).

In the study by Visoiu et al., 14.4% of patients had subsequent catheter-related complications, mainly minimal catheter leakage that did not affect the analgesic effect (15). Dadure et al. reported 20.1% of mechanical problems associated with catheter (mainly leakage and dislodgement) (25). In a study by Ganesh et al. (13), the catheter was accidentally withdrawn in 40.5% of patients. Despite the use of good fixation, Walker et al. noticed the occurrence of subcutaneous catheter migration that may result in secondary block failure (9). Gurnaney et al. had 4.2% catheter complications, 1.9% catheter failure, and only 0.07% of local inflammation (12). There were no differences in the risks and complications in inpatients and outpatients. It is necessary to improve the technique of catheters positioning and fixing (12, 24). Some authors recommend the use of a small drop of Dermabond (Ethicon, Raleigh, NC, USA) at the insertion site (12, 15, 16) to prevent leaking.

Visoiu et al. reported that 28% of patients had postoperative nausea/vomiting and/or itching (15). The technique did not work in only 6.9% of cases, but even this small percentage is unacceptable for patients and medical staff. In the study by Dadure et al. 14.7% patients had nausea/vomiting and only 1.5% urinary retention and 0.9% pruritus (24). Gable et al. reported postoperative nausea and vomiting in 5.9% of patients (14).

In the study by Walkers et al. (9), there were no permanent neurological complications of deep infection or local anesthetic toxicity, but most patients were older than 10 years. There were no permanent neurological complications of deep infection or LA toxicity in other studies as well (10, 15). The most common local complications are rare: local inflammation at the site of catheter placement (redness, swelling, or pain) and abscess at the catheter insertion site. Ecoffey noticed only superficial infections or blood vessel puncture (10). Studies have shown that perineural catheters infections are a rare occurrence and that the incidence is in correlation with the time that has passed since the catheter is placed (9, 12, 13). It is considered that the perineural catheters should be removed 3 days after the placement which reduces complications to a minimum (15), except in cases where the benefits to the patient overcomes the clinical risk of infection.

Many complications (e.g., paresthesia) are difficult to diagnose in infants and nonverbal children who cannot describe their symptoms accurately. Nevertheless, in a study by Polaner et al. (26) the incidence of serious complications that was detected in prospectively acquired unselected population was extremely small, and no sequelae lasting >3 months were reported in close to 15,000 regional anesthetics. There were no serious complications such as persistent neurological deficit. In these instances, we must rely on confidence intervals to provide an upper limit of possible incidence rates (for example, although there was no mortality reported in 9,156 neuraxial blocks, a mortality of 0–3.3: 10,000 is still consistent) (26).

Krane and Polaner believe that it cannot be determined whether the rare symptoms of LA (e.g., tinnitus) are objective or only placebo responses in children who are told to pay attention to these symptoms of LA toxicity (27).

Absolute contraindications for placement of perineural catheters are: allergy to local anesthetic and infection at the site of planned puncture. Relative contraindications are sepsis, prolonged PT and PTT, heart failure, neurological diseases, and patient refusal. Due to the small number of contraindications and improvements in the clinical, economic, and humanistic approach, perineural catheters are used more often nowadays (15).

CONCLUSION

Regional anesthesia is commonly used in addition to general anesthesia to provide adequate postoperative analgesia and better comfort. It provides sufficient analgesia and better comfort and it is rarely performed in a wake state. Postoperative course without the significant pain raises the morale of the child, parents, and medical staff. The surgeon as well as the anesthesiologist is pleased to see a peaceful, alert and cooperative child in the immediate postoperative period. From an ethical point of view, it is not justifiable to allow the child to suffer pain, when simple and safe techniques of regional anesthesia are easily complementing or replacing conventional-general anesthesia. The goal of a physician should always be to minimize the psychological and physical trauma of the patient, regardless of how young and immature the child is. Hospital stay will be forever remembered as a traumatic experience if pain is not adequately treated. Therefore, proper care of pain is of great importance.

The use of any technique of regional anesthesia depends on the estimated risk/benefit ratio. No published study reported sustained neurological complications or serious side effects after use of CPNB. It is possible to discharge patient home with the catheter, but it is necessary to provide adequate education for staff, patients, and parents, as well as to have dedicated anesthesiology team. It is extremely important to organize adequate monitoring of these patients by phone calls and visits by trained medical workers. Regardless of the numerous ethical and security problems in the design of pediatric studies, more prospective studies are needed to provide adequate evidence.

AUTHOR CONTRIBUTIONS

DS: conceptualization, investigation, project administration, visualization, and wrote the manuscript. MS: investigation, visualization, literature review and wrote the manuscript. ZS: literature review, providing regional anesthesia, visualization and investigation. IS: placing perineural catheters, providing regional anesthesia, visualization, and investigation. SD: investigation and supervision. IP: providing regional anesthesia, language supervision and made a final version of manuscript. MM: visualization, analysis of literature, and investigation.

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A Review of the Quadratus Lumborum Block and ERAS

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The use of truncal nerve blocks has been described since 2001. Since then, there have been many studies trying to understand the ideal clinical scenarios for its use. Since 2001, the transversus abdominis plane block has evolved in many ways including from landmark based technique to ultrasound guided and more recently, into the quadratus lumborum (QL) block. Its anatomical placement, concentration of local anesthetic, volume of local anesthetic, and anatomic placement have all been raised as clinical questions. This article will discuss the literature of the QL block in an effort to understand how it is best used in a variety of clinical scenarios.

Keywords: quadratus lumborum, truncal block, quadratus lumborum block, transversus abdominis plane block, ultrasound

INTRODUCTION

The truncal nerve blocks, as a part of perioperative pain management, were introduced into clinical practice over 40 years ago. Primarily these were the ilioinguinal–iliohypogastric (II–IH) block (1–4) and the rectus sheath block (5), mostly used in the pediatric anesthesia population. In the early years of the 21st century, the transversus abdominis plane (TAP) block was introduced in everyday practice, providing a much wider field of analgesia (6, 7). At first, these blocks were performed without ultrasound guidance, using landmark techniques. However, the clinical use of truncal block techniques have developed over time and their expansion was driven by introducing ultrasound into anesthesiology practice. Although the anatomical markers are reliably detected by ultrasound, the blocks of the anterior abdominal wall vary in both the distribution of the local anesthetics and the field of coverage. In the search for the wider analgesia coverage and long-lasting postoperative analgesia, the transversalis fascia plane block and the quadratus lumborum block (QLB) have been developed.

Quadratus lumborum block is a block of the posterior abdominal wall, "interfascial plane block," which is performed exclusively under ultrasound guidance. It was described by anesthesiologist Dr. Rafael Blanco (8) as a variant of the TAP block in 2007. Much later, he gave a detailed description of the block technique using the name QLB (9). In the spring of 2013, Dr. Jens Børglum from the University Hospital in Copenhagen (Denmark) published a new ultrasound-guided transmuscular QL blockade, describing the so-called "Shamrock sign," the sign of a shamrock for the detection of a local anesthetic injection point (10). In autumn 2013, Dr. MihaelaVisoiu (11), a pediatric anesthesiologist from the University Children's Hospital in Pittsburgh (USA), published a case report with continuous QLB for postoperative analgesia. Subsequently, there has been an increasing interest of the anesthesia community in the use of truncal blocks, and the number of publications on the topic of QLB is progressively growing.

MECHANISM OF ACTION

The crucial ultrasound landmark for block performance is the quadratus lumborum muscle (QLM), and the key to the analgesia lies in the thoracolumbar fascia (TLF) (12–15). TLF is a complex,

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connective tissue tubular structure formed by binding aponeuroses and fascia layers, which, enveloping the back muscles, connects the anterolateral abdominal wall with the lumbar paravertebral region. The TLF is on its medial side attached to the thoracic and lumbar vertebrae, cranially continuing with endothoracic, and caudally with the fascia iliaca, potentially ensuring the spread of anesthetics in the craniocaudal direction (16). The true mechanism of analgesia provided by QLB has not yet been fully clarified. It is believed that the local anesthetics spread along the TLF and the endothoracic fascia into the paravertebral space, is responsible in part for the analgesia. In 2011, Carney et al. (17) showed that contrast spreads from the L1–T5 segment of the paravertebral space. However, a recent publication (18), shows that contrast injected into the area around QLM (QL plane) does not spread into the paravertebral space and contrast injected into the paravertebral space does not spread around QLM. Hence the assumption that visceral analgesia results from the spread of anesthetics to the celiac ganglion or sympathetic trunk *via* splanchnic nerves, as is the case with the paravertebral block. This remains to be confirmed or denied by future research. The most recent publication on this topic is the abstract presented at the American Society of Anesthesiologists meeting in October 2017, which shows local anesthetic spreading into the paravertebral space, cranially to the T10 segment (19).

An additional mechanism of action of local anesthetics can be explained by the anatomical–histological characteristics of the TLF. Namely, in the superficial layer of the TLF, there is a thick network of sympathetic neurons. In the fascia, there are the high-threshold and low-threshold mechanoreceptors and pain receptors sensitive to the effects of the local anesthetics. These receptors play a role in the development of both acute and chronic pain. The QLB analgesia could be, at least partially, explained by local anesthetic blockade of these receptors (15, 20).

Different approaches to block performance are applied in everyday clinical practice, and differences in the width of the anesthetized field and the duration of analgesia are significant. So far, studies done on cadavers (18, 21–24) show that the injected contrast can spread cranially to the thoracic paravertebral space and intercostal spaces covering somatic nerves and the thoracic sympathetic trunk up to the T4 level. Blockade of the subcostal, iliohypogastric, and ilioinguinal nerve is consistent. Sometimes, genitofemoral and lateral femoral cutaneous nerve could be blocked. Caudally, contrast can reach lumbar nerve roots, but the results vary and new studies are needed to clarify the link between the type of QLB and the achieved analgesic effect. All of these data indicate that the QLB provides somatic and visceral analgesia.

Obviously, there are variations in the width of achieved analgesia, and in the number of dermatomes covered by QLB. In most of the cases, analgesia is achieved in T7–L1 dermatomes (10–14, 24–28), although there are descriptions of cranial spread to T4–T5 (13), and caudal spread to L2–L3 (22) dermatomes. The height of the block can be influenced by the choice of the site for the application of local anesthetics, both in relation to QLM and in relation to the distance from the iliac crest and costal margin (12, 13). The rate of the drug application (29), and the individual anatomical variations can also influence the height of the block.

TYPES OF QLB

Since the initial description, the block has experienced several modifications and today four types of the block are performed, which differ by the site of drug application. These are QLB 1 or lateral QLB, QLB 2 or posterior QLB, QLB 3, or anterior/transmuscular QLB, and QLB 4 or intramuscular QLB.

Quadratus lumborum block 1 implies the application of local anesthetics on the lateral side of QLM in the area of its contact with the transversalis fascia, at the level where transversus abdominis muscle (TAM) tapers off into its aponeurosis (30). One group of authors (12) states that the target site is between the fascia and the muscle, which can be seen as expanding space upon local anesthetic injection. They emphasize that medication should not be given between the fascial layers as the nerve endings are between the fascia and the muscle. Another group of authors (13) states that drug is administered in the space between the common aponeurosis of internal oblique muscle (IOM) and TAM and the transversalis fascia.

Quadratus lumborum block 2 implies the application of medication on the posterior side of the QLM between the QLM and the medial lamina of TLF which separates QLM from the latissimus dorsi muscle and paraspinal muscles [erector spinae muscles (ESM)]. This is laterally from the attachment of IOM aponeurosis (30), in the to the so-called lumbar interfascial triangle (14).

Quadratus lumborum block 3 implies the application of medication at the front of the QLM, at the level of its attachment to the transverse process of L4 vertebra. This can be seen under ultrasound as spreading of the local anesthetic between the QLM and the psoas major muscle (PMM) (10, 31). This approach assumes during ultrasound one is viewing the "Shamrock sign"—the transverse process of L4 vertebra is seen as a stem with ESM as posterior leaf, PMM as anterior leaf, and QLM as lateral leaf.

Quadratus lumborum block 4 implies the application of medication in the muscle itself.

Murouchi states that for QLB 1 and 3 a local anesthetic needs to be applied between the anterior layers of TLF and that its intramuscular approach does not involve the spread of local anesthetics into the interfascial space (28).

BLOCK TECHNIQUE

We perform lateral QLB (QLB 1) and posterior QLB (QLB 2) in our practice. During the block performance, the patient is in the supine position. **Figure 1** shows the cross-section of the cadaver abdomen in supination and a schematic presentation of anatomical structures for better understanding and easier performance of the QLB. If QLB is performed on the operating table, the operating table can be gently tilted to the opposite side to achieve a better exposure. If QLB is performed on a regular bed, a pillow can be placed under the lumbar spine. Alternatively, the patient could be asked to turn to the opposite side. The procedure begins by placing a transversally oriented linear or convex ultrasound probe between two distinct markers—the iliac crest and the costal margin at the level of

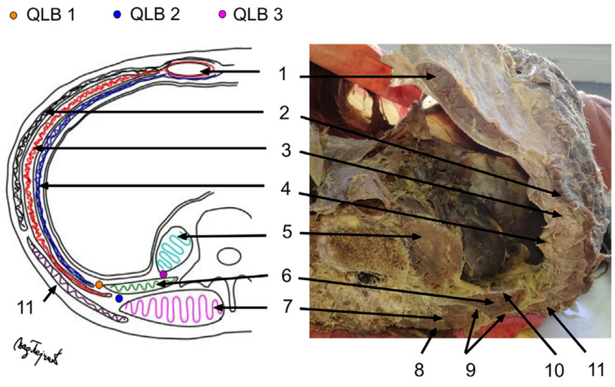

FIGURE 1 | Cross-section of the abdomen—a photo of cadaver and a scheme of anatomical structures. QLB 1—point of local anesthetic (LA) injection for QLB 1; QLB 2—point of LA injection for QLB 2; QLB 3—point of LA injection for QLB 3; 1—rectus abdominis muscle; 2—external oblique muscle; 3—internal oblique muscle; 4 –transversus abdominis muscle; 5—psoas major muscle; 6—quadratus lumborum muscle; 7—erectores spinae muscle; 8—lamina posterior of the thoracolumbar fascia; 9—lamina media of the thoracolumbar fascia; 10—lamina anterior of the thoracolumbar fascia; 11—latissimus dorsi muscle.

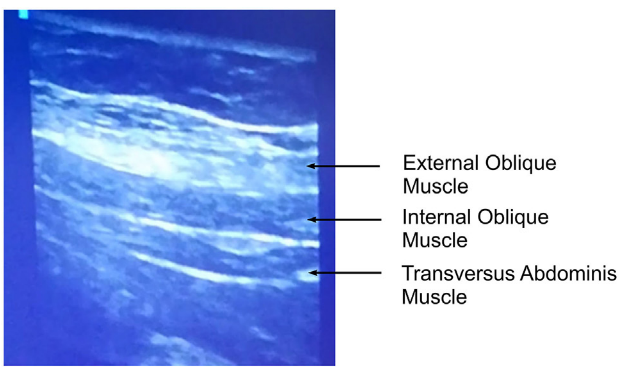

FIGURE 2 | Muscles of the anterolateral abdominal wall.

the anterior axillary line. The goal is to find three thin parallel muscles of the anterolateral abdominal wall, external oblique muscle, IOM, and TAM, from the outside to inside as in **Figure 2**. Moving the probe posteriorly, we follow narrowing of the muscles until the muscle fibers of TAM taper off into its aponeurosis at the level of the posterior axillary line. This is ultrasound-detected as a hyperechogenic sign (**Figure 3**), from which the QLM extends posteriorly and to the inside. Aponeuroses are seen as hyperechogenic structures, and muscles as hypoechogenic structures. If the image is lost during probe movement, we reposition probe to the starting point of scanning, looking for three parallel muscles, and then we continue scanning to the back, taking care that the probe is always perpendicularly placed on the skin surface and is following the body curvature. When we detect a remarkable hyperechogenic sign of the place where we want to inject a local anesthetic, we can improve the image by discrete tilting and rotation of the probe. If the hypoechogenic shadow blurs the image, it is necessary to add more gel that will improve the transmission of ultrasound waves from the probe to the skin.

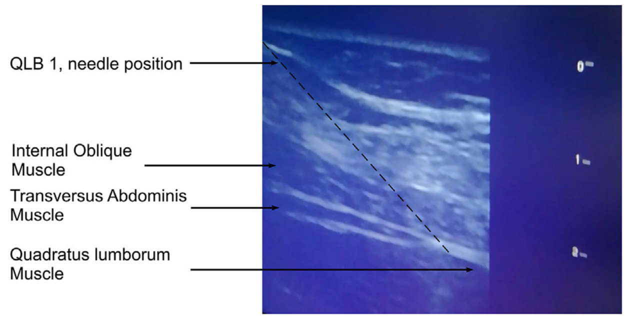

FIGURE 3 | Quadratus lumborum type 1 block—needle position.

The needle is introduced into the skin 1–2 cm above the probe (by "in plane" technique) and led through the muscles to the local anesthetic application site—posteriorly from the place where the TAM tapers off into its aponeurosis (we do not want the TAM perforation). The needle is advanced at 90° angle and only after the skin perforation we redirect needle in the desired direction. The TLF provides a characteristic elastic resistance to a blunt needle that is used for peripheral blocks, and TLF perforation is accompanied by double control—visual (ultrasound) and special tactile feeling due to loss of resistance. After a negative aspiration test, the injection of 1 ml of the solution provides visible hydrodisection—the accumulation of fluid in the form of a growing hypoechogenic shadow, which separates the muscle from the fascia, representing the third confirmation of the desired location. Then, the fractional administration of local anesthetics is performed. After every 5 ml of local anesthetic, it is necessary to do an aspiration test to confirm the extravascular location of the needle tip.

This technique is very easy to learn due to the fact that it is easy to find the key sonoanatomic markers for block performance. It can be learnt after only a few performance of the procedure (32).

When the catheter is placed for prolonged postoperative pain therapy, absolutely sterile working conditions are necessary (as for the epidural catheter placement or the central venous cannulation). This involves using caps, masks, sterile gloves, hand cleaning, sterile operating field, putting the probe into a sterile bag, and using sterile ultrasound gel. In the absence of sterile bags for the ultrasound probe and sterile gel, it is possible to improvise in the following way. An ultrasound probe with regular gel is placed in a sterile glove. The contact of the probe with skin can be improved by wetting skin with sterile saline.

For one-time administration of local anesthetic ("single shot" QLB), it is sufficient to apply clean technique according to many US regional anesthetic schools. This involves the use of regular gloves for single use without the preparation of a wide sterile field. It is necessary to use a cap and a mask. After identification of TAM and TLF, skin above the probe is cleaned with disinfectant. Insulated needle is held only at the "head," (without touching the metal part of the needle), and advanced through the cleaned skin. Only when we have an adequate ultrasound image and disinfected skin, we advance the needle through the skin and perform the block. A group of authors (33) recommends that a sterile transparent film (Tegaderm) should be placed over the probe and gel to additionally increase the safety and reduce the risk of infection.

For the performance of QLB, insulated block needles 50–150 mm in length are used, although for most patients the appropriate needle length is 100 mm.

There is still no consensus on the type, concentration, and volume of a local anesthetic used to perform QLB. QLB is performed by applying 15–30 mL (0.2–0.4 ml/kg) of a local anesthetic on the left and right side of the abdominal wall. 0.125–0.375% bupivacaine, levobupivacaine, or ropivacaine (12–14, 23, 25, 30, 34–37) can be used as local anesthetics. Many authors (26, 31, 35) recommend the addition of 2–4 mg dexamethasone to each side to extend the effect of the local anesthetic and, by some authors (38, 39), achieve the antiemetic effect. There is still no consensus on the effect of dexamethasone on the duration of peripheral nerve blocks either, but the most recent meta-analyses (39–41) indicate that perineurally administered dexamethasone prolongs the duration of the peripheral block and potentiates analgesia. We are currently complying with the recommended protocol from the Cornell Medical Center (Weill Cornell Medicine, New York, NY, USA), taking care that the patient does not receive a local anesthetic dose higher than the maximum allowed (2.5 mg/kg). We use 30 ml 0.25% bupivacaine/levobupivacaine with 2–4 mg dexamethasone per block. As a bilateral QLB is required for most procedures, the total dose is 60 ml of 0.25% (150 mg) bupivacaine/levobupivacaine with 4–8 mg of dexamethasone. For patients with a body weight of less than 60 kg, we use 20–30 ml of 0.20% bupivacaine/levobupivacaine with 2 mg dexamethasone per side.

The block can be performed postoperatively, on the operating table, immediately after waking up patient from general anesthesia, in the recovery room or in the intensive care unit. Patients who underwent neuraxial anesthesia are given QLB either before or after resolution of the block.

INDICATIONS

Quadratus lumborum block provides postoperative analgesia in a large number of surgical interventions and the list of indications is long.

The efficacy of QLB for postoperative analgesia following both cesarean section (8, 14, 30, 34, 35, 42–44) and gynecological laparoscopic procedures (25, 36) was shown. Additionally, the efficacy of QLB for postoperative analgesia was shown after abdominal surgery [small intestine (26) and colon (11, 27) resection, colostomy reconstruction (11), appendectomy (27), gastrectomy (45)], and for analgesia for anterior abdominal wall hernioplasty (46, 47) and orhcydopexy (47), both for open and laparoscopic procedures and for postoperative analgesia after open and laparoscopic nephrectomy (37, 48, 49).

As TAP block has its important place in postoperative analgesia after laparoscopic cholecystectomy, Elsharkawy (50) representing the American Society of Regional Anesthesia and Pain Medicine recommends the application of QLB for laparoscopic cholecystectomy (which we have confirmed in everyday practice on over 50 patients for the past 6 months).

There are more and more authors describing the application QLB for hip and femur surgery (31, 51–55) and lumbar vertebrae surgery (56, 57). A case study of the use of QLB for postoperative analgesia after femorofemoral bypass was published (58). A case of one-time administration of QLB in chronic pain treatment after the anterior abdominal wall hernia surgery with a multimonth effect after the block performance was also published (46).

QLB EFFICACY

All authors, which we have quoted so far, agree that QLB has an outstanding analgesic effect on pain reduction to 1–2/10 by Visual Analog Scale or Numeric Rating Scale pain scale, which usually last more than 24 h. Patients who receive QLB as part of a postoperative pain therapy, have lower pain levels both when resting and moving, which is important for early mobilization. The analgesic effect is as good as the one achieved by opioids, and there are no unwanted opioid effects such as nausea and vomiting (36). According to prospective studies published by Blanco et al.1 (4, 30) in 2015 and 2016, the need for morphine has been significantly reduced postoperatively in patients who received paracetamol, NSAID, and QLB as part of the multimodal postoperative analgesia compared to patients who received only paracetamol and NSAID, but did not receive QLB. Comparative studies have shown that the QLB covers a topographically broader field (Th7–Th12, compared to TAP Th10–Th12) (14, 25), and yields prolonged pain-free condition compared to the TAP block (24–48 h QLB versus 8–12 h TAP block) (14, 25, 47).

Quadratus lumborum block provides early and rapid pain relief in a high percentage of patients and allows early ambulation, which is one of the most important measures in the prevention of deep vein thrombosis and thromboembolic complications. So, this would be another important question that should be considered through future research—could QLB be used to reduce the incidence of postoperative thromboembolic complications?

QLB COMPLICATIONS

Complications associated with the performance of abdominal wall blocks are fortunately very rare and not described during QLB performance. Since QLB is a classical intramuscular medication injection, the possibility of infection is far lower than in performing the neuraxial blocks. So far, infections have not been described during the QLB performance. The advantage of QLB compared to other abdominal wall blocks is the fact that the passage of the needle and the site of the local anesthetic application are very distant from the peritoneal cavity, visceral abdominal organs, and large blood vessels. Therefore, needle trauma in terms of unintentional puncture of the peritoneum, intestine, liver, kidney, large blood vessels associated with blind methods (without ultrasound) of the TAP and II-IH block performance here is minimized. Performing a block under the control of ultrasound, with mandatory monitoring of the needle tip prior to injecting the drug, significantly increases the level of safety and efficiency of the technique. There are no data on neurological damage since the local anesthetic is not injected into the immediate proximity of the large nerve, but is injected into the space rich in small nerve endings. It is therefore generally accepted that QLB can be performed both under general and regional anesthesia (13).

An unwanted femoral nerve block is cited as a possible complication of QLB 3. A rational theoretical explanation lies in the immediate anatomical contact of the TLF and the iliac fascia and the possibility of spreading the anesthetic, down the iliac fascia causing weakness in the quadriceps (22, 52, 53, 59). Dam and associates (21) during the performance of QLB 3 do not puncture the PMM and do not get the contrast spreading caudally. This leaves us with a potential conclusion that if there are no punctures of the PMM, there is no unwanted quadriceps weakness.

Anterior abdominal wall blocks have the potential for local anesthetic systemic toxicity (LAST). For now, there is no LAST case with QLB. Namely, studies have shown that the concentration of local anesthetic (ropivacaine) in plasma is significantly lower after the performance of QLB comparing with than in the TAP block done by a lateral approach (13, 25). In any case, whenever regional blocks are performed, it is necessary to think of a potential LAST, take precautions to prevent LAST development and actively monitor the patient to timely spot the first signs and treat LAST.

As the QLB performance involves manipulation of the fascia where blood vessels exit from the paravertebral space, caution should be exercised in people receiving anticoagulant therapy due to the possible risk of hematoma (14).

As with any anesthetic procedure, it is necessary to take patient's written consent for the performance of the abdominal wall block, especially if the block is performed postoperatively in the intensive care unit or ward (13).

QLB AND ERAS PROTOCOL

Our review of literature did not result in any articles that would specifically discuss the role of QLB in ERAS protocols. Kim et al. recently published review on the role of TAP block as a part of ERAS protocol (60). They found that the use of TAP block resulted in significantly less opioid use, less postoperative pain and non inferiority was shown in comparison with thoracic epidural. Since QLB is similar to TAP block all of these findings should be subjects of new research. Other studies have shown less post-operative nausea and vomiting (36, 61), decreased post-operative sedation (62, 63), decreased length of hospital stay (64), earlier urinary catheter removal (65) when abdominal trunk blocks are used. This is another area where extensive research is needed. Improved early oral intake and early mobilization can be more easily achieved with good pain control and QLB has a great potential in this area of ERAS.

CONCLUSION

Quadratus lumborum block is a new form of the abdominal wall block which is relatively easily performed thanks to clear ultrasound anatomic markers. The block effect lasts 24–48 h and until now no complications have been described during the block performance. QLB is safe and has found its place in multimodal postoperative pain therapy in patients undergoing abdominal surgery, gynecological and obstetric procedures, and orthopedic interventions on hips, whether interventions are performed in general or spinal anesthesia, both in adults and in children. It follows from the above that QLB has the potential to significantly facilitate and improve postoperative pain therapy.

AUTHOR CONTRIBUTIONS

MA performed the proofreading of the translation of the article. NP and IV did the writing in Serbian and the literature search for the article.

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REVIEW
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Enhanced Recovery in Thoracic Surgery: A Review

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The main goal of enhanced recovery program after thoracic surgery is to minimize stress response, reduce postoperative pulmonary complications, and improve patient outcome, which will in addition decrease hospital stay and reduce hospital costs. As minimally invasive technique, video-assisted thoracoscopic surgery represents an important element of enhanced recovery program in thoracic surgery. Anesthetic management during preoperative, intraoperative and postoperative period is essential for the enhanced recovery. In the era of enhanced recovery protocols, non-intubated thoracoscopic procedures present a step forward. This article focuses on the key elements of the enhanced recovery program in thoracic surgery. Having reviewed recent literature, the authors highlight potential procedures and techniques that might be incorporated into the program.

Keywords: enhanced recovery, thoracic surgery, video-assisted thoracoscopic surgery, enhanced recovery after surgery, thoracic anesthesia

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INTRODUCTION

Despite of the advances in surgical and anesthetic techniques as well as improvements in perioperative care, major surgery is still associated with high rate of complications (1, 2). Postoperative complications are associated with prolonged hospitalization, delayed recovery, increased healthcare costs, and poor postoperative quality of life (3, 4). The concept of enhanced recovery after surgery (ERAS), also known as "fast-track," was derived from the need to minimize hospital length of stay and reduce hospital costs.

Enhanced recovery after surgery program is a multimodal plan of care aimed at optimizing patient before surgery, minimizing patient's intraoperative stress response, consequently reducing complications, decreasing hospital length of stay and accelerating recovery (5, 6).

The concept of ERAS was introduced in 1990s by Kehlet (7), and it was primarily intended for patients undergoing elective colorectal surgery (8). Afterward, it has spread to other surgical specialties, showing improvements in terms of clinical outcomes and costs (9). Many of the principles of enhanced recovery in colorectal surgery are adjusted to enhanced recovery protocols (ERP) in thoracic surgery. Although there are variations in care protocols among institutions, the goal of ERP in thoracic surgery is prevention of pulmonary complications as they are the main cause of increased morbidity and mortality in thoracic surgical population (10). The protocol presents an evidence-based approach to patient care which begins in the preoperative period, extends to entire intraoperative period, and ends until hospital discharge. Therefore, it consists of three phases: preoperative, intraoperative, and postoperative (**Figure 1**).

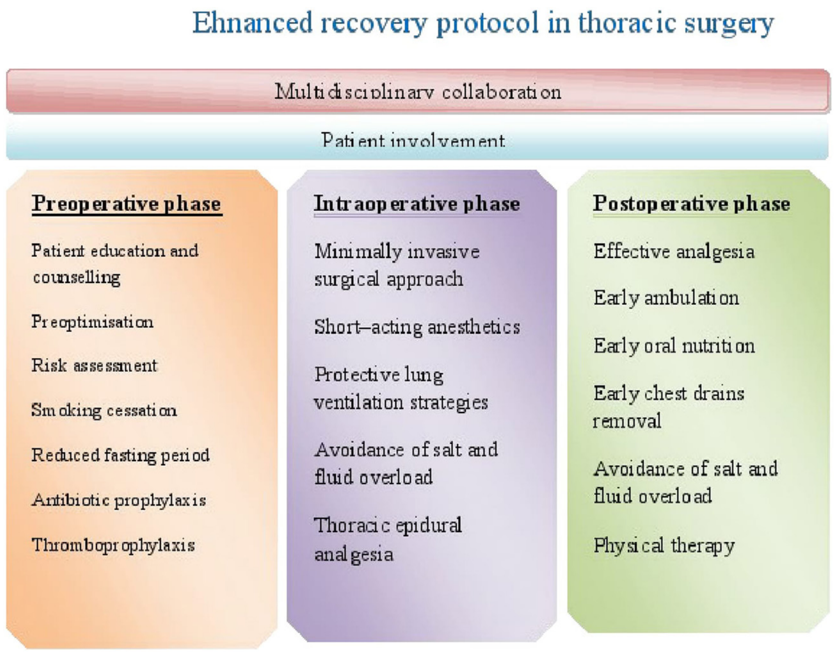

FIGURE 1 | The elements of enhanced recovery protocol in thoracic surgery.

In this article, we have reviewed the recent literature about ER in thoracic surgery. The PubMed and MEDLINE databases were searched using terms "enhanced recovery," "thoracic surgery," "anesthesia," "fast track," and "VATS." Publications from 2000 to 2017 were examined by the authors. To achieve better sensitivity, a search of references of review articles, systematic reviews, and meta-analysis were performed. The search results were limited to English language studies.

PREOPERATIVE PHASE

The main goal of preoperative assessment is to identify patients at higher risk, to address modifiable risk factors, and to optimize organ function before the surgery, so the patient could be in the best possible condition for the operation. Therefore, during preoperative phase, attention is focused on the risk assessment and optimization of patient's medical condition.

Anemia, malnutrition, and chronic obstructive pulmonary disease (COPD) are frequent in patients undergoing thoracic surgery and should be treated before the surgery. Malnutrition is common in cancer patients. It is associated with impaired wound healing, muscle weakness, immune dysfunction, leading to delayed recovery, prolonged length of stay, and costs (11). According to the European Society for Nutrition and Metabolism Guidelines, patients should be screened for malnutrition preoperatively, and those with increased risk should receive nutritional support for 10–14 days before the major surgery (12). Preoperative fasting from midnight is not necessary, as it was proven that patients given fluids 2–3 h preoperatively are not at greater risk of aspiration than those fasted for 12 h (13). Preoperative carbohydrate loading (the night before and 2 h before surgery) is recommended (12). There is evidence that preoperative administration of oral carbohydrate liquids is associated with faster recovery and reduced length of hospital stay (14).

Most of the patients undergoing thoracic surgery are high-risk patients. Preoperative risk assessment is essential for identification of higher-risk patients as they can require more intensive postoperative care and preoptimization. There are still controversies whether these patients should be included in ERAS programme.

Poor preoperative lung function, smoking, and physical inactivity are considered to be the risk factors for complications following thoracic surgery (15, 16).

It has been estimated that active smoking at the time of resection increases the risk of postoperative complications such as pneumonia, myocardial infarction, and stroke. It is also associated with a higher likelihood of death within 30 days after surgery (17). There are still controversies about the optimal time for smoking cessation. One study even reported an increase in perioperative pulmonary complications when smoking cessation occurred just before the surgery (18). Nevertheless, patients should be advised to stop smoking irrespective of timing of operation.

Improving lung function should be one of the main preoperative management strategies. With the aim to improve tolerance to the surgical procedure and enhance postoperative recovery, the concept of preoperative pulmonary rehabilitation was introduced. It integrates exercise training and self-management education. Some studies have shown that preoperative pulmonary rehabilitation can optimize functional state, decrease symptoms, and improve quality of life in patients with COPD (19). The interventions of pulmonary rehabilitation, including exercise training and smoking cessation, were also examined in patients with lung cancer and COPD undergoing lung resection. It has been shown that pulmonary rehabilitation, both before and after surgery significantly improves forced expiratory volume in 1 s (FEV_1), forced vital capacity, and quality of life (16, 20). Data from a meta-analysis and two systematic reviews have shown that preoperative exercise and smoking cessation in patients undergoing lung resection due to lung cancer, significantly improve pulmonary function and functional capacity, reduce postoperative morbidity and hospital length of stay. However, when exercises were performed only postoperatively, length of stay and postoperative morbidity did not reduce (21–23), which can be explained by the differences in the training programs among the studies.

Available data suggest that preoperative pulmonary rehabilitation, as the part of ERP in thoracic surgery, can improve exercise capacity, as well as reduce postoperative morbidity and mortality in patients with lung cancer. On the other hand, it is recommended not to delay an operation in patients with lung cancer in order to perform preoperative rehabilitation. In the context of aforementioned facts, consensus should be achieved about the training programs, as well as adequate duration of preoperative pulmonary rehabilitation.

Current ERAS guidelines recommend patient education and counseling (24). Patients should be given information about the surgical procedure, anesthesia, and recovery course. They should be encouraged to actively participate in their care as it can contribute to enhanced recovery.

Patient education, preoperative anesthetic assessment, and optimization of patient's medical condition present an essential part of preoperative phase of ERP in thoracic surgery.

During preoperative phase, special attention should be paid to the airway assessment. One—lung ventilation in patients with difficult airway can be very challenging. Chest radiography and computed tomography are important for airway assessment and selection of an appropriate double-lumen endotracheal tube (DLT). Identification of patients with difficult airway is essential for airway management planning and selection of an appropriate lung isolation device. In patients with already known or anticipated difficult airway the best option to establish an airway is by a single-lumen tube (SLT) while lung isolation can be achieved by bronchial blocker, or an SLT can be substituted with a DLT using an airway catheter technique (25).

INTRAOPERATIVE PHASE

During intraoperative period, many strategies and techniques can be applied to prevent pulmonary complications.

Surgical Techniques

The posterolateral thoracotomy (PLT), which is the traditional approach to lung resection, implies muscle-cutting incision. It provides good surgical access, but is associated with increased postoperative pain and reduced respiratory effort (26). With the aim to overcome disadvantages of PLT, muscle—sparing thoracotomy using anterolateral approach and video-assisted thoracoscopic surgery (VATS) were introduced.

Recent studies, including a meta-analysis (27), systematic review (28), and propensity-matched analysis, from Society of Thoracic Surgeons database (29) have shown significantly lower morbidity rate and shorter hospital stay in patients undergoing VATS lobectomy compared with open thoracotomy. The results from these studies are in line with recent findings from the database study from the European Society of Thoracic Surgeon Registry, which compared the outcome following VATS lobectomy versus open lobectomy in case-matched groups of patients (30). The study included 28,771 patients; 26,050 having thoracotomy and 2,721 having thoracoscopy. Compared with thoracotomy, patients undergoing VATS lobectomy had significantly lower incidence of total complications (29.1 vs. 31.7%), wound infection (0.2 vs. 0.6%), and atelectasis requiring bronchoscopy (2.4 vs. 5.5%). Patients undergoing VATS lobectomy had 2 days shorter hospital stay compared with those undergoing thoracotomy, and mortality at hospital discharge was significantly lower in this group (1.0 vs. 1.9%). Concerning patients older than 70 years, the results from this study showed significantly lower number of major cardiopulmonary complications and atelectasis, shorter length of stay, and reduced mortality in the VATS group of patients compared with patients undergoing thoracotomy. The data from these studies confirmed that in comparison to thoracotomy, lobectomies performed *via* VATS are associated with lower incidence of complications, shorter length of stay, and decreased mortality, even in high-risk patients (31). The benefits of VATS on long-term outcomes were also reported. A recent meta-analysis of 20 observational studies reported that compared with open lobectomies, VATS lobectomies were associated with improved long-term outcomes (32).

Due to its beneficial effects on patient recovery, VATS represent one of the main elements of an enhanced recovery in thoracic surgery. To minimize the injury during VATS, the idea of uniportal thoracoscopic surgery has risen. The perioperative outcomes of a single-port, two-port, and three-port approaches were studied. Recent study has shown that VATS single-port and two-port pulmonary resection were associated with decreased volume of drainage, shorter length of stay, and shorter duration of chest drainage (33). However, further randomized controlled trials with larger number of patients are needed to confirm the beneficial effects of single-port compared to three-port VATS pulmonary resections.

Anesthetic Management

Anesthetic management directed at improving patients' recovery includes maintenance of normothermia, the use of short-acting agents, protective lung ventilation (PLV), avoidance of fluid overload, and effective analgesia (34). Unlike intravenous anesthetics, volatile anesthetics inhibit hypoxic pulmonary vasoconstriction. However, some data suggest that there is no significant effect of volatile anesthetics on shunt when used in clinically relevant concentrations (35). Recent studies report the suppressive effect of volatile anesthetics and propofol on the alveolar inflammatory response during one-lung ventilation (OLV) (36).

Perioperative Fluid Management

One of the most severe pulmonary complications in thoracic surgery is an acute lung injury (ALI), presenting the main cause of mortality in patients undergoing lung resection (37). The main task of anesthesiologists is to prevent the development of

ALI focusing on the optimal fluid management, by balancing the risks for complications of fluid overload against the risks of hypovolemia and hypoperfusion. Fluid management in thoracic surgery is still controversial topic. There are disadvantages at both sides of regimes—liberal and restrictive. Numerous studies have demonstrated that excessive fluid administration can lead to postresection ALI (38–40).

It has been shown that administration of fluid >2l during pneumonectomy has negative effects on postoperative outcome (41, 42). Similar results are obtained in the studies that evaluated outcome in patients undergoing lesser pulmonary resections managed with high fluid loads (42, 43). On the other hand, there is concern that restrictive regimen can contribute to organ hypoperfusion leading to an acute kidney injury (AKI). In a retrospective study that included 1,442 patients undergoing thoracic surgery with crystalloid restriction <3 ml/kg/h, it was found that the incidence of AKI was 5.1%. The study concluded that fluid restriction neither increased nor was a risk factor for AKI (44). Recent data suggest that crystalloid administration should be <2 l intraoperatively, and <3 l during first 24 h with total fluid balance less than 20 ml/kg during the first 24 h postoperatively (42). Fluid restriction is not just important in prevention of ALI. It has been shown that fluid restrictive therapy leads to earlier resolution of already developed ALI without increasing the risk of AKI (45).

Considering the risk of AKI in a restrictive fluid management, normovolemic and goal-directed therapy protocols were examined. A prospective observational study examined the effects of normovolemia and protective lung ventilation on the development of ALI and found no increase in extravacular lung water (46). However, further studies are needed to find the optimal fluid regimen in patients undergoing pulmonary resections.

Protective Lung Ventilation

Tissue trauma during surgical intervention, lung hyperinflation, repetitive reexpansion of already collapsed alveoli, and reperfusion during OLV induce cytokine release leading to pulmonary inflammatory response (47).

It has been shown that despite potential hypoxemia, PLV reduces inflammatory response during OLV and consequently the incidence of ALI and postoperative atelectasis (48, 49). The aim of PLV is to minimize pulmonary trauma and avoid respiratory complications including lung injury. It can be achieved by avoiding overdistension and elevated plateau pressure, while providing adequate oxygenation and recruitment of alveoli (50). Although high tidal volumes (10 ml/kg/min) improve oxygenation during OLV, data from animal and human studies suggest that high tidal volumes and high pressures during ventilation are associated with lung injury (43).

Recommendations for OLV suggest that tidal volume of 4–6 ml/kg is protective (50). Protective OLV with low tidal volume is associated with increase in $PaCO_2$. Increase of respiratory rate decreases $PaCO_2$, but is associated with alveolar colapse–reexpansion cycles leading to atelectotrauma (50). Therefore, permissive hypercapnia is acceptable during protective OLV, while an adequate PEEP applied to the dependent lung keeps the alveoli open, provides oxygenation, and decreases lung injury. In patients with decreased functional residual capacity (FRC), PEEP applied to the dependent lung recruits alveoli and improves oxygenation. However, in patients with increased FRC, PEEP will decrease cardiac output and increase alveolar pressure, which will consequently increase vascular resistance in the dependent lung and increase hypoxemia by diverting blood flow to the non-dependent lung (51).

The value of PEEP should be adjusted according to the respiratory mechanics of the patient, as on the one hand it should prevent lung overdistension, and on the other hand, it should recruit alveoli without hemodynamic impairment.

POSTOPERATIVE PHASE

During postoperative period, the main goal of ERP is to promote early recovery. Early mobilization, adequate pain control, and postoperative pulmonary rehabilitation present the key elements of the postoperative ERP.

Pain Management

Pain after thoracic surgery impairs effective chest expansion, coughing, and breathing leading to postoperative atelectasis and pneumonia (52). Therefore, the main goal during postoperative period is to provide effective pain relief as it improves respiratory function and reduces postoperative complications. Regional anesthetic blockade in combination with systemic nonopioid analgesia present the basis of opioid sparing multimodal analgesia in thoracic surgery.

Thoracic epidural analgesia (TEA) is considered the gold standard technique for pain control after thoracic surgery and an essential part of ERAS protocols. In comparison with conventional analgesia techniques, TEA provides superior analgesia for post-thoracotomy pain (53), attenuates surgical stress response, having a positive impact on postoperative recovery. However, TEA has several disadvantages including hypotension, urinary retention, and muscular weakness. It can be overcome by performing thoracic paravertebral block (PVB). Recent meta-analysis and systematic reviews confirmed that PVB provides comparable analgesia to the TEA, but with statistically significant lower incidence of side effects, suggesting PVB as analgesic technique for major thoracic surgery (54, 55).

Although negative effects of morphine on respiratory function are described, intravenous patient-controlled analgesia (PCA) with morphine is widely used for pain control following thoracic procedures. To reduce the dose of morphine, ketamin was added to PCA morphine. It was reported that addition of low dose of ketamin to PCA morphine provides better analgesia than PCA morphine alone, reduces morphine consumption, and improves respiratory function (56).

Chest Drain Management

Chest tubes impair patient mobilization, exacerbate pain, and impose the risk of infection. Early chest tube removal improves forced expiratory volume in 1 s and enhances recovery of vital capacity after thoracic procedures (57). It also reduces pain, allows early mobilization of the patient, and results in shorter hospital stay. Therefore, early chest drain removal represents an important element of fast-tracking protocol in thoracic surgery.

Removal of drains is determined by the volume of fluid drainage. Majority of thoracic surgeons prefer leaving the chest tube until fluid drainage decreases to 250 ml/day or less, which prolongs hospital length of stay and delays discharge. Numerous studies have demonstrated that higher threshold for chest drain removal is safe. Nevertheless, there is still debate about the fluid threshold before chest drain removal. Recently, Bjerregaard et al. reported that chest drain removal after VATS lobectomy is safe despite volumes of serous fluid production up to 500 ml/day (58). Unlike these data, data from other studies suggest that 450 ml/day volume threshold for chest tube removal increases the risk for complications (59). However, the consensus on the fluid threshold before tubes removal should be achieved.

FUTURE DIRECTIONS

In the era of ERAS protocols, steps forward were made in the field of thoracoscopic surgery. With the aim to avoid complications related to tracheal intubation and to enhance postoperative recovery, efforts have been made to perform VATS procedures without tracheal intubation. The anesthetic technique consists of regional anesthesia and sedation in spontaneously single-lung breathing patient after performing an iatrogenic open pneumothorax (60). The inhibition of cough reflex is achieved by ipsilateral vagal blockade or stellate ganglion block (61, 62). However, open pneumothorax can compromise ventilation and oxygenation in a non-intubated patient leading to hypoxemia and hypercapnia due to carbon dioxide rebreathing from non-dependent lung. Hypercapnia is often mild and well-tolerated, while satisfactory oxygenation is usually maintained *via* face-mask (60). Recently, the first reports about the use of transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) in non-intubated VATS have appeared. It has been shown that in comparison to conventional oxygen masks, THRIVE with a flow rate at 20 l/min of oxygen, significantly improves oxygenation during non-intubated VATS, without expanding collapsed lung (63). Growing body of evidence suggests that non-intubated VATS procedures are safe and feasible to various thoracic procedures including pneumothorax management, wedge pulmonary resections, segmentectomy, lobectomy, as well as excision of mediastinal tumors (60). Recent studies reported that in comparison with double-lumen intubated general anesthesia, non-intubated thoracoscopic procedures were superior in terms of complication rate, overall hospital stay, and need for nursing care (62, 64, 65). Data from these studies suggest that non-intubated VATS could become an important element of ERP in the future.

CONCLUSION

Enhanced recovery protocol presents an evidence-based approach to patient care. Although there are variations in ERP among the institutions, the evidence suggests that implementation of ERPs in thoracic surgery significantly reduces postoperative complications and length of hospital stay. The role of anesthesiologists is very important during all the three phases of ERP. Minimally invasive surgical technique, adequate perioperative fluid management, protective ventilation, effective pain control, and patient's active collaboration are essential elements of ERP in thoracic surgery. In the era of fast-tracking, the results of studies regarding non-intubated VATS are promising.

AUTHOR CONTRIBUTIONS

All aforementioned authors contributed significantly to the final design of manuscript.

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Enhanced Recovery after Vascular Surgery

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The beginnings of the enhanced recovery after surgery (ERAS) program were first developed for patients in colorectal surgery, and after it was established as the standard of care in this surgical field, it began to be applied in many others surgical areas. This is multimodal, evidence-based approach program and includes simultaneous optimization of preoperative status of patients, adequate selection of surgical procedure and postoperative management. The aim of this program is to reduce complications, the length of hospital stay and to improve the patients outcome. Over the past decades, special attention was directed to the postoperative management in vascular surgery, especially after major vascular surgery because of the great risk of multiorgan failure, such as: respiratory failure, myocardial infarction, hemodynamic instability, coagulopathy, renal failure, neurological disorders, and intra-abdominal complications. Although a lot of effort was put into it, there is no unique acceptable program for ERAS in this surgical field, and there is still a need to point out the factors responsible for postoperative outcomes of these patients. So far, it is known that special attention should be paid to already existing diseases, type and the duration of the surgical intervention, hemodynamic and fluid management, nutrition, pain management, and early mobilization of patients.

Keywords: vascular surgery, recovery, postoperative management, intensive care, preoperative care

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INTRODUCTION

Enhanced recovery after surgery (ERAS) program or a "fast-track surgery" was first developed and successfully implemented in colorectal surgery (1), and was later reported in orthopedic (2, 3), cardiac (4), and vascular surgery (5, 6). The aims of this program are to improve the perioperative care of patients, avoid complications, accelerate recovery, shorten hospital stays and improve the patient's prognosis. Introduced by Danish surgeon Dr. Henrick Kehlet, this multimodal evidence-based approach program starts in the preoperative period and extends to the patient's release (1, 2).

It is possible to accelerate the patient's recovery, reduce complications and the length of hospital stay by changing factors which are responsible for prolonged recovery (1, 7, 8). Previous studies have shown the safety and efficiency of ERAS program, and they emphasize that for early recovery after surgery following factors are important: patient education, short-acting anesthetics, pain

Abbreviations: ERAS, enhanced recovery after surgery; ICU, intensive care unit; DVT, deep vein thrombosis; AAA, abdominal aortic aneurysm; AKI, acute kidney injury; NTG, nitrloglycerine; MAP, mean arterial pressure; ND, nasogastric drainage; PCA, patient-controlled analgesia; PCEA, patient-controlled epidural analgesia; CO, cardiac output.

management, fluid therapy, oral nutrition, and early mobilization (9, 10).

It is already proved in several studies that application of ERAS program reduces the length of hospital stay (11), decreases the surgical and non-surgical complications in postoperative period (12), and improves the outcome (13).

So far, the fields of interest in vascular surgery are ERAS in aortic (5) and carotid (6) surgery, but there are still not enough solid evidence to form a unique acceptable program.

PREOPERATIVE PERIOD

Preoperative assessment is as important as the intraoperative and postoperative period. It allows evaluation of risk and provides an opportunity to stabilize already existing disease and optimize organ dysfunction before surgery, as it is well known that postoperative organic dysfunction is undoubtfully associated with preoperative comorbidities. This period provides an opportunity for patient education, which refers to obtaining information about surgery itself, anticipated postoperative course, analgesia, and discharge. It is thought that in this way anxiety, the need for analgesics and the length of hospital stay can be reduced (1). The recommendations for ERAS in vascular surgery (including preoperative, intraoperative, and postoperative period) are shown in **Table 1**.

Special attention should be paid to premedication with an aim to reduce the stress response to surgery. Beta-blockers reduce the catecholamine level and thus reduce the perioperative and postoperative cardiovascular complications. Since surgical intervention is a stress that leads to activation of the sympathetic nervous system and catabolism, these medications with their anti-catabolic effect could have a positive impact on postoperative course. It is considered that alpha-2 adrenergic agonists, such as clonidine and dexmedetomidin, reduce myocardial ischemia, intraoperative blood loss, and postoperative nausea and vomiting (1).

Preoperative overnight fasting can lead to dehydration, and its avoidance reduces the risk of postoperative pain and nausea. It has even been proved that clear carbohydrate fluids given during this period can reduce the postoperative anxiety and endocrine response (1, 14).

INTRAOPERATIVE PERIOD

One of the major interventions in vascular surgery is an aortic surgery. Today available surgical techniques are endovascular and open repair. Study form Hertzer et al. showed that after elective open infrarenal aortic repair median length of stay in intensive care unit (ICU) is about 3 days and mortality rates are between 1.2 and 10.5% (15). Postoperative complications such as aneurysm rupture, thrombosis and graft migration are same after both surgical techniques, while endovascular repair has advantages in terms of length of intervention, blood loss, shorter length of mechanical ventilation, less malnutrition, and shorter hospital stay (16–18).

Special attention should be directed to intraoperative heat loss in order to avoid hypothermia and patient warming system should be strongly considered (16).

TABLE 1 | Recommendations for enhanced recovery program in vascular surgery.

Respiratory
Preoperative antibiotics use
Early extubation
Protective modes of ventilation
Prevention of ventilator-associated pneumonia
High-flow oxygen therapy or intermittent nasal continuous positive airway pressure after extubation
Breathing exercises
Cardiovascular
Monitoring for signs of myocardial ischemia
Goal directed fluid therapy
Maintaining the MAP above 80–90 mmHg
Renal
Monitoring of the amount of urine and creatinine clearance
Maintaining the normovolemia and electrolyte balance
Use diuretics with caution
Avoid fluid overload and dopamine
Nutrition
Without preoperative mechanical bowel preparation
Maintenance the glucose level < 215 mg/dl
Oral nutrition within the first 24–48 h after operation
Use prokinetics (metoclopramid and erithromycin)
Avoidance of nasogastric drainage or early removal
Monitoring of IAP
Pain management
PCEA 48 h before and 48 h after intervention
Avoid systemic opioid use
Other
Stabilize already existing disease and optimize organ dysfunction before surgery
Oral carbohydrate drinks before surgery
Minimize the time for surgical intervention
Patient education
Consider thromboprophylaxis
Avoid hypothermia
Early mobilization

POSTOPERATIVE PERIOD

A postoperative period in vascular surgery plays a pivotal role in the patient's recovery. The quality of postoperative care is essential for the successful recovery. Following the interventions in vascular surgery the most significant are considered to be: optimization of microcirculation after ischemic–reperfusion syndrome and inflammatory reaction caused by the operation itself, adequate fluid resuscitation, maintenance of satisfactory aerobic metabolism, stable blood glucose levels and adequate oxygen delivery, flow directed hemodynamic support, and use of vasodilators and vasoconstrictors with the goal of achieving adequate blood flow (19).

The spectrum of complications depends on the disease itself, its urgency and the surgical procedure (16). Some of these complications can appear in the early postoperative phase, but some of them can be manifested in the late postoperative period.

Immediately after operation, Crimi and Hill in their study point out the importance of resolving hemodynamic, pulmonary, renal, neurological, hematological, and gastrointestinal complications (20). The disorders of these organ systems are the result of ischemic–reperfusion injury.

Managing in the first postoperative day, mainly depends on the type of surgical intervention, the length of operation and the condition of the patient. During this period, it is important to be cautious about.

Hemodynamic Stability

Hemodynamic instability often occurs after major and complicated surgery. It is preferable to avoid hypertension, yet allowing adequate perfusion of vital organs. For this purpose, a combination of nitrloglycerine (NTG) and labetalol with some inodilators such as dobutamine is mostly recommended (19). The patients are often vasoplegic and hyperdynamic and require vasoconstrictors in the form of noradrenaline or vasopressin. This requires adequate invasive monitoring or the placement of pulmonary catheter. Oxygen delivery markers such as SvO_2 and serum lactate levels should also be monitored. Transesophageal ultrasound should be available, especially during the periods of hemodynamic instability (19).

Respiratory Failure

Respiratory failure, most commonly caused by infection and pulmonary pathology, is still the most common complication after surgery of thoracoabdominal aorta and occurs in about 30% of patients (20). Respiratory function is often most stable shortly after surgery and patients can usually be extubated within 6–12 h or even earlier. Only in rare cases of transfusion-related acute lung injury, or pulmonary infection exacerbation in high-risk patients, gas exchange remains compromised and requires prolonged ventilatory support. Additionally, major surgery and preexisted kidney disease can lead to significant pulmonary complications (21). If there is a risk of volotrauma, low tidal volumes can be used. Hypercapnia and respiratory acidosis are logical consequence of this ventilation mode, but if the patient does not have cerebral edema, this permissive hypercapnia is generally well tolerated with pH > 7.2 (22). If there is a need for lung recruitment and after separating from the ventilator, it is preferable to use high-flow oxygen therapy or intermittent nasal continuous positive airway pressure (19).

Factors such as: extreme age, comorbidities, extensive surgery, prolonged use of muscle relaxants and sedatives, preexisting pulmonary disease, postoperative hypothermia and fluid overload can lead to V/Q mismatch, hypoxia, and respiratory failure. Prevention of respiratory complications should start in the preoperative period using antibiotics and breathing exercises (22).

Myocardial Ischemia

Study of Landesberg et al. showed that transient myocardial ischemia developed among 21% of patients and myocardial infarction in 6.5% of cases (23). Combination of two precordial leads are more than 95% sensitive than troponin level for postoperative ischemia monitoring. If myocardial ischemic event occurs, supplemental oxygen, beta-blockers, afterload reduction agents, anticoagulants and antiplatelets should be administered. Percutaneous coronary intervention is also recommended, while postoperative fibrinolysis is a relative contraindication (22). If ischemic events are associated with signs of myocardial impairments, manifested by an increased need for inotropic use, reduced cardiac output (CO), cardiac arrhythmias or disorders of wall motility, urgent angiography can be indicated (19).

Bleeding and Coagulopathy

A typical consequence of aortic surgery is coagulopathy with subsequent bleeding. Early stabilization of coagulopathy is important in prevention of further complications. Special point-of-care laboratory tests such as thromboelastography or activated clotting time allow the treatment of such disorders (19). Preoperative administration of antifibrinolytics can be continued in the short postoperative period.

Liberal blood transfusions for treatment of massive bleeding are no longer in use because of high 30 days' adverse events among these patients. It is recommended that if hemoglobin is above 9 g/dl, transfusion should be avoided. When there is a need for correction of clotting factors deficiency, the dose of fresh frozen plasma should be 10–15 ml/kg of body weight, with a maximum dose of 30 ml/kg, and most important is that fresh frozen plasma should not be used as a volume expander (22).

Temperature Management

Immediately after surgery patients are often hypothermic, especially after long interventions. Maintaining an adequate body temperature in postoperative period is important for adequate oxygen supply, functioning of the coagulation system, hemodynamic stability, and neurocognitive integrity (19).

Neurologic Disorders

Typical complications following aortic surgery are stroke, spinal cord ischemia or generalized cognitive dysfunctions presented as delirium or confusion/agitation (19, 20). Study from Beydon et al. showed that lorazepam in premedication was associated with prolonged extubation time and a lower rate of cognitive recovery (24). But Scavee et al. showed that fear and anxiety increase the incidence of postoperative complications and that use of anxiolytics can be desirable (25).

Deep Vein Thrombosis (DVT)

The risk of DVT after open abdominal aortic aneurysm repair (AAA) is 2–33% without chemoprophylaxis, and 1–10.2% in patients who received postoperative enoxaparin (26). Previous studies, which had some limitations, have shown that because of low incidence of postoperative DVT or high risk of bleeding, there is no need for postoperative thromboprophylaxis (26).

Scarborough et al. in their study (6,000 patients) showed that the incidence of DVT after AAA is only 2.4%, but the limitation in this study was that they did not know which patient received thromboprophylaxis. They emphasize that the risk factors for DVT after open surgery are: length of surgery more than 5 h, obesity and ruptured aneurysmal disease (27).

For the time being, there are no unique guidelines for thromboprophylaxis. Although many studies in this field were conducted, they included small number of patients, so their conclusions cannot be considered as relevant.

Based on available data, the majority of vascular surgeons consider that the use of thromboprophylaxis should become a routine for patients undergoing AAA repair (27).

Special attention should be paid to patients with carotid surgery, especially those who develop some neurological deficit. Due to uncontrolled hypertension, cerebral hyperperfusion syndrome can develop, and this should be controlled with IV labetalol. Hypotension should be treated with volume infusion and phenylephrine (22).

In the late postoperative period the focus should be put on acute kidney injury (AKI) and intra-abdominal complications.

Acute Kidney Injury

The most common predictor factors for AKI are physiological reserve as well as the severity of atherosclerotic disease (28, 29). The incidence of postoperative AKI requiring dialysis ranges from 5 to 15%, and its occurrence is associated with a worse prognosis (30). Monitoring the amount of urine as well as creatinine clearance in postoperative period is crucial. Diuretics and dopamine can promote urine output, but integrity or functional reserve of glomerular function may be compromised (31). Patients with intra-abdominal pressure >25 mmHg are at risk for compartment syndrome development, which may cause AKI. In this group of patients it is important to maintain higher values of blood pressure and better oxygen delivery (22).

Intra-Abdominal Complications

Some of these complications are rare, such as mesenteric ischemia (2–5%), but the mortality rate is high (55–60%) (32). Cross-clamping the aorta may cause mesenteric ischemia with consequent reperfusion injury, translocation of the bacteria and systemic inflammatory response. After cardiopulmonary bypass, low CO can cause gut ischemia (where local vasodilatators, such as nitric oxide and papaverine, can be helpful) and colonic infarction with high mortality rate (89%) (33).

GUIDELINES FOR MANAGEMENT IN POSTOPERATIVE PERIOD

Hemodynamic Management

Hypoxia and hypertension in postoperative period can be harmful for patients. Hypertension is associated with increased incidence of strokes or aorta dissection. On the other hand, hypotension is associated with graft thrombosis and multiorgan failure, therefore, maintenance of adequate oxygen supply is crucial for kidneys, CNS, and spinal cord (22). The recommendations are to keep mean arterial pressure above 80–90 mmHg, as well as maintenance the systolic blood pressure above 130 mmHg. Achieving these values of blood pressure is not always easy in practice and often requires the use of vasodilatatotors—NTG and labetalol, vasoconstrictors—noradrenaline and vasopressin, and even inotropes such as dobutamin. Even with this support, fluid replacement can be a real challenge (19). Recent recommendations are based not only on the satisfactory pressure maintenance but also on tissue perfusion which is equally important (34). Among various types of arrhythmias, bradiarrythmias should not be treated if they are not associated with hemodynamic instability (35, 36).

Hemodynamic management is now directed not only toward the maintenance of satisfactory tissue perfusion but also toward flow directed approach, with clinical assessment of urine output and oxygen extraction index (19, 37). Recently, it has been showed that diuretics can improve venous drainage from the microcirculation, increase the oxygen extraction at cellular level and improve mitochondrial function (37).

Fluid Management

Many patients after operation do not have the ability to excrete fluids and sodium; on the other side, many of them are hypovolemic in this period (38). Crystalloid solutions like Ringer-lactate should be favourized during this period. Normal saline should be avoided due to hyperchloremic metabolic acidosis, which can reduce tissue perfusion and worsen the final outcome (19). In general, colloids are better in raising the blood pressure and improving the tissue perfusion, but they should be used with great caution due to renal toxicity and unfavorable effects on coagulation system (19). With limited evidence, it is advised to avoid them in patients with an already impaired kidney function (39).

Nutrition

Postoperative insulin therapy with the goal of maintenance the glucose level < 215 mg/dl (11.9 mmol/l) is mandatory for diabetic and non-diabetic patients (40). The relationship between high glucose levels and worse outcomes is a well-known concept. Study from Krinsley et al. showed that the mortality is twice as high when glucose level is above 140–150 mg/dl (41). An increase of glucose level for every 40 mg/dl carries a 30% higher risk of infection, graft failure, and longer ICU stay (42). Achieving these values is significant for wound healing, integrity of gastrointestinal system, and inflammatory response reduction (43).

Malnutrition in preoperative period is associated with muscle weakness, fatigue, immunological dysfunction, and slower wound healing. Some studies have proven that adequate nutrition even in the preoperative period can improve surgical outcome (44, 45). Restoration of bowel motility plays a very important role in the ERAS program since the beginning of food intake depends on it. Enteral feeding has fewer metabolic complications than parenteral nutrition (22), and it should be started as soon as possible in the postoperative period (6–8 h) (46). On the contrary, Ksienski et al. showed in their study that early oral nutrition should start within the first 24–48 h while gastric emptying occurs within 18 h after elective aortic aneurysm repair (47). If there is a postoperative disturbance in bowel motility, first-line choice therapy for prokinetic medications are metoclopramid and erythromycin (18).

The use of nasogastric drainage (ND) is not recommended and can even be harmful. It has been shown that in patients without ND bowel function returns earlier and that they have fewer pulmonary complications (18, 48).

Pain Management

Pain management in postoperative period is very important and one Cohrane review showed that use of epidural analgesia has fewer cardiovascular and renal complications compared with systemic opioid use with no difference in mortality (20). Patient-controlled epidural analgesia (PCEA) with local anesthetics provides better analgesic effect than patient-controlled analgesia (PCA) with intraveonous opioids, but there is no statistical difference in hospital stay and its outcome when these two techniques are compared (49). Additionally, based on available evidences for ERAS protocol, the PCA epidural analgesia is highly recommended (50). PCEA should begin 48 h before intervention and continue 48 h after operation (51). Criteria for discharge are: hemodynamic stability, urine output >0.5 ml/kg/h, adequate analgesia to make patients active, ability to consume solid fluid, and no indications for further surgical interventions (23, 49).

CONCLUSION

Although ERAS program was most studied and applied in colorectal surgery, recent studies suggest that it can be successfully applied in vascular surgery, too. The most important is establishing the guidelines and form a team whose members (surgeons, anesthesiologists, nurses, rehabilitation members, and nutritionists) should be familiar with ERAS program and must be motivated to carry out the program.

Since the field of vascular surgery is too broad, one cannot even expect that the conceptualization of just one program is sufficient for all areas in vascular surgery. For the moment, some acceptable guidelines for the postoperative management already exist, therefore, it is necessary to direct the attention to the preoperative status of a patient and improvements in surgical techniques.

AUTHOR CONTRIBUTIONS

RJ conceived of the presented idea. MS, AV, VD, and DM wrote the beginning version of the manuscript. MS, AV, RJ, VD, DM, AN, and TG contributed to the design of the research and the writing of the final version of the manuscript. RJ supervised the manuscript.

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