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Changing backgrounds and groundbreaking changes: gynecological surgery in the third decade of the 21st century, volume II

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Changing backgrounds and groundbreaking changes: gynecological surgery in the third decade of the 21st century, volume II

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Editorial: Changing backgrounds and groundbreaking changes: gynecological surgery in the third decade of the 21st century volume II

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Editorial on the Research Topic
Changing backgrounds and groundbreaking changes: gynecological surgery in the third decade of the 21st century volume II

The first volume of this Research Topic (RT) focused largely on patient safety and complication management (1). In this second volume, the submitted manuscripts also group around key contemporary themes. For instance, four papers are dedicated to the robotic approach (Ferrari et al., Kawamura et al., Neis et al., Ascione et al.), while four deal with cervical neoplasia (Ning et al., Zhang et al., Zeng et al., Li et al.). Among these, two evaluate a de-escalation of the surgical approach (Ning et al., Zeng et al.).

We believe that this RT accurately reflects the current discussions and evidence gaps in gynecologic surgery. In 2017, the LACC trial reshaped gynecologic oncology by demonstrating that laparoscopic radical hysterectomy (RH) for cervical cancer (CC) compromises treatment outcomes compared to the open approach (2). These findings were recently confirmed in the final overall survival analysis (3). Further analyses of the same dataset showed no difference in complication rates between open and laparoscopic RH (4), reaffirming the open approach as the standard of care for CC after two decades of laparoscopic RH evolution (3). Recently, the SHAPE trial demonstrated comparable oncological outcomes between simple hysterectomy (SH) and radical hysterectomy (RH) for early-stage, low-risk cervical cancer, confirming that surgical de-escalation can be considered safe in such cases (5). This RT includes a closely related meta-analysis by Zeng et al., examining the efficacy and safety of non-radical surgery for early-stage CC. The "groundbreaking changes" in CC surgery are accompanied by evolving anatomical knowledge, prompting a reassessment of the current anatomical classification of RH (6). In the coming years, the role of robotic approaches in CC treatment will be clarified by the RACC trial (estimated completion: May 2027) (7). Additionally, the newly launched LASH trial will address both surgical de-escalation and the relevance of surgical approach (8).

A decade ago, evaluations of robotic-assisted approaches primarily focused on feasibility, safety, and cost compared to conventional laparoscopy (9). These evaluations typically demonstrated similar complication rates and surgical outcomes, while favoring robotics for

improved dexterity, visibility, and surgeon comfort. However, higher costs remained a limiting factor, particularly in low-volume hospitals and resource-limited settings (9). Moreover, robotic-assisted surgery was almost exclusively associated with the pioneering da Vinci platform and its subsequent generations. Today, the market offers more than twenty robotic platforms, including various da Vinci variants (Intuitive Surgical Inc., California, USA), Senhance® (Asensus Surgical, North Carolina, USA), Versius (Cambridge Medical Robotics, UK), and the Hugo™ RAS system (Medtronic, Minneapolis, USA) (10, 11).

Technical advancements in robotic surgery have been applied early in endometriosis surgery, which is often characterized by extreme complexity and the necessity of nerve and fertility preservation. The review by Ferrari et al. addresses the role of robotic surgery in deep-infiltrating endometriosis, separately analyzing critical localizations such as colorectal, diaphragmatic, and sacral plexus endometriosis. Beyond summarizing current evidence, the authors highlight gaps in knowledge and emphasize the need for prospective randomized controlled trials. Kawamura et al. evaluated the feasibility of omitting a uterine manipulator during robotic-assisted hysterectomy without compromising patient safety. Their conclusion suggests that, unlike conventional laparoscopic hysterectomy—where a uterine manipulator is usually indispensable—the precision of robotic systems may reduce the necessity for a manipulator in certain cases. However, a "difficult" surgical field (e.g., ovarian casts or Douglas obliteration) and higher patient BMI still necessitate its use. In such cases, the employment of a fourth robotic arm could enhance surgical independence and resource efficiency. A surgeon's impact on patient safety is significantly influenced by surgical training, case volume, and various factors encompassed by the "human factor", including individual health, personality, and workload (9). Neis et al. used visualization techniques to analyze workflow consistencies and variabilities among surgeons performing robotic total laparoscopic hysterectomy, applying objective measurements to assess individual surgical behavior.

The collection of papers dedicated to robotic approaches is rounded out by the work of Ascione et al., which describes how the robotic-assisted approach can enhance fertility-preserving treatment of cornual pregnancy. This is the second paper in this RT addressing fertility-preserving approaches. Fertility-sparing surgery for early-stage CC patients is of great importance given the trend of childbearing shifting into the third and fourth decade of women's lives. The evaluation of clinicopathological characteristics by Ning et al., based on a large cohort of 10,629 stage I CC patients aged 15–39 years, provides valuable insights into fertility-sparing decision-making and represents an important contribution to this RT.

The work of Malanowska-Jarema et al. continues the evaluation of laparoscopic lateral suspension (LLS), which was suggested in Volume 1 of this RT as the new gold standard for treating pelvic organ prolapse (POP) (12). Their work provides evidence of the equivalence of LLS to laparoscopic sacrocolpopexy in terms of sexual function. This is a valuable contribution, as a contemporary "standard of care" for POP can only be established by evaluating a broad spectrum of outcomes.

An important part of this RT consists of carefully selected case reports. It is commendable that the journal still values case reports on par with studies with higher citation potential. Many journals have banned case reports in response to competitive pressures to optimize citation metrics and impact factors, as these productivity metrics (despite ongoing critiques) remain central to both academic careers and journal reputations (13). Notably, bibliometric studies have now evolved into an independent research field, as seen in the paper of Pérez-Reátegui et al. (14). However, without case reports, building a stable body of evidence for rare diseases would be nearly impossible (15). Two exemplary case reports in this RT focus on cervical tumors: one describes a rare ureteric-bud adenocarcinoma misdiagnosed as a cervical fibroid (Zhang et al.), while the other reports on benign cervical malakoplakia confused with CC (Li et al.). These cases underscore the continued importance of case reports, as demonstrated here in CC, since a small fraction of clinical presentations will always fall outside established frameworks, requiring an intuitive approach or treatment based on analogy to existing pathways (16).

To look forward, we predict that the renaissance of robotic surgery is occurring now, marking a shift from "robotic-assisted" to "robotic-guided" surgery through the implementation of artificial intelligence to integrate augmented reality and multimodal information (including imaging techniques, radiomics, and molecular diagnostics) into a virtually enhanced surgical field. These advancements will set new milestones in surgical approaches and personalized patient care. In the coming years, we anticipate further refinements in the surgical management of CC, informed by ongoing trials, as well as continued evolution in endometrial cancer treatment through molecular classifications and the establishment of sentinel node biopsy as the standard of care. We hope that, in rare diseases, continuous publication of case series—along with improved publication standards and integration of molecular analytics—will allow for reliable synthesis and cautious standardization of treatment approaches, including fertility-sparing criteria for rare malignancies (17).

We thank all authors who contributed to this issue and hope that their publications will contribute to and inspire further "groundbreaking changes" and "changing backgrounds" in gynecological surgery.

Author contributions

RW: Conceptualization, Project administration, Writing – original draft, Writing – review & editing. RS: Project administration, Writing – review & editing.

Conflict of interest

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

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Robotic surgery for deep-infiltrating endometriosis: is it time to take a step forward?

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Endometriosis is a chronic debilitating disease that affects nearly 10% of women of the reproductive age. Although the treatment modalities of endometriosis are numerous, surgical excision of the endometriotic implants and nodules remains the sole cytoreductive approach. Laparoscopic excision of endometriosis was proven to be beneficial in improving the postoperative pain and fertility. Moreover, it was also proved to be safe and efficient in treating the visceral localization of deep endometriosis, such as urinary and colorectal endometriosis. More recently, robotic-assisted surgery gained attention in the field of endometriosis surgery. Although the robotic technology provides a 3D vision of the surgical field and 7-degree of freedom motion, the safety, efficacy, and cost-effectiveness of this approach are yet to be determined. With this paper, we aim to review the available evidence regarding the role of robotic surgery in the management of endometriosis along with the current practices in the field.

KEYWORDS

endometriosis, robotic surgery, laparoscopy, diaphragm, urinary tract, Colon, rectum

1 Introduction

Endometriosis is one of the most common gynecologic diseases affecting nearly 10% of women of the reproductive age (1). Endometriosis is defined by the presence of endometrial-like glands and/or stroma out of the uterus (2, 3). The clinical manifestations of endometriosis could be broadly categorized into endometriosis-associated pain and infertility (4). The most commonly-reported symptoms of endometriosis are chronic pelvic pain, dysmenorrhea, and dyspareunia (5). On the other hand, infertility is reported to affect 30–50% of endometriosis patients (6). Although endometriosis has various forms and manifestations, superficial peritoneal endometriosis, ovarian endometriomas, and deep endometriosis are the three main types of the disease (7). Deep endometriosis has been historically defined as deep infiltrating endometriosis extending 5 mm below the peritoneal

surface (8). However, a recent international terminology consensus has argued that measuring depth in millimeters is inaccurate. It is now agreed that any endometrial-like tissue in the abdomen, extending on or under the peritoneal surface, is referred to as deep endometriosis (9). These lesions are typically nodular, capable of invading adjacent structures, and associated with fibrosis, leading to the disruption of the normal anatomy (9). Such lesions usually involve the retro-cervical space, the recto-vaginal septum, the uterosacral ligaments, as well as nearby organs such as the sigmoid colon, rectum, bladder, and ureters (10, 11). It should be noted that bowel endometriosis is a special subtype of deep endometriosis that should be only diagnosed when the muscular layer of the bowel wall is infiltrated with the disease (12, 13). Hormonal suppressive treatments with cyclic oral contraceptive pills, progestins, and gonadotropin-releasing hormones (GnRH) agonists and antagonists were proven to be safe and effective in treating the endometriosis-associated pain (14–16). However, those therapies are suppressive rather than cytoreductive, which means, in most cases, the symptoms recur with the suspension of the treatment. This becomes particularly problematic in cases of infertility or when the patient seeks conception. To date, surgical excision of endometriosis is the only cytoreductive approach with promising symptom-relief rates. Furthermore, surgery becomes unavoidable when organ damage is suspected or already detected (4, 17). The basic principles of the endometriosis excisional surgery are the uncomplicated resection of the visualized endometriotic lesions, performing adhesiolysis, and restoring the normal pelvic anatomy (18). Minimally invasive surgery (MIS) is actually the approach of choice since it demonstrated reduced blood loss, postoperative pain, and duration of hospitalization. In fact, the Enhanced Recovery After Surgery (ERAS) program recommends MIS to improve the postoperative patient recovery (19, 20). Nevertheless, the laparoscopic management of advanced and complex cases is challenging due to tissue alterations provoked by adhesions and the endometriosis-associated fibrosis (21). Despite the advantages of laparoscopy compared to open surgery and the development of laparoscopic 3D optics, the laparoscopic approach harbors technical limitations in terms of ergonomics and the limited range of motion (22). Robotic-assisted surgery was developed more than 30 years ago as a United States military project and received the approval of the Food and Drug Administration (FDA) in 2005 (23). Since then, robotic-assisted surgery has been widely implemented and adopted in gynecology (24). Robotic-assisted surgery was recently reported to have shorter operation time and less blood loss than laparoscopic surgery, with comparable outcomes (25). However, the available data in that regard is conflicting and more studies are required to justify this claim. Robotic-assisted surgery with its rapidly evolving technology can overcome much of the laparoscopic limitations, and represents a step forward toward a safer and more precise excision of the disease. Indeed, the EndoWrist® increases the range of motion and the robotic platform 3D vision avoids the problem of an unstable bi-dimensional image totally dependent on the assistant. Nonetheless, its superiority or at least non-inferiority in the management of deep endometriosis remains unclear due to the lack of research in the field. The present review aims to provide an update on the role of robotic-assisted surgery in managing endometriosis and summarize the main scientific findings in the literature.

2 Materials and methods

This work is a narrative review of the role of robotic-assisted surgery in deep-infiltrating endometriosis. A broad scope search of literature was conducted in Scopus, PubMed/Medline, ScienceDirect and the Cochrane Library. A combination of the following keywords was used: deep-infiltrating endometriosis, robotic surgery, robot-assisted laparoscopy. The search was restricted to only include articles in English language. Relevant papers of all types (i.e., original articles, video articles, and case reports) were assessed and included as appropriate.

3 Feasibility of the robotic-assisted surgery

Laparoscopic excisional surgery is the gold standard for the treatment of deep endometriosis. More recently, robotic-assisted surgery became more frequently adopted for the surgical management of endometriosis without clear indications. Available non-comparative studies of women that were operated robotically found a comparable complication rate between robotic-assisted surgery and laparoscopy with a significant reduction of pain symptoms. An improved quality of life at follow-up was also reported (22, 26–32). Nonetheless, very few studies that compared the two minimally invasive approaches in patients with r-ASRM stage III/IV endometriosis are available. To the best of our knowledge, there are only one randomized-controlled trial (RCT) (33) and two meta-analyses (34, 35) in that regard.

In 2010, Nezhat et al. (36) published for the first time a retrospective study comparing robotic-assisted surgery and laparoscopy in severe endometriosis. Although the outcomes and complication rates were comparable between the two groups, longer operative time and hospital stay were noted in the robotic group. The mean difference in the operation times was 61 min.

The safety and feasibility of robotic-assisted surgery was further confirmed by several studies that reported comparable outcomes and rates of intra-and postoperative complications (37–41).

In a large retrospective study by Nezhat et al. (41), the hospital stay was longer in the robotic-assisted group in contrast to the findings of other reports. In that study, only 23% of patients in the laparoscopy arm stayed overnight in the hospital against all the patients of the robotic arm without any complication in both groups (41). In our opinion, these findings may be related to a standardized protocol of postoperative discharge rather than an actual underlying difference between both approaches.

The total operative time was significantly shorter in the laparoscopy group in the majority of the studies (38, 40–42). Dulemba et al. (37) reported a non-significant difference in the length of surgery in accordance the multivariate analysis of Magrina et al. (39), which accounts for the impact of the higher number of procedures and radicality in the robotic group (39). In the same study, the authors reported a higher rate of histological confirmation of endometriosis in the robotic-assisted surgery group compared to the laparoscopic counterpart (80% vs. 56.8%, respectively). This could be attributed to the technology of the robotic platform and its three-dimensional visualization. Improved visualization could logically lead to improved detection of superficial lesions, which is of paramount importance in women reporting pelvic pain suggestive for endometriosis.

For some authors, obesity is a major limiting factor for laparoscopic surgery in terms of some technical aspects and the difficulties to access to the surgical spaces (40). Nonetheless, the available evidence supported the feasibility and safety of robotic-assisted gynecologic surgery in obese patients (43–46). In recent years, the wide spread of robotic platforms increased the number of women treated with minimally invasive approach (47, 48). Nezhat et al. (40) speculated that obese patients may benefit from robotic-assisted surgery more than normal-weighted patients. However, their study reported comparable outcomes and a significant higher total operative time in the robotic-assisted surgery arm compared to laparoscopic arm in the obese subgroup (40). Other authors addressed the increased amount of time to the multiple changing in table positioning but the proposal of a hybrid robotic-laparoscopic procedure was not demonstrated to be a time-saving option (38).

In 2017, Soto et al. (33) published a randomized controlled trial (LAROSE trial) enrolling 73 patients randomly assigned to laparoscopy or robotic-assisted surgery (33). To the best of our knowledge, this is the only trial available to date in that regard. Multivariate analysis showed no significant differences in total operative time, intraoperative complications and blood loss between the two groups. Nonetheless, only 33% of the patients had stage III/IV endometriosis and the intraoperative staging was significantly lower in the robotic arm. When taking in consideration the low rate of complications and adverse outcomes as well as the small sample size, the conclusion of the study may not be generalizable.

In a recent meta-analysis by Restaino et al. (35), the safety of robotic-assisted surgery was confirmed with a comparable rate of intra-and post-operative complications. In addition, the authors reported similar estimated blood loss quantities between the two groups. Moreover, robotic-assisted surgery was associated with longer operative time compared to laparoscopic surgery, even when excluding the docking time (35). Nonetheless, the authors concluded that the heterogeneity in outcomes of the included studies and the focus on the peri-operative window did not allow any conclusions on long-term pain relief, quality of life and fertility results (34, 35). Moreover, some of the considered studies enrolled both mild and severe endometriosis (33, 41) while other authors failed to report the stage of the disease, which contributed to the wide heterogeneity in the included population. Those results are in accordance with the results Chen et al. (34).

4 Colorectal endometriosis

Bowel endometriosis is a subgroup of deep endometriosis that involves the recto-sigmoid junction in the majority of the cases (65%), followed by the rectum (15–20%) (40, 49). In the available literature, its incidence was reported to be 4–38% in women with endometriosis and cyclic bowel symptoms, especially dyschezia and hematochezia (50). The surgical management is required after failure of conservative medical therapies and it should be tailored on the patient's symptoms and disease characteristics. Although clear guidelines are lacking, the choice between segmental resection with anastomosis, discoid resection or nodulectomy (shaving) is mainly based on the size, the depth of the lesions' invasion, the circumference of the disease and the coexistence of skip lesions (29, 51). In the last years, some authors considered the robotic-assisted surgery in cases of bowel endometriosis to overcome the complexity and technical difficulty of advanced stages allowing a smoother preparation of the rectum with an easier superior rectal artery sparing and simpler handling of the tissue during the anastomosis (23, 29). In a meta-analysis of a total of 3,079 women with recto-sigmoidal endometriosis, the statistical analysis demonstrated a higher rate of major complications for segmental resection (11.8%), followed by discoid resections (7.5%) and the rectal shaving technique (5.5%). In 92% of cases, a minimally invasive approach was used but robotic-assisted surgery was performed only in 1.7% of the patients (49).

In 2011, Nezhat et al. published two successful cases of bowel endometriosis managed with robotic segmental rectal resection and discoid resection demonstrating the feasibility of both approaches (28). In a small comparative study, Lim et al. (52) compared robotic-assisted anterior rectal resection with the open approach. The authors failed to detect any significant differences in total operative time, blood loss and length of hospitalization. A higher number of complications was reported in the laparotomy group, but the difference was not significant (52). In a cohort of 22 consecutive patients, robotic-assisted excision of bowel endometriosis was confirmed to be safe and feasible, with satisfactory short-term results and zero conversions to laparotomy (26).

In a recent prospective cohort study, the comparison between laparoscopy and robotic-assisted surgery did not yield in any differences in blood loss, intra-operative and postoperative complications, and voiding dysfunction rates. The robotic arm had a longer total operative time (221 ± 94 min vs. 163 ± 83 min, $p = 0.03$), a longer hospital stay (8 ± 4.4 vs. 6.5 ± 2.6 days, $p = 0.18$), a higher number of grade III complications (according to Clavien Dindo Classification) without reaching the statistical significance (53).

Raimondo et al. (54) published the results of a multicentric prospective cohort study comparing laparoscopy with robotic-assisted surgery. The data of the 44 enrolled women showed no differences in outcomes, complications, operative time (skin to skin) and improvement of symptoms at 12 months of follow-up. A longer operative room time in the robotic arm was reported (296 ± 80 min vs. 241 ± 72 min; $p = 0.020$). This is also consistent with the findings of Ercoli et al. (26).

5 Diaphragmatic endometriosis

Diaphragmatic endometriosis is a rare form of the disease. The exact incidence and prevalence of diaphragmatic endometriosis are unknown precisely yet. However, the prevalence of diaphragmatic endometriosis was reported to be 1.86–4.7% (55). The preoperative diagnosis is difficult and the management remains controversial (45, 46, 55, 56). It may cause catamenial symptoms or chronic pain. Nonetheless, some cases may be asymptomatic (57, 58).

Ceccaroni et al. reported the portion of the diaphragm behind the right hepatic lobe as the most frequent localization (57). Redwine (56) postulated the existence of sentinel lesion on the anterior part of the diaphragmatic peritoneum which could suggest the presence of more extended localization and may induce the surgeon to a complete retro-hepatic exploration (56). Symptomatic lesions are associated with a deep involvement of the whole thickness of the diaphragm and an association with symptomatic pelvic or bowel disease was reported in the totality of the cases (59, 60).

The management is a real challenge in particular for the rarity of the localization, availability of few case series, lack of guidelines and difficulty in the preoperative diagnosis. Complete surgical resection avoiding the opening of the thoracic cavity is the goal if a full-thickness excision is not required (61). Laparotomic, laparoscopic and robotic approaches were reported in the literature, associated with video-assisted thoracoscopy (VATS) when thoracic symptoms were present (27, 57, 60, 62). Thermal ablation was proposed for the superficial lesions and Ceccaroni et al. favored Argon Beam Coagulator (ABC) than electrocautery (57).

Abo et al. published a case series of 35 patients in which robotic-assisted endometriosis excision was performed over a period of 30 months (27). Among them 8 cases of diaphragmatic localization were reported. No major complications were related to the procedure but the extent of the disease and surgical technique was not described. Recently, Roman et al. published a proposal to standardize the surgical management using robotic surgery reporting the feasibility, safety and reproducibility of this approach (62). Moreover, cases of incidental tension pneumothorax during inspection of the abdomen in patients treated with robotic-assisted surgery is reported and the entire surgical team needs to be aware of this possibility (60, 63).

However, it should be noted that in a recent study of Naem et al. (55) patients with diaphragmatic endometriosis were followed up for a mean duration of 23 months. Although 78.9% of patients reported major postoperative improvement, the postoperative recurrence rates of diaphragmatic endometriosis-related symptoms were higher than expected, with complete pain relief being reported in 25–50% of patients. On the other hand, asymptomatic lesions that were left *in situ* remained asymptomatic after a follow up period of 6–14 months (55). Therefore, caution should be made before operating diaphragmatic endometriosis, especially in the asymptomatic cases, where treatment seems to be unnecessary, and appropriate patient counseling about what to exactly expect postoperatively should be carried out (55, 64).

6 Urinary endometriosis

The urinary tract is rarely an endometriosis localization occurring in 0.5 to 12% of women with pelvic endometriosis. The prevalence exceeds 50% in patients with deep endometriosis (65, 66). The urinary bladder is the most common site (80%), followed by the ureter (15%), kidney (3%) and urethra (2%) (65, 67). The definition and incidence of bladder endometriosis are different in the literature owing to the variation in the inclusion or exclusion of superficial serosal lesions. Related symptoms frequently include dysuria, hematuria, suprapubic pain and urinary frequency (65). Ureteral endometriosis is less frequent and most commonly affects the left distal ureter (68). It can be classified in extrinsic form when the ureter is involved by an external nodule and intrinsic form if mural invasion is present (68). The symptoms related to ureteral endometriosis may be lower back pain, recurrent urinary tract infections, and hematuria. However, it remains asymptomatic in around 50% of the cases and may lead to an ipsilateral silent kidney (65). When surgery is required, minimally invasive approaches were demonstrated to provide adequate outcomes and acceptable rate of complications in case of urinary tract endometriosis (67, 69). In case of bladder endometriosis, the majority of the authors suggested to perform partial cystectomy to achieve a complete resection of the nodule (65, 67, 68). According to literature, ureteral lesions may be removed with ureterolysis, segmental excision with end-to-end anastomosis or reimplantation (65, 67, 69).

In the literature there are no randomized trials or prospective studies comparing laparotomy with laparoscopy and robotic-assisted surgery in case of urinary tract endometriosis. However, case reports and case series demonstrated the feasibility and safety of the robotic-assisted laparoscopy (22, 27, 29, 65, 66, 68, 70–72). A French multicenter retrospective cohort including 232 patients reported the use of robotic surgery in 14.7% of the patients in comparison to laparoscopy and laparotomy in 74.1 and 11.2% of cases, respectively (68). Di Maida et al. (66) published a series of 74 women underwent minimally invasive surgery for urinary tract endometriosis. Twenty-eight (37.8%) were managed with laparoscopy and 46 (62.2%) with robotic-assisted surgery. The authors demonstrated the feasibility of the approach and reported an overall postoperative complication rate of 10.9% in the robotic group, which is consistent with the findings of Giannini et al. (70). A retrospective study compared laparoscopy and robotic-assisted surgery for the treatment of bladder endometriosis with partial cystectomy. No differences in term of surgical outcomes, perioperative complications, blood loss and recurrence rates were observed.

7 Sacral plexus endometriosis

Deep endometriosis involving the sacral plexus and the large nerves of the pelvis is deemed to be rare in gynecology (73). Although the first report of deep endometriosis of the sciatic nerve dates back to 1955 (74), very few data are available regarding its precise prevalence and optimal management. This may be attributed to the lack of awareness of this condition due to the lack of correlation between endometriosis, menstruation, and the resulting neurological symptoms (75). Deep endometriosis may involve the pelvic neural structures mainly in two ways. The first and most common form of neural involvement includes compressing the sciatic nerve and sacral roots due to the posterolateral extension of parametrial and rectovaginal endometriosis, causing intrapelvic nerve entrapment (76). It is noteworthy that rectovaginal nodules tend to involve the sacral roots S2, S3, and S4. While deep nodules of the parametrium with more superior lateral localization tend to involve the sciatic nerve (76). The second form of involvement is the direct infiltration of the nerves with endometriosis. This form is less common and was reported to account for nearly 33.5% of patients with recurrent sciatica (77). Pelvic nerve involvement with endometriosis causes a variety of somatic sensory and motor symptoms, with or without pelvic organ dysfunction (78, 79). In cases of sciatic nerve involvement, the patients often report cyclic sciatica. The term sciatica refers to pain along the distribution of sciatic nerve, usually referring to leg and gluteal pain (79). In addition, foot drop and alteration in the Achill's tendon reflex may be noticed (76). On the other hand, when the sacral roots are involved with endometriosis the patients suffer from perineal pain, altered sensations in the dermatomes S2 to S4, and pelvic organ dysfunction, such as constipation, vaginal dryness, urinary urgency or bladder atonia (76, 78). It should be noted that such symptoms do not necessarily originate from the sole involvement of the sacral roots, but the involvement of the hypogastric nerves, splanchnic nerves, and inferior hypogastric plexus in the large rectovaginal or parametrial endometriotic nodule (76).

Deep endometriosis involving the sacral roots and sciatic nerves was historically treated with laparoscopic detrapment of the involved structures in the means of neural decompression and shaving at the epineurium level. Less commonly, partial nerve resection was also applied (76–78, 80). Furthermore, laparoscopic identification and subsequent excision of peritoneal pockets resulted also in a postoperative resolution of the neurologic pain symptoms (79). The efficacy of such interventions is not estimated precisely yet, but the available reports indicate that pain symptoms tend to be improved postoperatively (76, 80). It should be noted that postoperative bladder dysfunction and the need for self-catheterization was recorded in 5.8% of the operated patients in the series of Roman et al. (76) over a year of follow-up. In the same series, the authors reported that *de novo* hyperesthesia, hypoesthesia, or allodynia were recorded in 17.2% of patients postoperatively (76).

On this basis, the role of the robotic-assisted surgery, which is basically a subdivision of laparoscopic surgery, is far from being determined. Available reports indicate that robotic surgery with its 3D image and the 7-degree of freedom of the robotic instruments increase the safety and the precision of the neural dissection (81, 82). Other authors used indocyanine green during robotic-assisted surgery for deep endometriosis to examine the vascularization of the hypogastric nerves and inferior hypogastric plexus, and subsequently their viability (83). To date, there are no studies comparing the operative and postoperative outcomes of robotic-assisted surgery compared to laparoscopy in terms of operative time, blood loss, short-and long-term postoperative neurologic symptoms.

8 Discussion

The available literature indicates the feasibility and safety of robotic-assisted surgery in treating deep endometriosis. However, drawing definitive conclusions regarding its superiority or non-inferiority for patients with advanced endometriosis is challenging due to several factors. These include the limited number of studies, their heterogeneity, and the predominance of retrospective designs. Additionally, comprehensive investigations into crucial long-term outcomes such as sustained pain relief, variations in quality of life, and fertility outcomes have been infrequent or inadequately conducted.

Nowadays, minimally invasive approaches are considered the gold standard for the surgical treatment of deep endometriosis and in this setting the robotic-assisted surgery may provide the technology to overcome some of the limitations of laparoscopy allowing a more ergonomic position, three dimensional vision and freedom of wrist movement (40). Some surgeons use robotic-assisted surgery in deep endometriosis claiming an advantage in complex pelvic pathology, obese patients and prior surgical history. However, such studies may be subject to selection bias (23, 29). Several studies demonstrated that the two main limitations to the spread of robotic-assisted surgery are longer operative time and higher costs (23). The increased total operative time is related partially to the phase of docking and intuitively to the specific learning curve of robotic-assisted surgery (84). Moreover, some authors underlined the need for changing the table position and hybrid conventional/robot-assisted laparoscopy in advanced procedures in consideration of the arm maneuverability in the extrapelvic surgical field and absence of interchangeability of the camera between ports (29, 41). Finally, robotic-assisted surgery lacks the tactile feedback and seemed to correlate with longer operative time, making the tissue dissection more difficult and the identification of the lesions limited (85). It should be noted that DaVinci (Intuitive Surgical, United States) has been the main surgical robot used by different surgical specialties worldwide. More recently, the Hugo™ RAS system (Medtronic, Minneapolis, United States) was introduced and implicated in the management of deep endometriosis (86). The initial experience with this new system indicated its safety in terms of perioperative complications and efficiency in terms of postoperative symptom relief (87, 88). However, the median docking time in one series could be considered long in comparison with the docking time required for DaVinci (87). This could be attributed to the learning curve, since this system is still new and the surgeons may not be very experienced, or due to the multiple bedside arms that should be brought to the operation theater and ducked.

Robotics surgery lead to substantial additional costs compared to laparoscopy, not only for the operative time but also the need of staff training, licenses and maintenance (89). However, recently a trend in cost reduction was registered due to shorter hospital stay, operative time and better resources' administration compared to initial experiences (90). These findings may suggest avoiding the overestimation of the costs drawback of robotic-assisted surgery and to run studies of suitable design investigating the economic impact in well trained and dedicated team.

One of the major complications of deep endometriosis treatment is the postoperative onset of sexual, rectal and voiding dysfunction that may affected more than 50% of the women (29, 91). Different expert groups described standardized approaches of nerve sparing with a systematic identification of the hypogastric nerves, pelvic splanchnic nerves and pelvic plexus in order to reduce denervation (18, 92, 93). Nonetheless, the preservation of the pelvic autonomic nerves requires not only excellent knowledge of pelvic anatomy, but also great laparoscopic technical skills (92). In this setting, all the latest technical development brought by robotic-assisted surgery may be considered especially helpful to increase the precision of the dissection and to improve autonomic nerve identification and preservation, providing better functional outcomes as demonstrated in the nerve-sparing robotic-assisted prostatectomy (94).

9 Conclusion

In conclusion, the quality of the available studies on robotic-assisted surgery in deep endometriosis is low despite the encouraging findings on peri-operative outcomes. On the other hand, long-term results about pain relief and pregnancy rates are lacking. We strongly believe that future well-designed studies are required to address these topics and to deeply understand possible advantages of robot-assisted surgery in deep endometriosis. Actually, a prospective randomized controlled single-center trial is ongoing (ROBEndo trial) aiming to evaluate the impact of robotic-assisted surgery for severe deep endometriosis at 6, 12 and 24 months postoperatively and we hope it will help to clarify the role robotic approach.

Author contributions

FAF: Conceptualization, Writing – original draft. YY: Resources, Writing – review & editing. AN: Resources, Writing – original draft, Writing – review & editing. FF: Writing – review & editing. FO: Writing – review & editing. HK: Supervision, Writing – review & editing. GM: Conceptualization, Methodology, Supervision, Writing – review & editing.

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Conflict of interest

GM works with the speakers Bureau at Intuitive Surgical.

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

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Case report: Ureteric bud intestinal-type adenocarcinoma involving the cervix was misdiagnosed as a large cervical fibroid

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Background: Malignant tumors of the ureteric bud are not common, and cervical involvement is even rarer. So far, there have been no such cases in the literature.

Case summary: A 50-year-old woman developed intermittent light bleeding in the past 7 months and lower abdominal pain in the past 2 months. The human papillomavirus 16 (HPV) DNA, P16 chemical staining, thinPrep cytology test (TCT), and cervical and cervical canal tissue biopsy were all negative. Pelvic color Doppler ultrasound exhibited incomplete mediastinal uterus and heterogeneous echo from the cervical canal to the posterior wall of the cervix. Pelvic contrast-enhanced CT showed left cervical mass, left retroperitoneal mass, absence of the left kidney, and mediastinal uterus. An increase in human epididymal protein 4 (HE4) (133.6 pmol/L) was detected, while other tumor markers were at normal levels. Based on these examination results, a diagnosis of "cervical fibroids, left retroperitoneal mass, incomplete mediastinal uterus, left kidney deficiency"[SIC] was conducted, and expanded hysterectomy, right adnexectomy, and left retroperitoneal mass resection were performed. Through intraoperative rapid pathological diagnosis, postoperative pathological diagnosis combined with the re-evaluation of laboratory, and imaging and intraoperative examination results, the patient was diagnosed with ureteric bud intestinal-type adenocarcinoma involving the cervix. The patient has been tracked and followed up for approximately 11 months. She underwent six courses of chemotherapy. At present, the medication has been discontinued for 4 months, and there is no recurrence, metastasis, or deterioration of the tumor.

Conclusion: For large masses of the cervix, it is feasible for the operation to be performed, improving the prognosis. There were a few limitations. A preoperative aspiration biopsy of masses was not performed to differentiate benign from malignant. Preoperative urography was not performed to clarify the function of the malformed urinary system structure. Partial cystectomy should be performed simultaneously with the resection of the ureteric bud for intestinal-type adenocarcinoma. In this case, a partial cystectomy was not performed, which can only be compensated with postoperative chemotherapy. Moreover, this patient did not undergo genetic screening, and it is currently

unclear whether there are any genetic mutations associated with ureteric bud intestinal adenocarcinoma.

KEYWORDS

ureteric bud intestinal-type adenocarcinoma, cervical metastatic intestinal-type adenocarcinoma, large cervical fibroid, metastatic malignancy, surgical treatment

1 Introduction

Ureteric bud refers to the structure that protrudes from the mesonephric duct during the development of the kidney. The ureteric bud gradually evolves into the ureter, renal pelvis, renal calyx, collecting duct, and kidney through extension and repeated branching. Therefore, underdeveloped ureteric buds can lead to the abnormal development of the urinary system (1, 2). Due to the absence of obvious symptoms, it is usually discovered incidentally (3). Under long-term inflammatory stimulation and a hypoxic environment, the ureteric bud may undergo malignant transformation and involve the cervix (4). In this case, a 50-year-old woman sought medical attention because of irregular vaginal bleeding and lower abdominal pain. The examination revealed a large lump in the cervix, which was negative for cervical virology, cytology, and histopathology. She was initially diagnosed with cervical fibroids. After laboratory, imaging, intraoperative findings, and pathological reassessment, a definitive diagnosis of ureteric bud intestinal-type adenocarcinoma involving the cervix was determined (Figure 1).

2 Case presentation

A 50-year-old woman experienced intermittent irregular vaginal bleeding for 7 months and developed lower abdominal pain in the past 2 months. The patient had no history of pregnancy or childbirth, family genetic history, or adverse environmental exposure, and no bad habits such as smoking and drinking. Human papillomavirus 16 (HPV) DNA testing and p16 immunostaining were both negative. The ThinPrep cytology test (TCT) showed atypical hyperplasia of the glandular epithelium. Pathological examination of cervical and cervical canal scraping tissues suggested chronic cervicitis with squamous epithelial hyperplasia. Pelvic ultrasound indicated an incomplete mediastinal uterus and heterogeneous echo from the cervical canal to the posterior wall of the cervix, with a size of approximately 7.0×5.6×5.2 cm. The cervical serosal layer protrudes outward with irregular morphology and clear boundaries. Blood flow signals were observed inside and around the cervix (Figure 2). Pelvic contrast-enhanced CT showed that the mediastinum was seen in the uterus up to the top of the cervical os, and double uterine cavity changes were observed. A mixed-density mass was seen on the left side of the cervix with cystic low-density shadows and visible septa inside. The maximum cross-sectional size was approximately 7.7×7.8 cm, and cord-like high-density shadows were around it. The left kidney was absent. A solid cystic mass was visible on the left side of the retroperitoneum at the same level as the lower pole of the right kidney, extending downward to the left side of the cervix. The maximum cross-sectional size was approximately 3.4×2.4 cm, and the length was approximately 15 cm. The boundary with the cervix was not clear (Figure 3). A lump of approximately 7.0×6.0×5.0 cm, tender and inactivity, was palpated on the left side of the cervix during the gynecological examination. Tumor marker tests showed human epididymis protein 4 (HE4) at 133.6 pmol/L, with alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate protein 199 (CA199), carbohydrate protein 125 (CA125), human chorionic gonadotropin (HCG), carbohydrate antigen 153 (CA153), carbohydrate antigen 724 (CA724), risk of ovarian malignancy algorithm (Roman) index (premenopausal and postmenopausal), and squamous cell carcinoma (SCC) antigen all within the normal range. Preoperative diagnosis: (1) cervical fibroids; (2) left retroperitoneal mass; (3) incomplete mediastinal uterus; and (4) left kidney deficiency. Due to the increase in protein marker HE4, preoperative preparation was performed for malignant tumor surgery with adequate intestinal tract preparation. After full communication with the patient and family, we planned to perform a total hysterectomy and explore the retroperitoneal mass location.

During the operation, it was observed that the cervix was significantly enlarged to the low left, and a mass of approximately 7.0×6.0×5.0 cm protruded from the left wall of the cervix with a relatively clear boundary with surrounding tissues. It had a spherical

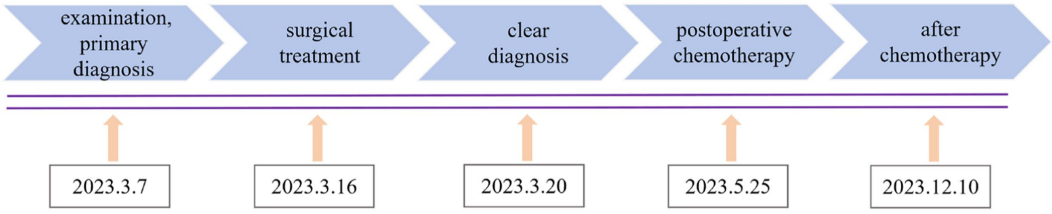

FIGURE 1
Timeline of historical and current episode of care.

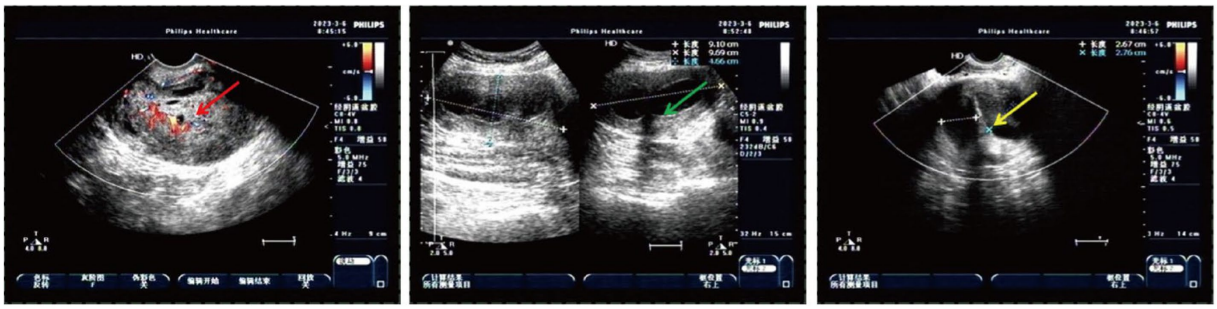

FIGURE 2
Heterogeneous echo on the left cervical wall and incomplete mediastinal uterus shown by pelvic ultrasound (The red arrow: heterogeneous echo on the left wall of the cervix detected with transvaginal ultrasound; the green arrow: heterogeneous echo on the left wall of the cervix detected with transabdominal ultrasound; and the yellow arrow: incomplete mediastinal uterus).

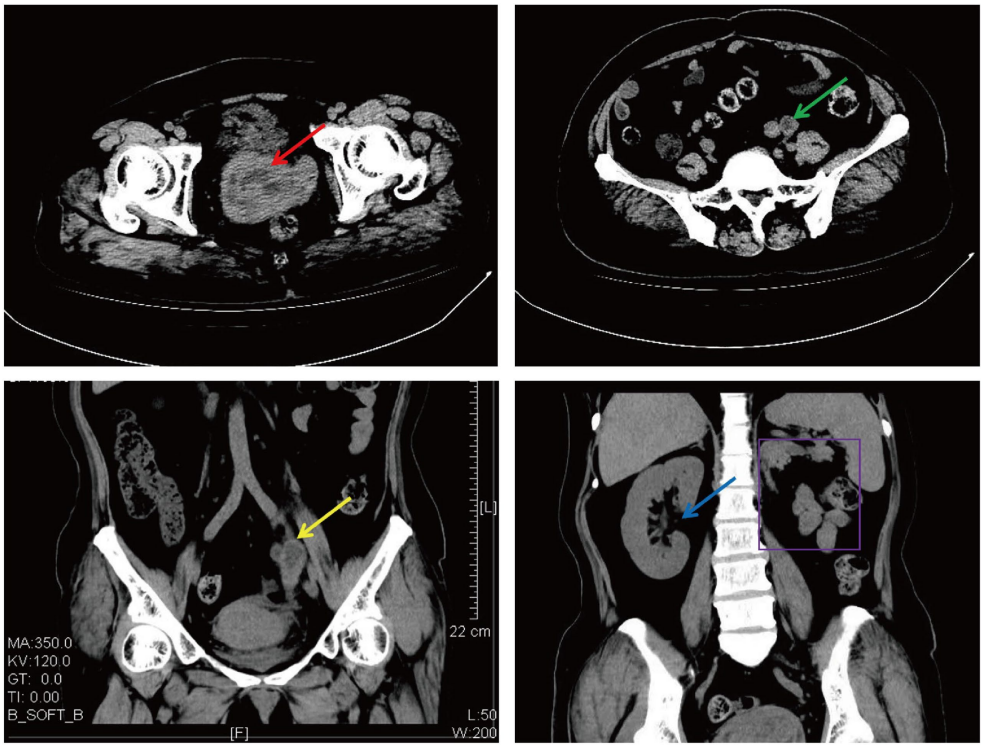

FIGURE 3
Cervical and left retroperitoneal mass shown on CT (The red arrow: a cervical mass; the green arrow: a horizontal left retroperitoneal mass; the yellow arrow: a coronal left retroperitoneal mass; the blue arrow: a coronal right kidney; and the purple border: a coronal left kidney absence).

shape, was isolated, and did not invade the rectum or bladder. The uterus, right ovary, and the complete large mass on the cervix were removed. The depth of the mass exceeded the external cervical os by 2 cm. The *ex vivo* specimen was cut open, and the tumor appeared to resemble smooth muscle tissue, with tough texture and multiple necrotic lesions. There was no tumor infiltration in the cervical canal. The results of rapid frozen pathology indicated a malignant cervical tumor. Intraoperative exploration revealed the other mass in the left retroperitoneum, approximately 15.0×3.0×2.0 cm in size, irregularly cylindrical in shape, with unclear boundaries with the surrounding area, especially closely adherent to the left cervical lesion, with gelatinous tissue on the surface. Intraoperative ultrasound examination showed that the mass lacked a complete renal pelvis structure, presented as a tubular cystic structure, and was interlinked but not connected to the bladder. The bladder was not involved, so a low-lying kidney was excluded. Based on preoperative imaging examination, intraoperative findings, and consultation with experienced urologists, this mass was considered an underdeveloped kidney and ureter, namely the ureteric bud. After explaining the situation to the patient's family, an informed consent form was signed to perform an expanded hysterectomy, right adnexectomy, and retroperitoneal mass resection. The retroperitoneal mass specimen was cut open and showed a nodular shape with irregular wall thickness, a closed cavity filled with pus, necrotic tissue, and gel-like liquid.

The postoperative pathological diagnosis suggested cervical adenocarcinoma with intestinal-type differentiation in the total hysterectomy specimen. The tumor volume was 7.0 × 6.5 × 5.0 cm. The cancer cells were poorly differentiated, and solid cell clusters were often seen. The maximum diameter of the cancer cluster was 0.25 cm, with necrosis in the center, lymphocyte infiltration, and abscess formation around the cancer nest. Cervical serosa showed the diffuse infiltration of cancer cells. No tumor was found in the vasculature or nerves. The pathological results of the retroperitoneal mass showed a muscular tubular structure, with adenocarcinoma presented both inside and outside the tube wall (Figures 4A,B). The immunohistochemical (IHC) results showed that the cervical mass exhibited PAX8 (−), CK7(−), ER(−), PR(−), and P16(−) (Figures 4C–G). Retroperitoneal mass presented PAX8 focal(+), GATA3 focal(+), CDX2(+), CK20(+), CK7(−), and P63(−) (Figures 4H–M).

3 Discussion

Intestinal-type cervical adenocarcinoma usually presents as HPV16 (+). In this case, the HPV test was negative, and both TCT and cervical biopsy were negative, which was one of the factors leading to the misdiagnosis. In addition, this cervical metastatic mass was non-endophytic and non-exophytic on the cervical surface, but a large and isolated lesion occurred on the left wall of the cervix, becoming another factor for the misdiagnosis.

This case presented two cancerous lesions, a mass on the left cervical wall and a retroperitoneal mass. Whether they are primary lesions, secondary lesions, or two non-metastatic cancer lesions is the diagnostic challenge we need to focus on. PAX8 is highly sensitive and specific for diagnosing tumors of Müllerian origin, thyroid, and upper urinary/renal tract (5–7). GATA3 can serve as a biomarker for upper urinary tract tumors (8, 9). CDX2, CK20, and CK7 are of great significance in identifying whether malignant tumors are accompanied by intestinal-type differentiation (10–12). In this case, the IHC indicators of the cervical mass showed PAX8 (−) and CK7(−), indicating that this malignant tumor did not originate from the Müllerian duct. The IHC indicators of retroperitoneal mass, PAX8 and GATA3 expressed focal (+), along with the absence of transitional epithelial cells of the ureteral organ observed under the microscope and the absence of the left kidney and ureter, suggesting that during embryonic development, the ureteric bud may have developed into part of the kidney and ureteral tissue, which could undergo malignant transformation and manifest as PAX8 focal (+). However, most of these structures have not developed into normal ureteral and renal structures, and immunohistochemistry can show PAX8 (−). The entire structure can cause infection and carcinogenesis under long-term inflammation and hypoxia environment (13). Based on the preoperative cervical virus, shed cells, histopathological examination results, imaging, and intraoperative findings, especially immunohistochemical results, it was speculated that the malignant tumor of the ureteral bud was the primary lesion, and the cervical lesion was a secondary lesion. Non-metastatic tumors were excluded, and the immunohistochemical PAX8 (−) results of the cervical mass can be explained. Meanwhile, CDX2 (+), CK20 (+), and CK7 (−) demonstrated that this malignant tumor was accompanied by intestinal-type differentiation, ultimately leading to the diagnosis of ureteric bud intestinal-type adenocarcinoma involving the cervix. Nevertheless, there was not enough evidence to rule out the possibility that the cervix was the primary lesion and metastasized to the ureteric bud, causing similar adenocarcinoma. Based on imaging and intraoperative findings, the cervix tumor was considered at least stage IIB if it was the primary lesion. However, due to congenital left kidney deficiency, it was impossible to determine whether its function was missing and reach the diagnostic criteria of stage III.

The ureteric bud is a precursor structure that develops into the ureter and kidney (14). In the embryonic stage, due to genetic defects or genetic mutations, abnormal development of the ureteric bud leads to renal and ureteral underdevelopment, usually accompanied by ipsilateral renal hypoplasia or renal absence, ipsilateral bladder trigone underdevelopment, with residual ureteral blind segments of varying lengths, small or absent ureteral openings, or ureteral atresia, which is replaced by fibrous bands (15–17). Usually, those with congenital abnormalities of Müllerian duct development are often accompanied by abnormalities of the urogenital system (18, 19). In this case, the patient had an incomplete mediastinal uterus, accompanied by the absence of the left kidney. During the surgery, a tubular structure containing gel-like pus was seen below the same level as the right kidney. The location and shape were consistent with the imaging findings. This tubular object was considered to be an underdeveloped ureter, namely the ureteric bud. Its normal smooth muscle structure might be damaged by tumor tissue or infection, leading to tissue necrosis, or carcinogenesis accompanied by intestinal-type differentiation. This condition might affect adjacent organs when in a closed cystic cavity for a long time.

According to the international conventional standards for the diagnosis and treatment of cervical cancer, the size, location, and depth of the mass have exceeded the surgical scope, so radiotherapy and chemotherapy should be carried out directly. In this case, surgical treatment was prepared due to preoperative misdiagnosis as cervical fibroids, and the isolated cancer lesion with clear boundaries with surrounding tissues made it possible to completely remove the lesion through surgical resection. The patient has been tracked and followed up for approximately 11 months. After surgery, in an external hospital, the whole-body PET scan showed no mass lesions in other parts of the body, and routine chemotherapy was performed. The patient has completed six courses of chemotherapy (carboplatin AUC 5 plus Paclitaxel 135 mg/m^2, every 21 days). The patient exhibited a high rate of adherence, and the chemotherapy process was uneventful, with no complications or serious adverse reactions. It cannot be ignored that during chemotherapy, the patient received health guidance and psychological support, which was beneficial for their recovery. At present, the medication has been discontinued for 4 months, and there is no recurrence, metastasis, or deterioration of the tumor. The patient is very satisfied with the overall treatment.

4 Conclusion

In summary, for large masses and isolated lesions on the lateral wall of the cervix, it is feasible for the operation to be performed by experienced doctors. The limitations of this study lie in the following points: First, preoperative aspiration biopsy of cervical masses and retroperitoneal masses was not performed to differentiate benign from malignant. Second, for patients with genitourinary malformations, especially those with confirmed mass by imaging and increased HE4

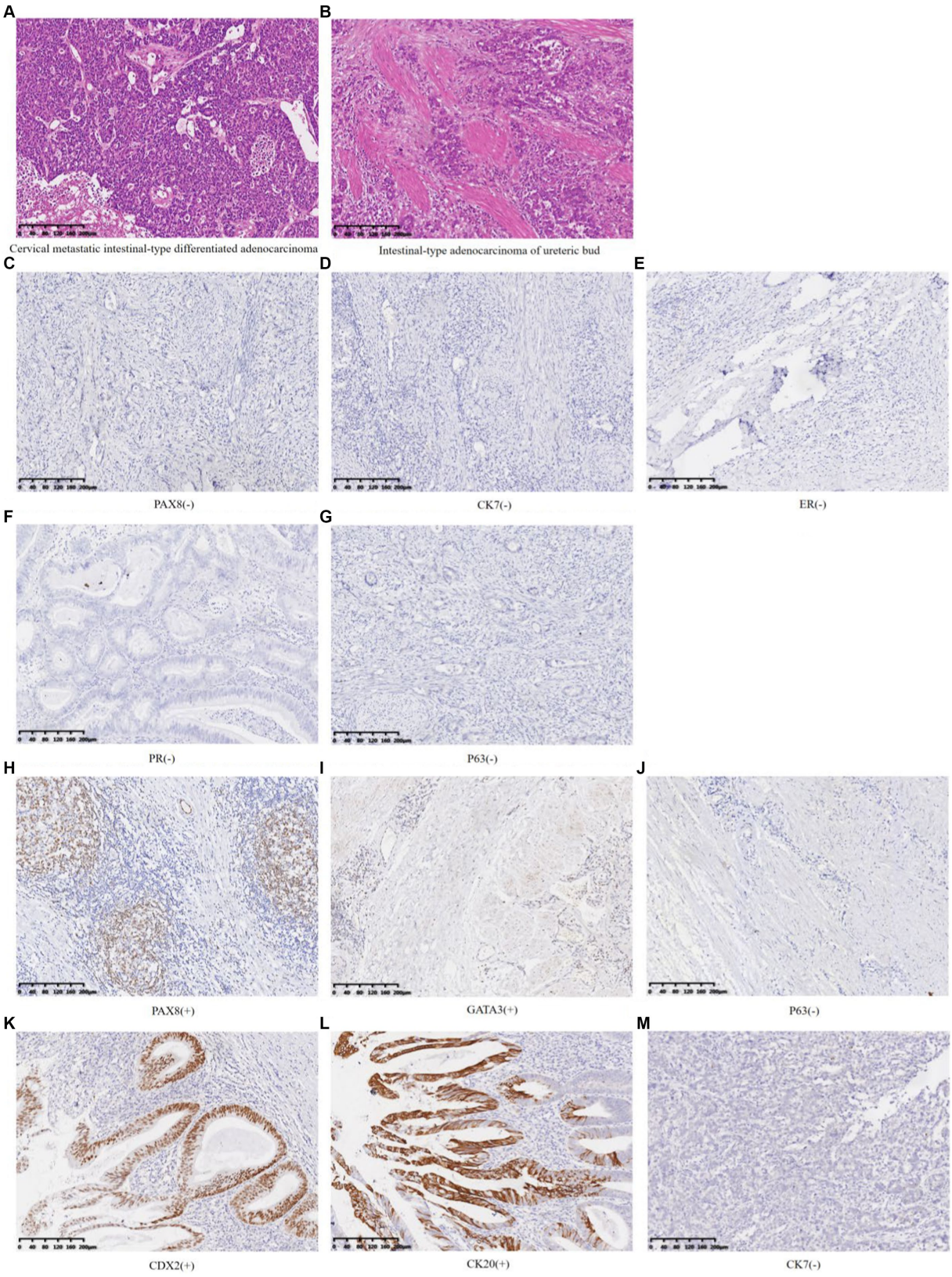

FIGURE 4
HE staining and immunohistochemistry of cervical masses and left retroperitoneal mass **(A)** Cervical metastatic intestinal-type differentiated adenocarcinoma (HE 10×). **(B)** Intestinal-type adenocarcinoma of the ureteric bud (HE 10×). **(C–G)** Cervical metastatic intestinal-type differentiated adenocarcinoma (IHC 10×). **(H–M)** Intestinal-type adenocarcinoma of the ureteric bud (IHC 10×).

levels, preoperative urography was not performed to clarify the function of the malformed urinary system structure. Third, partial cystectomy should be performed simultaneously with the resection of the ureteric bud intestinal-type adenocarcinoma. In this case, a partial cystectomy was not performed, which can only be compensated with postoperative chemotherapy. Finally, this patient did not undergo genetic screening, and it is currently unclear whether there are any genetic mutations associated with ureteric bud intestinal adenocarcinoma.

Data availability statement

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

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

L-lZ: Writing – original draft. LW: Writing – original draft. D-nZ: Writing – original draft. J-tW: Writing – review & editing. YL: Writing – review & editing. Y-pW: Funding acquisition, Writing – review & editing.

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Conflict of interest

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

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Efficacy and safety analysis of non-radical surgery for early-stage cervical cancer (IA2 ~ IB1): a systematic review and meta-analysis

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Objective: Radical hysterectomy has long been considered as the standard surgical treatment for early-stage cervical cancer (IA2 to IB1 stages), according to the 2009 International Federation of Obstetrics and Gynecology. This study aims to conduct an in-depth evaluation of the effectiveness and safety of non-radical surgery as an alternative treatment for patients with early-stage cervical cancer.

Methods: A systematic search of online databases including PubMed, Embase, and the Cochrane Library was conducted to identify relevant literature on surgical treatment options for early-stage cervical cancer. Keywords such as "cervical cancer," "conservative surgery," "early-stage," "less radical surgery," and "simple hysterectomy" were used. Meta-analysis was performed using Stata 15.0 software, which included randomized controlled trials (RCTs) and cohort studies.

Results: This meta-analysis included 8 eligible articles covering 9 studies, with 3,950 patients in the simple hysterectomy (SH) surgery group and 6,271 patients in the radical hysterectomy (RH) surgery group. The results indicate that there was no significant difference between the two groups in terms of the Overall Survival (OS) (HR = 1.04, 95% CI: 0.86–1.27, $p = 0.671$; Heterogeneity: $I^2 = 33.8\%$, $p = 0.170$), Disease Free Survival (DFS) (HR = 1.39, 95% CI: 0.59–3.29, $p = 0.456$; Heterogeneity: $I^2 = 0.0\%$, $p = 0.374$), Cervical Cancer Specific Survival (CCSS) (HR = 1.11, 95% CI: 0.80–1.54, $p = 0.519$; Heterogeneity: $I^2 = 11.9\%$, $p = 0.287$) and recurrence rate (RR = 1.16, 95% CI: 0.69–1.97, $p = 0.583$; Heterogeneity: $I = 0.0\%$, $p = 0.488$). However, the mortality rate (RR = 1.35, 95% CI: 1.10–1.67, $p = 0.006$; Heterogeneity: $I^2 = 35.4\%$, $p = 0.158$) and the rate of postoperative adjuvant therapy (RR = 1.59, 95% CI: 1.16–2.19, $p = 0.004$; Heterogeneity: $I^2 = 92.7\%$, $p < 0.10$) were higher in the SH group compared to those in the RH group. On the other hand, the incidence of surgical complications was lower in the SH group (RR = 0.36, 95% CI: 0.21–0.59, $p = 0.004$; Heterogeneity: $I^2 = 0.0\%$, $p = 0.857$) than that in the RH group. Subgroup analysis revealed that patients in the IB1 stage SH group had a significantly higher mortality rate compared to those in the RH group (RR = 1.59, 95% CI: 1.23–2.07, $p < 0.001$; Heterogeneity: $I^2 = 0.0\%$, $p = 0.332$). However, there was no significant difference in mortality rates between the two groups for patients at stage IA2 (RR = 0.84, 95% CI:

0.54–1.30, $p = 0.428$; Heterogeneity: $I^2 = 26.8\%$, $p = 0.243$). In the subgroups positive for Lymphovascular Space Invasion (LVSI), patients in the SH group had a significantly higher mortality rate than those in the RH group (RR = 1.34, 95% CI: 1.09–1.65, $p = 0.005$; Heterogeneity: $I^2 = 41.6\%$, $p = 0.128$). However, in the LVSI-negative subgroups, there was no significant difference in mortality rates between the two groups (RR = 0.33, 95% CI: 0.01–8.04, $p = 0.499$).

Conclusion: For patients with early-stage cervical cancer patients at IA2 without LVSI involvement, comparisons between the two groups in terms of OS, DFS, CCSS, recurrence rate, and mortality rates revealed no statistically significant differences, indicating that the choice of surgical approach does not affect long-term survival outcomes for this specific patient group. For patients at IB1 and IA2 stages with LVSI involvement, while there were no significant differences between the two groups in OS, DFS, CSS, and recurrence rate, a significant increase in mortality rates was observed in the SH group. This indicates a potential elevated risk of mortality associated with SH in this subset of patients. Notably, the incidence of surgical complications was significantly lower in the SH group compared to the RH group, highlighting the safety profile of SH in this context. Significantly, among patients in the SH group, an increase in the rate of postoperative adjuvant treatment is associated with a higher occurrence of treatment-related complications. To facilitate more precise patient selection for conservative surgical management, future prospective studies of superior quality are imperative to gain deeper insights into this matter.

Systematic review registration: PROSPERO (CRD42023451609: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023451609).

KEYWORDS

early stage, cervical cancer, conservative surgery, less radical surgery, simple hysterectomy

1 Introduction

Presently, cervical cancer stands as a prevalent malignancy within the female reproductive tract, securing its position as the fourth most threatening cancer to women's health, following breast, colorectal, and lung cancers. It has become a significant global public health issue. In 2020, there were 604,000 new cases of cervical cancer worldwide, with an incidence rate of 15.6 per 100,000 people, and 342,000 deaths, resulting in a mortality rate of 8.8 per 100,000 people (1). Fortunately, thanks to the widespread availability of screening technologies, an increasing number of cervical cancer cases are being diagnosed at an early stage.

For patients with cervical cancer at International Federation of Gynecology and Obstetrics (FIGO) stages IA2 to IB1, Radical Hysterectomy (RH) combined with pelvic lymphadenectomy is considered the fundamental approach for early-stage cervical cancer treatment (2). However, the traditional RH procedure involves the removal of the uterine main ligaments, sacrouterine ligaments, and parametrial tissue, a process that may inflict damage on the pelvic autonomic nervous system, leading to disruption of the pelvic floor support structure's anatomy (3, 4). These factors increase the risk of perioperative complications such as bleeding, damage to the ureter and bladder, and postoperative complications like fistulas, urinary retention or incontinence, and sexual dysfunction (5). Although past National Comprehensive Cancer Network (NCCN) guidelines have recommended radical hysterectomy for patients with IA2 and IB1 stage cervical cancer, there is currently no RCT evidence to prove that this standard surgical procedure, which has a history of over 120 years, has better oncological outcomes compared to non-radical surgeries (6).

To further investigate the feasibility of employing non-radical surgical approaches for patients with early-stage cervical cancer, this study utilizes a meta-analysis method to synthesize findings from relevant clinical research. We compared the effectiveness and safety of SH versus RH in the treatment of early-stage cervical cancer, aiming to assess the relative merits of these two surgical techniques.

2 Methods

The meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (7).

2.1 Data selection

2.1.1 Research types

Randomized controlled trials (RCTs), observational studies, cohort studies, etc.

2.1.2 Research subjects

The study encompassed women diagnosed with early-stage cervical cancer, specifically stages IA2 to IB1. Research articles that merged data from IA2 and IB1 stages with additional stages (including IA1 LVSI, IB2, and IIA) were incorporated into the table and appropriately annotated. The analysis covered histological variants like adenocarcinoma, squamous cell carcinoma, and adenosquamous carcinoma.

2.1.3 Intervention measures

The control group was treated with a RH ± Pelvic lymphadenectomy, while the experimental group received SH treatment ± Pelvic lymphadenectomy.

2.2 Outcome measures

Primary outcome measure: Overall Survival (OS) refers to the duration from the moment of randomization to death from any cause. Secondary Outcome Measures include: 1. Disease-Free Survival (DFS): Calculated from the initiation of treatment, it represents the period throughout which a patient remains free from any recurrence or progression of cervical cancer. 2. Cervical Cancer-Specific Survival (CCSS): CCSS measures the time from treatment initiation to death specifically caused by cervical cancer. 3. Mortality Rate: This encompasses the proportion of patients who pass away due to any cause following cervical cancer treatment, during the follow-up period. 4. Recurrence Rate: Referring to the proportion of cervical cancer patients experiencing disease reappearance after treatment during the follow-up period, recurrence is strictly defined as an invasive event, excluding any *in situ* developments. 5. Postoperative Adjuvant Therapy Rate: This measure indicates the proportion of patients that receive additional adjuvant treatment (e.g., chemotherapy, radiotherapy, or hormone therapy) subsequent to surgical intervention. 6. Incidence of Surgical Complications: This quantifies the frequency at which patients encounter complications during and after surgery.

2.3 Literature screening and data extraction

A thorough systematic literature search was conducted to identify relevant studies investigating the outcomes of SH in women with early-stage cervical cancer (IA2 to IB1). A comprehensive search strategy employing keywords including "early-stage cervical cancer," "simple hysterectomy," and "radical hysterectomy" was implemented across multiple databases such as Embase, PubMed, Cochrane Library, and other relevant sources. In addition, a manual screening of references was performed to ensure maximum coverage of the available literature. Studies meeting the following exclusion criteria were excluded from the analysis: (1) duplicate publications; (2) studies lacking essential data for the present research; (3) studies published in languages other than English; (4) overview articles, case reports, conference papers, and similar sources; (5) studies focusing on histological types other than those specified, such as clear cells, serous, and neuroendocrine; (6) studies reporting new trials of adjuvant therapies, including chemotherapy (CT) or radiotherapy; and (7) studies solely examining IA1 or lower or IB2 or higher stages, unless these results were combined with IA2 to IB1 cases. Data extraction from each included study was performed using standardized tables, capturing relevant information such as the first author, publication year, study design, study population, intervention measures, outcome indicators, and more. Notably, our research has been prospectively registered with the PROSPERO database (registration number: CRD42023451609), ensuring transparency and accountability in the research process.

2.4 Literature quality evaluation

To evaluate the quality of the retrospective survey, a 9-star Newcastle Ottawa Scale (NOS) was used, with the lowest 6 stars being considered as high quality (8). The RCTs included in the study referred to the Cochrane Collaboration Network's setting of the bias risk assessment entry (9), and the bias risk of each study was independently evaluated: A random number table, computer randomization, coin tossing, poker or envelope washing, drawing lots, and rolling dice with a score of 1 point were used. Additionally, the blind method was used to give 1 point, 1 point was for not losing outcome data, and propensity analysis was used, 1 point was for reporting non-selective outcomes, The study showed no other sources of bias, giving a score of 1, The total score was calculated based on each score. Finally, calculate the total score for each study based on these criteria.

2.5 Statistical analysis methods

The meta-analyses were conducted using Stata 15.0 software. Initially, the heterogeneity among included studies was assessed using the Chi-square test (test level $\alpha = 0.10$). If no statistical heterogeneity was detected among the studies ($p > 0.05$, $I^2 < 50\%$), a fixed-effect model was employed for analysis; conversely, if statistical heterogeneity was present ($p < 0.10$, $I^2 > 50\%$), a random-effects model was utilized, with subgroup analyses and sensitivity analyses conducted to explore the sources of heterogeneity. Hazard Ratios (HR) and 95% Confidence Intervals (CI) were employed to evaluate OS, DFS, and CCSS, while Relative Risks (RR) and 95% CI were utilized to assess mortality rates, recurrence rates, rates of postoperative adjuvant therapy, and incidence of surgical complications. Publication bias was evaluated through Egger's test, Begg's test, and funnel plots with Stata 15.0. Subgroup analyses, for instance, based on study type, disease staging, sample size, and other factors, were planned within the meta-analysis for detailed examination and comparison. Furthermore, sensitivity analyses were conducted to assess the impact of the quality of included studies on the overall findings. Results from the meta-analysis, including effect sizes and confidence intervals, were graphically represented using forest plots and other methods as necessary. Additional statistical techniques were applied as needed to interpret and analyze heterogeneity among studies. All findings were presented in tables and graphs, accompanied by concise concluding paragraphs.

3 Results

3.1 Process diagram of literature retrieval

After conducting a comprehensive search across major databases, a total of 864 relevant articles were identified. Following

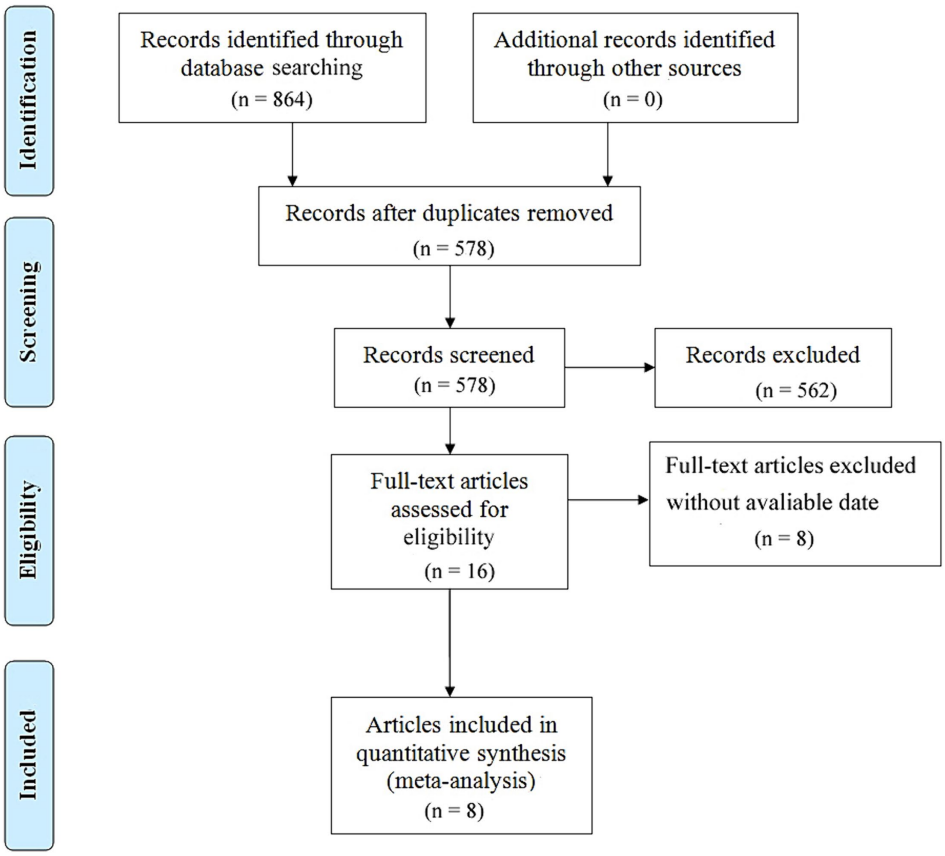

FIGURE 1
Flow chart of the meta-analysis.

the removal of duplicates, 578 articles remained. Subsequently, a detailed review of the titles and abstracts of these articles was carried out based on predefined inclusion and exclusion criteria, resulting in 562 articles being excluded. After a thorough full-text review, 8 articles covering 9 studies were ultimately selected, involving literature numbered (10–17). The specific selection process is illustrated in Figure 1.

3.2 Basic characteristics of collected literature

This study included a total of 10,221 early-stage cervical cancer patients, comprising 3,950 patients who underwent SH (Querleu-Morrow type A and Piver type I hysterectomy) and 6,271 patients who received RH (Querleu-Morrow type B (B1 + B2) and type C (C1 + C2), Piver Type II and type III radical hysterectomy). In these 9 studies, all patients were diagnosed with cervical cancer ranging from stages IA2 to IIA. Among the studies, six explicitly reported using the 2009 version of the FIGO staging system, while the other three did not specify which version of the FIGO staging was used. However, all nine studies provided detailed reports on the maximum diameter of the tumor and information that is crucial for understanding and assessing the clinical relevance of the study findings. The types of studies encompassed 4 RCTs and 4 cohort studies. Of these, 4 studies were conducted in the United States, 3 in China, and 2 in other countries, with sample sizes ranging from 40 to 3,931. Table 1 provides the basic information of the original literature. Table 2 lists the patients' characteristics from the original literature. The pathological types of tumors among the included cervical cancer patients consisted of adenocarcinoma, squamous cell carcinoma, and adenosquamous carcinoma. The vast majority of patients (87.53%) had tumors with a diameter of less than 2 cm, and the tumor diameter in all patients was less than 4 cm. Approximately 14.44% of cases were positive for LVSI. Among all patients who underwent lymph node (LN) assessment, about 5.75% demonstrated positive LN.

3.3 Quality evaluation results of collected literature

In this study, we employed RevMan 5.4 software to assess the risk of bias in RCTs. Among the included four studies, there was a low to moderate risk of bias demonstrated in aspects such as the generation of random sequences, blinding measures implemented for participants and researchers, and the completeness of reported outcomes. Overall, the quality assessment of these RCTs indicates that the studies involved have a moderate risk of bias (Supplementary Figures S1, S2 for details). Furthermore, based on the NOS scores, all five cohort studies included in this meta-analysis were rated as high-quality research (Supplementary Table S1).

TABLE 1 Characteristics of studies included in this meta-analysis.

Study, year	Study design	Country	Duration	Sample size (SH/RH)	Age (SH/RH)	Median follow-up (months)	Stage (year)	Summary statistics
Landoni 2012	RCT	Italy	1981–1986	62/63	55 (34–82)/44 (24–72)	≥280	IB1-IIA (NR)	OS: HR: 0.53 (0.25–1.12) DFS: 70% SH, 86% RH
Wang 2017	RCT	China	2002–2014	70/70	44.04 ± 8.46/43.03 ± 8.59	75	IB1 (2009)	OS: 100% SH, 98.5% RH ($p = 0.32$) RFS: HR 0.49 (0.04–5.37)
Chen 2018	RCT	China	2006–2011	45/56	50 (34–75)/47 (24–72)	≥60	IA2-IB1 (2009)	OS: HR: 0.49 (0.12–2.10)
Tseng 2018	Cohort	USA	1998–2012	807/1764	median: 37	79	IB1 (2009)	DSS: HR: 1.01 (0.69–1.45)
Sia 2019 1	Cohort	USA	2004–2015	683/847	NR	56	IA2 (NR)	OS: HR: 0.68 (0.37–1.25)
Sia 2019 2	Cohort	USA	2004–2015	1388/2543	NR	53	IB1 (NR)	OS: HR: 1.31 (0.97–1.75)
Liu 2021	Cohort	China	2014–2019	182/258	44.5 ± 12.8/44.3 ± 12.3	39/45	IA2 (2009)	OS: HR: 1.122 (0.319–3.493) DFS: HR: 1.608 (0.640–4.041)
Du 2022	Cohort	USA	1998–2015	693/650	NR	97/107	IA2 (2009)	OS: HR: 1.078 (0.764–1.522) CSS: HR: 1.536 (0.782–3.021)
Carneiro 2023	RCT	Brazil	2015–2018	20/20	37 (34–50.5)/37.5 (34–44)	52.1	IA2-IB1 (2009)	OS: HR: 0.48 (0.07–3.35) DFS: 95% SH, 100% RH ($p = 0.30$)

SH, simple hysterectomy; RH, radical hysterectomy; OS, overall survival; DFS, disease-free survival; NR, not reached.

TABLE 2 Patients characteristics of studies included in this meta-analysis.

Study, year	Type of surgery		Tumor size		LVSI(+)	LN(+)	Adjuvant therapy		Recurrences		Deaths		Complications	
	RH	SH	<2 cm	2–4 cm			RH	SH	RH	SH	RH	SH	RH	SH
Landoni 2012	63	62	8	117	52	13	35	43	8	14	12	18	24	8
Wang 2017	70	70	140	0	0	4	2	2	2	1	1	0	10	3
Chen 2018	56	45	101	0	25	0	23	22	10	5	5	3	12	3
Tseng 2018	1764	807	1,414	1,157	NR	444	507	217	NR	NR	NR	NR	NR	NR
Sia 2019 1	847	683	1,530	0	143	17	79	138	NR	NR	38	22	NR	NR
Sia 2019 2	2,543	1,388	3,931	0	615	48	496	578	NR	NR	111	98	NR	NR
Liu 2021	258	182	440	0	67	NR	23	48	6	5	11	10	NR	NR
Du 2022	650	693	1,343	0	NR	34	87	150	NR	NR	NR	NR	NR	NR
Carneiro 2023	20	20	40	0	9	3	4	6	0	1	1	2	5	3
Total	6,271 (61.3%)	3,950 (38.6%)	8,947 (87.5%)	1,274 (12.4%)	911 (14.4%)	563 (5.7%)	1,256 (20%)	1,204 (30.4%)	26 (3%)	26 (3%)	179 (4.6%)	153 (6.2%)	51 (24.4%)	17 (8.6%)

SH, simple hysterectomy; RH, radical hysterectomy; NR, not reached.

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3.4 Meta-analysis results

3.4.1 OS

Data on OS were obtained from a comprehensive analysis of seven studies (12–17). The studies exhibited minimal heterogeneity, indicated by an I^2 value less than 50%, which justifies the adoption of a fixed-effect model. ($I^2 < 50\%$) HR served as the effect measure, and the meta-analysis results revealed no significant difference in OS between the SH group and the RH group. Specifically, there was no statistically significant difference in the risk of death between patients in the SH group and those in the RH group (HR = 1.04, 95% CI: 0.86–1.27, $p = 0.671$; Heterogeneity: $I^2 = 33.8\%$, $p = 0.170$) (Figure 2).

3.4.2 DFS

DFS were obtained from two studies (10, 13). With low heterogeneity observed between these studies ($I^2 < 50\%$), a fixed-effect model was applied. Utilizing HR as the effect measure, the meta-analysis results indicated that there was no statistically significant difference in DFS between patients in the SH group and those in the RH group, suggesting that the risk of disease recurrence or death was similar for both groups (HR = 1.39, 95% CI: 0.59–3.29, $p = 0.456$; Heterogeneity: $I^2 = 0.0\%$, $p = 0.374$) (Figure 3).

3.4.3 CCSS

CCSS were sourced from two studies (11, 15). The heterogeneity among these studies for CCSS was low ($I^2 < 50\%$), leading to the application of a fixed-effect model. Meta-analysis, utilizing HR as the measure of effect, demonstrated that there was no significant difference in CCSS between patients in the SH group and those in the RH group (HR = 1.11, 95% CI: 0.80–1.54, $p = 0.519$; Heterogeneity: $I^2 = 11.9\%$, $p = 0.287$) (Figure 4).

3.4.4 Recurrence rates

Data on recurrence rates were derived from five studies (10, 12–14, 16). With low heterogeneity observed among these studies ($I^2 < 50\%$), a fixed-effect model was employed. The meta-analysis, using RR as the effect measure, found no significant difference in recurrence rates between patients in the SH group and those in the RH group (RR = 1.16, 95% CI: 0.69–1.97, $p = 0.583$; Heterogeneity: $I^2 = 0.0\%$, $p = 0.488$) (Figure 5).

3.4.5 Mortality rates

Data on mortality rates were obtained from seven studies (10–14, 16, 17). With low heterogeneity among these studies ($I^2 < 50\%$), a fixed-effect model was applied. The meta-analysis, utilizing RR as the effect measure, indicated that the mortality rate in the SH group was higher than in the RH group (RR = 1.35, 95% CI: 1.10–1.67, $p = 0.006$; Heterogeneity: $I^2 = 35.4\%$, $p = 0.158$) (Figure 6).

3.4.6 The rate of postoperative adjuvant therapy

Data on the rate of postoperative adjuvant therapy were collected from nine studies (10–17). With high heterogeneity among these studies ($I^2 > 50\%$), a random-effects model was employed. The meta-analysis, using RR as the measure of effect, indicated that the rate of postoperative adjuvant therapy in the SH group was higher than in the RH group (RR = 1.59, 95% CI: 1.16–2.19, $p = 0.004$; Heterogeneity: $I^2 = 92.7\%$, $p < 0.10$) (Figure 7).

3.4.7 The incidence of surgical complication

Data on the incidence of surgical complications were derived from four studies (10, 14, 16, 17). With low heterogeneity observed among these studies ($I^2 < 50\%$), a fixed-effect model was applied. The meta-analysis, utilizing RR as the measure of effect, indicated that the incidence of postoperative complications in the SH group was lower

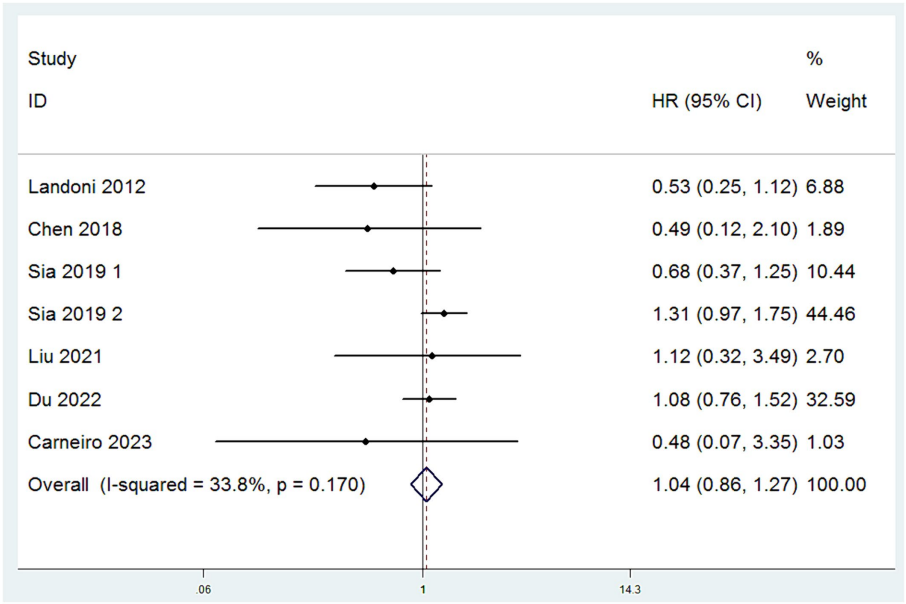

FIGURE 2
Forest plots for overall survival (OS).

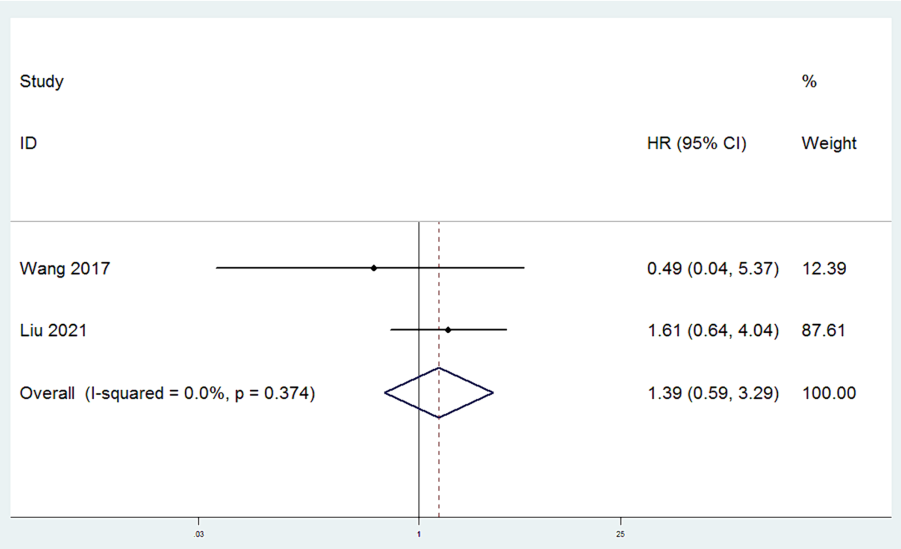

FIGURE 3
Forest plots for disease free survival (DFS).

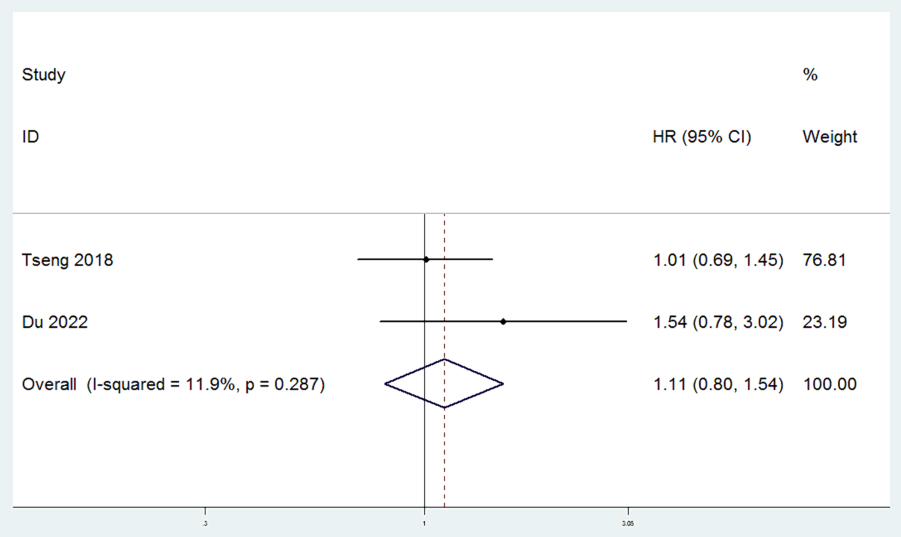

FIGURE 4
Forest plots for Cervical Cancer Specific Survival Rate/Disease Specific Survival Rate (CCSS).

than in the RH group (RR = 0.36, 95% CI: 0.21–0.59, $p < 0.001$; Heterogeneity: $I^2 = 0.0\%$, $p = 0.857$) (Figure 8).

3.5 Subgroup analysis

An extensive analysis of subgroups based on various influencing factors was conducted and the outcomes are summarized in Table 3. The findings revealed a significant disparity in mortality rates between patients with Stage IB1 cervical cancer who underwent SH compared to those who underwent RH, with the former group exhibiting a notably higher mortality rate (RR = 1.59, 95% CI: 1.23–2.07, $p < 0.001$; heterogeneity: $I^2 = 0.0\%$, $p = 0.332$). Conversely, for patients in the Stage IA2 subgroup, there was no statistically significant variance in mortality rates observed between those who underwent SH and RH procedures (RR = 0.84, 95% CI: 0.54–1.30, $p = 0.428$; heterogeneity: $I^2 = 26.8\%$, $p = 0.243$). Subsequently, within the subgroup of patients testing positive for LVSI, individuals who underwent SH exhibited a significantly higher mortality rate compared to their counterparts who had RH (RR = 1.34, 95% CI: 1.09–1.65, $p = 0.005$; heterogeneity: $I^2 = 41.6\%$, $p = 0.128$). However, there was no statistically significant difference in mortality rates between the SH and RH groups among the LVSI negative subgroup (RR = 0.33, 95% CI: 0.01–8.04, $p = 0.499$). In the LN-positive subgroup, there was no statistically significant

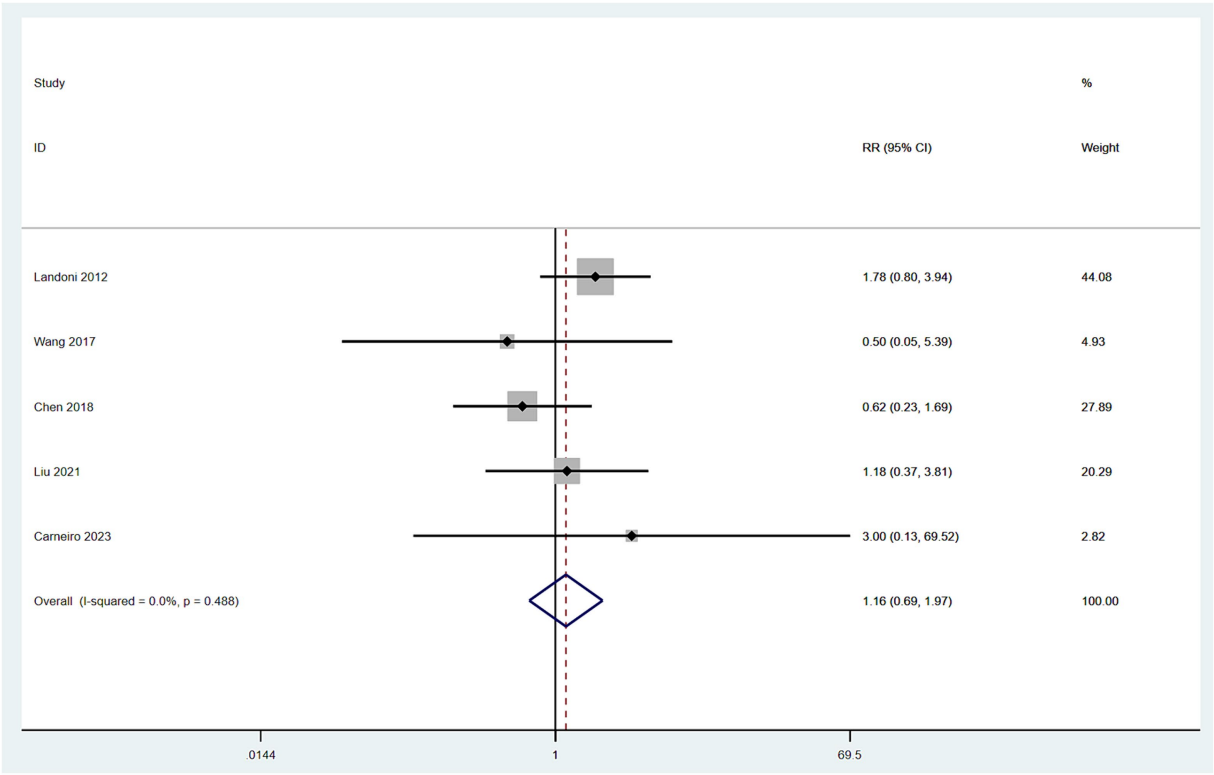

FIGURE 5
Forest plots for recurrence rate.

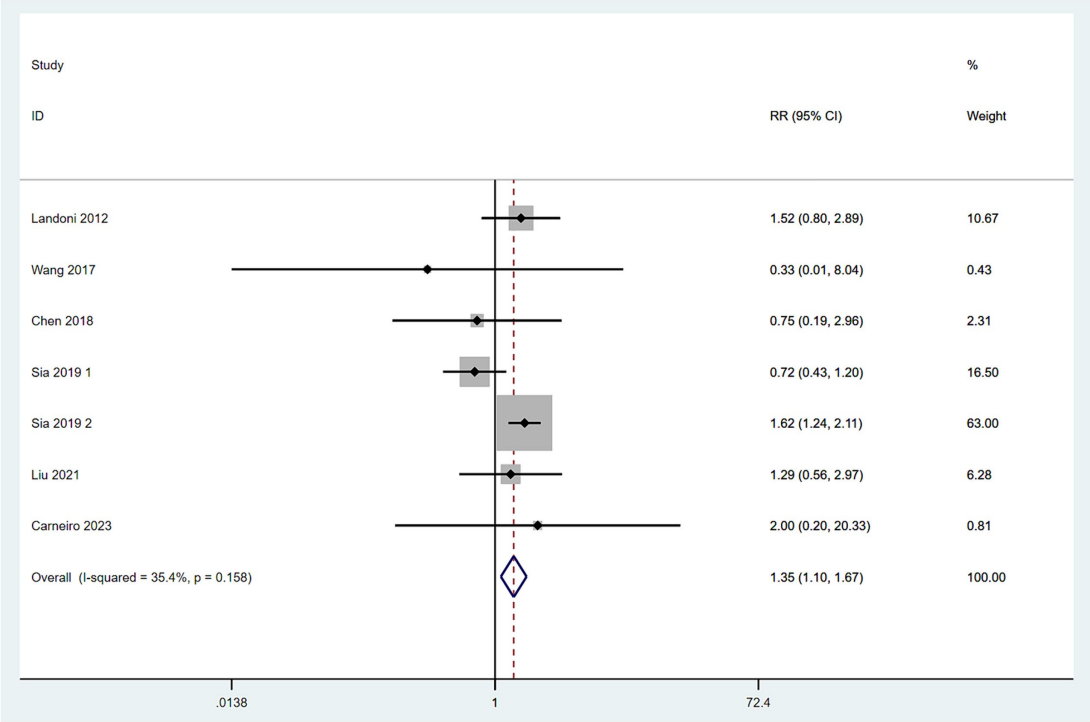

FIGURE 6
Forest plots for mortality rate.

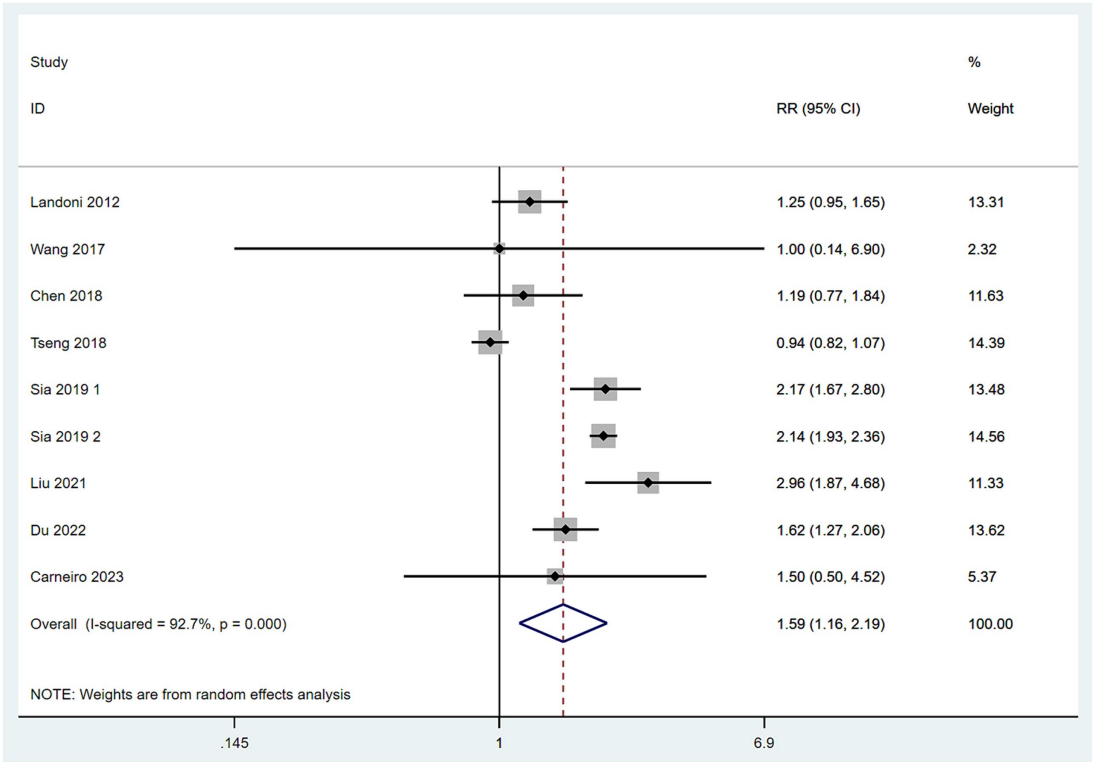

FIGURE 7
Forest plots for postoperative adjuvant therapy rate.

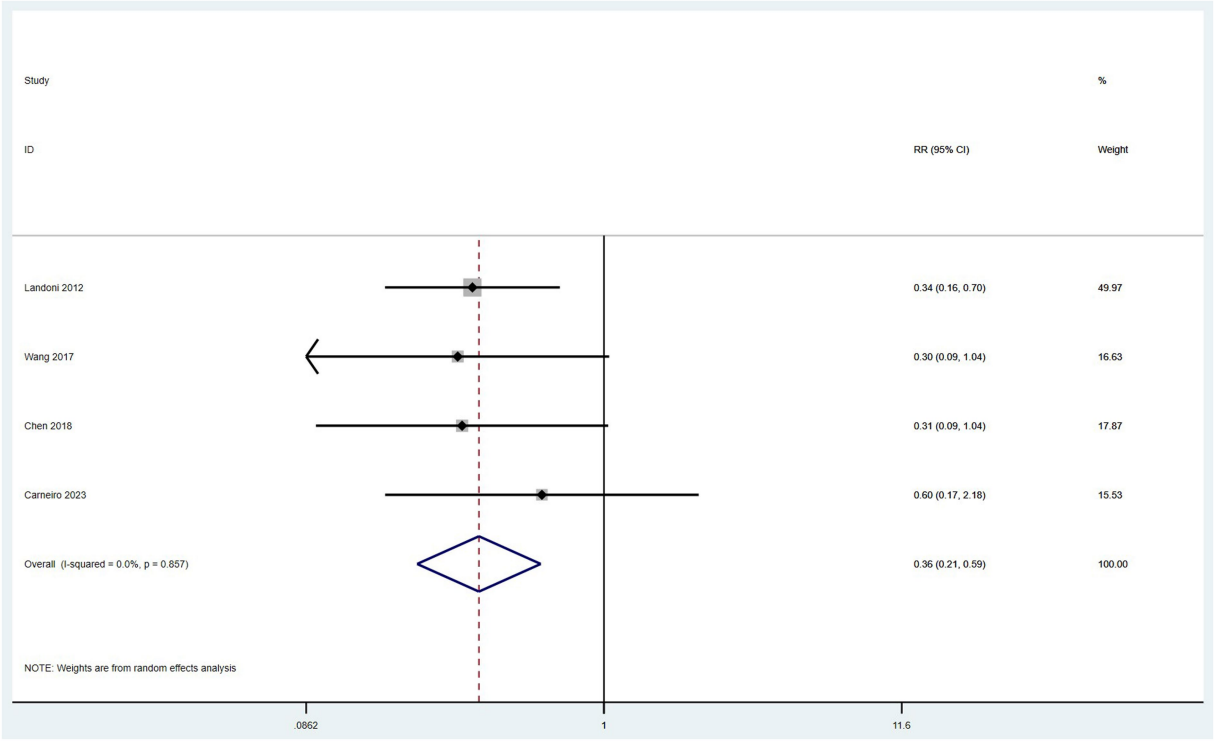

FIGURE 8
Forest plots for surgical complication rate.

TABLE 3 Subgroups analysis for mortality rate.

Subgroup	No. of studies	RR(95%CI)	*p*	I^2 (%)	Ph
Stage					
IA2	2	0.84 (0.54–1.30)	0.428	26.8	0.243
IB1	2	1.59 (1.23–2.07)	<0.001	0	0.332
Study design					
RCTs	4	1.32 (0.76–2.29)	0.332	0	0.635
Cohort	3	1.16 (0.66–2.05)	0.599	73.7	0.022
LVSI					
Positive	6	1.34 (1.09–1.65)	0.005	41.6	0.128
Negative	1	0.33 (0.01–8.04)	0.499	–	–
LN					
Positive	5	1.23 (0.77–1.94)	0.384	53.2	0.073
Negative	1	0.75 (0.19–2.96)	0.677	–	–

difference in mortality rates between the SH and RH groups (RR = 1.23, 95% CI: 0.77–1.94, $p = 0.384$; heterogeneity: $I^2 = 53.2\%$, $p = 0.073$), and this was also true for the LN-negative subgroup (RR = 0.75, 95% CI: 0.19–2.96, $p = 0.677$). Likewise, when stratified by study type, the comparison of mortality rates between the SH and RH groups within RCTs or cohort studies did not yield statistically significant differences. (RR = 1.32, 95% CI: 0.76–2.29, $p = 0.332$; heterogeneity: $I^2 = 0.0\%$, $p = 0.635$) or the cohort study subgroup (RR = 1.16, 95% CI: 0.66–2.05, $p = 0.599$; heterogeneity: $I^2 = 73.7\%$, $p = 0.022$).

3.6 Sensitivity analysis

Sensitivity analysis was conducted by altering the type of effect model or by excluding individual studies from the outcome analysis. In the evaluation of overall survival rates, the systematic removal of individual original studies in a stepwise manner did not elicit substantial alterations in the results, demonstrating consistent findings and minimal fluctuation. This stability suggests that the outcomes obtained from this meta-analysis are resilient and possess a high degree of reliability (Figure 9). In the assessment of heterogeneity, when I^2 exceeds 50%, sensitivity analysis is required. For outcomes with significant heterogeneity, such as the rate of postoperative adjuvant therapy, a sensitivity analysis was conducted by sequentially excluding each included study to assess the stability of the related results. In the investigation concerning the frequency of postoperative adjuvant therapy, the progressive exclusion of individual original studies did not induce substantial changes in the results and exhibited minimal variability, underscoring the robustness and insensitivity of the meta-analysis findings (Supplementary Figure S3).

3.7 Publication bias analysis

To assess publication bias for the reported OS, we created a funnel plot that demonstrated good symmetry (Figure 10). Additionally, we performed Begg and Egger tests. The publication bias for OS, based on the Begg test, was not significant ($p = 0.368$) (Supplementary Figure S4). Similarly, the Egger test yielded comparable results ($p = 0.06$) (Supplementary Figure S5).

4 Discussion

For an extensive period, RH combined with pelvic lymphadenectomy has been the standard surgical approach for patients with cervical cancer at FIGO stages IA2-IB1 (18). Discussions about employing less radical surgical treatments for early-stage cervical cancer patients have been ongoing. Research indicates that in patients who meet specific criteria, less radical surgery can be utilized without compromising survival outcomes, offering a new treatment option for early-stage cervical cancer patients (19, 20).

4.1 Key findings of this study

In this study, 3,950 patients in the SH group and 6,271 patients in the RH group were included to assess the efficacy and safety of SH and RH surgeries in the treatment of early-stage cervical cancer patients. Our findings indicate no significant differences between the SH and RH surgery groups in terms of OS, DFS, CCSS, and recurrence rates. However, the mortality rate and the rate of postoperative adjuvant therapy were higher in the SH group than those in the RH group, while the incidence of surgical complications was lower in the SH group. To our knowledge, this study is the first meta-analysis to compare the treatment efficacy of SH and RH in early-stage cervical cancer patients with the largest sample size involved. A total of seven studies reported the number of patient deaths. In the RH group, out of 3,857 patients, 179 died, indicating a mortality rate of 4.64%. In the SH group, out of 2,450 patients, 153 died, suggesting a mortality rate of 6.24%. In the research conducted by Wu et al. (21), it was found that the mortality rate for patients at stage IA2 was 2.7%, while for those at stage IB1, the rate was 7.3%. This disparity in mortality rates highlights the impact of disease progression on patient outcomes. The overall average mortality rate reported in the study by Wu et al. was 5.5%. Also, Wu et al. (21) presented a systematic review on the treatment of early-stage cervical cancer patients who underwent less radical surgery, pooling data from 21 studies involving 2,662 patients. Among these patients, 36.1% were classified as stage FIGO IA1 and 61.0% as IB1. The mortality rate was 4.5% in the RH group and 5.8% in the SH group. The estimated and reported HR values indicate no significant correlation between mortality rates among IA2 stage patients undergoing radical and less radical surgeries, although the mortality rate for IB1 stage disease might increase, which aligns with the findings of our study. Hence, in this present study, to further understand the significant differences in mortality rates between the two groups, a more detailed approach was adopted, conducting subgroup analyses based on tumor staging, LVSI status, LN status, and the type of the original study. The aim of this analysis was to uncover which factors most critically affected the survival outcomes of patients in the SH group. The results indicated that patients who were treated with SH at the positive LVSI status and those in the early stage of IB1 cervical cancer exhibited significantly higher mortality rates compared to those undergoing RH. A study (22) suggests that the positive status of LVSI in early cervical cancer tissue may significantly increase the

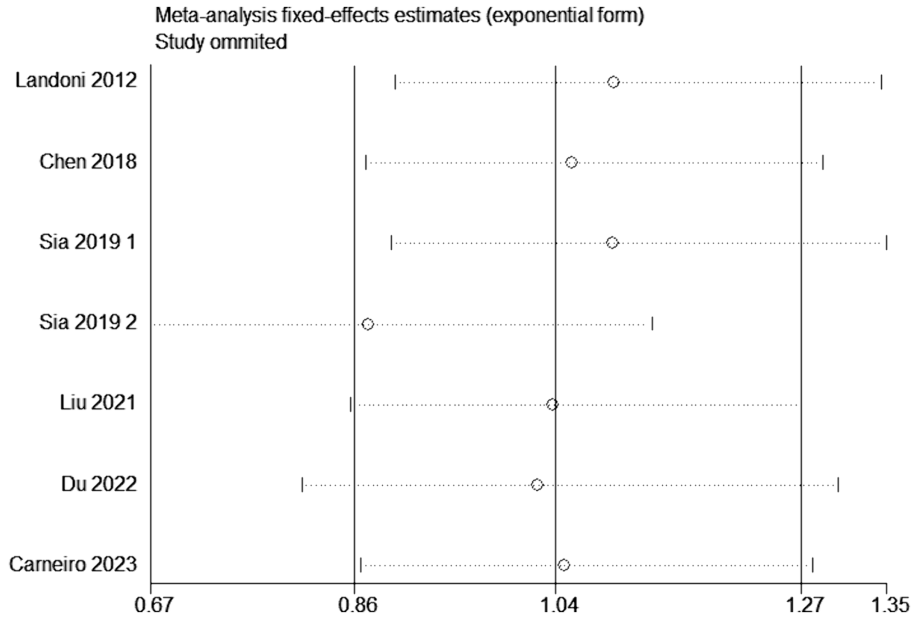

FIGURE 9
Sensitivity analysis for the meta-analysis (OS).

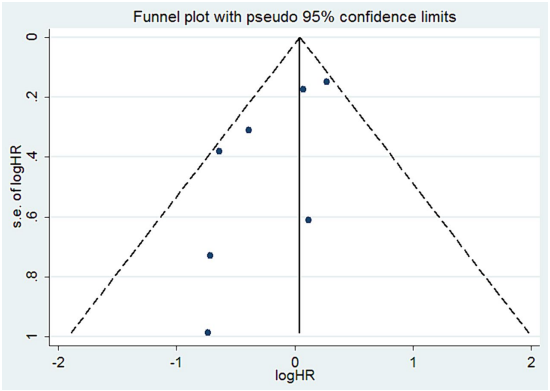

FIGURE 10
Publication bias detected by funnel plots for OS.

risk of LN metastasis, thereby seriously affecting the prognosis of patients. For patients with cervical cancer, the relationship between LVSI and clinical prognosis exhibits a complexity not witnessed in the straightforward correlations seen with parametrial infiltration and LN metastasis. The formation of neoangiogenesis and neolymphangiogenesis crucial for tumor expansion predominantly originates from the cervical stroma. Theoretically, an increase in cervical stromal infiltration depth escalates the chances of intravascular spread of cancer emboli. Therefore, a rise in the depth of tumor infiltration corresponds to an augmented frequency of LVSI. For early cervical cancer patients receiving SH treatment, the meticulous preoperative assessment of LVSI, ideally accomplished through methods such as cervical conization, emerges as a pivotal step. This step significantly enhances the condition evaluation process and treatment efficacy, laying a solid foundation for treatment planning. In our analysis, roughly 30.48% of patients in the SH cohort and 20.02% in the RH cohort required postoperative adjuvant therapy. However, given the nature of our systematic review and meta-analysis, the specific rationales behind the postoperative adjuvant therapy in individual studies remain beyond our scope. Previous studies identifying the primary factors leading to postoperative adjuvant therapy (10–17) cited tumor depth stromal invasion, positive LN metastasis, LVSI, positive margins, grade 3 tumors, and parametrial invasion. Particularly noteworthy was the investigation by Wu et al. (21) revealing a higher utilization rate of adjuvant therapy (comprising radiation or chemotherapy) in the SH group at 30.7% compared to 16.7% in the RH group, a trend closely mirrored in our findings. In managing early-stage cervical cancer, the inclination towards less radical surgical approaches aims to mitigate the associated morbidity linked to aggressive surgical interventions. Notably, four studies documented surgical complications, with incidences of 24.4% (51 out of 209 patients) in the RH group and 8.63% (17 out of 197 patients) in the SH group. Predominant complications encompassed lymphedema, lymphocysts, and the occurrence of urinary incontinence. Importantly, for patients in the SH group, the higher the postoperative adjuvant treatment rate, the higher the incidence of treatment-related complications. Therefore, it is crucial to accurately screen patients who are suitable for SH and avoid them receiving adjuvant therapy after surgery.

4.2 Discussion on the use of SH in minimally invasive or open surgery for early cervical cancer patients

According to a study by Violante Di Donato et al. (23), the ten-year OS rates of early low-risk cervical cancer patients who underwent minimally invasive RH were not significantly different

from those who underwent open RH (98% vs. 96%; $p = 0.995$). However, open RH remains the standard surgical method for cervical cancer patients, and minimally invasive RH should only be performed in clinical trials. In another study by Giacomo Corrado et al. (24), no significant differences were found in recurrence rates, distant metastasis risk, DFS, and OS between minimally invasive and open RH for patients with IB1 to IB2 stage cervical cancer. Nevertheless, the aforementioned studies did not explore the safety of minimally invasive SH for early low-risk cervical cancer patients. The LACC Trial study (25) showed that patients with tumor diameters >2 cm had worse prognoses with minimally invasive surgery, while those <2 cm did not reach statistical significance due to the small sample size. However, based on the number of DFS events, minimally invasive surgery (7/75) still demonstrated a higher occurrence compared to open surgery (0/65). On a related note, Liu et al. (13) examined the impact of minimally invasive surgery on the survival rate of patients with IA2 stage cervical cancer and found no significant change in survival rate. It is important to highlight that this study did not include patients with IB1 stage cancer. In the ConCerv trial (19), 96% of the patients underwent minimally invasive SH surgery, and no recurrences were observed during a 2-year follow-up period. Another trial, the SHAPE trial, demonstrated that neither open nor minimally invasive surgery affected the recurrence risk for early low-risk cervical cancer patients. Overall, for those patients who meet specific criteria, minimally invasive surgery to perform SH appears to be an effective alternative strategy to open surgery. However, this assumption needs to be further verified through more high-quality RCTs.

4.3 How to screen suitable patients for SH

In recent years, a growing body of research has been dedicated to exploring the feasibility of employing less radical surgical methods for managing early-stage cervical cancer patients (26–32). The primary objective of employing SH treatment for early-stage cervical cancer patients is to accurately stratify patients based on the presence or absence of parametrial invasion risk prior to surgical intervention. Patients with favorable pathological features are associated with a notably low incidence of parametrial invasion, eliminating the need for complete removal of the parametrial area (33–35). A significant update in the latest NCCN guidelines (36) pertains to the management of low-risk patients with IA2-IB1 stage cervical cancer following cone biopsy. Specifically, patients meeting stringent criteria including the absence of LVSI, negative surgical margins, histologically confirmed squamous carcinoma or ordinary type adenocarcinoma (limited to G1 or G2), a tumor size not exceeding 2 cm, an invasion depth within 10 mm, and lacking radiographic evidence of metastasis, may be candidates for cervical conization and pelvic LN dissection (or sentinel LN evaluation) if fertility preservation is desired. Otherwise, SH + pelvic LN dissection (or sentinel LN evaluation) is recommended. However, the latest European guidelines (37) diverge from the 2023 NCCN version, recommending SLN biopsy for patients at the IA2 stage contingent upon LVSI status, while endorsing radical hysterectomy for those at IB1 stage. Notably, a study by Landoni et al. (14) shows that patients at stages IB1-IIA (tumor diameter ≤ 3 cm) undergoing Piver type I surgery (extrafascial hysterectomy, bilateral salpingectomy, and upper third vaginal resection), exhibit comparable recurrence and survival outcomes. In summary, our study suggests that for cervical cancer patients at stage IA2 and those with negative LVSI, SH treatment is an effective and safe alternative to RH. However, for patients with positive LVSI and those at stage IB1, SH treatment may adversely impact their mortality risk. Although the quality of certain randomized controlled trials reviewed within this investigation is susceptible to moderate bias, limiting the precision of our conclusions, patients presenting with early-stage cervical cancer appear to demonstrate favorable overall survival rates regardless of the surgical approach adopted, particularly those at the IA2 stage devoid of LVSI, reflecting discrepancies with the 2023 NCCN guidelines but echoing the sentiments of the 2023 European guidelines. Moreover, for early-stage (IA2 to IB1) cervical cancer patients, SH significantly reduces complications associated with surgery compared to RH. Efforts to refine patient selection criteria for less extensive surgical interventions hinge upon forthcoming evidence stemming from high-caliber randomized controlled trials.

4.4 Ongoing research

The most recent findings from the SHAPE trial (38) were presented at the 2023 American Society of Clinical Oncology annual meeting. Over an average follow-up of 4.5 years, the 3-year pelvic recurrence rate for patients undergoing SH was 2.52%, compared to 2.17% for those undergoing RH. This resulted in a marginal variance of 0.35%, aligning with the upper limit of the 95% confidence interval at 2.32%, which fell below the predefined upper limit of 4%. Furthermore, the prevalence of early postoperative surgical complications within a 4-week window stood at 42.6% in the SH group compared to 50.6% in the RH group ($p = 0.04$). Subsequently, the occurrence of delayed postoperative adverse events following the initial 4 weeks recorded figures of 53.6% in the SH group and 60.5% in the RH group ($p = 0.08$). This study indicates that for early low-risk cervical cancer patients, SH is not inferior to RH. The Gynecologic Oncology Group trial 278 is evaluating the impact of non-radical surgery on functional outcomes such as lymphedema, bowel, and sexual functions in patients with stage IA1 with LVSI and IA2 to IB1 stage (tumor diameter ≤ 2 cm). The publication of these high-level evidence clinical study results may provide strong evidence-based medicine support for the use of less radical surgery in treating early low-risk cervical cancer patients.

4.5 Study highlights and limitations

This study represents the latest meta-analysis work in the field concerning this topic. By extensively collecting and synthesizing related literature from multiple databases, this research meticulously selected high-quality RCTs and cohort studies. This is the first time that gold-standard oncological outcomes, such as OS, have been incorporated into a comprehensive evaluation. Furthermore, the study conducted a thorough analysis of key indicators, including DFS, CCSS, mortality rates, recurrence rates, rates of postoperative adjuvant therapy, and rates of surgical complications, leading to more comprehensive and reliable conclusions. In conducting subgroup analyses, this study specifically considered key factors

affecting treatment outcomes, including FIGO stages, types of studies, and LVSI status, and LN status. To ensure the fairness and reliability of the research, publication bias was assessed through funnel plots, Egger's test, and Begg's test for the included literature, showing no significant bias. Additionally, sensitivity analyses confirmed the robustness of the meta-analysis results. Overall, the findings of this study provide important reference for the individualized surgical choices of patients with early-stage cervical cancer and may have significant implications for clinical practice. However, there are some limitations to this study that need to be acknowledged. (1) There is significant variability in the criteria for selecting SH among original studies. It is important to note that this manuscript does not primarily utilize the Querleu-Morrow classification because Simple Hysterectomy, Querleu-Morrow Type A, and Piver type I hysterectomy represent different surgical approaches. Specifically, there is a distinction in definition between Querleu-Morrow type A and Piver type I. These differences somewhat limit the ability to further precisely analyze the study results. (2) There is a scarcity of research on perioperative and long-term complications associated with SH, which is a key driving factor for considering SH as an alternative to RH. (3) Some key findings are derived from large-scale population-based cohort registries, which have a lower level of evidence compared to RCTs. (4) Based on the available primary literature, it is currently not possible to differentiate recurrence rates into categories of pelvic and extra-pelvic recurrences. In conclusion, while this study offers guidance for clinical practice, further research is required to accurately identify patients who meet these treatment criteria. The limitations of this study are expected to be addressed in the ongoing large-scale prospective studies.

5 Conclusion

The meta-analysis conducted in this study elucidates the following key findings: (1) For cervical cancer patients at stage IA2 and those with negative LVSI, no significant differences were found between the SH and RH groups in terms of OS, DFS, CCSS, RR, and mortality, indicating that the type of surgery does not affect the long-term survival outcomes for these patients. (2) For patients at stage IB1 or IA2 with positive LVSI, although no significant differences were observed between the SH and RH groups in OS, DFS, CCSS, and recurrence rate, a notable increase in mortality was observed in the SH group, suggesting that the type of surgery may increase the mortality risk for these patients. (3) In terms of safety, the SH group experienced significantly fewer surgery-related complications compared to the RH group. Significantly, among patients in the SH group, an increase in the rate of postoperative adjuvant treatment is associated with a higher occurrence of treatment-related complications. Therefore, when choosing surgical treatment options for early-stage cervical cancer patients, a comprehensive consideration of the specific characteristics of the case is essential, including the staging of the tumor, LVSI status, the patient's personal preferences, and the expected progression of the disease, among other factors. Through a thorough assessment and careful weighing of the pros and cons, clinicians can furnish patients with an evidence-based and personalized treatment plan. Such an approach not only maximizes treatment efficacy but also reduces surgery-related complications, thereby benefiting early-stage cervical cancer patients to the greatest extent. Future research will be directed towards how to more accurately select patients suitable for less extensive surgery, which will become a key area of study in this field.

Data availability statement

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

Author contributions

SZ: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. SX, YX, PY and CH: Conceptualization, Data curation, Investigation, Writing – review & editing. LL and XJ: Funding acquisition, Supervision, Writing – review & editing.

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Conflict of interest

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

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2024.1337752/full#supplementary-material

FIGURE S1
Risk of bias graph for randomized controlled trials (RCTs).

FIGURE S2
Risk of bias summary for randomized controlled trials (RCTs).

FIGURE S3
Sensitivity analysis for the meta-analysis (Postoperative adjuvant therapy rate).

FIGURE S4
Publication bias detected by Begg's funnel plots for OS.

FIGURE S5
Publication bias detected by Egger's funnel plots for OS.

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Case report: A rare case of malacoplakia resembling a malignant tumor of the cervix: a case report and review of the literature

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Malacoplakia is a rare chronic granulomatous disease that mostly affects the gastrointestinal tract and urinary tract of immunocompromised patients; malacoplakia rarely effects the female reproductive tract. Here, we report a 56-year-old patient who underwent thymectomy for thymoma and myasthenia gravis prior to developing cervical and vaginal malacoplakia. The patient presented with recurrent vaginal bleeding. We discovered that there were alterations in the cervical cauliflower pattern during colposcopy, which is suggestive of cervical cancer. Pathological examination of the lesion tissue showed that a large number of macrophages aggregated, and M-G bodies with concentric circles and refractive properties were observed between cells. Immunostaining for CD68 and CD163 was positive, and special staining for D-PAS and PAS was positive. The discovery of *Escherichia coli* in bacterial culture can aid in the diagnosis of malacoplakia. Following surgery, we performed vaginal lavage with antibiotics in addition to resection of local cervical and vaginal lesions. This study provides a fresh perspective on the management of genital malacoplakia.

KEYWORDS

malacoplakia, malignant tumor of the cervix, pathology, vaginal bleeding, case report

1 Introduction

A relatively rare granulomatous condition called malacoplakia primarily impacts the urinary system, but it can also affect the gastrointestinal tract, testicles, prostate, and other organs (1). The causes of malacoplakia and its pathophysiology are unclear. Nonetheless, most studies indicate a strong correlation between infection and the onset of malacoplakia (2). These infections were primarily caused by Acidophilus, Klebsiella species, and *Escherichia coli*. Malacoplakia has also been linked to immunodeficiency, which is thought to be caused by a malfunction in the process of killing intracellular bacteria (3). There is currently little research on malacoplakia in the female vaginal canal. Diagnosing and treating malacoplakia are more difficult for professionals due to its unusual clinical presentation, and clinical misdiagnosis is highly common. The two main treatments for cervical malacoplakia are hysterectomy and antibiotic therapy (2, 4–12).

However, the disadvantages of hysterectomy are obvious, including short-term infections, peripheral organ damage, increased morbidity, and long-term complications such as pelvic organ prolapse and urinary incontinence (13). At present, the treatment and prognosis of malacoplakia patients with uterine preservation are unclear. The cases and treatments reported below provide new ideas for the clinical treatment of genital tract malacoplakia (14).

2 Case reports

At the beginning of 2021, a 56-year-old Chinese woman who complained of recurrent vaginal bleeding for one week visited our hospital. The patient had previously undergone thymectomy due to myasthenia gravis combined with type B2 thymoma, and she had no history of diabetes, AIDS, tuberculosis, etc. Gynecological examination of the patient at the time of treatment revealed that the 5 * 5 cm cauliflower-like mass on the anterior lip of the cervix involved the vault and easily bled when touched. A gynecologic ultrasound revealed that the cervix was enlarged with solid tumor formation. The outpatient department was highly suspicious of a cervical malignant tumor, so further colposcopy (Figure 1A) and tissue biopsy were performed. Colposcopy revealed that the cervical surface showed cauliflower-like changes, involving the upper 1/3 of the posterior vaginal wall, the upper 1/3 of the left vaginal wall, the front segment of the right vaginal wall, and the front 1/2 of the vaginal wall. No obvious white epithelium was observed, and the iodine test was negative. The microscope showed that a large number of macrophages (tissue cells) aggregated, and concentric and refractive small bodies, called MG bodies, were seen between tissue cells. They can be seen inside or outside the cytoplasm of macrophages (tissue cells) and are characteristic for diagnosing soft spot disease. Immunohistochemical staining for CD68 and CD163 was used to identify tissue cells, while D-PAS and PAS were used to visualize MG bodies. The discovery of *Escherichia coli* in bacterial culture can aid in the diagnosis of soft spot disease. Antibiotics be combined with surgical hysterectomy based on the results of drug sensitivity tests. Due to religious beliefs, the patient refused uterine removal, so she was given 0.2 g intravenous amikacin once a day according to the drug sensitivity test. After one month of treatment, the vaginal bleeding of the patient stopped, the colposcopy mass was smaller than before, and the focus was limited to the cervical surface in the second month (Figure 1B). At the end of 2022, after the patient was infected with COVID-19 and had mild COVID-19 pneumonia, vaginal bleeding occurred again. Pelvic magnetic resonance imaging (MRI) revealed a large cervical space occupying the protrusion into the vagina; this space was thought to be a result of malacoplakia, although cervical malignancies were not excluded (Figure 2). After communicating with the patient, the patient asked to keep their uterus, and after signing the informed consent form, cervical lesion resection + vaginal wall lesion resection was performed. Microscopy revealed a diffuse inflammatory lesion with a large number of tissue cell clusters (Figure 3A, 100X). In the background of tissue cells, there were varying numbers of plasma cells and lymphocytes, and there may have been bleeding and a small amount of neutrophils (Figure 3B, 100X). Characteristic soft spot bodies (Michaelis Gutmann bodies, MG bodies) were also observed inside and outside the tissue cells. Soft spot bodies were round or oval in shape, with clear boundaries, refractive, alkaline homogeneous shapes, or ring-like structures resembling "owl's eyes" (Figure 3C, 400X). MG bodies are formed by incomplete degradation of bacterial calcification. Immunohistochemistry revealed CD68- and CD163-positive tissue cells (Figures 3D, E, 200X), while PAS staining revealed purplish red soft macular bodies (Figure 3F, 400X). After surgery, the method of antibiotic administration was changed, and tobramycin/dexamethasone eye ointment + 0.2 g amikacin were mixed with local vaginal lavage. More than one year after surgery, the disease is well controlled, and there has been no recurrence.

3 Discussion

Malacoplakia has been recognized since before 1900 as a very rare disease that is characterized by defects in the mononuclear phagocyte system (15). Malacoplakia related to the female reproductive system is rare. Malacoplakia is usually associated with an immunosuppressive state, indicating that immunity plays an important role in its pathogenesis. Different manifestations of malacoplakia include malignant tumors, SOT, human immunodeficiency virus (HIV), and autoimmune diseases (16–18).

3.1 Demographic patterns of malacoplakia of the cervix: age and racial disparities

A previous study revealed that malacoplakia had a high prevalence in the southwestern United States, with patients ranging in age from as young as 6 weeks to as old as 85 years of age (19), usually with the highest prevalence in patients >50 years of age (20). The most recent case of cervical malacoplakia is reported in this paper. To date, a total of 14 cases of cervical malacoplakia have been reported, including that in the present paper, among which the youngest woman was only 27 years old, the oldest patient was 83 years old, and there were 11 cases in women over 50 years old, accounting for 78.57% of all cases; these ages are close to the ages of onset of other malacoplakia diseases (2, 4–12).

3.2 Pathogenesis of malacoplakia of the cervix

The etiology and pathogenesis of cervical malacoplakia are still unclear, and the main underlying mechanisms are various microbial infections and immune dysfunction (21). In this case, *Escherichia coli* was found in the vaginal secretions, so we believe that microbial infection may be one of the important factors involved in the pathogenesis of cervical malacoplakia. Moreover, the occurrence of malacoplakia is related to functional defects in macrophages, which block the degradation of phagocytic bacteria by lysosomes, resulting in excessive undigested bacterial debris in the cytoplasm (22–24). Our patient had previously undergone a thymectomy for myasthenia gravis with type B2 thymoma. Thymoma-associated myasthenia gravis is a paraneoplastic disease, and myasthenia gravis is the most widely reported autoimmune disease associated with thymoma (25). There is evidence that cholinergic receptor agonists, such as chlormethine, combined with antibiotics may improve the function of macrophages by correcting lysosomal defects. Therefore, we speculate that cholinergic receptor antibodies in malacoplakia patients may affect the function of macrophages, thus driving the phagocytosis of pathogenic bacteria in patients (26). Therefore, we hypothesized that the patient's previous history of myasthenia gravis combined with thymoma may have induced the development of malacoplakia.

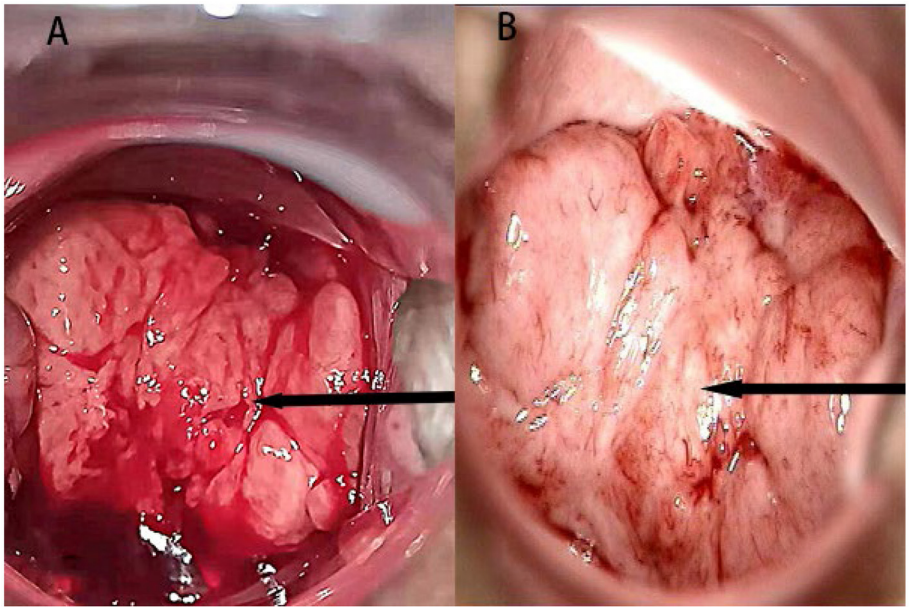

FIGURE 1
(A) A colposcopic image at the time of initial diagnosis; the arrow points to the lesion. **(B)** Review of the colposcopic image in the second month of treatment; the arrow points to the lesion.

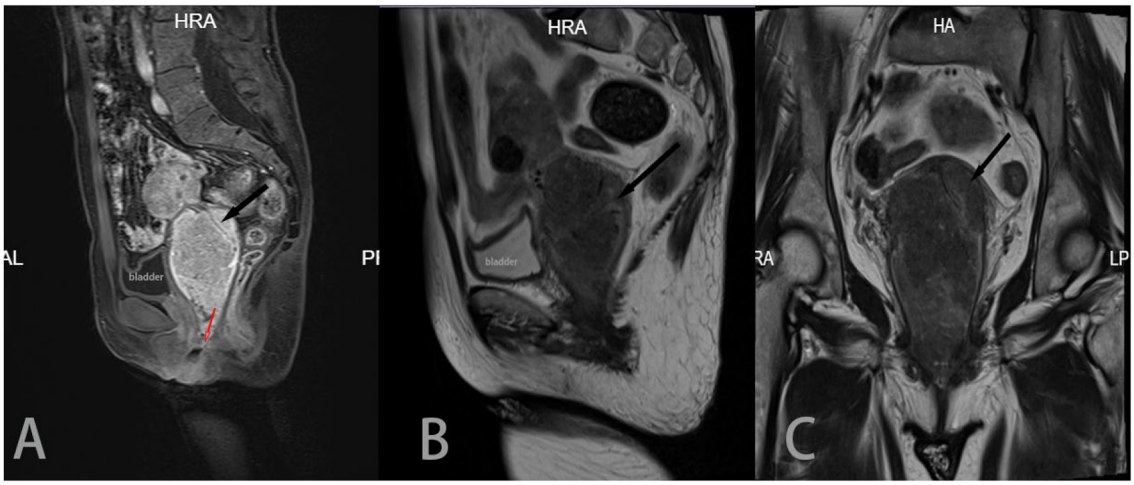

FIGURE 2
Sagittal T2 **(A)**, sagittal T1 enhancement **(B)** and coronal T2 **(C)** images all show a large cervical mass protruding into the vagina, with a size of approximately 50 * 58 * 91 mm. The mass invaded the cervical interstitium (black arrow), and the surrounding low-signal basal ring was still apparent. In **(B)**, and the lesion appeared in the vagina, occupying 2/3 of the vaginal cavity (red arrow). The uterine body was compressed and moved upward.

3.3 Challenges in the clinical diagnosis of malacoplakia of the cervix: overlapping symptoms

Most patients with malacoplakia present with abnormal vaginal bleeding and ulcerative changes in the cervix, which can be seen with the naked eye (27). The similarity of clinical manifestations often leads us to overlook cervical malacoplakia and misdiagnose it as a malignant tumor of the cervix (28). Our patient saw a doctor due to abnormal vaginal bleeding. During gynecological examination and colposcopy, a cauliflower-like cervical tumor was found. Ultrasound revealed that the cervix was enlarged with a solid tumor-like appearance. Because cervical cancer was suspected, we conducted a colposcopy examination and found that the lesion was soft, yellow, slightly raised, and fused into a 5 * 5 cm cauliflower-like plaque. A histological biopsy was taken. However, to our surprise, the pathological report suggested that this was a case of malacoplakia. Here, we emphasize the clinical significance of

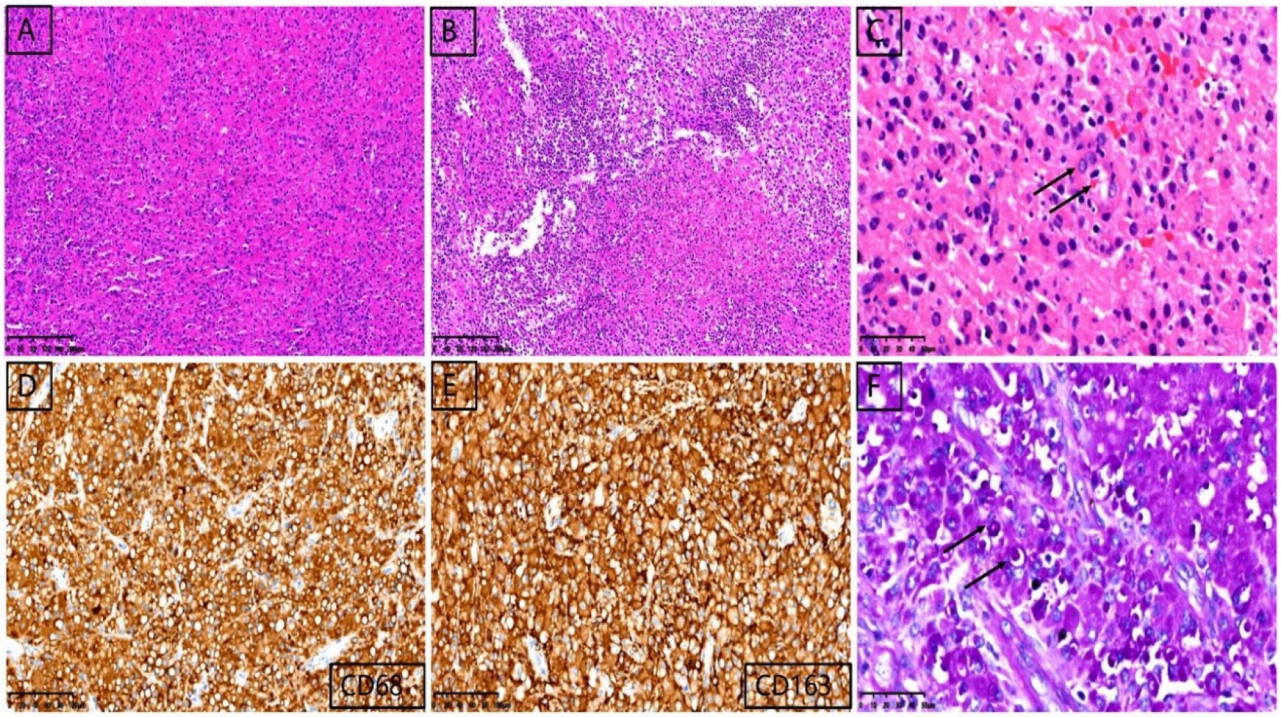

FIGURE 3
Pathological images of cervical lesions. Microscopy revealed a diffuse inflammatory lesion with a large number of tissue cell clusters [**(A)**, 100X]. In the background of tissue cells, there were varying numbers of plasma cells and lymphocytes, and there may have been bleeding and a small amount of neutrophils [**(B)**, 100X]. Characteristic soft spot bodies (Michaelis Gutmann bodies, MG bodies) were also observed inside and outside the tissue cells. Soft spot bodies were round or oval in shape, with clear boundaries, refractive, alkaline homogeneous shapes, or ring-like structures resembling "owl's eyes" [**(C)**, 400X]. MG bodies are formed by incomplete degradation of bacterial calcification. Immunohistochemistry revealed CD68- and CD163-positive tissue cells [**(D, E)**, 200X), while PAS staining revealed purplish red soft macular bodies [**(F)**, 400X].

malacoplakia in the differential diagnosis of gynecological diseases. Malacoplakia may mimic malignant tumors, which can be a challenge for obstetricians and gynecologists.

3.4 Identification of malacoplakia in the genital tract

To date, there have been fewer than 40 reported cases of female genital malacoplakia, 14 of which were cervical malacoplakia (including this case); most of these patients presented with vaginal and endometrial soft spots, and ovarian and fallopian tube invasion was rarer (29). Malacoplakia involving the cervix, endometrium and vagina has similar clinical manifestations, mainly abnormal uterine bleeding, postmenopausal vaginal bleeding and increased secretions (30). The ultrasound characteristics of endometrial malacoplakia include anechoic fluid expansion in the endometrial cavity in the acute stage, irregular and heterogeneous thickening, and endometrial hypopogenicity in the chronic stage; gynecological examinations generally have no specific findings (31). The imaging characteristics of cervical malacoplakia include a hypoechoic space in the cervix. Cervical lesions can be detected via gynecological examination and confirmed via cervical lesion biopsy. Vaginal malacoplakia can be detected through gynecological examination, vaginal lesions, and biopsy, and abnormalities can be detected in the uterus and cervix (7). Ovarian and tubal malacoplakia often manifest as abdominal pain and abdominal discomfort before surgery, and imaging can reveal space in the accessory area. Operations can show that lesions directly spread and invade the surrounding tissues, similar to tumors, but postoperative pathology will suggest malacoplakia (32).

3.5 Pathological features of malacoplakia of the cervix

Malacoplakia is a chronic granulomatous disease that is characterized by a large number of tissue cells that are visible under the microscope, with a background of small lymphocytes, plasma cells, and neutrophils (26). Among them, circular or oval shaped cells are observed, with clear boundaries, refraction, alkaline homogeneity, or a ring-like structure resembling "owl's eyes". Immunohistochemically, there are more CD68 and CD163 positive tissue cells, and unstained circular or oval vacuolar structures can be seen inside tissue cells (29). The MG bodies are specifically stained with D-PAS. PAS can mark MG bodies, which are purple–red in color. The diagnosis is consistent with soft spot disease. Due to the rarity of this disease, its clinical symptoms and general features are nonspecific, and there is a lack of sufficient understanding. Thus, misdiagnosing this disease as a malignant

TABLE 1 Summary of the previous cases reported of malacoplakia of the uterine cervix in literature along with our case.

Age	Clinical presentation	Initial diagnosis	Anamnesis	Treatment	Follow-up	Reference
64	Reproductive tract bleeding	Not described	Transitional cell carcinoma of the urinary bladder. Nulligravid. Use prednisone	Antibiotic treatment after a cervical biopsy	The vaginal vault recurred 2 years after surgery.	(7)
71	Reproductive tract bleeding; abdominal pain	Not described	Cholecystectomy	Hysterectomy Electrocautery of vaginal lesion	No recurrence	(5)
83	Reproductive tract bleeding	Not described	Xanthogranulomatous pyelonephritis	Hysterectomy	The vaginal stump recurred 14 months after surgery.	(11)
69	Uterine prolapse Cervical ulceration	Uterine prolapse. Proctopto-ma	Uterine prolapse	Hysterectomy. Partial resection of the vagina	Not reported	(27)
60	Reproductive tract bleeding	Therioma	Rheumatoid. Use cortisol	Not reported	Not reported	(4)
74	Reproductive tract bleeding	Therioma	No	Antibiotic	Not reported	(8)
27	Reproductive tract bleeding Cervical ulceration	Cervical malignancy	AIDS(Acquired immune deficiency syndrome)	Antibiotic	Follow-up failure	(2)
36	Reproductive tract bleeding Cervical ulceration	Cervical malignancy	AIDS(Acquired immune deficiency syndrome)	Died before treatment	Died before treatment	(2)
81	Reproductive tract bleeding	Cervical malignancy	Nulligravid	Not reported	Not reported	(12)
78	Reproductive tract bleeding. Abdominal pain	Cervical malignancy	Sjögren's syndrome. Use cortisol.	Hysterectomy	There was no recurrence at 13 months after surgery.C	(29)
72	Reproductive tract bleeding	Cervical malignancy	Use cortisol	Died before treatment	Died before treatment	(9)
66	Reproductive tract bleeding	Cervical malignancy	No	Antibiotic	Not reported	(9)
78	Reproductive tract bleeding	Not described	No	Antibiotic	Not reported	(10)
56	Reproductive tract bleeding	Cervical malignancy	Myasthenia gravis. Thymoma	Resection of the cervical and vaginal lesions	There was no recurrence at 12 months after surgery.	Present case

tumor, especially using frozen specimens obtained during surgery, is easy, and misdiagnosis and missed diagnoses can occur. Therefore, differential diagnosis is necessary. (1) The differential diagnosis for endometrial poorly differentiated carcinoma is as follows: when malacoplakia occurs in the uterine cavity, it often manifests as vaginal bleeding, menstrual changes, ultrasound detection of a space occupying the uterine cavity, and microscopic masses of tissue cells that are easily mistaken for epithelial cells. Especially during intraoperative frozen sectioning, due to the lack of fixed tissue and atypical cell morphology, malacoplakia can be misdiagnosed as poorly differentiated endometrial carcinoma. In endometrial cancer, CK (AE1/AE3) and vimentin are positive, while CD68 is negative, and the Ki67 proliferation index is significantly greater than that in malacoplakia (33, 34). (2) The differential diagnosis for malignant melanoma is as follows: when malacoplakia is accompanied by bleeding, the lesion appears dark brown. Under a microscope, tissue cells are prone to morphology similar to that of malignant melanoma cells. Malignant melanoma cells exhibit obvious atypia, with large purple–red nucleoli visible and melanin visible in the cytoplasm. The immunohistochemical markers HMB-45, Melan-A, and S-100 are positive (35). (3) Xanthogranulomatous and histiocytic endometritis are commonly observed in postmenopausal women and are characterized by vaginal bleeding or fluid flow, often accompanied by cervical stenosis or pyometra with generally brownish yellow brittle tissue. Microscopically, patients with xanthogranulomatous and histiocytic endometritis show a large number of tissue cells with eosinophilic or foam-like cytoplasm. The cytoplasm is also rich in lipids or hemosiderin. There are also plasma cells, lymphocytes and neutrophils in the background (36, 37). Unlike malacoplakia, these patients lack characteristic MG bodies. This disease can be distinguished based on medical history.

3.6 Individualized management of malacoplakia of the cervix

Currently, there are no definitive guidelines for the treatment of malacoplakia. The main therapeutic approaches are antimicrobial therapy, a reduction in the use of immunosuppressive drugs and surgical treatment (23, 24). Quinolone antimicrobials (methotrexate, ciprofloxacin) have good cell membrane penetration and are therapeutically effective. However, quinolones block neuromuscular transmission, and there is a possibility of myasthenia gravis (38, 39). Early antimicrobial treatment before malacoplakia causes severe and extensive pathological damage can prevent this pathological damage (40). In this case, the patient was sensitive to aminoglycoside antibiotics, so we administered amikacin and tobramycin ointment for anti-infection treatment. In addition, another treatment strategy is immunotherapy. Cholinergic receptor agonists and vitamin C can alleviate immune dysfunction. Ascorbic acid can enhance lysozyme damage caused by immune deficiency. Therefore, the combination of antibiotics, vitamin C, and cholinergic drugs may have a certain effect (41–44).

Surgery may be recommended when conventional drug therapy fails (2, 4–12). Thirteen cases of cervical malacoplakia have been reported; three patients were treated with antibiotics, five were treated with hysterectomy, and the remaining five were either not treated or died before treatment. Hysterectomy was performed in all surgically treated patients, which may be related to the difficulty of distinguishing cervical malacoplakia from cervical malignancy (29) (Table 1). Due to differences in culture and religious beliefs, most Chinese women want to preserve the uterus. For our patient, we intravenously administered antibiotics they were sensitive to immediately after diagnosis. In the first month, the cervical space occupation tended to decrease. However, after infection with COVID-19, the cervical space occupied became larger. This effect may be related to COVID-19 attacking the immune system (45, 46). Due to the special anatomical properties of the cervix, we first performed a colposcopic biopsy before the operation, and the pathology confirmed cervical malacoplakia. Therefore, we developed a personalized operation involving the resection of cervical lesions and vaginal wall lesions. We also administered a special vaginal lavage after surgery. The optimal duration of antibiotic therapy for patients with malacoplakia is unclear, and typically ranges from 12 weeks to 6 months (14). We chose to administer the drug vaginally for 3 months continuously, and the patient did not relapse within 12 months after surgery.

4 Conclusion

Malacoplakia is a rare systemic disease that is usually seen in immunocompromised patients, and the common treatment regimen is intravenous or oral antibiotics combined with total hysterectomy. In our case, we used the first treatment protocol involving antibiotic vaginal lavage after combined resection of cervical and vaginal lesions, which was a new approach for the treatment of cervical malacoplakia. Early and accurate diagnosis and individualized treatment are the basis for improving patient prognosis, and we hope that in future studies, we can explore the etiology, pathogenesis, imaging characteristics, and treatment modalities of cervical malacoplakia in greater depth to improve the quality of life of patients and the cure rate of this disease.

Data availability statement

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

Ethics statement

The studies involving humans were approved by Ethics Committee of Ningbo No.2 Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

JL: Writing – original draft, Writing – review & editing. JM: Software, Writing – original draft, Writing – review & editing. JW: Data curation, Writing – review & editing. ZZ: Funding acquisition, Resources, Writing – review & editing.

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Conflict of interest

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

Publisher's note

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Global scientific production on gasless laparoscopy: a bibliometric analysis

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Objectives: To characterize the bibliometric characteristics of the global scientific production of original research on gasless laparoscopy in the Web of Science Core Collection (WoSCC) platform.

Materials and methods: A bibliometric study of original articles published up to the year 2023 was carried out. Articles were included following the selection criteria in the Rayyan web application, indexed in the Scopus database. The bibliometric analysis was performed using the Bibliometrix program in the R programming language and VOSviewer. The bibliometric characteristics evaluated were articles, journals, citations, publications, ten most mentioned articles, journals with the highest number of publications, authors and institutional affiliations; and cooccurrence of terms.

Results: A total of 223 publications were included, with the highest number of articles being published in the years 1999 and 2014. The publication with the most citations was found to be a randomized trial by Galizia G in 2001 with 132 citations. We identified 846 authors involved in the production of articles on gasless laparoscopy, with Nakamura H being the most productive author with 15 articles between the years 2007 and 2020, followed by Takeda A and Imoto S, all three affiliated with "Gifu Prefectural Tajimi Hospital". The country with the highest production was Japan with 64 publications, followed by China and Italy with 46 and 18 publications, respectively. In the top 10 journals with the highest number of publications, "Surgical Endoscopy—Ultrasound and Interventional Techniques" is in first place with 20 articles published on gasless laparoscopy; in addition, most of these are located in Q1 and Q2. Regarding the terms or keywords, it was found that the initial studies had terms related to the disadvantages of pneumoperitoneum and later focused on more specific topics of the application of gasless laparoscopy.

Conclusions: Production on gasless laparoscopy has stagnated, with the topics of interest currently being its application in new, less invasive techniques. The most productive countries are found in the Asian and European continents, with little information collected in Latin America. This fact makes it necessary to increase the production of studies to promote this technique and its possible advantages.

KEYWORDS

bibliometrics, minimally invasive surgical procedures, laparoscopy, humans, pneumoperitoneum bibliometrics, pneumoperitoneum

Abbreviations

BJAG, Brad Jhefferson Arge Gamarr; JPR, Javier Pérez Reátegui; AHV, Akram Hernández-Vásquez; RDR, Renato Díaz-Ruiz; WoSCC, web of science core collection; NTC, number of total citations; SCP, single country publications; MCP, multiple country publications.

1 Introduction

Lack of access to timely surgical interventions causes high morbidity and mortality in less developed countries (1). The supply of professionals per 100,000 inhabitants in these countries is 5.5, being as low as 0.7, in stark contrast to the 56.9 that can be found in more developed countries (2). On the other hand, more than 90% of the world's population, mainly living in less developed regions, lack timely access to surgery (1), resulting in delayed and often inadequate treatment (3).

Surgery is the first-line management in multiple pathologies. Likewise, minimally invasive surgery, or conventional laparoscopy (4), is the first choice for emergencies as well as for elective procedures, such as cholecystectomies or ectopic pregnancies (1, 5, 6). The known advantages of laparoscopy are a shorter recovery time and hospital stay and less postoperative pain, which favor its use (7). However, laparoscopy requires a producing pneumoperitoneum using CO2 to create the working space in the abdominal cavity (8). Nonetheless, despite the advantages mentioned above, conventional laparoscopy presents some complications or difficulties, such as the need for general anesthesia or hemodynamic and acidobasic alterations caused by pneumoperitoneum, requiring constant monitoring and increasing the cost of surgery (8, 9). This has a great impact in low-income countries, where many patients opt for open surgery or no surgery at all (9).

Given the possible complications of conventional laparoscopy due to pneumoperitoneum, the first publications aimed at solving this problem appeared in the 80s and the 90s. Gasless laparoscopy involves the creation of an intra-abdominal working space (10, 11), by traction of the abdominal wall and sometimes in combination with a low-pressure pneumoperitoneum (10, 12). The first gasless laparoscopic cholecystectomy was performed by Erich Mühe in 1985, after which different methods and devices emerged to achieve this approach (13).

Gasless laparoscopy may be a surgical alternative in countries with fewer economic resources (14), due to its cost savings (9, 15, 16). Several studies included in a systematic review have shown that gasless surgery has similar results to conventional laparoscopy in general surgery and gynecology (17). By not requiring a pneumoperitoneum, there is greater hemodynamic stability, being an option for patients at high cardiovascular risk (16, 18) and may even be considered in patients with an unfavorable American Society of Anesthesiologists classification (19). When comparing the use of conventional laparoscopy with gasless laparoscopy in gynecological pathologies, better operating and bleeding times were reported with the latter approach (20). Therefore, despite the limitations of gasless laparoscopy, this procedure could be a more comfortable alternative with similar results to conventional laparoscopy.

The limitations of gasless laparoscopy described in the literature include low methodological quality and small sample size, limiting the certainty of its results in clinical surgical management (14, 17, 20). Among other important points that are not mentioned in these studies are the severity of the complications identified, the surgeon's experience, or patient comorbidities, precluding correct interpretation of the results and research trends in this field (9). In addition, gasless laparoscopy is expected to have the same versatility as conventional laparoscopy, being a promising line of research (19). Greater dissemination and knowledge of this approach could result in expanding topics of research interest in surgical procedures used in other regions of the world, such as India (7). A bibliometric study, which seeks to analyze trends in article, author and journal output, using qualitative and quantitative indicators, would provide a basis for the main topics addressed, as well as the countries or authors with the highest output in gasless laparoscopy, or how much progress has been made in recent years in this field. However, no such study has been carried out to date (21). For this reason, the present study aimed to establish the bibliometric aspects of the global scientific production of original publications on gasless laparoscopy in the Web of Science Core Collection (WoSCC) platform until 2023.

2 Materials and methods

2.1 Type of study and source of data

A bibliometric study of original articles on gasless laparoscopic surgery was developed on the WoSCC platform (Science Citation Index Expanded™, Social Sciences Citation Index®, Arts & Humanities Citation Index®, Emerging Sources Citation Index), to develop a performance analysis and bibliometric mapping of the data obtained. WoSCC was used because it has records of articles from the most impactful journals globally and is composed of up to ten citation indexes. WoS coverage has expanded enormously over the years, reaching around 34,000 journals to date (22). WoSCC has also been widely used in bibliometric studies, proving to be a selective, structured and balanced platform with comprehensive citation links and enhanced metadata supporting a wide range of informational purposes (21, 23).

2.2 Search strategy

The search and identification of publication records on gasless laparoscopy was performed on January 23, 2024, using the following terms and specifications: TS = (gasless OR "without gas" OR isobaric) AND (laparoscop* OR celioscop* OR peritoneoscop* OR laparoendoscop* OR laparo-endoscop* OR "endoscopic surgery") and Article (Document Types).

The initial search strategy was developed by three of the authors (A. G. B., P. R. J. and A. H. V.) and then reviewed by a physician specialized in pediatric surgery (R. D. R.), for subsequent approval by all the investigators.

2.3 Eligible criteria and data acquisition

A review of the records independently identified in Rayyan was performed by two investigators (A. G. B. and P. R. J.) to assess compliance with each of the study inclusion criteria. These

criteria were: original articles addressing the topic of gasless laparoscopy, published up to 2023, articles published in English and Spanish, articles including any research design, original articles that apply to live human models, original articles on abdominopelvic surgery, and original articles on abdominal-pelvic surgery (24). Using the Accession Number of the records obtained in WoSCC, a search was performed on January 28, 2024, to retrieve their metadata and export this information to a Plain Text file. This file was imported into the Notepad program to homogenize the fields of authors (AU), affiliations (C3), and Keywords Plus® to finally obtain a text file that was analyzed.

2.4 Statistical data analysis and display

Bibliometric indicators were obtained through the use of the Bibliometrix package in the R programming language (25). VOSviewer 1.6.20 (Leiden University, Leiden, The Netherlands) was also used (26), for the construction of author "networks", institutional affiliations and Keywords Plus®.

The absolute number of articles, journals, citations, annual number of publications, the ten most cited articles, the journals with the highest number of publications, and the co-authorship networks based on authors, institutional affiliations and Keywords Plus® co-occurrence were presented. The analysis of the networks was developed by means of the full counting method, normalization method by association, node repulsion and node attraction with VOSviewer default values, cluster resolution at 1.00, minimum cluster size at 1, weight according to the number of documents, and term temporality networks based on the average annual publication following the methodology applied in a previous study and the VOSviewer manual (27, 28). For the Keywords Plus® (ID) cooccurrence network, a threshold was applied for cooccurrence in titles and abstracts with at least one mention.

2.5 Ethical considerations

The execution of the study did not require the approval of an ethics committee because it was a study using published articles.

3 Results

A search of the WoSCC database yielded a total of 441 articles on gasless laparoscopy up to December 2023. After a review of the titles and abstracts in Rayyan, the sample was reduced to 223 articles, which were included for further analysis. The time period covered was between the years 1993 and 2023, with the years 2014 and 1999 having the highest number of articles published with 17 and 15, respectively (Figure 1). On average, each article has been cited 12.8 times.

3.1 Most productive authors

A total of 846 authors were found to be involved in the production of articles on gasless laparoscopy.

Table 1 shows the 10 most productive authors with their corresponding country and the institution with which they are

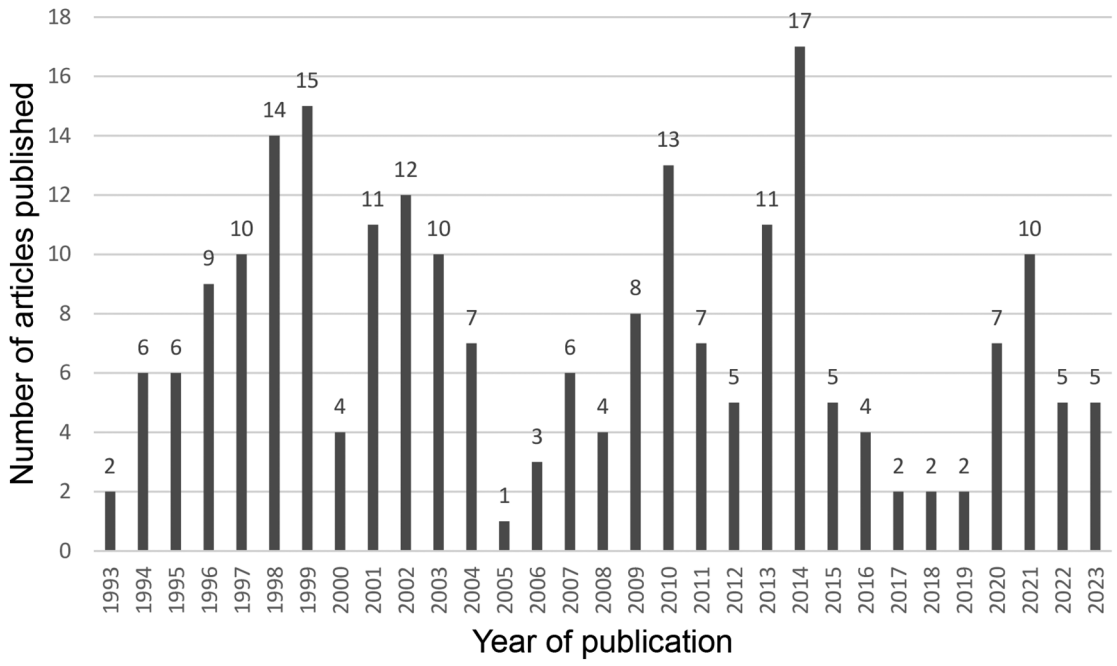

FIGURE 1
Publication trends of gasless laparoscopy articles in WoSCC 1993–2023.

affiliated. It can be seen that Nakamura H., affiliated with "Gifu Prefectural Tajimi Hospital", stands out as the author with the highest production on gasless laparoscopy with a total of 15 articles between 2007 and 2020. He is followed by Takeda A and Imoto S, with 13 and 10 articles, respectively, both affiliated with the same institution. Of The 10 authors with the highest production, had Japan, Taiwan and Germany as the corresponding countries. Paolucci V. and Gutt CN. presented the greatest production on gasless laparoscopy between 1994 and 1998, being among the authors with greater representation in these years, unlike the others who showed greater production at the beginning of the 21st century.

3.2 Articles and journals

Table 2 lists the 10 most cited articles on gasless laparoscopy, being "Hemodynamic and pulmonary changes during open, carbon dioxide pneumoperitoneum and abdominal wall-lifting cholecystectomy. A prospective, randomized study", the first on the list with 132 citations, published by Galizia G in 2001. The second most cited article is "Gasless laparoscopy and conventional instruments. The next phase of minimally invasive surgery" by Smith R S in 1993 with a total of 99 citations.

A total of 100 sources of information were found. Table 3 shows the 10 journals with the highest number of publications

TABLE 1 Top ten authors with the highest production of articles on gasless laparoscopy in the WoSCC (*N* = 223).

Rank	Author's name	Articles published	% of total publications	Country[a]	Affiliation[a]	H index[a]
1	Nakamura H	15	6.73	Japan	Gifu Prefectural Tajimi Hospital	17
2	Takeda A	13	5.83	Japan	Gifu Prefectural Tajimi Hospital	18
3	Imoto S	10	4.48	Japan	Gifu Prefectural Tajimi Hospital	13
4	Lin MT	10	4.48	Taiwan	National Taiwan University Hospital	43
5	Paolucci V	9	4.04	Germany	Ketteler-Krankenhaus	19
6	Gutt CN	8	3.59	Germany	Klinikum Memmingen	29
7	Yang CY	8	3.59	Taiwan	National Taiwan University Hospital	36
8	Kihara K	7	3.14	Japan	Tokyo Medical and Dental University	41
9	Mori M	7	3.14	Japan	Graduate School of Medicine	83
10	Wang MY	7	3.14	Taiwan	National Taiwan University Hospital	24

NA, not available.
[a]Collected from WoSCC.

TABLE 2 Top ten most cited articles on gasless laparoscopy in WoSCC 1993–2023.

Rank	Title	Authors	Year of publication	Journal	Total citations	Citations per year	NTC
1	Hemodynamic and pulmonary changes during open, carbon dioxide pneumoperitoneum, and abdominal wall-lifting cholecystectomy. A prospective, randomized study	Galizia G et al.	2001	Surgical endoscopy and other interventional techniques	132	5.50	5.17
2	Gasless laparoscopy and conventional instruments. The next phase of minimally invasive surgery	Smith RS et al.	1993	Archives of surgery	99	3.09	1.60
3	Splanchnic and renal deterioration during and after laparoscopic cholecystectomy: a comparison of the carbon dioxide pneumoperitoneum and the abdominal wall lift method	Koivusalo AM et al.	1997	Anesthesia and analgesia	76	2.71	3.30
4	A comparison of gasless mechanical and conventional carbon dioxide pneumoperitoneum methods for laparoscopic cholecystectomy	Koivusalo AM et al.	1998	Anesthesia and analgesia	65	2.41	4.08
5	Gasless laparoscopic cholecystectomy: comparison of postoperative recovery with conventional technique	Koivusalo AM et al.	1996	British Journal of Anaesthesia	63	2.17	3.61
6	Randomized clinical trial of the effect of pneumoperitoneum on cardiac function and haemodynamics during laparoscopic cholecystectomy	Larsen JF et al.	2004	British Journal of Surgery	61	2.90	3.34
7	Cardiorespiratory effects of laparoscopy with and without gas insufflation	McDermott JP et al.	1995	Archives of surgery	58	1.93	2.81
8	Gasless laparoscopic ovarian cystectomy during pregnancy: comparison with laparotomy	Akira S et al.	1999	American journal of obstetrics and gynecology	55	2.12	2.21
9	Randomized comparison between low-pressure laparoscopic cholecystectomy and gasless laparoscopic cholecystectomy	Vezakis A et al.	1999	Surgical endoscopy and other interventional techniques	52	2.00	2.09
10	Changes in urinary output during laparoscopic adrenalectomy	Nishio S et al.	1999	BJU International	45	1.73	1.81

NTC: total number of citations/average n° of citations of all documents published in the same years.

TABLE 3 Top ten journals with publications on gasless laparoscopy (*N* = 223) WoSCC 1993–2023.

Rank	Source title	Articles published	% of articles	Quartile category[a]
1	Surgical endoscopy-ultrasound and interventional techniques[b]	20	8.97	NA
2	Surgical endoscopy and other interventional techniques[b]	14	6.28	Q1
3	Journal of laparoendoscopic & advanced surgical techniques	10	4.48	Q4
4	Hepato-gastroenterology	9	4.04	Q4
5	Journal of minimally invasive gynecology[c]	9	4.04	Q1
6	European journal of obstetrics & gynecology and reproductive biology	8	3.59	Q3
7	Journal of the American Association of gynecologyc laparoscopists	6	2.69	NA
8	Surgical laparoscopy endoscopy & percutaneous techniques[c]	6	2.69	Q4
9	International journal of urology	5	2.24	Q3
10	JSLS-Journal of the Society of laparoendoscopic surgeons	5	2.24	NA

NA, not available.
[a]Collected from WoSCC.
[b]Both journals correspond to the same one, the current name being surgical endoscopy and other interventional techniques.
[c]Both journals correspond to the same one, the current name being journal of minimally invasive gynecology.

on gasless laparoscopy. The first place is held by Surgical Endoscopy-Ultrasound and Interventional Techniques with 20 articles followed by Surgical Endoscopy and Other Interventional Techniques and the Journal of Laparoendoscopic & Advanced Surgical Techniques, with 14 and 10 articles, respectively.

3.3 Most productive countries

Table 4 shows the top 10 correspondent countries of the authors in terms of production on gasless laparoscopy, of which 5 belong to Asia, 4 to Europe and 1 to the United States. Japan is the country with the highest production with 64 articles, followed by China with 46, and Italy and the United States with 18 articles each.

In terms of the number of citations per article, Table 5 shows that Japan remains in the lead with 741 in total with an average of 11.58 citations per article, followed by Italy with 371 and 20.61, respectively. However, countries such as Finland, Denmark and Greece published articles with higher impact, presenting a higher average number of citations of 70.50, 31.00 and 52.00, respectively.

TABLE 4 The top ten corresponding author countries with the most articles published on gasless laparoscopy in the WoSCC 1993–2023 (*N* = 223).

Rank	Country	Articles	% of articles	SCP	MCP
1	Japan	64	28.70	64	0
2	China	46	20.63	45	1
3	Italy	18	8.07	18	0
4	United States	18	8.07	15	3
5	Germany	12	5.38	12	0
6	Korea	10	4.48	9	1
7	Turkey	6	2.69	6	0
8	Denmark	5	2.24	5	0
9	Thailand	4	1.79	4	0
10	United Kingdom	4	1.79	0	4

SCP, single country publications; MCP, multiple country publications.

TABLE 5 The top ten countries with the most cited articles published on gasless laparoscopy in the WoSCC 1993–2023.

Rank	Country	Total citations	Average article citations
1	Japan	741	11.58
2	Italy	371	20.61
3	United States	358	19.89
4	China	350	7.61
5	Denmark	155	31.00
6	Finland	141	70.50
7	Germany	77	6.42
8	Turkey	68	11.33
9	Sweden	55	27.50
10	Greece	52	52.00

3.4 Most used key terms

In terms of keywords, 385 terms were identified. Figure 2 shows the network of the most frequently used key terms by year. We found that the most used terms were “laparoscopic cholecystectomy”, “management” and “surgery”, especially between 2005 and 2010. The terms most present at the beginning of the century were “malignancy”, “metastases”, “carbon dioxide embolism” and “blood-flow”; as opposed to those most used in recent years such as “single-port”, “children”, “pain” or “antibiotic-therapy”. Likewise, Figure 3 presents the network of terms grouped by co-occurrence, showing that terms such as “carcinoma”, “port-site metastases” or “invasive surgery” appear together. Likewise, “respiratory changes”, “hemodynamic changes” and “carbon dioxide embolism” also tend to appear together.

3.5 Most productive institutions

Regarding institutions, Figure 4 shows the network of affiliations producing literature on gasless laparoscopy. The most

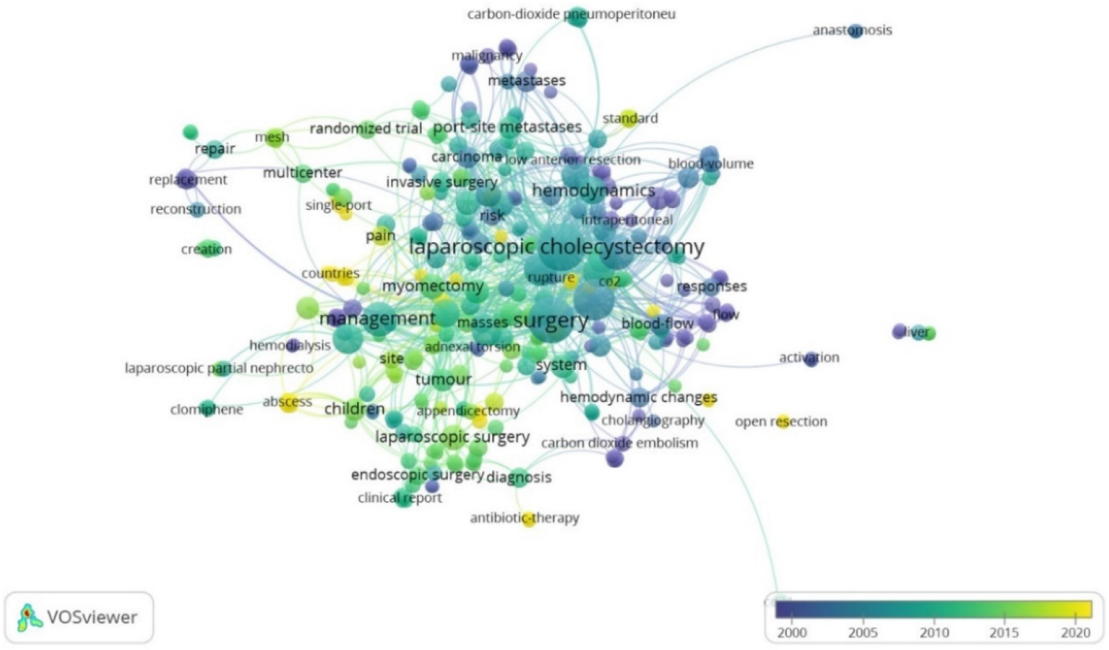

FIGURE 2
Network of the most frequently used key terms by year.

relevant institutions are the University of Leeds (29) in England and Maulana Azad Medical College together with the Karunya Institute of Technology and Sciences in India. These three institutions show multiple collaborations with other organizations and with each other.

4 Discussion

Despite the demonstrated benefits of gasless laparoscopy, the production of articles on this subject has stagnated over the years. It is possible that the improvement in surgical or anesthesiological management of situations that might contraindicate pneumoperitoneum has favored conventional laparoscopy to remain as the intervention of choice.

We found that 1999 and 2014 were the years in which the largest number of articles were published, showing a sustained trend in the number of articles published throughout the decades. Likewise, data corresponding to authors with the highest production were identified, as well as the countries and terms that were most relevant throughout all the years of production.

Nakamura H is the author with the most publications, with all the research having been conducted at the "Gifu Prefectural Tajimi Hospital" in Japan. With a total of 15 articles between 2007 and 2020, this author is among those with the greatest range of activity over time. The topics addressed by Nakamura remain consistent, dealing mostly with the laparoscopic management of adnexal tumors through a single incision, as shown in the publication of a study in 2011 including a series of 100 cases. The latest publications by Nakamura consist of case reports involving the treatment of pregnant women and even the successful management of ectopic pregnancies (30).

The most cited article is "Hemodynamic and pulmonary changes during open, carbon dioxide pneumoperitoneum and abdominal wall-lifting cholecystectomy. A prospective, randomized study" published by Galizia G in 2001 with a total of 132 citations. This study was published in the journal Surgical Endoscopy and Other Interventional Techniques which has the second highest number of publications on gasless laparoscopy, with 14 in total. The study by Galizia consisted in the measurement of various cardiovascular parameters in three study groups, maintaining the same conditions in all the groups and altering only the surgical approach. Thus, the results of this study were completely objective and with few biases, making this study a reference and a good basis for further research (31).

Regarding the most productive journals, it was of note that they were focused on specialized aspects of surgery rather than general aspects, which could have greater diffusion. As expected, surgical journals were more oriented towards conventional laparoscopy since gasless laparoscopy is a less known or used technique and may not be of interest to a journal with broader vision.

Japan leads the scientific production with a total 64 articles on gasless laparoscopy which, according to the corresponding authors, focus mainly on the evaluation of this technique in gynecological pathologies. In addition, in the period from 2014 to 2020 the number of laparoscopic hysterectomies increased considerably from 16,016 to 27,755, observing a trend towards the use of minimally invasive interventions which corresponded to more

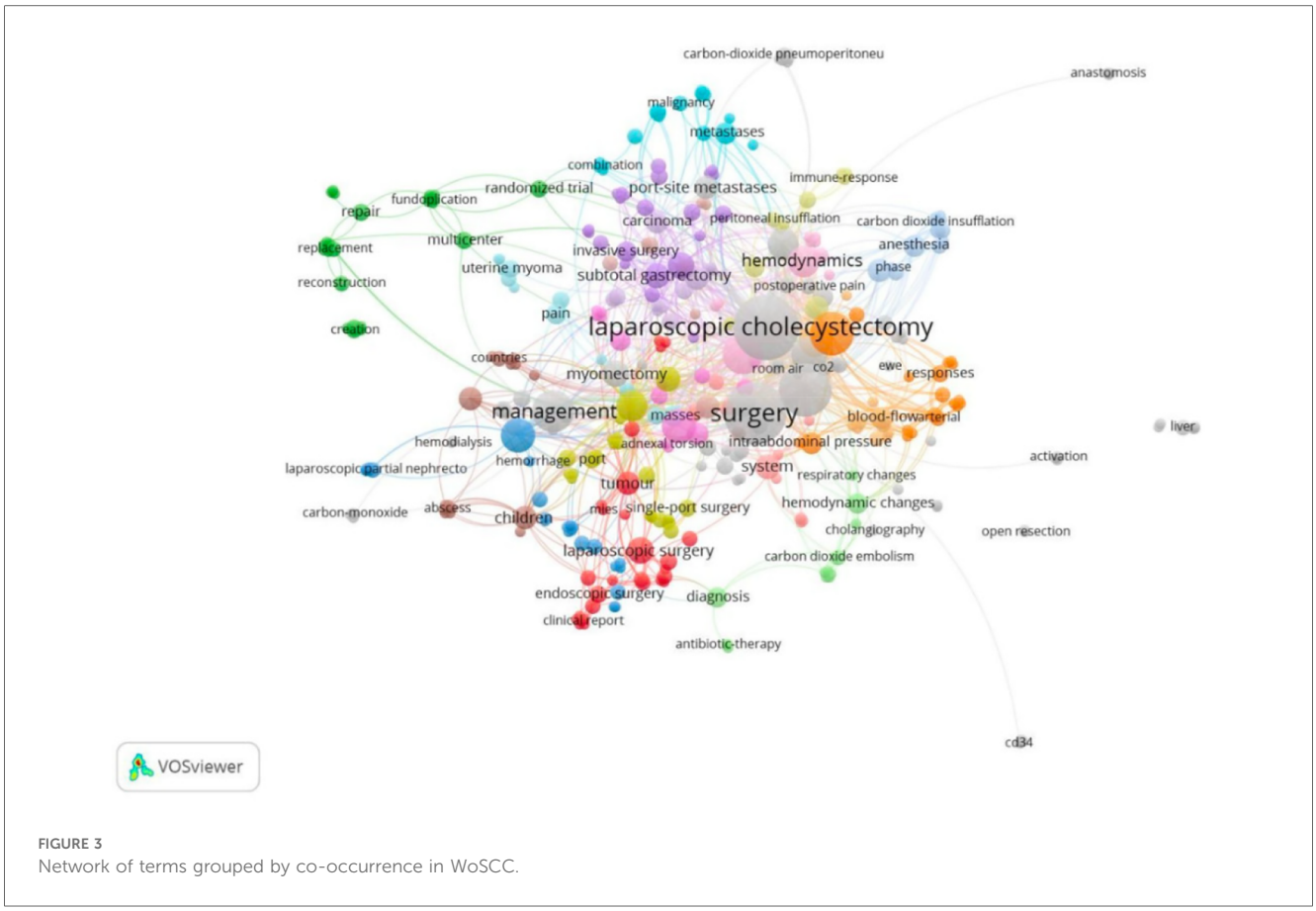

FIGURE 3
Network of terms grouped by co-occurrence in WoSCC.

than 50% of the hysterectomies performed since 2019 (32). This makes this country an important niche for research in this field. On the other hand, according to Scimago Journal and Country Rank, Japan ranks seventh in scientific production until 2020 (33). China, follows the same ranking, occupying second place in scientific production on gasless laparoscopy. In contrast to these results, no Latin American country is included among the top ten authors in terms of number of publications. This may be due to the lesser research funding which mainly comes from the government in this region, and to the fact that socioeconomic conditions do not favor investment in research (34). Despite this, given the inequality in the region, gasless laparoscopy should be considered a viable option (35). However, a possible lack of knowledge of this technique, lack of surgeons who have the necessary expertise to train other physicians or the fact of centralizing surgical interventions, may be factors that prevent the investigation and even the implementation of this technique in our setting.

On the other hand, the publications on gasless laparoscopy with the highest impact belong to countries such as Finland, Greece or Denmark, which is probably due to the methodology used or the objectives set. The Finnish author Koivusalo AM stands out with three of the five most cited articles. These studies present a reliable methodology since they apply a strict control of both the pre-surgical interventions and the target parameters during and after surgery (36–38). This author presented relevant results related to the length of the procedure, demonstrating the benefits of gasless laparoscopy over conventional laparoscopy in the involvement of various organs.

With respect to the keywords found, initially terms such as "malignancy" or "metastases" predominated, showing the interest in the earlier years in the risk of dissemination due to the use of conventional laparoscopy in oncologic pathologies caused by pneumoperitoneum (39). Several publications at that time reported a risk of dissemination and recurrence of oncologic pathologies at the trocar insertion sites after laparoscopy (40, 41), which led to interest in the use of gasless laparoscopy in cancer management. However, Mo X et al. conducted a meta-analysis in 2014 refuting an increased risk for recurrence (42). In recent years, the most used terms are "single-port", "children" or "antibiotic-therapy" showing the new tendency of authors to combine this gasless surgical technique with the use of fewer access points, or to extend its application to children.

We also evaluated the networks of terms that were grouped in clusters according to the line of research or areas of application of gasless laparoscopy. The complications of pneumoperitoneum have been an important area of study in gasless laparoscopy, since terms such as "respiratory changes", "hemodynamic changes" or "carbon dioxide embolism" have frequently been mentioned, demonstrating

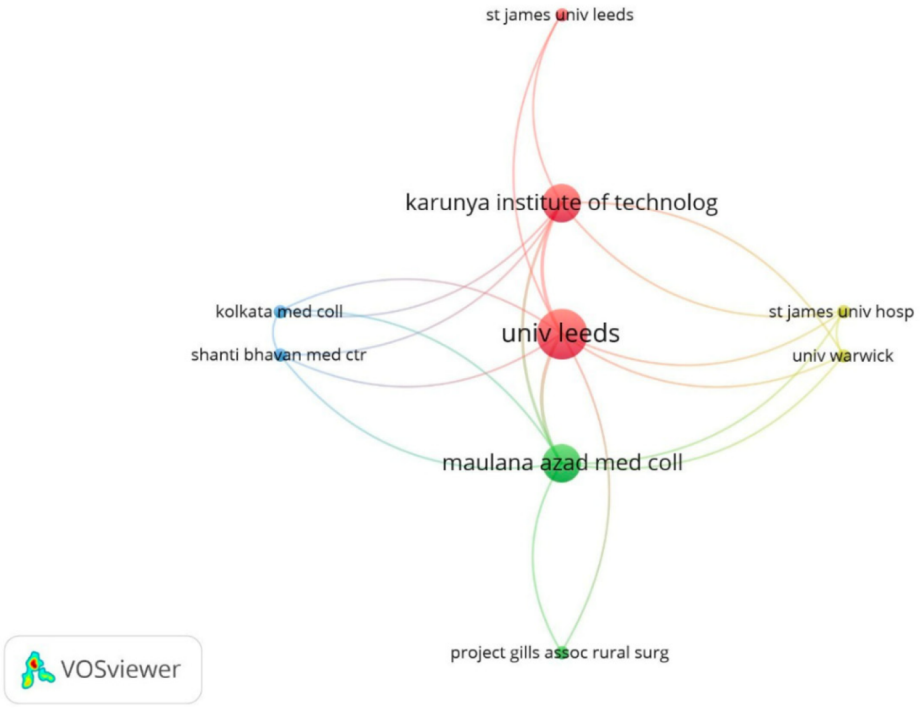

FIGURE 4
Network of institutional affiliations with the highest production on gasless laparoscopy in WoSCC.

that gasless laparoscopy presents an advantage by having minimal alterations in these parameters (43). The network of terms "subtotal gastrectomy", "invasive surgery", "carcinoma" or "port-site metastases", suggests research on the use of this technique in surgical-oncological management, in which it has been successfully used in different gastrointestinal pathologies (44). Likewise, its relationship with terms such as "uterine myoma" and "myomectomy" indicates its application in gyneco-oncologic pathologies, in which the aim is to provide more precise information to help choose the most appropriate surgical approach according to the characteristics of the patient to be treated (45).

As for affiliations, again there was an absence of Latin American institutions, reaffirming the lack of research in this field in the region. Institutions belonging to India or England stand out for great mutual cooperation, all being educational institutions. However, India is not among the most productive. This can be explained by the fact that probably, the corresponding authors of the publications were from another institution and the rest were omitted for the analysis. Project GILLS is a project carried out by surgeons in rural India that aims to increase the number and variety of surgical interventions in the area (46). Different organizations can collaborate with the project either financially or with material or human resources, and among these collaborators there is the University of Leeds, thus explaining its position as the most productive institution.

Gasless laparoscopy has demonstrated benefits in reducing hospital costs and hospitalization days (15, 17). Specifically, gasless laparoscopy for appendectomy has shown similar results to conventional laparoscopy in terms of operative time, surgical complications, and hospital stay, with the added advantage of lower hospital costs (15). Although it presents a higher conversion rate compared to conventional laparoscopy in gynecological surgeries, gasless laparoscopy still results in shorter hospitalization periods compared to conventional laparoscopic abdominal and gynecological surgeries (17). Moreover, due to its lower associated costs, the gasless laparoscopic technique can be implemented in low-income countries, as has been successfully done in India (7).

Currently, energetic vessel sealing devices, such as the harmonic scalpel, are used in laparoscopic procedures. Their use in laparoscopic cholecystectomy, compared to other hemostasis management devices, has shown benefits including shorter hospital stays, reduced operative time, fewer perioperative complications, and less postoperative pain (47). A systematic review also indicates similar advantages of these new energy devices over monopolar or bipolar devices in gynecologic laparoscopy (48). While these new energy devices (harmonic scalpel, LigaSure, EnSeal) may incur higher costs than monopolar or bipolar devices, the cost savings associated with gasless laparoscopy could offset these expenses. Therefore, the use of energetic devices in gasless laparoscopy warrants evaluation in future prospective studies.

Regarding the limitations of our study, the use of WoSCC as the only database means that studies published in other databases, such as Scopus or MEDLINE, may have been omitted. It is known that different databases have a varied coverage of journals according to geographical areas. Scopus and WoSCC have been shown to under-record journals from Africa and South America compared to other regions of the world (49). Another limitation is the exclusion of articles applied to animal or cadaveric models, which could create a bias in our analysis as it is possible that important information, such as new methods or applications of this surgical technique, could be omitted. However, WoS offers a large amount of data and information about the articles, which increases the quality of the analysis of the journals and has allowed standardization of the data. Furthermore, approximately 99.11% of the journals indexed in WoSCC are also indexed in Scopus, which does not cause significant differences (50). Additionally, documents in languages other than English may have been ignored since only English documents were included, potentially overlooking relevant studies published in other languages. In the future research, literature related to gasless laparoscopy should be collected from multiple bibliographic databases to provide a more comprehensive overview of scientific production in this field.

In conclusion, the results of the present study show a low and oscillating production of scientific output on gasless laparoscopy. Initially the focus of the studies on this technique was on the complications of pneumoperitoneum and the feasibility of the technique. Later research is aimed at new applications of gasless laparoscopy, such as single incision laparoscopy or its application in children. The most productive authors are located in Japan, the country with the highest number of publications according to the corresponding author. To date, this is the first study analyzing the scientific production on gasless laparoscopy, showing the current state of research in this field and laying the groundwork for possible future publications.

Data availability statement

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

Author contributions

JP-R: Conceptualization, Data curation, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. BA-G: Conceptualization, Data curation, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. RD-R: Investigation, Validation, Writing – review & editing. AH-V: Data curation, Formal Analysis, Methodology, Project administration, Software, Supervision, Validation, Writing – original draft, Writing – review & editing.

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Conflict of interest

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

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Novel workflow analysis of robot-assisted hysterectomy through objective performance indicators: a pilot study

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Introduction: The curriculum for a da Vinci surgeon in gynecology requires special training before a surgeon performs their first independent case, but standardized, objective assessments of a trainee's workflow or skills learned during clinical cases are lacking. This pilot study presents a methodology to evaluate intraoperative surgeon behavior in hysterectomy cases through standardized surgical step segmentation paired with objective performance indicators (OPIs) calculated directly from robotic data streams. This method can provide individual case analysis in a truly objective capacity.

Materials and methods: Surgical data from six robot-assisted total laparoscopic hysterectomies (rTLH) performed by two experienced surgeons was collected prospectively using an Intuitive Data Recorder. Each rTLH video was annotated and segmented into specific, functional surgical steps based on the recorded video. Once annotated, OPIs were compared through workflow analysis and across surgeons during two critical surgical steps: colpotomy and vaginal cuff closure.

Results: Through visualization of the individual steps over time, we observe workflow consistencies and variabilities across individual surgeons of a similar experience level at the same hospital, creating unique surgeon behavior signatures across each surgical case. OPI differences across surgeons were observed for both the colpotomy and vaginal cuff closure steps, specifically reflecting camera movement, energy usage and clutching behaviors. Comparing colpotomy and vaginal cuff closure time needed for the step and the events of energy use were significantly different ($p<0.001$). For the comparison between the two surgeons only the event count for camera movement during colpotomy showed significant differences ($p=0.03$).

Conclusion: This pilot study presents a novel methodology to analyze and compare individual rTLH procedures with truly objective measurements. Through collection of robotic data streams and standardized segmentation, OPI measurements for specific rTLH surgery steps can be reliably calculated and compared to those of other surgeons. This provides opportunity for critical standardization to the gynecology field, which can be integrated into individualized training plans in the future. However, more studies are needed to establish context surrounding these metrics in gynecology.

KEYWORDS

robot-assisted total hysterectomy, surgical data science, objective performance indicators, surgical workflow, intuitive data recorder, surgical annotation, Da Vinci surgical system

Introduction

Since the introduction of the da Vinci Surgical System in the 1990s, its use has gained importance in gynecology and other surgical fields (1–3). Since then, Intuitive has established curricula to be completed before the surgeon uses the da Vinci Surgical System in the operating room, as robotic surgery performance has been shown to be dependent on the expertise of the surgeon (4). However, there is still limited understanding of a true surgical learning curve (5). Most studies define the learning curve of robotic surgery via reduced surgical time, docking time, console time, rates of complications, blood drop, and time of hospital stay (5–7). Moreover, many assessments are time-and resource-consuming, subjective, not reproducible, and poorly comparable across surgeons.

One of many ways to look at surgical behavior and the improvement of robotic surgical skills may be the analysis of workflows using individual application of camera movement, energy use and clutching to reposition the hands within the console during specific surgical steps. These robotic data streams can be captured directly from the da Vinci Surgical System using an Intuitive Data Recorder (IDR, Intuitive Surgical Ltd., Sunnyvale, California, United States) (8). Recently, the field of surgical data science has emerged, with a growing interest in objective performance indicators (OPIs), metrics calculated directly from the robotic system's data streams, that provide truly objective measurements and behaviors within individual surgeries (9, 10). OPIs have been utilized in other surgical specialties to correlate with surgical skill, workflow, and outcomes (11, 12), but no studies have been performed for gynecology procedures.

This feasibility study, which is the first in the gynecology space, introduces a methodology specific robot-assisted total laparoscopic hysterectomy (rTLH) and utilizes it to evaluate surgical workflow and intraoperative behaviors using OPIs. With more research in this space, such objective parameters will enable surgeon proficiency identification and tailored training to the learning surgeon.

Materials and methods

Raw data collection and annotation

Six rTLH were performed at the Department of Women's Health at the University Hospital of Tübingen using the da Vinci Si surgical system (Intuitive Surgical Ltd., Sunnyvale, California, United States). Synchronized video and accompanying robotic data streams were captured using an IDR on loan from Intuitive Surgical for the purpose of this study. All data were encrypted (AES-256) and stored on the Intuitive Data Recorder. Data were copied to an external hard disk (with encrypted access) and sent to Intuitive Surgical for professional annotation. No sound was recorded and neither patient nor surgeon were identifiable from the recordings. Date and time markers were part of the data captured from the da Vinci Surgical System, data allowing identification of the patient was not forwarded to Intuitive. Video annotation started with the insertion of the camera to the abdominal cavity. Video scrubbing algorithm was used to block out endoscope events outside of the body to guarantee patient and OR staff anonymity.

Each video was segmented into functional surgical steps specific to rTLH by a professional annotator (LP), a data scientist trained in gynecologic anatomy and all surgical steps of rTHL. The annotator indicated the start and stop times of each step according to a standardized annotation card (Table 1), which provides a detailed start and stop action for the specific surgical step (Figure 1). Each step may occur multiple times, identifying when a surgeon alternates between steps. As annotations were limited to functional steps, gaps between steps could also be identified. These include cleaning of the camera, change of instruments, surgeon idle time, etc. When a surgeon switched from one surgical step to the next within 2 seconds, no gap would be inserted by the annotator. Metric data that can be extracted via the IDR from the robot are: frequency of camera movement, energy use and clutch use for each side. Within each surgical step these parameters were used to calculate surgical activity within the time parameters of each step. Hereby OPIs can now be analyzed for each individual surgical step. These provide a truly objective measure of surgical behavior that can be attributed to specific rTLH steps. Since during colpotomy and closure of the vaginal cuff camera movement, use of energy and clutch use are frequently applied in every hysterectomy and therefore a large amount of data was available, these two surgical steps were examined in detail.

Ethics statement

Ethical approval was obtained from the Ethics Committee of Tübingen University Medical Faculty and University Hospital (621/2018BO1). Three operations, each performed by two experienced da Vinci surgeons, were selected to evaluate the feasibility of the method in this pilot study.

Statistical analysis

Statistical analysis was performed with Microsoft excel and R version 4.3 and RStudio version 2023.06.1 + 524 using the tidyverse

TABLE 1 Functional surgical steps utilized for annotation during rTLH.

	Surgical step name
1	Mobilize Colon/Removal of Adhesions (optional)
2	Dissection of Fallopian Tube (Left/Right side) (optional)
3	Dissection of IP Ligament (Left/Right side) (optional)
4	Dissection of Utero-Ovarian Ligament (Left/Right side) (optional)
5	Division of the Round Ligament (Left/Right side)
6	Division of the Broad Ligament (Left/Right side)
7	Bladder Flap Creation
8	Division of Uterine Vessels (Left/Right side)
9	Colpotomy
10	Removal of the Uterus
11	Vaginal Cuff Closure

Steps are listed in the order in which they first appear during a standardized laparoscopic hysterectomy. As not all steps might be required during hysterectomy step 1 to 4 are optional steps. The order of the individual steps may vary depending on the individual operation.

Abbreviations: OPI, objective performance indicator; rTLH, robot-assisted total laparoscopic hysterectomy.

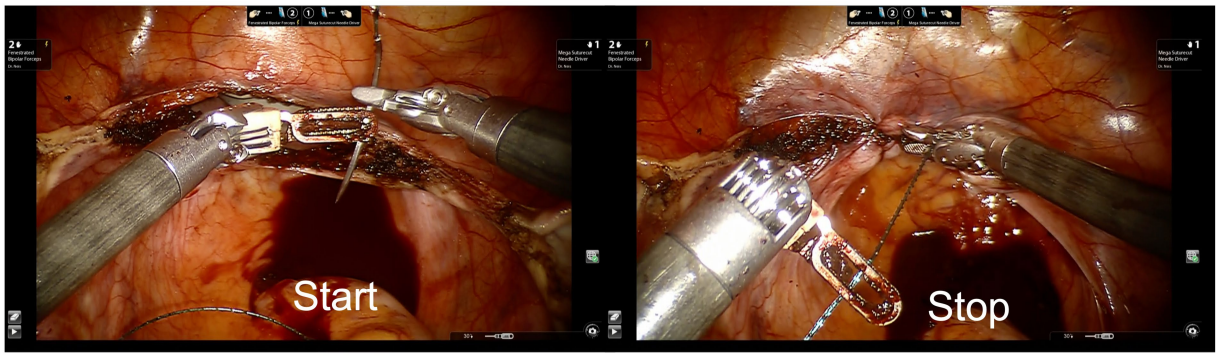

FIGURE 1
Images depicting start and stop moments for segmentation of hysterectomy. Vaginal cuff closure is presented as an example here. The surgical step begins with the clamping of the needle in the needle holder and ends with the cutting of the barbed thread after complete closure of the colpotomy.

(2.0.0) packages. Statistical comparisons were carried out with the student's *t* test. The data are expressed as the mean ± standard deviation. *p* values of <0.05 indicate statistical significance.

Results

Visualization of standardized surgical steps across two experienced surgeons enable rTLH workflow comparison

Individual steps across six rTLH cases from two experienced surgeons, who performed more than 30 TLHs using the da Vinci surgical system, were segmented, plotted, and compared (Figure 2). Case numbers 1–3 were performed by surgeon A, while cases 4–6 were performed by surgeon B. Patient characteristics are displayed in Table 2. By displaying each individual step over time, it is possible to observe the sequence of surgery exactly. Roughly similar sequence patterns were observed across the individual surgeries and across the two surgeons, with dissection of the fallopian tube followed by dissection of the round ligament, dissection of the broad ligament, bladder flap creation, division of the uterine vessels, colpotomy with removal of the uterus, and vaginal cuff closure using a barbed thread (Figure 1). An obvious difference observed was that surgeon A began with the hysterectomy on the left side, while surgeon B began on the right side. Despite the side differences on which surgery was stared, hereafter the surgical steps of all 6 surgeries follow the standard surgical steps described in the annotation card (Table 1—steps 5 to 11).

Additionally, all cases display both blank time periods with no surgical steps indicated and surgical step switching. Blank periods occur when the change between surgical steps last longer than two seconds, e.g., due to change of instruments, need to obtain additional equipment such as retrieval bags or morcellators, or idle time. Gaps were observed in all six surgeries. Surgical step switching in all cases indicates that although a general workflow can be observed, the surgeon would perform a step for a certain duration, then return to that same step, displaying unique workflow signatures.

Individual differences across cases can be observed, as well. In surgery no. 3, extensive adhesiolysis was performed at the beginning of the procedure (Figure 2, broad orange bar). This may not be required in all cases, as variable presence of adhesions may eliminate the need for this step. Additionally, surgery no. 4 exhibits a longer duration for removal of the uterus, which follows the colpotomy. This case represents a patient with a large uterus myomatosus, which could not be retrieved through the vagina, so a laparoscopic morcellation was performed. This is similar to surgery no. 6, although the removal of the uterus is in reverse order to surgery no. 4. In this particular surgery, a vaginal morcellation was performed for large uterus myomatosus followed by laparoscopic suturing of the colpotomy. Together, this visualization uncovers both similarities and differences in individual hysterectomies and reflects unique components to aide in analysis of surgical workflow. Patient characteristics are displayed in Table 2.

Step transition probabilities elucidate consolidated workflows of rTLH

Figure 3 shows the probability of the sequence of the surgical steps of all six rTLH surgeries. Lighter squares indicate a higher probability and black indicates that the transition never occurred. All surgeries start with the default "start" step and then the next step with highest probability is "mobilize colon/removal of adhesions (optional)," but "dissection of fallopian tube (r side) (optional)" and "division of the broad ligament (r side)" also occur with smaller probability. As most surgeries end with the vaginal cuff closure this square is the lightest in the last line. In one case the uterus was morcellated due to the size after the vaginal cuff closure, so there is also a square indicating the probability of the removal of the uterus which is darker than the one for vaginal cuff closure.

Surgical step order was determined from the calculated median fractional step order, but if a step had both a left and a right variant (e.g., Division of the Broad Ligament), then right was ordered before left. This fixed ordering provided consistency, as the right and left variants of a step had similar fractional step orders. Dissection of the infundibulopelvic ligament was excluded in this figure, as this step occurred only twice, once left and once right in case 5. A linear progression of the individual surgical steps from the upper left to the lower right corner of the diagram is apparent. Deviations from the direct diagonal indicate deviation from the standardized sequence of the individual surgical steps.

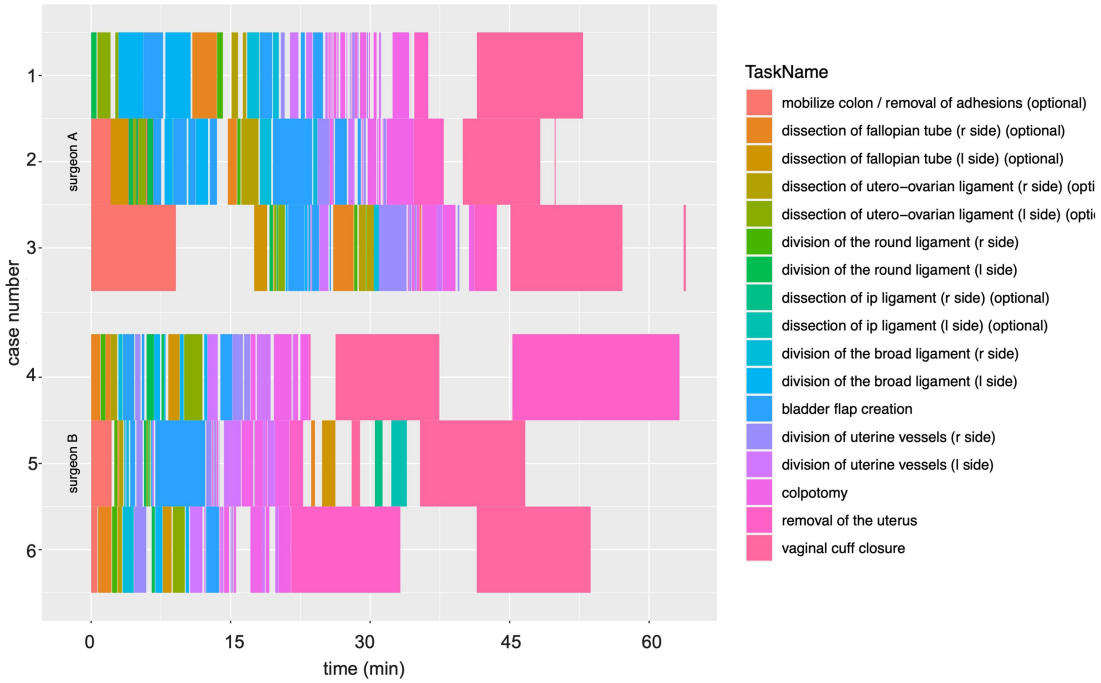

FIGURE 2
Visualization of surgical workflows across six unique rTLH cases enables objective workflow comparisons. Each color bar represents a surgical step with the length of the bar corresponding to its duration. Gaps between steps indicate idle time or surgical activity not aligned to the standardized hysterectomy steps. The existence of multiple bars of the same step name represent step switching by the surgeon or pause from the surgeon. All cases exhibited step switching and lapses between surgical steps, with each case exhibiting an individualized signature, enabling insights into surgical technique and workflow.

TABLE 2 Patient characteristics.

Pat. No.	1	2	3	4	5	6
Surgeon	A	A	A	B	B	B
Indication	Adenomyosis Fibroids	Fibroids	Fibroids	Fibroids	Fibroids	CIN III, Hypermenorrhea
Age (years)	47	44	45	45	58	49
BMI (kg/m^2)	22.3	21.8	20.5	38.5	35.3	21.0
Uterus weight (gram)	240	368	202	375	104	130
Duration (min)	75	72	85	103	82	65
Special feature	Peritoneal Endometriosis	–	Adhesions, Ovarian cyst	Laparoscopic morcellation	Adnexectomy, Adhesions	Vaginal morcellation, Deep infiltration Endometriosis: Adhesions
Previous abdominal surgeries	Diagnostic laparoscopy	–	Cesarean section, Transversal laparotomy because of adhesions	Laparoscopic cholecystectomy	Cesarean section	–

Note that the center diagonal, consisting of a surgical step followed by the same surgical step, is almost black with the exception of "vaginal cuff closure" indicating, that there was an alternation of steps. The parallel diagonal lighter lines beside the "black" line indicate a tendency of surgeons to keep working on the same side.

OPI comparisons for colpotomy and vaginal cuff closure

OPIs have been shown to provide insight into intraoperative surgeon behavior (13, 14). In addition to comparison of surgical step duration and workflow, data captured directly from the robotic data streams, such as events of energy use, clutching behavior, and camera movements were calculated into OPIs and observed. For detailed analysis of OPIs we choose the two most complex and standardized surgical steps of TLH: colpotomy and vaginal cuff closure. When comparing colpotomy to vaginal cuff closure for all six surgeries time (seconds) needed for the step (281.1 ± 83.7 vs. 677.5 ± 81.0) and the events of energy use (38.2 ± 11.3 vs. 6.3 ± 3.1) were significantly different ($p < 0.001$) (see Figure 4). For the events of camera movement and clutch use no differences were observed.

Importantly, OPI differences between the two surgeons were observed (see Figure 5). In comparable time of the respective steps,

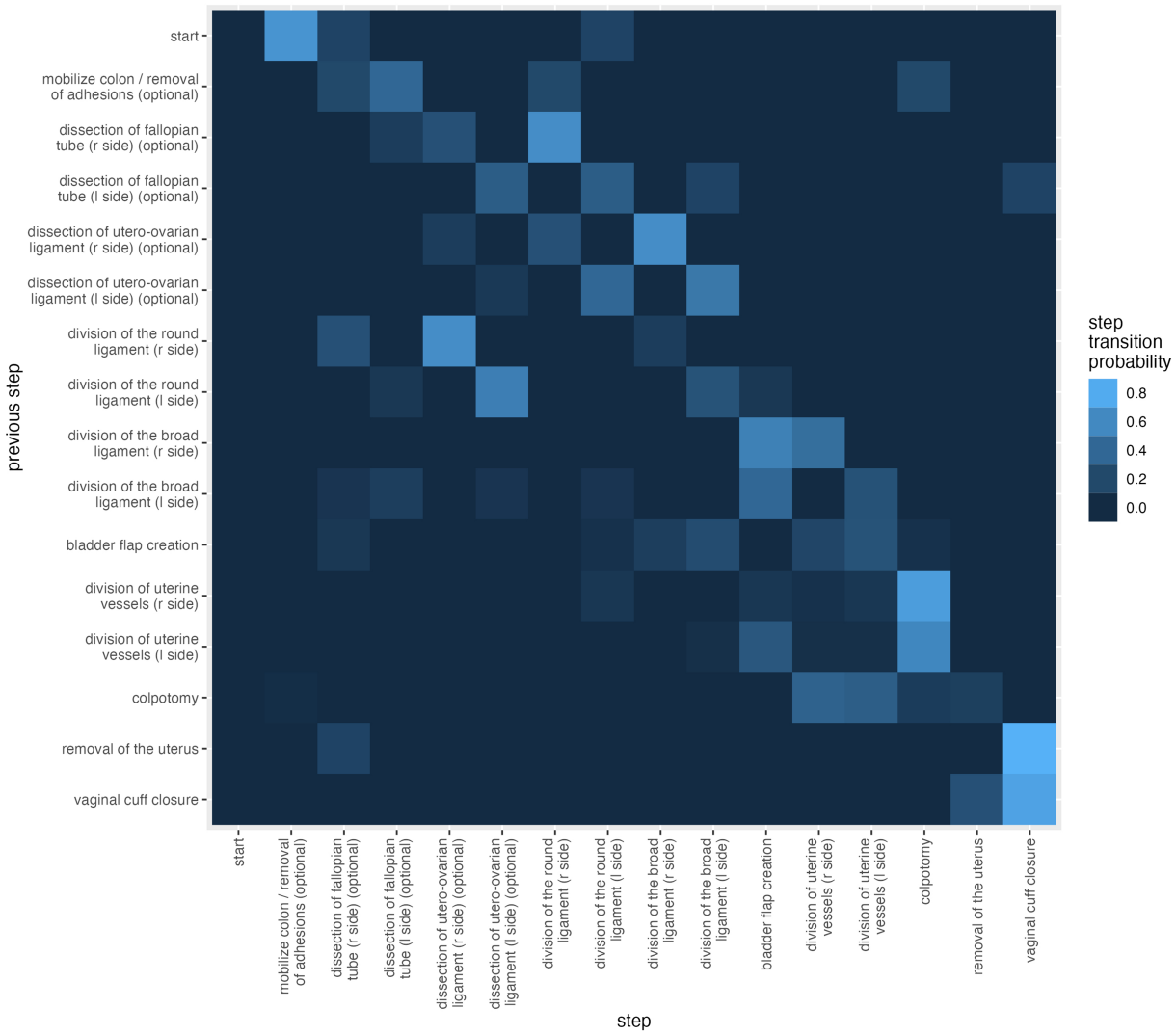

FIGURE 3
Step transition probability from six procedures from two surgeons combined. The ordering is right/left for paired steps.

the event count for camera movement varies significantly between the two surgeons during the colpotomy step (surgeon A: 35.3 ± 7.6, surgeon B: 18.3 ± 5.3; $p = 0.03$) but not for vaginal cuff closure (surgeon A: 21.7 ± 15.1, surgeon B: 14.7 ± 5.3; $p = 0.28$). Clutching event count (addition of event clutch left, right and both) showed no significant differences between the two surgeons performing colpotomy and vaginal cuff closure (colpotomy: surgeon A: 7.3 ± 3.1, surgeon B: 2.7 ± 0.5; $p = 0.051$ and vaginal cuff closure: surgeon A: 9.0 ± 0.8, surgeon B: 6.3 ± 4.9; $p = 0.25$). Use of energy during colpotomy and vaginal cuff closer showed no significant difference between the two surgeons (colpotomy: surgeon A: 35.3 ± 9.3, surgeon B: 41.0 ± 12.3; $p = 0.09$ and vaginal cuff closure: surgeon A: 4.3 ± 2.4, surgeon B: 8.3 ± 2.5; $p = 0.32$), despite energy use was, as typical for this step, more frequently during colpotomy. Outliers in the frequency of current application indicate difficulty in hemostasis at the vaginal edges. Although the difference in clutching during colpotomy is not significant, there is a trend towards more actions for surgeon A, which provides preliminary feasibility for the need for future investigation.

Discussion

This study provides the gynecology field a novel methodology to investigate OPIs in rTLH. We utilize this method to compare surgical workflows and surgeon behaviors across cases and surgeons. We show that annotation and visualization of independent surgical steps enables workflow comparisons across individual surgeries, as well as identification of OPIs differences and similarities in surgeon behavior. This could be a tool to monitor and adjust learning plans for gynecologic robotic surgery trainees. Together, this work lays the foundation for future gynecology studies using case segmentation and OPIs.

Hysterectomy is a highly standardized operation with fixed sequential surgical steps (15). As such, it was an ideal model to visualize surgical workflow changes for a small data set across two surgeons. In the step transition probability analysis (Figure 3), a clear workflow can be seen reliably from step to predicted step, supporting the high standardization of this procedure. We do observe a slight divergent dimming in the middle of the heat map, illuminating two

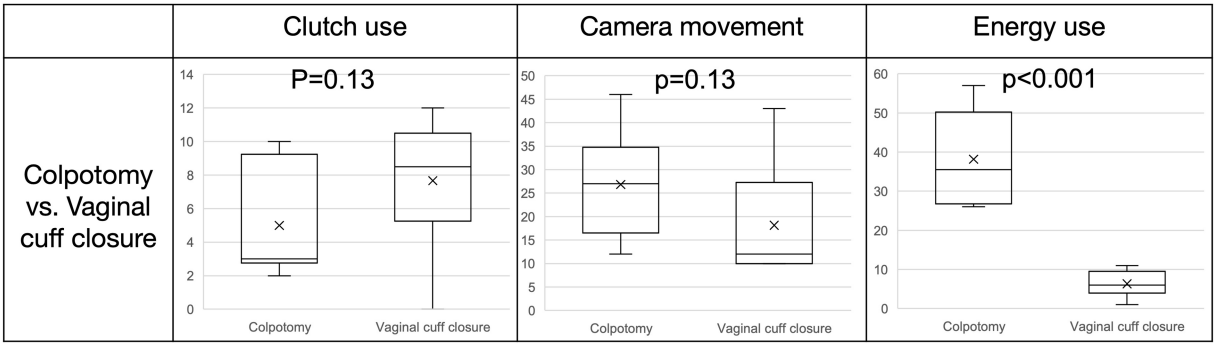

FIGURE 4
Whisker box plot. Comparison of event counts (clutch use, camera movement and energy use) between colpotomy and vaginal cuff closure for all six surgeries.

distinct surgical approaches across surgeons; Surgeon A began hysterectomies on the left side and Surgeon B on the right side. Together, this work provides feasibility for unique surgical workflow signatures, which could be used for training, identification of complex cases, surgical techniques, and more. Metchik demonstrated that using a forward and backward entropy, similar to our model, behavioral patterns in the change between individual surgical steps can be shown in order to improve learning curves and workflows (16).

In this study, we analyzed the two most standard surgical steps in rTLH in detail: colpotomy and closure of the vaginal cuff. Since the circumference of the vagina must be viewed during the colpotomy, this surgical step exhibits high counts of camera movements. The use of energy is also high during this step as the vagina is opened by using monopolar energy. Despite both surgeons being experienced in rTLH, remarkably, clear OPI differences were observed. Thus, with the help of OPIs, not only can surgical workflow be elucidated, differences in surgical techniques and preferences can be identified and compared. In the future, it may be possible to distinguish between different surgeons and different surgeries based on the analysis of OPI signatures alone.

Our proposed methodology may enable tailored gynecology learning plans and opportunities to track learning progress. Although this study compared surgeries performed by experienced surgeons, it is likely that there will also be differences between experts and trainees, as has been shown in previous OPI studies in other specialties (10, 13). Other studies have shown the potential for similar metric data to track learning progression, such as Turner's et al work in simulator studies (17) and Ma's et al work in tissue models (18). These and other investigations of OPI utility have been increasing for the past 5 years, showing promise for surgical workflow analysis, training, skill, and correlation to patient outcomes (18, 19). This work is most prevalent in urology (13, 14, 18, 19), with limited published work emerging in the thoracic (9, 10) and general surgery specialties (8, 11, 20). However, no studies to date have utilized such technologies and methodologies in gynecology. As such, much work is needed in clinical gynecology cases to validate this potential.

International societies such as the European Society for Gynaecological Endoscopy (ESGE) have recognized the importance of developing structured training in robotics and have drawn up their own curriculum (Gynaecological Endoscopic Surgical Education and Assessment—GESEA programme) (21). In the future, analyses of segmented videos and OPIs could become part of such a structured learning concept in order to objectively quantify learning progress and possibly compare it with a large group of robotic surgeons.

The addition of visualization of surgical workflows, as shown in Figure 2, to the analysis of OPIs provide the additional advantage of identifying difficult situations during the surgery. This can be helpful in monitoring learning progress. Unusual situations can be reviewed retrospectively using video to identify deviations from the standard to fine tune training.

Although we present significant advantages to OPI evaluations, this study has a number of limitations. It must be noted that this work is a feasibility study on the use of a recorder for video and metric data for the use of the da Vinci Surgical System, which initially covers only six surgeries. Further studies are needed to support the data presented here and pave the way for routine use of OPI measurements. Additionally, this study does not utilize any trainees or surgeons that are in the initial stages of their learning curve, which will be critical for future studies. Although we evaluate surgeon behavior use as it pertains to camera manipulation, energy use, and clutching, we did not investigate any kinematic indicators of performance, which will be needed to elucidate surgeon behaviors in the future. Since a barbed thread was used for the vaginal flap closure, the knotting, which requires special fine motor skills, was not part of the study.

Together, the foundation laid in this work opens the door to countless and critical future investigations for truly objective characterizations and inquiry of intraoperative surgical behaviors, which can be used to train exceptional surgeons objectively and efficiently, leading to better patient outcomes.

Conclusion

This pilot study presents a novel methodology to analyze and compare individual hysterectomy procedures across surgeons with truly objective measurements. Through collection of robotic data streams and standardized segmentation of hysterectomy cases, OPI measurements for specific rTLH surgery steps can be reliably calculated and compared to those of other surgeons. Utilization of this methodology provides opportunity for critical standardization to the gynecology field, which could be integrated into individualized training plans in the future. However, more data is needed to establish context surrounding these metrics as they pertain to gynecology.

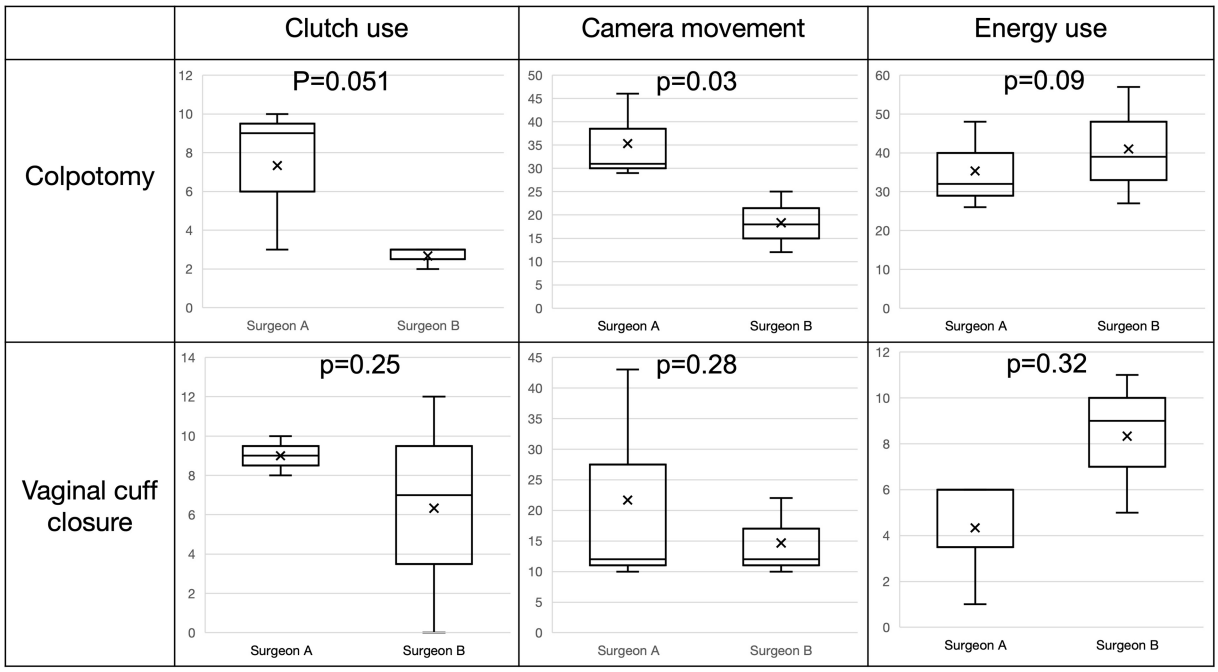

FIGURE 5
Event counts for clutch use, camera movements, and energy use can be compared across surgeons for specific steps. Box and whisker plots comparing event counts of clutching, camera movements, and energy use during colpotomy (top) and vaginal cuff closure (bottom) for Surgeon A and B during rTLH. "*x*" represents mean.

Data availability statement

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

Ethics statement

The studies involving humans were approved by the Ethics Committee of Tübingen University Medical Faculty and University Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

FN: Conceptualization, Data curation, Formal analysis, Project administration, Writing – original draft. SB: Conceptualization, Writing – review & editing. AB: Writing – review & editing. MS: Writing – original draft, Writing – review & editing. LP: Data curation, Formal analysis, Writing – review & editing. XL: Data curation, Formal analysis, Writing – review & editing. ME: Data curation, Formal analysis, Writing – review & editing. CW: Writing – review & editing. TD: Data curation, Formal analysis, Visualization, Writing – original draft. CR: Writing – review & editing. BK: Conceptualization, Writing – review & editing.

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Conflict of interest

MS, LP, XL, and ME were employed by Intuitive Surgical Inc.

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

Publisher's note

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Adoption strategies of fertility-sparing surgery for early-stage cervical cancer patients based on clinicopathological characteristics: a large retrospective cohort study

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Background: The demand for fertility-sparing surgery (FSS) is increasing among patients with early-stage cervical cancer (CC). This study aimed to evaluate the feasibility of local excision as an alternative to hysterectomy in stage I CC patients aged 15–39 years—commonly referred to as adolescents and young adults (AYAs)—with varying clinicopathological characteristics.
Methods: Using the Surveillance, Epidemiology, and End Results (SEER) database, we identified patients diagnosed between 2000 and 2020. We examined treatment interventions across different age groups, degrees of histological types, tumor differentiation, and tumor stages. The effect of local excision vs. hysterectomy was assessed by comparing overall survival (OS) and disease-specific survival (DSS) rates.
Results: A total of 10,629 stage I AYA cervical cancer patients were included in this study. Among these patients, 24.5% underwent local excision for fertility preservation, while 67.3% underwent radical hysterectomy. For patients with cervical squamous cell carcinoma (SCC), long-term outcomes favored local excision over hysterectomy, and a similar trend was observed in those with adenosquamous cell carcinoma (ASCC). However, the prognosis was comparable among patients with cervical adenocarcinoma (AC). In patients with well- and moderate- differentiated tumors, local excision demonstrated superior OS compared to hysterectomy. No significant differences in prognosis were found between the two surgical interventions for patients with poorly differentiated and undifferentiated tumors. In stage IA patients, local excision was considered a viable alternative to hysterectomy. In stage IB1–IB2, FSS yielded prognostic outcomes comparable to those of hysterectomy. Conversely, patients with stage IB3 exhibited significantly shorter 5-year OS and DSS following local excision than those who underwent hysterectomy.

Conclusion: In stage IA–IB2 (diameter ≤4 cm) AYA patients, local excision may serve as a viable option for fertility preservation. The histological type of SCC, AC, and ASCC, along with differentiation, should not serve as restrictive factors in determining fertility preservation strategies for these patients. Patients with early-stage, well- or moderately-differentiated SCC may benefit from local excision surgery, even when fertility preservation is not the primary objective.

KEYWORDS

early-stage cervical cancer, fertility preservation, local excision, hysterectomy, prognosis

1 Introduction

Cervical cancer (CC) is the most prevalent malignancy of the female reproductive system, with significant global health implications (1). In 2022, there were an estimated 662,301 new cases and 348,874 deaths attributed to cervical cancer worldwide (2). Among these figures, individuals aged 15–39 years—commonly referred to as adolescents and young adults (AYAs)—accounted for 105,728 new cases and 32,575 deaths, making CC the third most common cancer and the second leading cause of cancer-related mortality among young females (2). Despite the implementation and increasing uptake of cancer initiatives in numerous countries, the incidence of CC among young women has shown a troubling upward trend in certain regions in recent years (3).

For patients diagnosed with early-stage CC, the standard treatment is radical hysterectomy with or without pelvic lymph node dissection. The 5-year survival rate for stage I CC patients exceeds 90% (4). Currently, the focus of treatment for young patients has shifted from solely improving survival rates to enhancing quality of life (5). Given that the AYA demographic encompasses prime reproductive years, fertility preservation is a crucial consideration for maintaining a satisfactory quality of life. As societal trends increasingly lead young women to marry later in life, many of these individuals express a strong desire to conceive following a cancer diagnosis (6–9). Moreover, studies have indicated that the loss of fertility in women with a history of gynecological malignancies can adversely affect their mental health and sexual function (10). Consequently, preserving fertility in AYA cervical cancer patients has emerged as a significant challenge.

For those patients who prioritize fertility preservation, available surgical options for fertility-sparing surgery (FSS) include conization or simple cervical excision, as well as (vaginal or abdominal) radical trachelectomy. However, the feasibility of FSS is influenced by various factors, such as age at diagnosis, tumor pathological characteristics, and International Federation of Gynecology and Obstetrics (FIGO) stage. While extensive follow-up studies at several medical institutions have substantiated the efficacy of local excision to some extent, comprehensive research offering a broad spectrum of FSS options across diverse patient populations is lacking. Thus, there is an urgent need for extensive studies to evaluate the safety of local excision compared with hysterectomy in patients with varying clinicopathological characteristics (11). This study endeavored to investigate the treatment modalities for stage I AYA cervical cancer patients, and to assess the safety of local excision as an alternative to hysterectomy across different patient profiles. By doing so, we seek to establish a framework for the personalized selection of FSS, thereby providing a theoretical foundation for clinical decision-making in this patient population.

2 Materials and methods

2.1 Data source

The data for this study were sourced from the Surveillance, Epidemiology, and End Results (SEER) database, a resource supported by the National Cancer Institute (NCI) of the United States. Encompassing approximately 30% of the U.S. population, the SEER database furnishes comprehensive data on patient demographics, tumor-related characteristics, diagnosis, treatment modalities, and subsequent follow-up. For the purposes of this study, the SEER*Stat 8.4.3 version was utilized to aggregate data from patients spanning the period from 2000 to 2020. The SEER database upholds stringent measures to safeguard patient confidentiality, and research conducted utilizing this database is not contingent upon obtaining ethical approval post-application review. Importantly, this study adhered to the principles outlined in the Helsinki Declaration.

2.2 Study cohort selection

Initially, patients with cervical lesions were identified by selecting the ICD-10 codes "C53.0–C53.9". We subsequently collected basic patient information, including age, marital status, and ethnicity, as well as socioeconomic factors such as income and residence. Additionally, we gathered data on tumor characteristics, including pathological type, tumor differentiation, and FIGO staging, along with information regarding treatment and prognosis. Patients were categorized into four groups according to age: 15–24 years, 25–29 years, 30–34 years, and 35–39 years. Further stratification was performed based on marital status, dividing patients into married, single (including unmarried), or separated (including divorced, separated, or widowed) individuals. Ethnicity information primarily categorized patients into black, white, and other ethnic groups. Based on income status, patients were divided into three groups: high, medium, and low, with thresholds set at $35,000–$75,000

annually. Residential information stratified patients into urban and rural groups. The histological differentiation types were identified as squamous cell carcinoma (SCC), adenocarcinoma (AC), adenosquamous carcinoma (ASCC), and other subtypes. Patients were divided into Grade 1–2 (well and moderately differentiated) and Grade 3–4 (poorly differentiated and undifferentiated) groups according to their histological grade. Based on the description of surgical information, patients who underwent hysterectomy, local excision, or did not undergo surgery were included, excluding cases with only lesion destruction or inadequate surgical records. Local excision surgeries include "Local tumor excision, NOS", "Local tumor excision with electrocautery", "Local tumor excision with cryosurgery", "Cone biopsy with gross excision of lesion", "Dilatation and curettage; endocervical curettage (for *in situ* only)", "Excisional biopsy, NOS", "Cone biopsy", "Cone biopsy with gross excision of lesion", "Trachelectomy; removal of cervical stump; cervicectomy". Hysterectomy surgeries include "Total hysterectomy", "Modified radical or extended hysterectomy", "Radical or extended hysterectomy", "Hysterectomy, NOS", and "Pelvic exenteration". Survival indicators were collected, including survival time, survival status, and causes of death. Patients with missing survival data were excluded. Overall survival (OS) was defined as the time from diagnosis to death, whereas disease-specific survival (DSS) was defined as the time from diagnosis to death specifically attributable to cervical cancer. Duplicate patient IDs were eliminated to ensure data integrity. The detailed filtering process was shown in Figure 1.

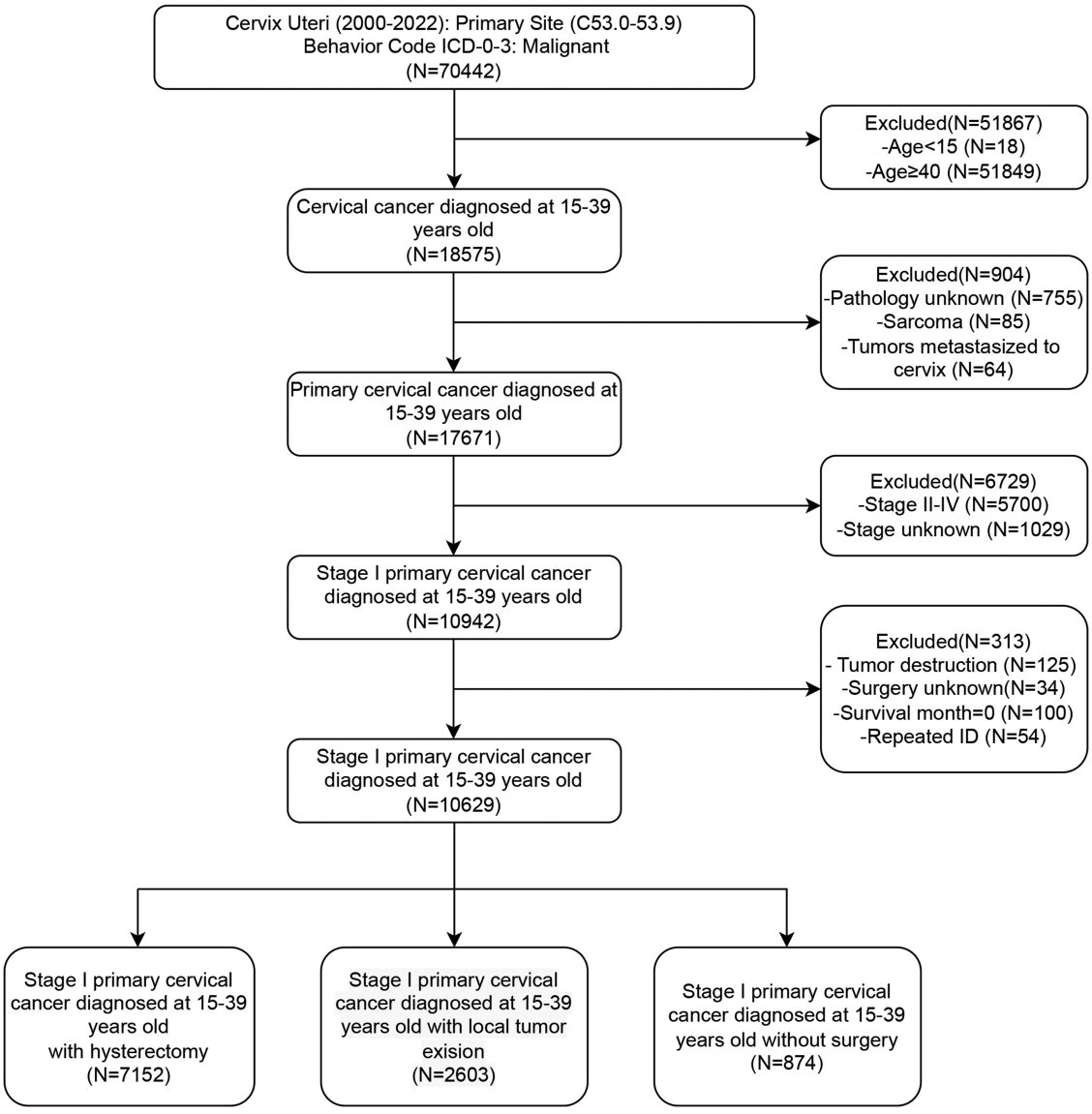

FIGURE 1
Screening flowchart.

2.3 Statistical analysis

Kaplan-Meier curves were generated to depict the prognosis of patients receiving different surgical interventions, and distinctions between these curves were evaluated through the log-rank test. Multivariate Cox regression analyses were applied to scrutinize the factors impacting prognosis, with the significance of these factors quantified by hazard ratios (HRs) and 95% confidence intervals (CIs). Statistical analyses and graphical representations were conducted using SPSS 26 and GraphPad Prism 9. A significance threshold of $P < 0.05$ was established to determine statistical significance.

3 Results

3.1 Patient clinical and pathological characteristics

We conducted a retrospective analysis of 10,629 stage I AYA cervical cancer patients between 2000 and 2020. Patients were categorized into three groups based on their surgical interventions: 67.3% of the patients (7,152 cases) underwent radical hysterectomy, 24.5% (2,603 cases) underwent fertility-preserving local excision, and 8.2% (874 cases) did not undergo any surgical intervention. The majority of patients (approximately 80%) were aged between 30 and 39 years. Notably, more than 50% of patients undergoing hysterectomy were in the 35–39 years group, while the highest proportion of those undergoing local excision were in the 30–34 years group. In terms of marital status, 54.2% of the patients who received a hysterectomy were married, suggesting that they may have already had children and experienced a decreased desire for fertility preservation. Conversely, a greater proportion of patients who underwent local excision were single or unmarried, indicating a greater desire for fertility preservation. Histologically, SCC was the most common subtype, accounting for 64.9%, followed by AC at 29.9%. ASCC and other histological types accounted for only 3.8% and 1.4%, respectively. In terms of FIGO stage, patients undergoing hysterectomy were evenly distributed in stages IA and IB, while the patients who underwent local excision were mostly in the earlier stage IA (72.1%), and the majority of those who did not undergo surgery were in the later stage IB (75.4%). Most of the patients who did not undergo surgery received radiotherapy and/or chemotherapy, whereas lower than 10% of the patients who underwent local excision received concurrent radiotherapy and/or chemotherapy (Table 1).

3.2 Treatment choice and prognostic impact of surgery in stage I CC

Surgical intervention has emerged as the primary treatment modality for AYA patients with stage I CC (Figure 2A). Among this cohort, a greater proportion of individuals in the 15–24 years group underwent local excision (local excision: 48.2% vs. hysterectomy: 42.0%). As age increased, the adoption of local excision declined gradually, whereas the preference for hysterectomy rose steadily. Among patients aged 35–39 years, only 14.9% chose local excision, whereas 76.8% underwent hysterectomy (Figure 2A). Survival analysis revealed that among all stage I AYA patients, those who underwent local excision exhibited significantly superior OS and DSS outcomes in comparison to those who underwent hysterectomy ($P < 0.001$) (Figures 2B,C).

3.3 Factors affecting the prognosis of stage I CC patients

The prognostic analyses indicated favorable outcomes for local excision over hysterectomy as a treatment option for AYA with stage I CC. However, these findings pertain to the cohort as a whole, and may not necessarily apply to every individual seeking fertility preservation. Importantly, patients' baseline characteristics, tumor attributes, and socioeconomic factors, play crucial roles as prognostic determinants. The different combinations of these factors for each patient may lead to distinct outcomes. Therefore, our study encompassed a range of variables, including age, marital status, race, income, residence, pathological subtype, histological differentiation, FIGO stage, and surgical approach, to conduct a comprehensive multivariate Cox regression analysis investigating the factors influencing OS and DSS in the patients. Our findings revealed that pathological subtype, differentiation, and stage were independent tumor factors influencing prognosis (Table 2). Upon adjusting for these variables, the choice between local excision and hysterectomy did not significantly impact OS (HR: 0.987; 95% CI: 0.8–1.218; $P = 0.904$) or DSS (HR: 1.033; 95% CI: 0.794–1.343; $P = 0.810$) in AYA patients with stage I CC.

3.4 Surgical interventions for stage I CC patients with various pathological subtypes

The multivariate Cox regression analyses highlighted the significance of pathological subtype, differentiation, and FIGO stage as independent factors influencing the prognostic outcomes of the patients. Subsequently, we delved into a stratified examination of these three tumor characteristics to explore potential differences in prognosis associated with distinct surgical interventions. Initially, we conducted separate analyses for SCC, AC, ASCC and other epithelial types of CC. Notably, the utilization of local excision tended to decrease with increasing age in patients with SCC and AC, dropping from approximately 50% in the 15–24 years group to 16.6% for SCC and 12.6% for AC in the 35–39 years group (Figures 3A,D). In contrast, the proportion of patients who underwent local excision remained consistently a low level for ASCC and other types across all age groups (ASCC: 9.9%–25.0%; others: 9.4%–24.3%) (Figure 3G, Supplementary Figure S1A). Prognostic analysis demonstrated

TABLE 1 Clinicopathologic profiles of stage I AYA cervical cancer with different surgery interventions.

Characteristics	Total *n* (%)	Hysterectomy *n* (%)	Local excision *n* (%)	None *n* (%)
Total	10,629 (100)	7,152 (100)	2,603 (100)	874 (100)
Age				
15–24	367 (3.5)	154 (2.2)	177 (6.4)	36 (4.1)
25–29	1,810 (17.0)	934 (13.1)	738 (28.4)	138 (15.8)
30–34	3,776 (35.5)	2,473 (34.6)	991 (38.1)	312 (35.7)
35–39	4,676 (44.0)	3,591 (50.2)	697 (26.8)	388 (44.4)
Marital state				
Marriage	5,210 (49.0)	3,878 (54.2)	1,009 (38.8)	323 (37.0)
Single	3,854 (36.3)	2,250 (36.1)	1,218 (46.8)	386 (44.2)
Separated	905 (8.5)	681 (9.5)	158 (6.1)	66 (7.6)
Unknown	660 (6.2)	343 (4.8)	218 (8.4)	99 (11.3)
Race				
Black	955 (9.0)	571 (8.0)	225 (8.6)	159 (18.2)
White	8,649 (81.4)	5,971 (83.5)	2,048 (78.7)	630 (72.1)
Others	864 (8.1)	543 (7.6)	261 (10.0)	60 (6.9)
Unknown	161 (1.5)	67 (0.9)	69 (2.7)	25 (2.9)
Income				
Low	84 (0.8)	64 (0.9)	8 (0.3)	12 (1.4)
Media	6,402 (60.2)	4,409 (61.6)	1,399 (53.7)	594 (68.0)
High	4,142 (39.0)	2,679 (37.5)	1,196 (45.9)	267 (30.6)
Rural/Urben				
Urben	9,470 (89.3)	6,317 (88.5)	2,410 (92.8)	743 (85.4)
Rural	1,132 (10.7)	819 (11.5)	186 (7.2)	127 (14.6)
Pathology				
SCC	6,893 (64.9)	4,399 (61.5)	1,821 (70.0)	673 (77.0)
AC	3,180 (29.9)	2,501 (32.5)	750 (26.9)	174 (18.2)
ASCC	406 (3.8)	318 (4.4)	61 (2.3)	27 (3.1)
Others	150 (1.4)	114 (1.6)	21 (0.8)	15 (1.7)
Grade				
1–2	5,033 (47.4)	3,710 (51.9)	1,082 (41.6)	241 (27.6)
3–4	2,080 (19.6)	1,600 (22.4)	282 (10.8)	198 (22.7)
Unknown	3,516 (33.1)	1,842 (25.8)	1,239 (47.6)	435 (49.8)
Stage				
IA	5,195 (48.9)	3,145 (44.0)	1,877 (72.1)	173 (19.8)
IB	5,238 (49.3)	3,913 (54.7)	666 (25.6)	659 (75.4)
I	196 (1.8)	94 (1.3)	60 (2.3)	42 (4.8)
Radiation				
No	8,592 (80.8)	5,993 (83.8)	2,354 (90.4)	245 (28.0)
Yes	2,037 (19.2)	1,159 (16.2)	249 (9.6)	629 (72.0)
Chemotherapy				
No	9,145 (86.0)	6,414 (89.7)	2,413 (92.7)	318 (36.4)
Yes	1,484 (14.0)	738 (10.3)	190 (7.3)	556 (63.6)

OS, overall survival; DSS, disease-specific survival.

that the therapeutic efficacy of local excision surpassed that of hysterectomy in patients with SCC (OS: 96.8% vs. 95.1%, $P = 0.004$; DSS: 97.9% vs. 96.0%, $P = 0.001$). A similar trend was observed in patients with ASCC (OS: 93.9% vs. 85.9%, $P = 0.027$; DSS: 93.9% vs. 87.8%, $P = 0.078$). Additionally, the treatment outcomes of local excision were comparable to those of hysterectomy in patients with AC (OS: 97.1% vs. 96.9%, $P = 0.353$; DSS: 97.5% vs. 97.6%, $P = 0.729$). Although the prognosis of ASCC is significantly lower than that of SCC and AC, the findings suggest that ASCC should not serve as a limiting factor for AYA with stage I CC to consider FSS (Figures 3B,C,E,F,H,I). In the context of other types of stage I CC, our analysis did not reveal a significant difference in efficacy between local excision and hysterectomy (Supplementary Figures S1B,C). However, it is important to note that the 5-year survival rate for other pathological types fell below 80%. Given the substantial surgical risks involved, the adoption of the FSS in patients with other histological types of CC warrants careful consideration and caution.

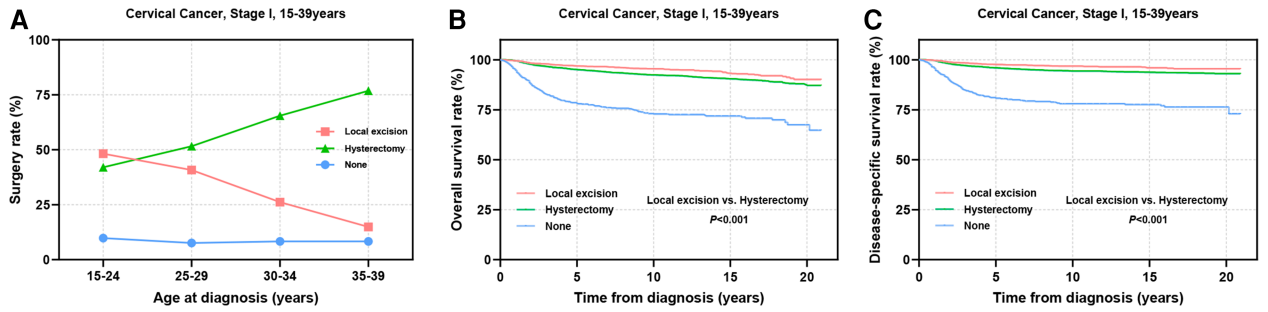

FIGURE 2
Prognosis of AYA stage I patients undergoing different types of surgical interventions. **(A)** The rate at which patients underwent local excision or hysterectomy; **(B,C)** OS and DSS of AYA stage I patients receiving local excision or hysterectomy.

3.5 Surgical interventions for stage I CCs of different degrees of histological differentiation

Tumors with low differentiation often indicate an increased potential for metastasis and a less favorable prognosis. Subsequently, we conducted a stratified analysis on patients based on differentiation status. Among patients with well or moderately differentiated tumors, it was observed that younger individuals tended to undergo local excision, while the utilization of local excision in patients with grade 3–4 tumors was lower than that in patients with grade 1–2 tumors (Figures 4A,D). Prognostic analyses revealed that substituting hysterectomy with local excision surgery in patients with well or moderately differentiated tumors is a viable option (OS: 97.3% vs. 95.9%, $P = 0.034$; DSS: 97.8% vs. 96.8%, $P = 0.089$) (Figures 4B,C). Although, grade 3–4 differentiation status emerged as an independent factor influencing prognosis, the prognosis of patients who underwent different surgical procedures did not appear to be significantly influenced solely by differentiation status (OS: 89.2% vs. 89.3%, $P = 0.587$; DSS: 90.5% vs. 90.2%, $P = 0.476$) (Figures 4E,F).

3.6 Surgical interventions for stage I CC patients at different tumor stages

The stage of cervical cancer plays a crucial role in determining prognosis and guiding surgical decision-making. Subsequently, we performed a stratified analysis on patients at stage IA and IB. Among patients at stage IA, the percentage of patients receiving local excision was notably high at 66.3% in the 15–24 years group, this percentage gradually declined to 22.3% with age advancing (Figure 5A). Conversely, for patients at stage IB, the adoption of local excision remained relatively low across all age groups (8.4%–24.7%) (Figure 5D). In the stage IA group, there were no significant disparities in OS (98.5% vs. 98.6%, $P = 0.853$) and DSS (99.4% vs. 99.2%, $P = 0.762$) between patients undergoing local excision and those receiving hysterectomy (Figures 5B,C). Similarly, among patients at stage IB, no statistically significance was observed in OS (91.4% vs. 92.2%, $P = 0.961$) and DSS (92.1% vs. 93.2%, $P = 0.926$) between the two surgical choices (Figures 5E,F).

The international application of FSS for CC patients remains controversial, primarily concerning the tumor size threshold. ESGO 2023 suggests that patients with SCC and HPV-related AC with a maximal tumor diameter ≤2 cm may be considered for FSS, while the National Comprehensive Cancer Network (NCCN) guidelines propose the possibility of fertility preservation for select stage IB2 (2 cm < diameter ≤ 4 cm) patients (12, 13). Thus, we further subdivided stage IB into IB1–IB3 for analysis. The results showed that the proportion of stage IB1 patients receiving local excision ranged from 9.3% to 37.5% (Figure 6A). For patients in IB2 stage, thia percentage decreased to 5.9%–20% (Figure 6D). Only 3.0%–8.9% of patients in IB3 stage underwent FSS (Figure 6G). Prognostic evaluation indicated comparable 5-year survival rates between the local excision and hysterectomy for stage IB1 patients (5-year OS: 94.7% vs. 95.9%, $P = 0.563$; 5-year DSS: 95.2% vs. 96.5%, $P = 0.904$) (Figures 6B,C) and stage IB2 patients (5-year OS: 88.0% vs. 89.0%, $P = 0.780$; 5-year DSS: 89.1% vs. 90.3%, $P = 0.727$), suggesting that FSS may be considered for stage I patients with tumor diameters of 2–4 cm (Figures 6E,F). In IB3 patients, although there was no statistically significant difference in long-term survival rates and DSS between the two surgical interventions (Figures 6H,I), patients undergoing local excision showed significantly reduced 5-year OS and DSS (5-year OS: 77.8% vs. 83.4%; 5-year DSS: 79.0% vs. 85.5%). Therefore, careful consideration is imperative for stage IB3 AYA patients opting for local excision.

3.7 Causes of death in AYA stage I CC patients

This study also investigated the cumulative mortality rates (CMRs) attributed to diverse causes of death in cervical cancer patients (Figures 7A–H). Patients undergoing local excision exhibited notably lower rates of cancer-related mortality in comparison to those undergoing hysterectomy ($P < 0.001$, Figure 7A). However, the mortality rate stemming from

TABLE 2 Multivariate Cox analysis of prognostic factors in stage I AYA cervical cancer patients.

Characteristics	OS		DSS	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age				
15–24	Reference		Reference	
25–29	1.25 (0.82–1.90)	0.309	1.16 (0.71–1.88)	0.556
30–34	1.39 (0.92–2.08)	0.114	1.23 (0.78–1.97)	0.376
35–39	1.42 (0.95–2.12)	0.092	1.06 (0.67–1.69)	0.798
Marital state				
Marriage	Reference		Reference	
Single	1.48 (1.26–1.73)	<0.001	1.30 (1.08–1.57)	0.006
Separated	1.54 (1.23–1.93)	<0.001	1.39 (1.05–1.84)	0.020
Unknown	1.51 (1.12–2.03)	0.007	1.29 (0.88–1.90)	0.192
Race				
Black	Reference		Reference	
White	0.77 (0.63–0.94)	0.009	0.67 (0.53–0.84)	0.001
Others	0.99 (0.73–1.34)	0.943	0.97 (0.69–1.36)	0.851
Unknown	0.18 (0.04–0.72)	0.015	0 (0–6.302 × 10^{53})	0.879
Income				
Low	Reference		Reference	
Media	0.65 (0.35–1.22)	0.179	0.69 (0.32–1.51)	0.349
High	0.57 (0.30–1.09)	0.089	0.66 (0.30–1.47)	0.308
Rural/Urben				
Urben	Reference		Reference	
Rural	1.07 (0.86–1.33)	0.563	1.00 (0.76–1.33)	0.975
Pathology				
SCC	Reference		Reference	
AC	0.71 (0.59–0.85)	<0.001	0.76 (0.61–1.00)	0.015
ASCC	1.69 (1.32–2.16)	<0.001	1.99 (1.51–2.61)	<0.001
Others	1.94 (1.27–2.97)	0.002	2.47 (1.59–3.82)	<0.001
Grade				
1–2	Reference		Reference	
3–4	1.37 (1.16–1.62)	<0.001	1.55 (1.28–1.88)	<0.001
Unknown	0.87 (0.72–1.06)	0.160	0.76 (0.60–0.98)	0.033
Stage				
IA	Reference		Reference	
IB	2.66 (2.21–3.19)	<0.001	4.50 (3.46–5.86)	<0.001
I	1.41 (0.86–2.34)	0.177	2.39 (1.26–4.52)	0.008
Surgery				
Hysterectomy	Reference		Reference	
Local excision	0.99 (0.80–1.22)	0.904	1.03 (0.79–1.34)	0.810
None	3.19 (2.68–3.80)	<0.001	3.50 (2.86–4.29)	<0.001

OS, overall survival; DSS, disease-specific survival; HR, hazard ratio; CI, confidence interval; SCC, squamous cell carcinoma; AC: adenocarcinoma; ASCC, adenosquamous cell carcinoma.

infectious diseases was significantly elevated in the former group ($P = 0.026$, Figure 7B). Patients receiving hysterectomy displayed a heightened CMR linked to gastrointestinal and cardiovascular ailments during the initial phases of follow-up, although these differences did not reach statistical significance (Figures 7C–H).

4 Discussion

With the increasing trend of conceiving age, the demand for fertility preservation in early-stage CC patients has gained prominence. The recommendation of FSS remains to be more individualized and precise. This study delved into the interventions and outcomes of 10,629 AYA with stage I CC. In this cohort, approximately one-third of the patients opted for FSS, with this percentage increasing to nearly 50% among patients aged 15–24 years. Our study demonstrated that the outcomes of local excision surgery were comparable to those of hysterectomy in the whole AYA stage I CC patients, aligning with findings of Ying Chen's study (4). However, variations in pathological type, tumor differentiation, and FIGO stage influenced the surgery choices of patients.

SCC stands as the predominant histological type of CC, followed by AC, ASCC, and others (14, 15). With the widespread adoption of cervical screening and HPV vaccination, the incidence of SCC has gradually declined, while the prevalence of AC has been increasing (14). Studies have suggested a poorer prognosis associated with AC and ASCC compared to SCC (16–18), although some studies have reported no discernible difference in prognosis upon considering tumor staging (19, 20). Our study specifically investigated stage I cervical cancer patients aged 15–39 years and found that the prognosis of patients with AC is significantly better than that of patients with SCC, whereas ASCC is associated with a worse prognosis than SCC. This disparity in prognosis also influences the choice of FSS. Notably, young patients with cervical ASCC are notably less likely to choose local excision compared to those with SCC or AC. Even within the 15–24 years group, only 25% of patients choose FSS, whereas the percentage among patients with SCC and AC is nearly 50%. Further prognosis analyses suggested that patients with SCC may derive greater benefit from local excision. For patients with AC, local excision is a viable option since hysterectomy has not shown superior survival outcomes. In the case of ASCC patients, although their prognosis may be less favorable than that of SCC patients, there is no evidence indicating that FSS negatively impacts the prognosis of ASCC patients. While additional adjuvant therapy may be necessary based on the specific pathology, ASCC should not be considered a limiting factor in the decision-making process concerning fertility preservation for AYA stage I patients.

Histological differentiation appeared to affect decision-making regarding fertility preservation. Fewer than 15% of patients with poorly differentiated or undifferentiated tumors chose FSS. Safety evaluations suggested that patients with well or moderately differentiated (grade 1–2) tumors tend to benefit more from local excision. In patients with poorly differentiated and undifferentiated tumors, local excision led to comparable outcomes with hysterectomy. We believe that tumor differentiation should not be a decisive factor for AYA stage I patients considering FSS, especially among patients with SCC, AC, or ASCC histopathological types. However, lower differentiation is often accompanied by an advanced stage at the time of initial diagnosis. This correlation may have influenced the adoption of FSS for patients with poorly differentiated CC.

Tumor stage is a key factor affecting the prognosis of CC patients and is also an important factor for considering the FSS in young CC patients. In our study, more than 50% of AYA

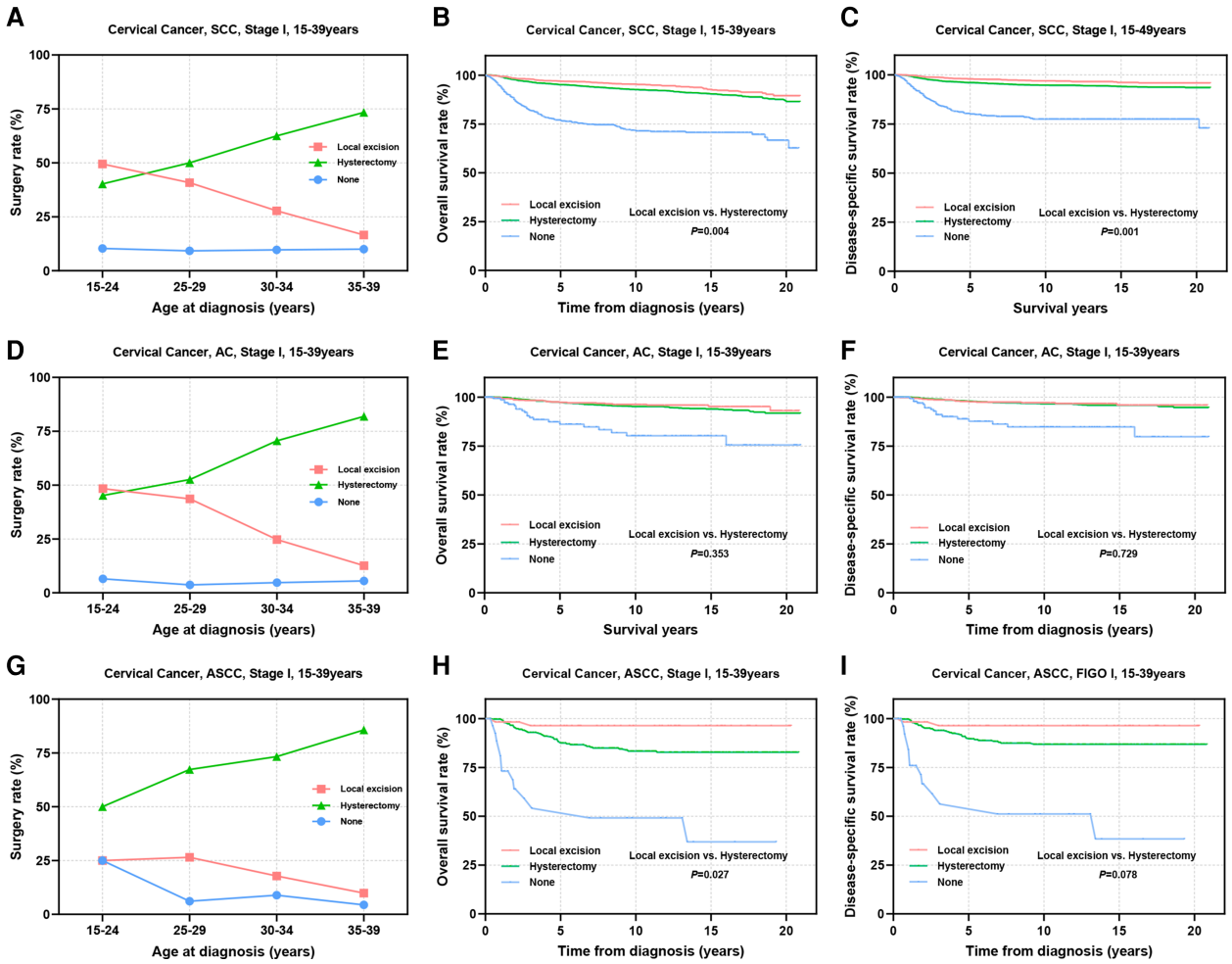

FIGURE 3
Prognosis of AYA stage I patients with different pathologic types receiving different types of surgical interventions. **(A,D,G)** Rates of patients with SCC, AC, ASCC receiving local excision or hysterectomy; **(B,C)** OS and DSS of stage I SCC patients undergoing local excision or hysterectomy; **(E,F)** OS and DSS of stage I AC patients undergoing local excision or hysterectomy; **(H,I)** OS and DSS of patients with stage I ASCC undergoing local excision or hysterectomy.

patients at stage IA underwent local excision surgery. Concerns regarding the impact of stage progression on prognosis affect the choice of fertility preservation. The proportion of stage IB2-IB3 AYA patients receiving local excision experienced a sharp decline. Previous studies and guidelines such as the NCCN 2024 and the ESGO have consistently confirmed the safety and feasibility of FSS in stage IA-IB1 patients (12, 13, 15, 21, 22). Similarly, our study in a larger cohort validated the viability of local excision as an alternative to hysterectomy for preserving fertility in stage I AYA patients. However, recommendations for fertility preservation in stage IB2-IB3 patients remain controversial. The safety and efficacy of neoadjuvant chemotherapy combined with local excision as a treatment option for preserving fertility have been gradually explored in early-stage CC patients. A meta-analysis showed that neoadjuvant chemotherapy combined with local excision was a viable option for fertility preservation in patients with a tumor diameter of 2–4 cm, with an efficacy rate of 92% and a postoperative recurrence rate of 6.1% (23). The ongoing prospective CONTESSA study (NCT 04483557) plans to include patients with tumor sizes of 2–4 cm who wish to preserve fertility, exploring the option of FSS for patients who have achieved complete or partial response after neoadjuvant chemotherapy (residual lesion <2 cm), and the results will be ready by 2025 (24). In our research, we demonstrated that local excision surgery had comparable prognostic outcomes to hysterectomy in a cohort of more than 1,400 patients at stage IB2. The high recurrence rate reported in some other studies of stage IB2 patients may be due to the tumor itself rather than the choice of surgery type. Recent studies have confirmed notable pregnancy and live birth rates following FSS in stage IB2 patients (25, 26). Overall, FSS was feasible in stage IA-IB2 AYA patients. For patients at stage IB3, consistent with most studies and guideline recommendations, our study revealed that the 5-year

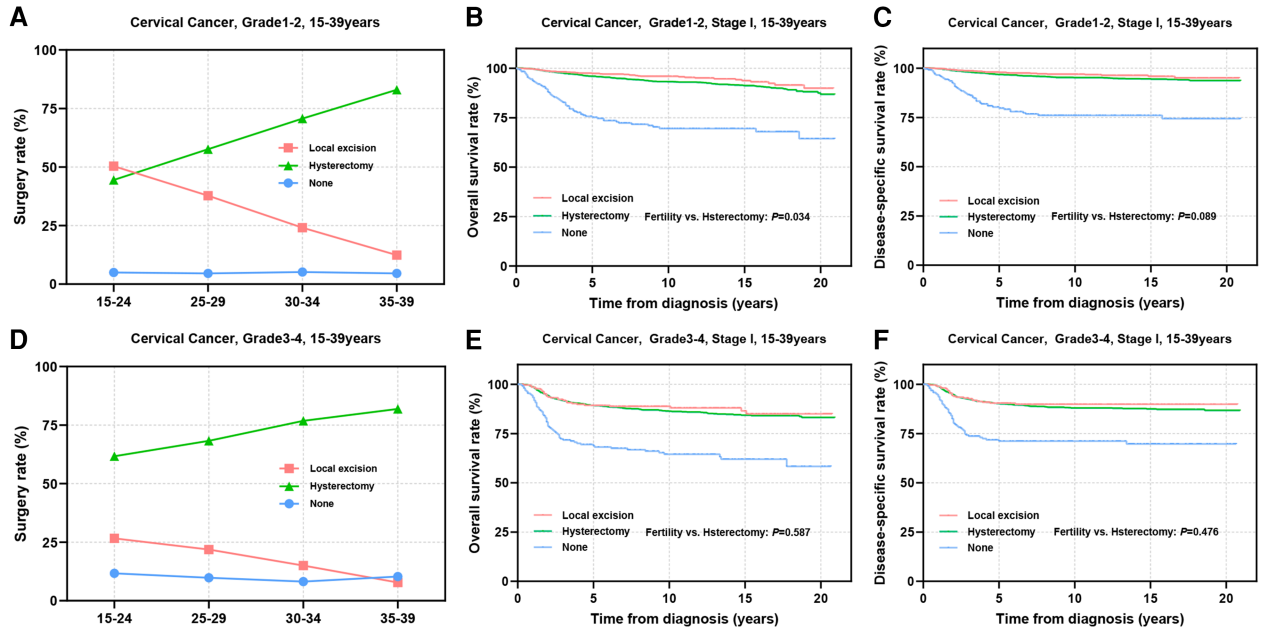

FIGURE 4
Prognosis in patients with different pathologic differentiations undergoing different types of surgical interventions. (A,D) The rate of Grade 1–2 (A) and Grade 3–4 (D) differentiated patients receiving local excision or hysterectomy; (B,C,E,F) OS and DSS of Grade1-2 (B,C) and Grade3-4 (E,F) differentiated patients undergoing local excision or hysterectomy.

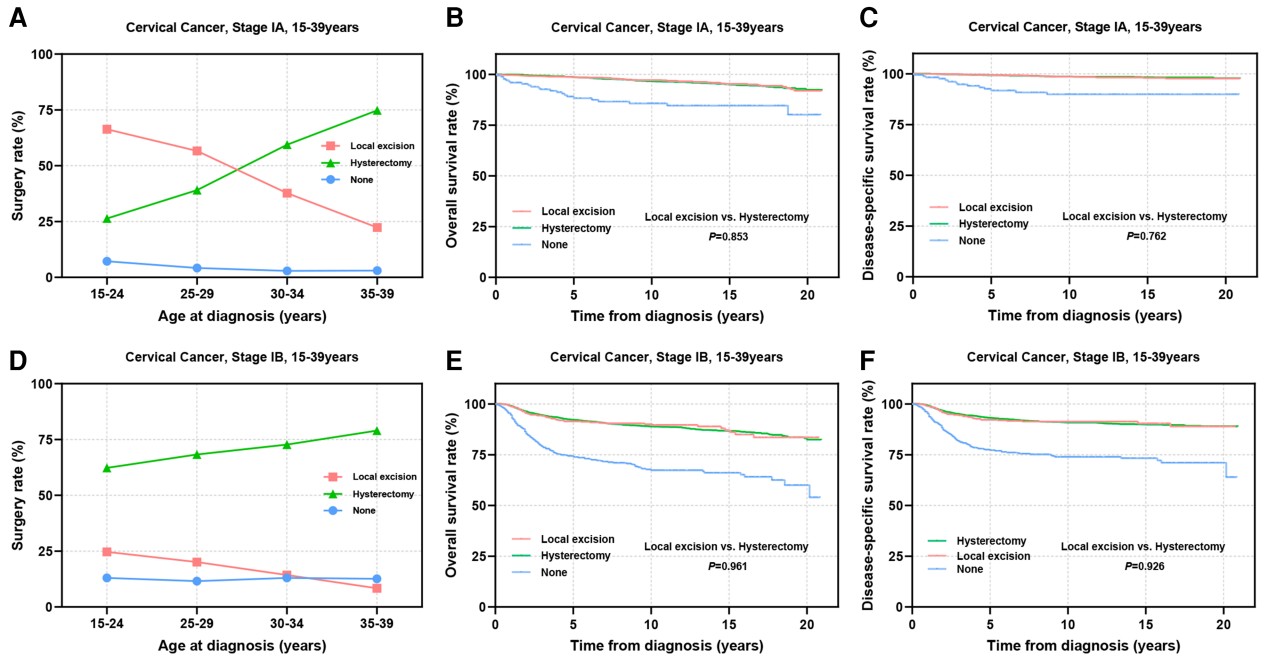

FIGURE 5
Prognosis in AYA stage IA and IB patients undergoing different types of surgical interventions. (A,D) The rate of stage IA (A) and stage IB (D) patients receiving local excision or hysterectomy; (B,C,E,F) OS and DSS of stage IA (B,C) and stage IB (E,F) patients undergoing local excision or hysterectomy.

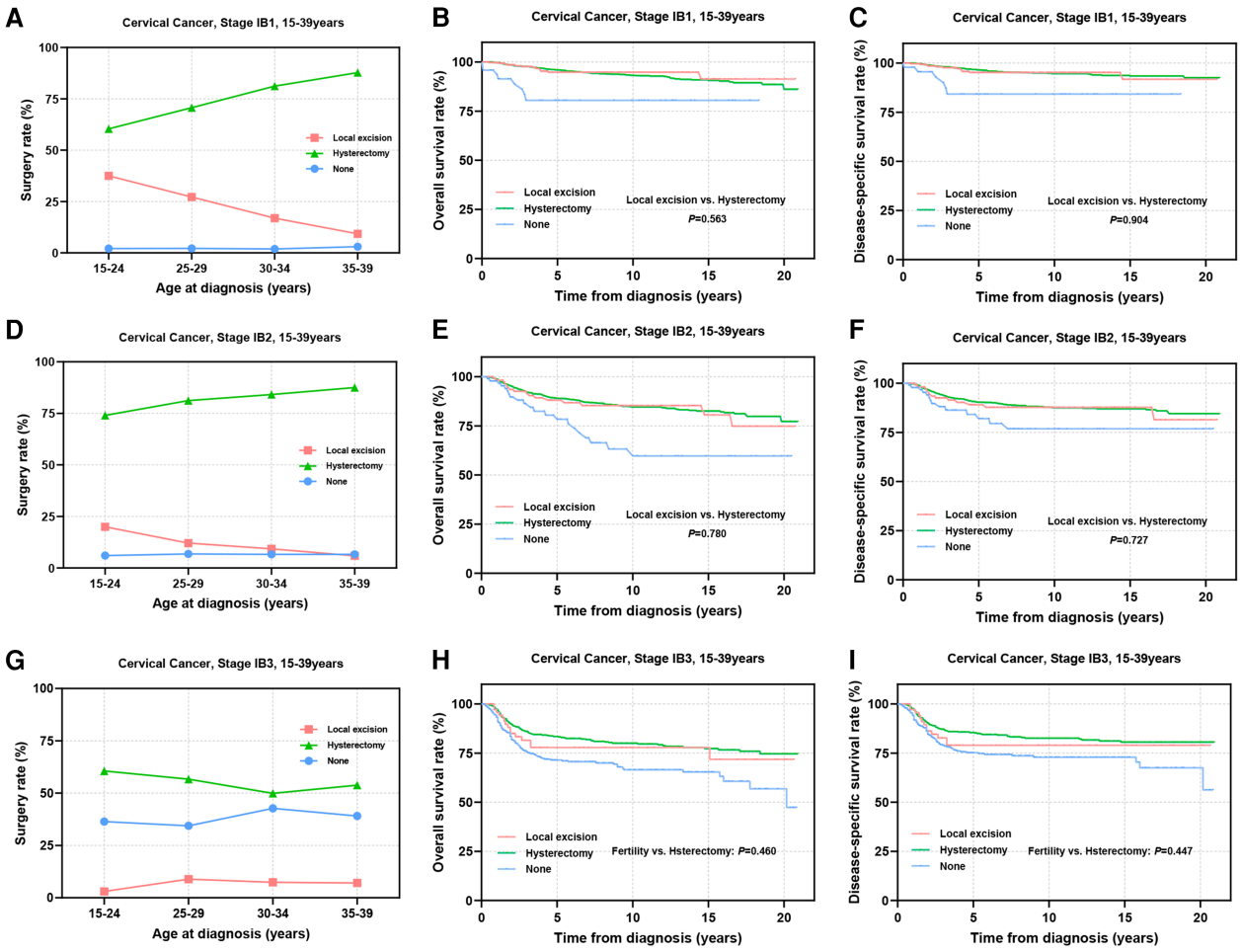

FIGURE 6
Prognosis of stage IB1-IB3 AYA patients undergoing different types of surgical interventions. **(A,D,G)** Rates of patients at stage IB1, IB2, IB3 receiving local excision or hysterectomy; **(B,C)** OS and DSS of stage IB1 patients undergoing local excision or hysterectomy; **(E,F)** OS and DSS of stage IB2 patients undergoing local excision or hysterectomy; **(H,I)** OS and DSS of patients with stage IB3 undergoing local excision or hysterectomy.

survival rate of patients who underwent local excision surgery was significantly lower than that of patients who underwent hysterectomy in these patients, even though adjuvant chemotherapy was very common in this patient population. Therefore, careful consideration is warranted regarding FSS for stage IB3 patients.

Comprehensive preoperative and intraoperative evaluations are needed for implementing FSS. It is crucial to utilize pelvic MRI, PET-CT, and other examinations to evaluate lymph node involvement and deep stromal tissue infiltration. Lymphovascular space invasion (LVSI)is a risk factor for lymph node metastasis and indicates a poor prognosis in early-stage cervical cancer (27). For stage IA patients without LVSI, lymph node dissection is optional, while for patients with LVSI, pelvic lymph node dissection or sentinel lymph node (SLN) assessment is imperative (12, 27). In early-stage cervical cancer, SLN evaluation has been shown comparable prognostic value to traditional pelvic lymph node dissection (28). Both the ESGO guidelines and the NCCN guidelines recognize the effect of SLN assessment in lymph node evaluation for FSS (12). These evaluations play a pivotal role in identifying individuals at high risk of recurrence and ensuring their exclusion from FSS (2, 29). The high incidence of complications associated with radical surgeries has led to a shift toward less radical surgery for early-stage, low-risk CC, offering fertility-sparing options for patients (30). In our study, we observed that patients with early-stage, well- or moderately-differentiated SCC may benefit from local excision surgery, even if fertility preservation is not the primary goal. For the selection of surgical paths, the minimally invasive surgical approach may be more preferable to the laparotomic approach, for it can reduce the occurrence of complications and improve the postoperative pregnancy rate without increasing the recurrence rate (18, 31). Following surgery, vigilant monitoring and consideration of adjuvant radiotherapy or chemotherapy based on tumor characteristics are important for improving patient prognosis (32–35).

While our study provides insights, it has limitations. Retrospective analysis, despite its large case count, can only

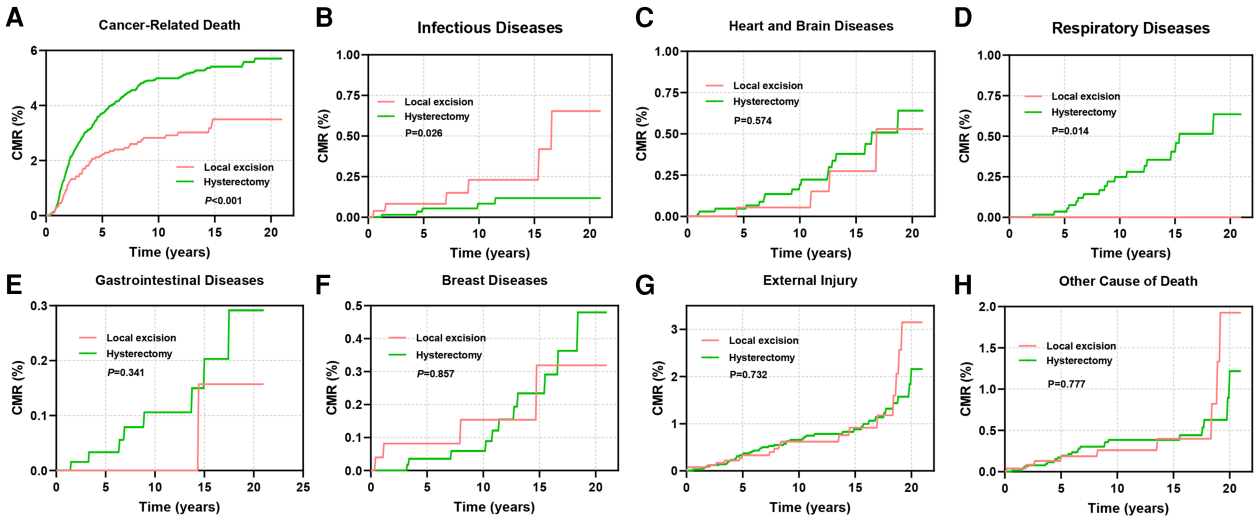

FIGURE 7
CMR among AYA stage I patients undergoing different types of surgical interventions. **(A)** CMR due to cancer-related diseases; **(B)** CMR due to infectious diseases; **(C)** CMR due to diseases of the heart and brain; **(D)** CMR due to respiratory diseases; **(E)** CMR due to gastrointestinal diseases; **(F)** CMR due to breast diseases; **(G)** CMR due to external injury; **(H)** CMR due to other causes of death.

offer evidence for local excision as a viable alternative to hysterectomy for FSS in AYA stage I CC patients. Prospective studies are necessary for definitive guidance. Second, the absence of detailed information on specific surgical approaches, extent of surgery and lymphovascular invasion information in the database, as well as surgical heterogeneity due to longer study timeline, impedes a more comprehensive assessment of the prognostic impact of various surgical choices. Third, while the ultimate objective of FSS is to maintain fertility potential, the database also lacks long-term follow-up data, posing challenges in evaluating the final fertility outcomes across different age groups, tumor characteristics, and surgical interventions.

5 Conclusion

The pathological type, low degree of differentiation, and relatively advanced tumor stage limit the choice of fertility preservation for AYA patients with stage I CC. In AYA patients with stage IA or IB2, the efficacy of local excision surgery and hysterectomy was comparable. Tumor differentiation should not be a restrictive factor for fertility preservation in stage I AYA patients.

Data availability statement

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

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

YN: Conceptualization, Investigation, Writing – original draft. XG: Formal Analysis, Resources, Writing – original draft. YK: Formal Analysis, Resources, Writing – original draft. YW: Formal Analysis, Resources, Writing – review & editing. TT: Writing – review & editing. YC: Data curation, Validation, Writing – review & editing. YY: Data curation, Validation, Writing – review & editing. KL: Writing – review & editing. ZC: Funding acquisition, Supervision, Writing – review & editing.

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Conflict of interest

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

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2024.1456376/full#supplementary-material

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Identifying key predictors for uterine manipulator use in robotic simple hysterectomy: a retrospective cohort analysis

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Background: Robotic simple hysterectomy (RSH) is the most common robotic gynecologic surgery in the United States. Uterine manipulators are commonly used to handle the uterus during laparoscopic surgery, but few studies have examined their necessity in RSH. This study retrospectively compares RSH cases with and without the use of manipulators, and identifies predictors for their intraoperative use.

Materials and methods: This retrospective cohort study included patients undergoing RSH for benign pathologies at Kawasaki Medical School from October 2020 to December 2022. Patients with malignancies were excluded. The robotic surgeries were performed by three skilled surgeons using the four-arm da Vinci Xi surgical system. Data on perioperative and operative parameters were collected, including age, body mass index (BMI), history of abdominal surgery, disease type, presence of ovarian cysts, and operative time. Statistical analyses were performed using EZR software, with multivariate logistic regression to identify predictive factors for uterine manipulator use.

Results: The study included 113 patients who underwent RSH without a uterine manipulator and 58 with one. Patients without a manipulator were older, while those with a manipulator had higher BMIs and a higher prevalence of ovarian chocolate cysts and Douglas obliteration. Operating time was shorter without a manipulator. Independent predictors for manipulator use were higher BMI, presence of ovarian endometrioid cysts, and Douglas obliteration.

Conclusion: RSH without a uterine manipulator is feasible and can reduce the need for surgical assistants. Predictors for manipulator use include higher BMI, ovarian cysts, and Douglas obliteration. The use of a fourth robotic

arm can enhance surgical independence and resource efficiency. Further research is needed to assess the long-term cost-effectiveness and outcomes of this approach.

KEYWORDS

robotic simple hysterectomy, robot-assisted simple hysterectomy, uterine manipulator, da Vinci Xi surgical system, pouch of Douglas obliteration, operative assistant

1 Introduction

Hysterectomy is the most frequent surgical procedure performed on women with uterine benign diseases accounting for approximately 90% of hysterectomies (1). Before surgical robots, laparoscopy was the only minimally invasive option, limited by its steep learning curve and need for advanced training. Since the United States Food and Drug Administration approved the da Vinci robot (Intuitive Surgical) in 2005, advancements in robotic technology have greatly increased its use in gynecologic surgeries. At present, robotic simple hysterectomy (RSH) is now the most common robotic gynecologic surgeries in the United States (2, 3).

The greatest advantage of robotic surgery compared with laparotomy or laparoscopy is the saving in human resources. The equipment for RSH is slightly more expensive per procedure than for total laparoscopic hysterectomy (TLH), but performing 45 or more RSH procedures becomes more cost-effective than TLH (4, 5). The use of uterine manipulators is well established and it is clear that uterine manipulators offer the easiest way to handle the uterus during surgery (6). TLH without a uterine manipulator has been reported to reduce operative time and the need for a pelvic assistant (7). However, few studies have examined whether manipulators are necessary for RSH. In this study, we aimed to retrospectively compare cases of RSH with and without the manipulator and identify predictors for the intraoperative use of manipulators.

2 Materials and methods

2.1 Study design and data collection

This study was reviewed and approved by the Human Research Ethics Committee of Kawasaki Medical School (trial registration no.: 5043-03). After institutional review board approval, this study was designed as a retrospective cohort study. Patients who underwent RSH at the Women's Medical Center, Kawasaki Medical School from October 2020 and December 2022 were included. Inclusion criteria encompassed RSH for benign pathologies, including fibroids, adenomyosis, cervical diseases (such as high-grade cervical intraepithelial neoplasia), and endometrial diseases (such as endometrial hyperplasia without atypia). All patients provided consent before the procedure. Patients with indications of malignancy were excluded from this study.

The robotic surgeries were performed by three skilled surgeons (surgeons A, B, and C). Surgeon A was awarded a class B International license by The Japanese Society for Robotic Surgery and is a proctor in The Japan Society for Endoscopic Surgery and Intuitive Surgical; Surgeon B holds a class B domestic license from The Japanese Society for Robotic Surgery and is a proctor in Intuitive Surgical; and Surgeon C is a proctor in Intuitive Surgical. Each surgery was assisted by a gynecological resident who had at least 1 year of experience in robotic surgeries, having participated in more than 30 cases.

We collected the data regarding perioperative parameters: age, body mass index (BMI), history of abdominal surgery, types of disease, presence of ovarian chocolate cysts, presence of pouch of Douglas obliteration, and operative parameters as follows: estimated blood loss, operating time defined as the time from skin incision to skin closure for RSH, concomitant procedures, and uterine weight excised.

2.2 Surgical procedures

Under general anesthesia, the patient was placed in a lithotomy position with Trendelenburg tilt. All robotic procedures utilized the four-arm da Vinci Xi surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA). Initially, an 8-mm endoscope port trocar was inserted 3 cm above the umbilicus using the direct closed method to establish pneumoperitoneum. Three 8-mm robotic ports were then inserted under direct vision on the same horizontal line, spaced 8 cm apart at the level of the endoscope port. The second arm managed the endoscope, while the first arm operated fenestrated bipolar forceps and the third arm managed Maryland bipolar forceps using the double bipolar technique (8). The fourth arm utilized Cadiere forceps to manipulate the uterus, eliminating the need for a uterine manipulator. Suturing was performed using the Suture Cut needle driver on the Maryland bipolar forceps on the third arm, which enabled both suturing and cutting of threads. For suction and intra-abdominal needle transport, the Probe Plus II (Ethicon, Tokyo, Japan) was introduced through the third arm. However, when it was necessary to pull the uterus or bowel toward the head to ensure a clear surgical field, a uterine manipulator was used.

The hysterectomy procedure followed our standard operating procedure for conventional RSH (9). Briefly, the round ligament was transected initially, followed by dissection of the broad ligament anteriorly and posteriorly using the double bipolar method with the Maryland bipolar and fenestrated bipolar forceps. Dissection of the bladder from the proximal vagina was followed by incision and expansion of the peritoneum of vesico-uterine pouch to identify and ligate the ureter and uterine artery, including the ureter-uterine artery crossover point, with 2-0 Vicryl (Ethicon, Tokyo, Japan) sutures. The uterine artery and ascending branches of the uterine vessels were ligated at two points with C 2-0 Vicryl (Ethicon, Tokyo, Japan) and coagulated using the fenestrated bipolar forceps before transecting with the Maryland bipolar

forceps. The cardinal ligaments were transected, and colpotomy was performed with the Maryland bipolar forceps, followed by vaginal extraction of the uterus. A large uterus was divided into removable segments and extracted vaginally. Closure of the vaginal cuff was achieved using interrupted 0-Vicryl (Ethicon, Tokyo, Japan) sutures. A video clip summarizing the RSH technique is available (Supplementary Video 1).

2.3 Statistical analysis

Statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) (10). Data was represented as median and interquartile ranges (IQR) for non-parametric variables, and categorical variables are described as frequency and percentage and compared between the groups using Mann–Whitney's U test (for numeric non-parametric variables) or Fisher's exact test (for categorical variables). Multiple logistic regression analyses were performed to investigate potential influencing factors to evaluate RSH with a uterine manipulator, employing a forward stepwise methodology to identify independent predictive factors. Specifically, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated in the multivariate analyses, controlling for potential confounders such as age, BMI, history of abdominal surgery, types of diseases, location of fibroids, console surgeons, presence of ovarian endometrioid cysts, presence of pouch of Douglas obliteration, and extracted uterine weight. These factors relate to securing the operative field before or at the start of surgery. Factors such as operative time and operative blood loss, which occur after surgery begins, were excluded as adjustment factors because they were not related to whether manipulators were used. However, for console surgeons, there was a significant difference in the number of RSH surgeries among surgeons. Therefore, console surgeon was included as an adjustment factor. Statistical significance was set at $P < 0.05$.

3 Results

The characteristics of patients who underwent RSH without a manipulator (113 patients) and RSH with a manipulator (58 patients) are summarized in Table 1. Patients in RSH without a manipulator were significantly older than those in RSH with a manipulator (median 48.0, IQR 45.0–51.0 versus median 46.5, IQR 42.3–50.0, $P = 0.04$), and BMI was significantly higher in RSH with a manipulator than in RSH without a manipulator (median 25.7, IQR 22.6–29.0 versus median 23.8, IQR 20.8–27.1, $P = 0.02$). There were no statistically significant differences in the types of benign disease excluding the presence of cervical or broad ligament fibroid between the groups. The percentage of cervical or broad ligament fibroids was significantly higher in the RSH with a manipulator group than that in RSH without a manipulator group (13.8 versus 4.4%, $P = 0.03$). There were no statistically significant differences in the history of abdominal surgery between the groups. The percentage of presence of ovarian chocolate cysts was significantly higher in the RSH with a manipulator group than in the RSH with a uterine manipulator group (22.4 versus 3.5%, $P < 0.01$). The percentage of pouch of Douglas obliteration was significantly higher in the RSH with a manipulator group than in the RSH with a uterine manipulator group (25.9 versus 1.8%, $P < 0.01$).

The surgical outcomes of RSH without a uterine manipulator and RSH with a uterine manipulator are summarized in Table 2. Operating time was significantly shorter in RSH without a uterine manipulator than in RSH with a uterine manipulator (125.0, IQR 112.0–138.0 versus 148.5, IQR 133.0–172.5). Both estimated blood loss and uterine weight were not significantly different between the groups. For console Surgeon A, the percentage of RSH with a uterine manipulator was significantly higher than that of RSH without a uterine manipulator (65.6 versus 38.9%, $P < 0.01$). For console Surgeon B, the percentage of RSH with a uterine manipulator was significantly lower than that of RSH without a uterine manipulator (3.4 versus 48.7%, $P = 0.02$). For console Surgeon C, there was no significant difference in the percentage of RSH with and without a uterine manipulator.

Predictive factors for uterine manipulator use during RSH are summarized in Table 3. Multivariate logistic analysis showed that BMI (adjusted OR: 1.15, 95% CI 1.04–1.26, $P < 0.01$), the presence of ovarian endometrioid cysts (OR: 5.25, 95% CI 1.19–23.10, $P = 0.03$), and the presence of pouch of Douglas obliteration (OR: 32.6, 95% CI 3.73–285.00, $P < 0.041$) were independent predictive factors for uterine manipulator use during RSH. Adjusting explanatory variables, history of abdominal surgery, uterine weight, and cervical or broad ligament fibroids were not significant predictors for uterine manipulator use during RSH.

4 Discussion

In this study, we showed for the first time that independent predictors of uterine manipulator use during RSH were BMI, presence of endometrial cysts in the ovary, and Douglas obliteration.

The use of manipulators for RSH is the technique derived from imitation methods of the TLH. In TLH procedures, several studies have highlighted the importance of uterine manipulators in reducing complications during hysterectomy (6, 11). In fact, a uterine manipulator is routinely used as the gold standard in TLH to allow better exposure of the anatomical spaces, consequently lower the overall complication rate, and to prevent bowel and ureteral injuries (12, 13). On the other hand, recently, the use of uterine manipulators has been increasingly discouraged in laparoscopic and robotic surgery. The use of the uterine manipulator in TLH might be avoided in malignant tumor because it is suggested to increase concerns regarding the dissemination of malignant cells to the vaginal cuff and the peritoneal cavity through the fallopian tubes when the uterine manipulator is used for endometrial carcinoma (14). Therefore, there have been many reports of TLH without manipulators in recent years (15), although TLH without the use of a manipulator is a more demanding surgical procedure (16–19). This is because the learning curve for performing TLH without a uterine manipulator is likely to be longer (20, 21). Because robotic surgery has advantages such as a short learning curve, even in RSH, uterine manipulators tend not to be used for endometrial cancer (22).

TABLE 1 Patient characteristics in both RSH without and with a uterine manipulator.

	RSH without a uterine manipulator (n = 113)	RSH with a uterine manipulator (n = 58)	P-value
Age, years	48.0 (45.0–51.0)	46.5 (42.3–50.0)	0.04
BMI, kg/m^2	23.8 (20.8–27.1)	25.7 (22.6–29.0)	0.02
Types of diseases			
Fibroids, number (%)	73 (64.6)	39 (67.2)	0.73
Adenomyosis, number (%)	32 (28.3)	16 (27.6)	0.92
Cervical disease, number (%)	3 (2.7)	2 (3.4)	1.00
Endometrial disease, number (%)	5 (4.4)	1 (1.7)	0.67
Presence of ovarian endometrioid cyst, number (%)	4 (3.5)	13 (22.4)	< 0.01
Presence of pouch of Douglas obliteration, number (%)	2 (1.8)	15 (25.9)	< 0.01
History of abdominal surgery, number (%)	7 (6.2)	5 (8.6)	0.56

Data are presented as median (interquartile range) or number (percentage). RSH, robotic simple hysterectomy; BMI, body mass index.

TABLE 2 Surgical outcomes in both RSH without and with a uterine manipulator.

	RSH without a uterine manipulator (n = 113)	RSH with a uterine manipulator (n = 58)	P-value
Operating time, min	125.0 (112.0–138.0)	148.5 (133.0–172.5)	< 0.01
Estimated blood loss, ml	25.0 (10.0–53.0)	37.5 (10.0–69.0)	0.18
Uterine weight, g	182.0 (138.0–260.0)	211.0 (135.5–364.0)	0.28
Console surgeons, number (%)			
A	44 (38.9)	38 (65.5)	< 0.01
B	55 (48.7)	17 (3.4)	0.02
C	14 (12.4)	3 (5.2)	0.14

Data are presented as median (interquartile range) or number (percentage). RSH, robotic simple hysterectomy.

TABLE 3 Predictors of uterine manipulator use during RSH.

	Adjusted odds ratio* (95% confidence interval)	P-value
BMI	1.15 (1.04–1.26)	< 0.01
History of abdominal surgery	2.35 (0.56–9.76)	0.24
Uterine weight	1.00 (0.99–1.00)	0.14
Cervical fibroid	2.68 (0.62–11.60)	0.19
Presence of ovarian endometrioid cyst	5.25 (1.19–23.10)	0.03
Presence of pouch of Douglas obliteration	32.6 (3.73–285.0)	< 0.01

*Adjusted for age, body mass index, the types of disease, and the console surgeons. RSH, robotic simple hysterectomy.

Recent studies on uterine manipulators in gynecological surgery provide mixed insights. Ongoing research may provide clearer guidelines for their optimal use in various gynecological surgeries. To date, there is no conclusion to the debate on whether a uterine manipulator should or should not be used for TLH, although recent studies on uterine manipulators in gynecological surgery provide mixed insights. In particular, some reports of surgical approaches for a TLH without a uterine manipulator (23) raised concerns over the use of a uterine manipulator for uterine cancers during TLH (24, 25). The meta-analysis by Scutiero et al. (26) suggests that while manipulators don't significantly impact overall or disease-free survival in endometrial cancer cases, they may increase the risk of positive peritoneal cytology. The prospective randomized trial found that the use of a uterine manipulator during minimally invasive staging for early-stage endometrial cancer does not significantly impact lymph vascular space invasion or patient outcomes (27). Therefore, uterine manipulators are expected to be in increasing demand. On the other hand, Cianci et al.'s (28, 29) reviews highlight the importance of tailoring surgical approaches to individual cases, especially for fibroid treatment and large uterine. Their study on laparoscopic hysterectomy conversions indicates that uterine size significantly affects procedural success, with manipulators potentially less effective for very large uterine (28, 29). Overall, while uterine manipulators offer benefits in visualization and ease of minimally invasive procedures, their use should be carefully considered based on factors like uterine size, cancer risk, and patient characteristics. Hence, it is the new era to adapt to hysterectomy even if a manipulator was not available. Zygouris et al. (15) concluded the feasible and safe technique using grasping forceps for uterine manipulation instead of a uterine manipulator from a large clinical study, if performed by well-trained, experienced laparoscopic surgeons. Moreover, Abdel Khalek et al. (11) advise that surgeons

performing TLH should decide on a case-by-case basis whether a uterine manipulator is necessary and, if so, which type best suits the procedure.

The study by Gallotta et al. (30) demonstrates that robotic surgery (RS) is a feasible and safe option for elderly (65–74 years) and very elderly (≥ 75 years) women undergoing gynecologic oncologic procedures. While their study doesn't specifically address uterine manipulators, the precision of robotic systems may reduce the need for extensive manipulation, potentially benefiting older patients with more fragile tissues (30). Although there were no elderly patients in this study, it may provide the basis for further development into robotic sacrocolpopexy does not use manipulators if this study has advanced and establish as a manipulator-free RSH.

Robotic surgery is considered as advantageous for reducing human resources, but an assistant is still needed. When a uterine manipulator is used, at least two assistants are required. Additionally, the assistant must work in a confined space with the patient's legs spread, causing significant stress during surgery. Determining whether a uterine manipulator can be used before or immediately after surgery helps reduce the number of assistants needed for the procedure. Perrone et al. (31) described that RSH with the assistance of the fourth robotic arm instead of a uterine manipulator may reduce the need for uterine manipulation because the operating time was not different from TLH without a uterine manipulator done by the experts. Our technique of RSH without a uterine manipulator is consistent with the very same concept. Recently, Barger et al. (32) described that adding a fourth robotic arm to the standard three port setup can markedly improve robotic hysterectomy without a uterine manipulator. In this study, RSH utilizing four arms also allowed us to complete the hysterectomy without a uterine manipulator; however, even with four arms, a manipulator was necessary in cases with increased BMI, the presence of ovarian endometrioid cysts, and the presence of pouch of Douglas obliteration. In those cases, the console surgeon's independence may be somewhat diminished, as an additional surgical assistant is required. On the other hand, reducing human resources for surgery would deprive fellows or residents of the opportunity to enter robotic surgery. In fact, Hall et al. (33) reported that few fellows were deemed competent enough to independently operate the robot with only 15% being able to perform an entire hysterectomy. Therefore, recent curriculum for OB/Gyn residents and fellows reduces barriers by providing protected time away from clinical duties to provide a reproducible platform for the early acquisition of advanced robotic skills outside of the operating room to standardize mastery-based training for the next generation of robotic surgeons (34).

The difficulty of performing a hysterectomy increases when fibroids are located in the cervix or the broad ligament. In laparoscopic surgery, where manual traction is not possible, the location of the fibroids particularly affects the surgical difficulty. Our study found no association between the use of uterine manipulators and cervical or broad ligament fibroids when adjusted for explanatory variables. Of the 13 cases with cervical or broad ligament fibroids, eight were performed by Surgeon A, five by Surgeon B, and none by Surgeon C (data not shown). These results may be influenced by differences in surgeon experience and should be interpreted with caution.

Although this is a robot-specific study, it may be necessary to consider whether robotic surgery is more significant than laparoscopic surgery. In a previous review, RSH had a longer operating time than TLH (35). However, in the recent RCT-only meta-analysis, there was no difference in operating time between RSH and TLH, and those are now rated as equivalent operative techniques (36). Both the decade of surgeons' experience and robotic development realized the democratization and widespread of robotic surgery and might reduce the operating time. However, there is no doubt that robotic surgery will surpass laparoscopic surgery in the future. Although the current challenge lies in the training of surgeons and the development of the operating room of the future, In the era of digital surgery, robotic platforms serve as computer interfaces capable of integrating various real-time data analysis modalities, and the next decade enables advanced systems to provide augmented surgical vision through augmented reality, improved surgical decisions using artificial intelligence, and enhanced surgical maneuvers through the advancement of robotic instruments (37). In addition, recent meta-analysis demonstrates that 3D vision systems offer significant advantages over 2D systems in laparoscopic surgery, particularly in terms of improved depth perception, precision, and task completion time (38). All robotic systems always include 3D vision systems, and could be especially beneficial for the training of surgeons to enhance spatial awareness and precision afforded by 3D vision. Pavone et al. (39) have systematically studied the advantages and advancements of robotic platforms in gynecological surgery, and the potential benefits of robotic approaches are sufficient strength for endometriosis surgery (40) and superior to laparoscopic approaches for severe cases such as deep endometriosis through a meta-analysis (41). Furthermore, those foundations are more established when they combine structured training in skill development, novel techniques such as ultrasound-guided robotic surgical procedures, and the integration of imaging technologies (42, 43). Therefore, the potential benefits in the next decade would also depend on the widespread adoption of robotic surgery systems in gynecological surgery settings emphasizing technological advancements, comparative effectiveness, training methodologies, and the integration of imaging techniques.

Our study had several limitations. First, the data may have incomplete information that was not fulfilled in the patient record because of the retrospective nature of the study, which limits the generalizability of our findings. In this retrospective study, there was the possible allocation biases arising from the retrospective comparison between RSH without a uterine manipulator and RSH with a uterine manipulator because of the non-randomized nature of the study design. Therefore, we further need to analyze with a propensity-matched analysis to decrease biases arising from different covariates if both cases are increased, or further prospective trials are needed to confirm our results. Second, three surgeons from our robotic surgical team performed the surgeries. Although most surgeons in the team were trained at the same institution, biases resulting from individual surgeon differences cannot be excluded. Moreover, the most proficient surgeon (Surgeon A) required a uterine manipulator for RSH, which may have resulted in an unbalanced distribution of surgical difficulty and may have impacted the statistical analysis. Third, In the current landscape, other robotic systems have been developed, and the Hugo^{TM} RAS (Medtronic, Minneapolis, MN, USA)

or hinotori^{TM} system (Medicaroid Corporation, Kobe, Japan) for hysterectomy has demonstrated effectiveness (44–46). It has raised the possibility of different results to operate with other robotic systems, although Matsuura et al. (47) described that surgeons who are already proficient in performing robotic surgery with da Vinci X can safely perform surgeries with the new models when three robotic systems were compared. The study's main strength is its description of a four-arm approach to hysterectomy using the da Vinci Xi without a uterine manipulator, which enabled minimal dependence on an assistant. Although previous reports have shown the superiority of a four-arm hysterectomy approach for malignant gynecological diseases (48), this is the first study to demonstrate the superiority of this hysterectomy approach for benign gynecological diseases. Furthermore, this report seems worthwhile because pelvic occupying diseases, such as enlarged uterine fibroids, are more difficult to treat robotically than with radical total hysterectomy.

In conclusion, the routine use of a fourth robotic arm during RSH provides the operating surgeon with greater independence during critical phases of the procedure without the requirement of a uterine manipulator and assistant. This advantage translates into non-dependence on an assistant and the conservation of human resources as well as medical resources such as a uterine manipulator. Although the initial investment in robotic surgical systems is high, we need further longitudinal research on whether shorter hospital stays, reduced postoperative complications, and quicker recovery times, can significantly lower overall healthcare costs.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: Raw data were generated at Kawasaki Medical School. Derived data supporting the findings of this study are available from the corresponding author YO on request. Requests to access these datasets should be directed to yoshimon@med.kawasaki-m.ac.jp.

Ethics statement

The studies involving humans were reviewed and approved by the Human Research Ethics Committee of Kawasaki Medical School (trial registration no.: 5086-01). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

SK: Data curation, Methodology, Writing – original draft, Writing – review & editing. KO: Writing – original draft, Writing – review & editing. YO: Conceptualization, Supervision, Writing – review & editing. TT: Writing – original draft, Writing – review & editing. HF: Data curation, Methodology, Writing – review & editing. KT: Data curation, Methodology, Writing – review & editing. HO: Data curation, Methodology, Writing – review & editing. YM: Data curation, Methodology, Writing – review & editing. WS: Data curation, Methodology, Writing – review & editing. MSu: Formal analysis, Writing – review & editing. TM: Supervision, Writing – review & editing. EK: Supervision, Writing – review & editing. MSh: Supervision, Writing – review & editing. KS: Supervision, Writing – review & editing.

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Conflict of interest

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

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2024.1462632/full#supplementary-material

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Case report: Robotically-treated spontaneous interstitial pregnancy on tubal stump

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To report a rare case of a right interstitial pregnancy spontaneously occurring in a patient who had previously undergone homolateral salpingo-oophorectomy, and to propose possible explanations for the mechanisms involved in the genesis of this rare scenario. A 32-year-old G3P1 female presented to our emergency room with symptoms related to a suspected ectopic interstitial pregnancy managed in another hospital using a conservative pharmacological approach. After discussing the risks, firstly she underwent a transvaginal ultrasound examination, then a diagnostic hysteroscopy to clarify the unclear ultrasound finding, followed by a successful robot-assisted laparoscopic cornual resection. Hysteroscopy demonstrated an empty uterine cavity, confirming the suspect of pregnancy localization into the interstitial portion of the tubal stump. Through the robot-assisted laparoscopic approach, all the trophoblastic tissue was removed without causing significant damage to the surrounding myometrium and preserving the patient's fertility. No post-operative complications were recorded. The robotic approach successfully allowed the cornual resection, with minimal blood loss and optimal suturing of the uterine defect. Although our knowledge is still limited, it is possible that the pregnancy nested in the tubal residue after being properly fertilized into the intact tube. However, it cannot be ruled out that there have been remodeling phenomena of the tubal residue so that it has acquired the ability to intercept the oocyte.

KEYWORDS

interstitial pregnancy, ectopic pregnancy, robotic surgery, fertility, case report

1 Introduction

Ectopic pregnancy is defined as a blastocyst implantation outside the uterine cavity with a fallopian tube placement rate of ≥95.5%. Interstitial pregnancies (IPs) represent 2–4% of ectopic pregnancies (1). The "interstitial pregnancy" is defined as the gestational sac implant within the proximal tubal segment, which is located within the uterine wall muscles (2). A correct diagnosis of IP may be difficult, and it necessitates appropriate ultrasound interpretation and training. Treatment options include conservative medical management or surgical intervention.

2 Case description

A 32-year-old woman, G3P1, presented to our emergency room complaining of lower abdominal pain (Visual Analogue Scale (VAS) score: 8) with no vaginal bleeding. The patient

had a surgical history of a right laparotomic adnexectomy when she was a child because of a cystic teratoma. According to her health records, the woman was attempting to conceive, but in April 2023, a different hospital admitted her as a suspect of cornual pregnancy with a serum beta human chorionic gonadotropin (β-hCG) level of 15,000 mUI/mL and an ultrasound showing the presence of a gestational sac with a single live embryo, with a crown-rump length (CRL) of 6 mm, and biometry corresponding to 6 weeks +2 days located in the right angular area of the uterus. The patient was first treated with methotrexate 50 mg twice, one week apart. The first β-hCG level determination was made 48 h later, and then every 24 h showed a decrease (T1: 8,782; T2: 7,882; T3: 7,261; T4: 6,152 mlU/ml) until June 2023, when she arrived at our emergency room. She had fair condition: her vital signs were stable and within normal limits. She was conscious, though she felt uncomfortable. The patient reported spontaneous pelvic pain which was difficult to localize. At the abdominal physical exam, tenderness to deep palpation was noted in her right lower quadrant radiating to the hypogastrium. Blumberg and Rovsing signs were negative. An ultrasound examination was performed, revealing in the right angular area the presence of a 25×26 mm neoformation, with an intense peripheral vascularization suggesting an ectopic pregnancy in the right angular area and little free blood in the pouch of Douglas (Figure 1). The blood tests showed: hemoglobin 10.4 g/dL; white blood cell (WBC) count 7,800/mL, with 70% neutrophils; C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) were just slightly increased; serum β-hCG level 25.4 mUI/mL. The patient was admitted to our Obstetrics and Gynecology Unit, and a diagnostic hysteroscopy was performed, which showed a regular endometrial cavity, regular tubal ostia, and no neoformation inside the uterine cavity (Figure 2). So, a diagnosis of interstitial ectopic pregnancy on the tubal stump was made. Although β-hCG levels were declining and a wait-and-see approach would have been appropriate, due to the persistence of symptoms, the ultrasound evidence of a richly vascularized formation, the reproductive desire, and the peculiar pathological condition to be addressed, we opted for the surgical approach after detailed counseling and obtaining written informed consent. Furthermore, in our experience with ectopic pregnancies (3), the choice of methotrexate in this case was questionable from the outset, and surgery seemed the preferred route. A robotic-assisted laparoscopy was performed using the *Da Vinci® Robotic Surgical System*. At the introduction of the optical trocar, the presence of oval tumefaction corresponding to the right corner of the uterine was observed (Figure 3A). This finding was compatible with the suspicion of ectopic pregnancy, of course. The left ovary appeared normal. The right ovary was absent for prior surgery. It was not possible to distinguish the boundary between the uterus and the remaining tubal portion due to the alteration of the usual anatomical relationships. No hemoperitoneum in the pouch of Douglas was detected. After the injection of a vasoconstrictor agent inside the pregnancy (20 U of diluted vasopressin in 100 mL of normal saline solution), an incision of the serosa was made (Figures 3B–C). The dissection plane between the myometrium and the suspected gestational sac was identified. So, without damaging the endometrial cavity, the pregnancy as well as surrounding tissue were removed, and an accurate hemostasis on the uterine breach was obtained. Hence, a wedge resection of the right angular part of the uterus (Figures 3D–E). The tissue samples were placed in an endo-bag and extracted through one of the laparoscopic accesses. The uterine wall was then repaired with a double-layer suture by self-blocking monofilament (*V-Loc 2.0* barbed-suture type) (Figure 3F). Eventually, the samples were analyzed by pathologists. The histology confirmed the diagnosis, showing the presence of decidual cells and fragments of myometrium with adenomyosis. The procedure had no complications. The patient was discharged 48 h after surgery. The clinical conditions were satisfactory, and the patient had an immediate return to daily activities without complaining of any symptoms.

3 Discussion

The most common site of ectopic pregnancies is the fallopian tube. Only 2 to 4% of all ectopic pregnancies occur in the interstitial or cornual part of the uterus. The terms cornual and interstitial ectopic pregnancy have been used interchangeably until now. According to literature, the rudimentary horn of a unicornuate uterus or of a septate/bicornuate uterus is where the true cornual pregnancy occurs (4, 5). The angular pregnancy is also frequently mistaken for an interstitial or cornual pregnancy. Angular pregnancies develop anatomically just medial to the utero-tubal junction, at the lateral angle of the endometrial/uterine cavity, and medial to the round ligament (5). Since there is not agreement on the exact ultrasonic characteristics of these three entities, the literature improperly

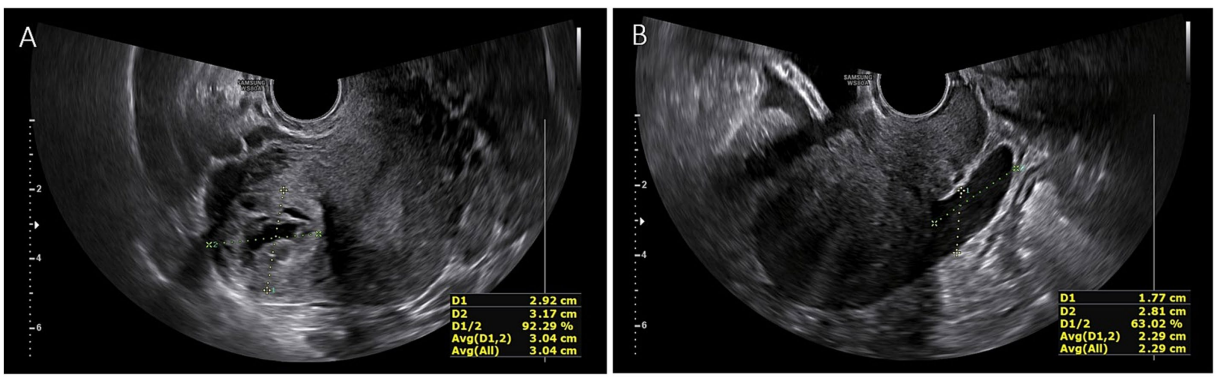

FIGURE 1
(A) Ultrasonographic finding. A 25×26 mm neoformation, with an intense peripheral vascularization in the right angular area suggesting an ectopic pregnancy; **(B)** Free fluid in the pouch of Douglas.

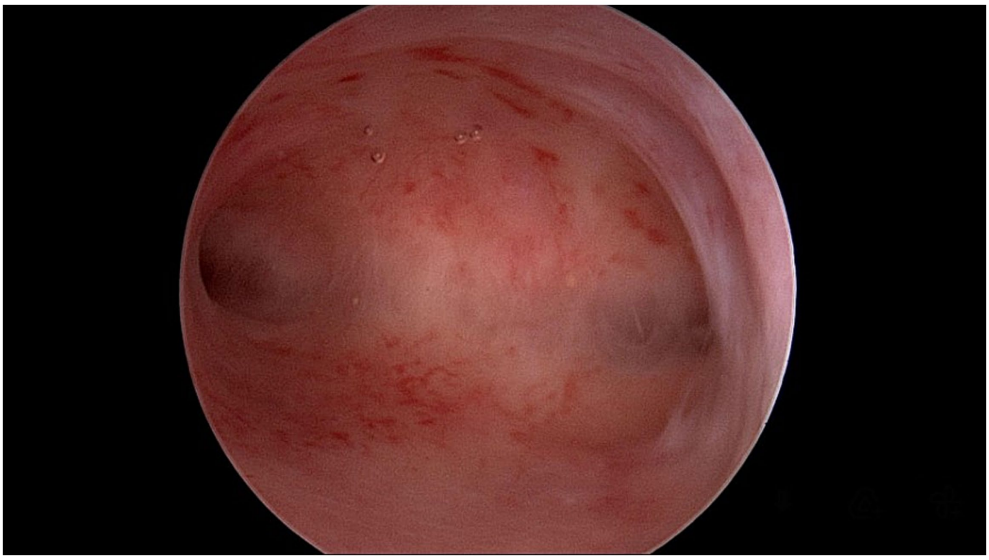

FIGURE 2
Diagnostic hysteroscopy shows an empty uterine cavity with visible tubal ostia.

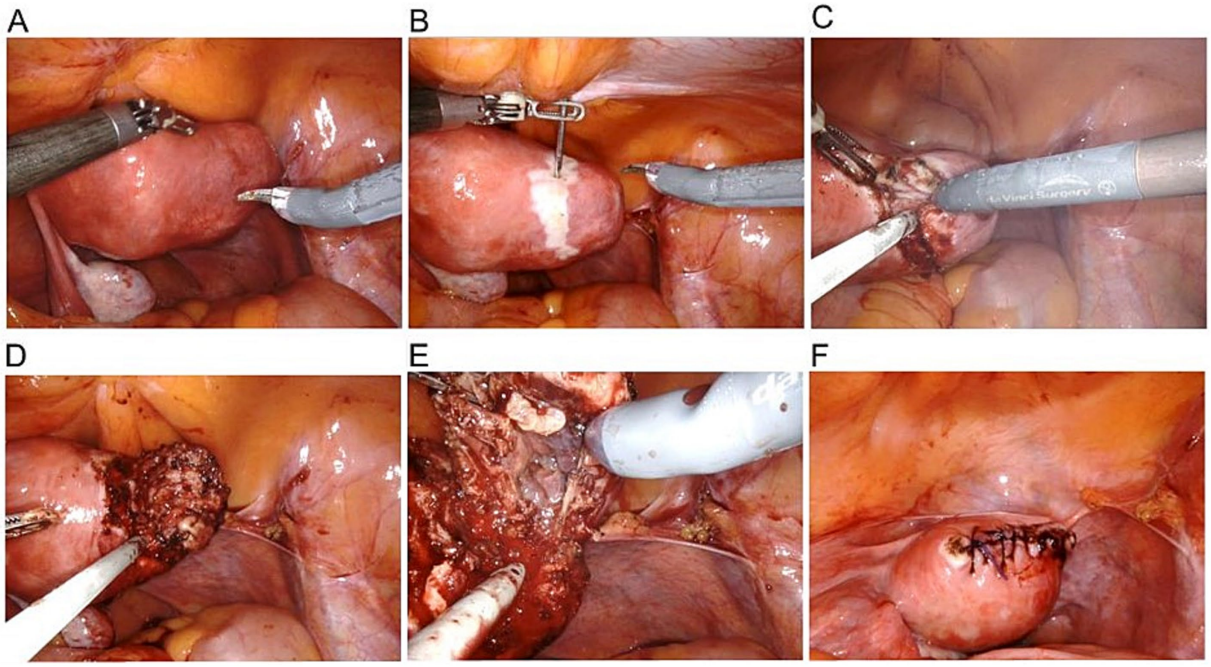

FIGURE 3
(A) Robotic view of interstitial pregnancy; **(B)** Perilesional injection of 20 U of diluted vasopressin in 100 mL of normal saline solution; **(C)** Incision of the serosa and cleavage plan identification; **(D)** Pregnancy and surrounding myometrium resection; **(E)** Gestational sac; **(F)** Uterine wall repair with double-layer suture.

interchanges them. While interstitial or cornual pregnancies can be considered ectopic pregnancies to be terminated, an angular pregnancy should be regarded as a possibly viable intra-uterine eccentric pregnancy since it may be carried to term in some cases (6). Patients may complain of vaginal bleeding or abdominal pain, be asymptomatic, or have their IP discovered after an ordinary early pregnancy ultrasound. Only patients with a diagnosed IP who are hemodynamically stable and have no clear concerns of early rupture, such as large gestational sac or rapidly rising β-hCG levels, should be considered for conservative therapy (both expectant and medical management) (7). For women with an IP with declining serum β-hCG levels (regardless of ectopic mass size or baseline serum β-hCG levels), expectant care is an acceptable first-line strategy (8, 9). Single-dose or multiple-dose courses of methotrexate are employed in medical management. With a failure rate for conservative medical care ranging from 9 to 65% in prior studies, surgical

intervention may still be required if the ectopic pregnancy ruptures. A feasible and safe alternative to systemic methotrexate administration is direct methotrexate injection into the interstitial ectopic pregnancy. Historically, the likelihood of the effectiveness of conservative treatment was estimated using a β-hCG threshold of 5,000.00 mIU/mL. Surgical management of IPs represents an essential option since it provides permanent treatment. Women with IPs who are hemodynamically unstable and/or have ultrasound findings suggesting an incipient or recent pregnancy rupture should have prompt surgery. Patients who receive expectant or medical treatment are at a higher risk of persistent interstitial pregnancy and must be monitored for serial β-hCG values until resolution. The laparoscopic treatment of interstitial pregnancies has been becoming more frequently performed (8), supplanting the classic laparotomic approach. Laparoscopic treatment provides some advantages over laparotomy, including a shorter hospital stay, a faster return to normal activities, and fewer healthcare expenses (10). Over the last few decades, many different kinds of techniques have been developed, including cornuostomia, salpingotomy, and cornual resection (11). Regardless of the surgical technique, blood loss is an inherent hazard of the surgical program. Due to the extremely vascularized interstitial pregnancies (12), multiple strategies can be used before making a cornual incision to minimize intraoperative blood loss: vasopressin injection into the peri-cornual area, electric cauterization of the incision area, endo-loop application to create a para-cornual tourniquet, and an encircling suture around the cornua. Worries are related to electrocoagulation procedure which would weaken the area and possibly increase the risk of uterine rupture in the future by harming the myometrium underneath and delaying the revascularization process. We believe that cautious coagulation of the surrounding myometrium does not compromise the uterine integrity but rather helps to avoid post-operative bleeding. In addition, we maintain that the use of intralesional vasoconstrictors is essential to decrease the hemorrhagic risk and guarantee the surgeon a clean surgical field. To date, the use of robotic surgery for the management of ectopic pregnancies has already been described in the international literature. Ansari et al. reported the first description of robot-assisted cornual ectopic excision, listing the advantages of this technique (13). Robot-assisted surgery (RAS) has been criticized for longer operative times compared to traditional laparoscopy. Some procedures, particularly difficult ones, may actually take less time to complete due to the increased precision provided by the robotic tools and wider eyesight (14, 15). Indeed, in our experience, three-dimensional and magnified vision enables greater overall accuracy, the breadth of surgical gestures simplifies difficult maneuvers, such as suturing, and significantly reduces operating times. In addition to the well-known benefits of laparoscopy, RAS allows for precision surgery. This results in greater respect for anatomy and minimal healthy tissue injury, which we hypothesize may play a role in preserving fertility. About the "docking time" that affects the *Da Vinci® Robotic Surgical System*, the most important variable is surely the experience of the operating team. Indeed, many studies have analyzed robotic surgical learning curves on the *Da Vinci* platform and have suggested that the longer operative times associated with RAS decrease as surgeons become more familiar with the technology (16). Through adequate training, our staff has acquired the right skills to perform robotic docking and set-up time-effectively, so the overall operating time was not much different from that of conventional surgery (Figure 4). Previous tubal surgery constitutes an independent risk factor for the development of ectopic pregnancies (17). Considering that our patient underwent monolateral salpingo-oophorectomy during childhood, it remains to be explained how the pregnancy was implanted in the interstitial tubal portion. To hypothesize about the circumstances leading to this scenario, it is plausible that the oocyte has been fertilized in the intact tube and subsequently migrated into the control-lateral tubal stump. This transfer could be facilitated by intrauterine fluid currents. Alternatively, some Authors suggest that an ovum could have transmigrated and passed through a fistula into the tubal stump, where successive sperm fertilization and local embryo nidation occurred (18). However, unknown is the mechanism that could allow the oocyte to be intercepted by a mutilated tube, in which the fimbrial structures that should capture it are now abolished. An attractive explanation might be that the tubal stump remodeled throughout the years, gaining the ability to intercept the oocyte released by the contralateral ovary. Moreover, to support this proposal, there is some evidence that the uterus undergoes remodeling processes after surgical procedures (19). So, considering the possibility of future remodeling of the uterus, it is reasonable to assume the precision of the robotically assisted system was perfectly suited to this rare condition. The only studies found in the literature referring to ectopic pregnancy after a previous tubal surgery concern patients with prior salpingectomy undergoing *in-vitro* fertilization (IVF) and embryo transfer (20). The strength of this work is that we have described an absolutely rare case with truly innovative surgical management. The hope is to encourage scientific research on this topic, considering that the literature is still rather limited, and to stimulate collective interest in deepening the etiopathogenesis of ectopic pregnancies. However, the superiority of robotic surgery over traditional laparoscopy

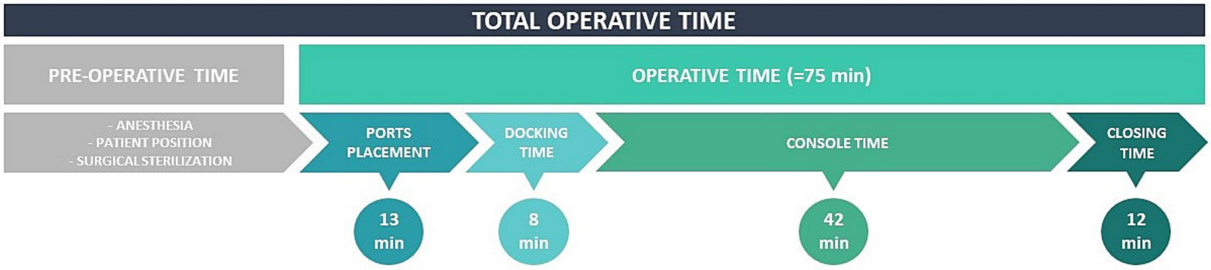

FIGURE 4
Summary of operating room timeline.

remains to be defined in a larger case study. Indeed, the main limitation of our work is that a single case of interstitial pregnancy on the tubal stump is described, which limits generalizability. Unfortunately, interstitial pregnancies are very rare. As a result, it is difficult to understand if our approach is applicable on a large scale.

4 Conclusion

IP remains a truly rare condition. We believe that robotic surgery represents a feasible and safe strategy for the surgical treatment of IPs and can offer some advantages, such as shorter surgical time, magnification of the operative field, wide mobility of the robotic arms, minimal invasiveness, and minimal blood loss, while minimizing the risks. Nevertheless, a pilot study could validate our positive surgical management. Finally, further evidence is needed to conclusively explain the pathophysiological mechanisms underlying the development of spontaneous IPs on the tubal stump.

Data availability statement

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

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

MA: Writing – original draft, Writing – review & editing, Data curation, Investigation. LD: Writing – original draft, Writing – review & editing. GD'A: Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Investigation. MP: Writing – original draft, Writing – review & editing, Investigation, Supervision. RW: Writing – original draft, Writing – review & editing, Supervision, Validation, Visualization. AD: Writing – original draft, Writing – review & editing, Validation, Visualization. GB: Writing – original draft, Writing – review & editing, Supervision, Validation, Visualization.

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Conflict of interest

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

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Comparison of sexual function between laparoscopic lateral suspension and laparoscopic sacrocervicopexy with the use of the PISQ-IR questionnaire

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Introduction and hypothesis: We aimed to analyze the quality of sexual life of patients with apical vaginal wall prolapse who had undergone laparoscopic lateral suspension (LLS) and laparoscopic sacrocolpopexy (LSC).

Methods: We performed a secondary analysis of sexual outcomes of a previous randomized control trial comparing LLS and LSC in 89 women with symptomatic POP stage ≥ II. We evaluated sexually active (SA) and non-sexually active women (NSA) using the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire-IUGA-Revised (PISQ-IR). Women were reviewed over a period of 1 year post-surgery.

Results: Analysis of the entire PISQ-IR questionnaire indicates that surgical treatment of POP resulted in an improvement of the quality of sexual life in 21 (80.76%) in the group of sexually active women after LSC and in 20 (83.33%) in the group of SA patients after LLS. In both groups of patients, dyspareunia was not observed.

Conclusion: In conclusion, the quality of sexual life in SA group of patients improved significantly after both surgical procedures. The quality of sexual life of surveyed women significantly improved after curing POP symptoms.

KEYWORDS

pelvic organ prolapse, lateral suspension, sacrocervicopexy, sexual function, pelvic organ prolapse/incontinence sexual questionnaire—IUGA revised (PISQ-IR)

1 Introduction

Pelvic Organ Prolapse (POP) primarily affects women of menopausal age and has a detrimental impact on their quality of life. In addition to causing unpleasant symptoms, POP often leads to a deterioration of sexual function (1, 2).

The number of women undergoing surgery for POP increases each year (3, 4). However, studies show that sexual function differs after various surgical procedures (5–7).

Apical suspension procedures can be broadly categorized into transvaginal and abdominal approaches. Abdominal procedures can be performed via laparotomy, conventional laparoscopy,

or robotic-assisted laparoscopy. Transvaginal apical suspension methods include native tissue repairs and mesh-based repairs.

1.1 Sacrocolpopexy

Traditionally, sacrocolpopexy has been performed through a laparotomy, known as abdominal sacrocolpopexy (ASCP). However, over the past decade, minimally invasive techniques, including laparoscopic (LSCP) and robotic sacrocolpopexy (RSCP), have become increasingly favored due to their advantages such as shorter recovery times, reduced postoperative pain, and smaller incisions compared to the open abdominal method. Laparoscopic sacrocolpopexy (LSCP) is now regarded as the gold standard for treating apical prolapse, although it requires more advanced surgical expertise. Operating near the sacral region carries potential risks, including neurological, ureteral, or vascular injury, and postoperative bowel issues are frequently reported. Moreover, periostitis, although rare, can occur due to the weak anterior longitudinal ligament at the site of sacral attachment, increasing the risk of periosteal penetration during surgery.

Compared to vaginal procedures, ASCP is associated with higher morbidity, particularly in terms of longer operative times (notably for laparoscopic or robotic approaches), extended hospital stays, delayed return to normal activities, and increased costs. Additionally, sacrocolpopexy may involve mesh-related complications, such as erosion, infection, or pain, although these complications are rare with the use of modern surgical techniques (8–15).

Laparoscopic lateral suspension (LLS) Laparoscopic lateral suspension with mesh has emerged as a promising technique, offering both excellent anatomical and functional outcomes. The uniqueness of LLS lies in the placement of the T-shaped mesh, where the lateral arms are passed through a subperitoneal tunnel along the lateral abdominal wall, exiting just above the iliac crest. This approach minimizes the risk of injury to major blood vessels, nerves, or the bowel and ensures symmetrical, tension-free suspension along the vaginal axis. LLS is primarily indicated for the treatment of anterior pelvic organ prolapse and apical descent. It is particularly useful in cases where access to the sacral promontory is challenging, such as in the presence of dense adhesions, sigmoid megacolon, or when the left common iliac vein is positioned low and partially obstructs the promontory.

Like other mesh-based procedures, LLS carries risks of mesh-related complications, including erosion, infection, and pain. Although the mesh is placed at a distance from the vaginal mucosa, these complications can still occur. While LLS has demonstrated favorable short-to medium-term outcomes, long-term data remain limited when compared to procedures such as sacrocolpopexy. Several studies and reviews have noted a higher risk of recurrence in the anterior compartment after LLS compared to sacrocolpopexy, underscoring the need for further research into its long-term efficacy (16–19).

1.2 Pectopexy

Pectopexy, introduced by Banerjee and Noé in 2010 (20), is a viable alternative to sacrocolpopexy for pelvic organ prolapse repair. Like sacrocolpopexy, pectopexy employs a macroporous, monofilament mesh; however, instead of attaching to the presacral ligament, the mesh is secured to the right and left pectineal ligaments, supporting the anterior and/or posterior vaginal walls. Pectopexy offers several advantages, including a shorter operative time and a lower rate of complications compared to laparoscopic sacrocolpopexy. Additionally, it is particularly beneficial for obese patients, providing a safer and more effective option than traditional sacrocolpopexy in this population. Despite its advantages, pectopexy also has certain drawbacks. One of the primary concerns is the lack of long-term data compared to sacrocolpopexy, limiting our understanding of its durability and effectiveness over time. Additionally, pectopexy may have a higher risk of anterior compartment prolapse recurrence due to its lateral mesh fixation, which may not provide as robust support for the vaginal apex as sacrocolpopexy. There is also the potential for complications such as mesh erosion, infection, and pain, which are risks associated with any mesh-based procedure. Finally, while pectopexy avoids the risks related to sacral nerve and vascular injury seen in sacrocolpopexy, it can still pose a risk to nearby structures, including the obturator nerve and vessels, during fixation to the pectineal ligaments (20–24).

1.3 Sacrospinous ligament fixation

Sacrospinous ligament fixation (SSLF) is a widely recognized and frequently reported transvaginal procedure for addressing apical prolapses using native tissue techniques. This minimally invasive approach offers several advantages, including reduced recovery times, making it an appealing option for women who wish to avoid abdominal surgery or who may not be suitable candidates for sacrocolpopexy. Despite its benefits, SSLF may lead to complications such as vaginal asymmetry, which may impact sexual function. Additionally, during the procedure, there is a risk of injury to critical neurovascular structures located in proximity to the surgical site. When compared to sacrocolpopexy, the recurrence of prolapse is higher (25, 26).

1.4 Ipsilateral uterosacral ligament fixation

Ipsilateral uterosacral ligament fixation (USLS) is a surgical technique that suspends the vaginal apex to the proximal remnants of the uterosacral ligaments via an intraperitoneal approach. This method effectively restores the vaginal axis, thereby mitigating the higher incidence of retroflexion commonly seen with sacrospinous ligament fixation (SSLF). However, patients with more severe prolapse or significant pelvic floor laxity have been noted to experience a higher recurrence rate following this procedure. Additionally, USLS carries the risk of potential injury to adjacent structures, including the ureters and nearby nerves, which necessitates careful surgical technique and consideration during the operation (27–30).

1.5 Transvaginal mesh procedures

Transvaginal mesh procedures involve the insertion of synthetic mesh through the vaginal wall to provide robust and durable support for prolapsed organs. This surgical approach is particularly beneficial in cases where prolapse affects not only the vaginal apex but also the anterior and/or posterior compartments. However, these procedures

carry a significant risk of complications, including mesh erosion, infection, pain, and dyspareunia. The use of mesh in vaginal surgeries has also led to numerous legal challenges, prompting restrictions in some countries due to safety concerns. As a result, careful consideration of the risks and benefits is essential when evaluating the use of transvaginal mesh for pelvic organ prolapse repair (31–33).

1.6 McCall culdoplasty

McCall culdoplasty was not initially designed specifically for the treatment of vaginal vault prolapse, it has been shown to effectively prevent recurrence after hysterectomy. Among the various techniques for suspending the vaginal apex during vaginal hysterectomy, McCall culdoplasty is the most commonly performed procedure. This technique involves obliterating the posterior cul-de-sac and plicating the uterosacral ligaments across the midline.

A large study conducted at the Mayo Clinic demonstrated a high success rate in preventing prolapse recurrence among patients who underwent McCall culdoplasty, with the majority expressing satisfaction with their outcomes. Therefore, McCall culdoplasty appears to be an effective method for preventing vaginal vault prolapse following primary repair after hysterectomy, with minimal associated morbidity (34–37).

Obliterative surgery, including total colpocleisis and LeFort partial colpocleisis, is another option for managing apical pelvic organ prolapse (POP). However, these procedures are typically reserved for elderly women, those with significant medical comorbidities, or individuals who are no longer sexually active (38).

Several studies suggest that laparoscopic surgery for POP may confer significant benefits comparing to the vaginal approach (39–44). Unfortunately, there is a lack of consensus regarding the optimal way of surgery to preserve women's sexual function (45).

Laparoscopic sacrocolpopexy remains the gold standard in the treatment of apical prolapse and it is recommended in sexually active patients (14, 42). Laparoscopic lateral suspension turned out to be an alternative procedure and has proved good anatomical as well as functional outcomes (46–54). However, there are only a few studies that describe the impact of laparoscopic lateral suspension on sexual function using validated questionnaires (55, 56).

Pelvic Organ Prolapse/Incontinence Sexual Questionnaire—IUGA Revised (PISQ-IR) is condition—specific measure of sexual function in women with PFD (Pelvic Floor Disorders) (57). Despite the growing demand for validated measures of sexual dysfunction, the PISQ-IR has not been widely used in patients who have undergone laparoscopic urogynaecological procedures. This underutilization highlights a significant gap in our understanding and management of sexual dysfunction in this population.

The aim of this study was to compare sexual function outcomes between laparoscopic lateral suspension and laparoscopic sacrocervicopexy, assessed before surgery and 12 months postoperatively.

2 Materials and methods

This retrospective observational study included 100 women referred to our department and qualified for surgery from January 2018 to December 2021. We performed a secondary analysis of sexual outcomes of a previous randomized control trial comparing LLS and LSC (53).

Preoperative data collected included age, parity, body mass index, and hormonal status.

The study inclusion criteria were: symptomatic apical prolapse stage ≥ II according to the Pelvic Organ Prolapse Quantification (POP-Q) system, sexually active women (SA), sexually not active women (NSA), all women who were able to understand and write in Polish.

The exclusion criteria included: a history of previous urogynecological surgeries, including prolapse/incontinence surgery and hysterectomy; active malignancy; posterior vaginal wall prolapse ≥ II stage.

Stress urinary incontinence was not an exclusion criterion, but patients were informed that only surgical repair of POP would be performed. 43 patients were qualified for laparoscopic sacrocervicopexy, and 46 for laparoscopic lateral suspension. All women underwent concomitant laparoscopic supracervical hysterectomy, which is a standard procedure in our department. All surgical procedures were performed by an experienced surgical team. In our study, we utilized a polypropylene mesh with a pore size of 1 mm and a product weight of 65 g/m^2 for LLS and SCP procedures".

The study was approved by our institutional ethic committee, and patients who met the inclusion criteria signed informed consent prior to participation in the study. Eleven patients were excluded because they did not meet all inclusion criteria or met at least one exclusion criterion.

2.1 The applied questionnaire

The patients completed a validated Polish questionnaire, the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire—IUGA Revised (PISQ-IR) before undergoing surgery and 12 months postoperatively. The data were collected through face-to-face interviews conducted by an experienced urogynecologist (EMJ).

PISQ-IR is the disease-specific questionnaire to assess the women's sexual function in both sexually active (SA) and inactive women (NSA) with PFD (Pelvic Floor Disorders) (57, 58).

PISQ-IR consists of two parts. Part 1, for not SA (NSA) women, and contains four domains – specific subscales (Condition – specific—NSA—CS, Partner-related—NSA—PR, Global Quality—NSA-GQ, Condition Impact—NSA-CI). Part 2, for sexually active (SA) women with six domains – specific subscales (Arousal-Orgasm—AO, Condition-specific—CS, Partner-related—PR, Desire – D, Condition Impact – CI, Global Quality—GQ).

In the PISQ-IR questionnaire, the first question (Q1) describes the engagement in sexual activity and sound: "Which of the following describes you?" According to this, we enrolled patients to two groups SA and not SA. The enrolment process is shown in Figure 1.

Data was collected by face to face interview and from the patient's medical records. Physical examination was conducted one month after surgery, including POP-Q evaluation. The information collected from patients' medical records included anamnesis and the patients' physical examination results. All women underwent post-operative follow-up within 3–6 months postoperatively to assess recurrent prolapse or mesh exposure or other potential complications of the surgery. A personal interview 12 months after surgery was carried out

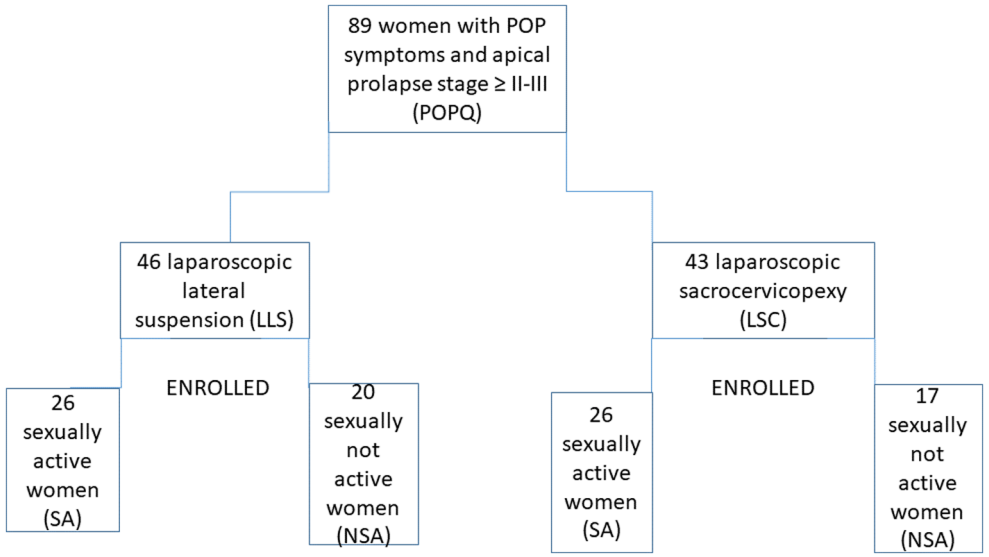

FIGURE 1
Study flowchart.

by an experienced urogynaecologist EMJ. In this interview, the patients were requested to answer a PISQ IR questionnaire.

2.2 Statistical analysis

Based on the collected data, a database was created using Microsoft Excel® 2013 (15.0.5589.1000) MSO (15.0.5589.1000) (32-bit), from Microsoft Office Standard 2013, Microsoft Corporation, manufacture code DG7GMGF0D7FX:0002. The data were statistically analyzed using Gretl software version 2017a. Comparisons were made between LLS and LSC preoperatively and 12 months postoperatively; the p value was obtained using a t-test. The significance level was assumed to be $p < 0.005$.

3 Results

In the analyzed group of 89 female patients, 52 (58.42%) were sexually active (SA) and 37 (41.57%) were inactive (NSA). All of the patients were qualified for surgery because of pelvic organ prolapse (POP). We have observed significant improvement of POP after both procedures. Tables 1, 2 present anatomic outcomes before and after both surgeries.

26 (60.46%) sexually active and 17 (39.53%) inactive patients were qualified for laparoscopic promontofixation surgery, while in the group of patients qualified for laparoscopic lateral suspension surgery, 26 (60.46%) were sexually active and 20 (43.47%) inactive.

In the group of 17 NSA women qualified for laparoscopic promontofixation surgery: 9 (52.94%) women had non-intercourse due to the lack of a partner (NSA-PR), 8 (47.05%) women had non-intercourse due to the lack of intercourse despite having a partner, of which in 2, the lack of desire for intercourse was the result of prolapse (NSA-CS). From the non-intercourse groups due to the surgical reduction of POP, both patients returned to sexual activity.

TABLE 1 Anatomic outcomes in patients undergoing laparoscopic sacrocervicopexy with mesh.

POP-Q parameters	Preoperative		Follow-up		p
	Mean	SD	Mean	SD	
Aa	0.86	0.91	−1.49	1.18	0.000
Ba	1.70	1.10	−1.37	1.50	0.000
Ap	−0.72	0.73	−1.63	0.79	0.000
Bp	−0.72	0.73	−2.09	1.77	0.000
C	0.35	1.53	−5.44	2.51	0.000
gh	3.91	0.57	2.84	0.78	0.000
pb	2.33	0.81	2.63	0.62	0.022
tvl	10.00	–	10.00	–	

POP – Q – Pelvic Organ Prolapse Quantification System, SD – Standard Deviation, p – value <0.0001.

In a group of 26 SA women scheduled for laparoscopic promontofixation surgery, 17 (65.38%) patients stated that they "significantly" or "very much" avoid sexual activity due to the prolapse of the reproductive organ (SA-CI). The remaining 9 (34.61%) patients replied that the problem of prolapse did not determine their sexual activity. Despite this, a total of 21 (80.76%) women experienced an improvement in the quality of their sexual life after the surgery, due to the reduced feeling of discomfort associated with the improvement of anatomical conditions.

In the group of 20 NSA women qualified for lateral suspension surgery: 4 (20%) women did not have intercourse due to the lack of a partner, 16 (80%) women did not have intercourse due to the lack of willingness to have intercourse, despite having a partner, of which 9 women did not want to have intercourse caused by POP (NSA-PR, NSA-CS). From the group of women who did not have sexual intercourse due to the POP, all patients returned to sexual activity after the surgery.

In a group of 26 SA women qualified for laparoscopic lateral suspension surgery, 15 patients answered that they avoid "significantly"

TABLE 2 Anatomic outcomes in patients undergoing laparoscopic lateral suspension with mesh.

POP-Q parameters	Preoperative		Follow-up		*p*
	Mean	SD	Mean	SD	
Aa	1.02	0.54	−1.65	0.95	0.000
Ba	1.91	0.51	−1.57	1.20	0.000
Ap	−0.41	1.09	−1.57	1.05	0.000
Bp	−0.46	0.98	−2.07	2.12	0.000
C	0.30	1.41	−5.39	2.75	0.000
gh	4.09	0.41	2.96	0.70	0.000
pb	2.17	0.97	2.47	0.69	0.025
tvl	10.00	–	10.00	–	

POP – Q – Pelvic Organ Prolapse Quantification System, SD – Standard Deviation, *p* – value <0.0001.

or "very much" sexual activity due to the POP (SA-CI). The remaining 11 patients replied that the problem of POP did not determine their sexual activity. Despite this, 20 (76.92%) women had a significant improvement in their quality of life due to the improvement of depression symptoms.

After both surgeries, no patient in the NSA and SA groups reported dyspareunia or other health problems.

Despite the lack of sexual activity due to reluctance to have intercourse or the lack of a partner, NSA women in both study groups assessed the subjective quality of sexual life (NSA-GQ-) as "sufficient and satisfactory," both before and after surgical treatment. In response to the questionnaire question "How much does the lack of sexual activity bother you?" answered "Not at all" or "A little".

In contrast to NSA patients who did not have sexual intercourse due to a POP, who answered the same question "It bothers me a lot" or "It bothers me a lot." This indicates that the POP was the reason for not having intercourse.

In the group of SA patients, after both procedures, there was no significant improvement in the quality of life in terms of the feeling of orgasm or sexual desire (SA-O, SA-D domain). In the entire SA group operated on, a "positive" or "very positive" influence of the sexual partner on the perceived sexual desire was found, but the surgery did not improve the degree of sexual interest (SA-P domain).

Analyzing the entire questionnaire, surgical treatment to correct the reduction contributed to the improvement of the quality of sexual life in 21 (80.76%) of 26 in the group of sexually active women after promontofixation surgery and in 20 (76.92%) of 26 in the group of SA patients (sexually active) after side suspension surgery (Table 3). Therefore, the quality of sexual life in this group of patients improved significantly after both surgical procedures. The treatment of the symptoms of POP significantly influenced the improvement in the quality of sexual life of the surveyed women (Figure 2).

There was no significant statistical difference between groups in improvement in sexual quality of life after both procedures in NSA women. A total of 11 women in the NSA group returned to sexual activity.

TABLE 3 Change in sexual status at 12-months.

	Preoperatively	Postoperatively
NSA at baseline	37 (41.57%)	11(29.72%)
Change from NSA to SA	11 (29.72)	11(4%)
SA at baseline	52 (58.42%)	41 (78.84)
Change from SA to NSA	0 (0%)	0 (0%)

4 Discussion

According to the International Continence Society (ICS) and the International Urogynecological Association (IUGA) Pelvic Organ Prolapse (POP) is defined as „the descent of one or more of the anterior vaginal wall, posterior vaginal wall, the uterus (cervix) or the apex of the vagina, or the perineum (perineal descent)" (59). The symptoms of Pelvic Organ Prolapse (POP) experienced by women can have a significant impact on their biopsychosocial, psychological, and social well-being. According to patient-reported outcome measures (PROMs), women with POP reported moderate levels of pain during sexual intercourse and low levels of bodily pain. Furthermore, POP was found to have a low to moderate impact on sleep quality, energy levels, quality of life, and sexual function domains, while its impact on physical symptoms and general health perception domains was relatively low. The results of PROMs assessing physical functioning varied widely, ranging from low to high impact (60, 61).

Sexual health, as defined by the World Health Organization, is a state of complete physical, mental, and social well-being related to sexuality. It encompasses not just the absence of disease or infirmity, but also emotional health (62). Sexual functioning is defined as "absence of difficulty moving through the stages of sexual desire, arousal, and orgasm, as well as subjective satisfaction with the frequency and outcome of individual and partnered sexual behavior" (63). Patient-reported outcome measures (PROMs) questionnaires provide a valuable patient-centered perspective on the effectiveness of surgical interventions for Pelvic Organ Prolapse (POP). However, it's crucial to carefully choose a prolapse-specific questionnaire that is both validated and prelevant to the patient's condition. This ensures an accurate and thorough portrayal of their experiences and outcomes.

To assess female sexual functioning, various questionnaires such as the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire—IUGA Revised (PISQ-IR), Female Sexual Function Index (FSFI), International Consultation on Incontinence Questionnaire–Vaginal Symptoms Module (ICIQ-*VS*), Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-12 (PISQ-12) can be used. The ICIQ-VS questionnaire may not be the best choice for obtaining a comprehensive understanding of a patient's condition, as it solely focuses only on vaginal symptoms and is comparatively shorter (4 main questions). The Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ) and its short form version, the PISQ-12, are the only current validated condition-specific female sexual function questionnaires purposively developed to assess sexual function in women with UI and/or POP (64, 65).

PISQ-12 is a shortened version of the PISQ-31 questionnaire presented in 2001. This questionnaire is used to assess sexual function in heterosexual patients with diagnosed POP and/or UI who have been sexually active over the last 6 months. It should not be used for patients who have no partner or are sexually inactive (66). The International Urogynecological Association (IUGA) Sexual Function Working Group undertook a comprehensive re-evaluation of the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire (PISQ), with the primary objectives of refining its psychometric properties, expanding its applicability to women who are not sexually active and

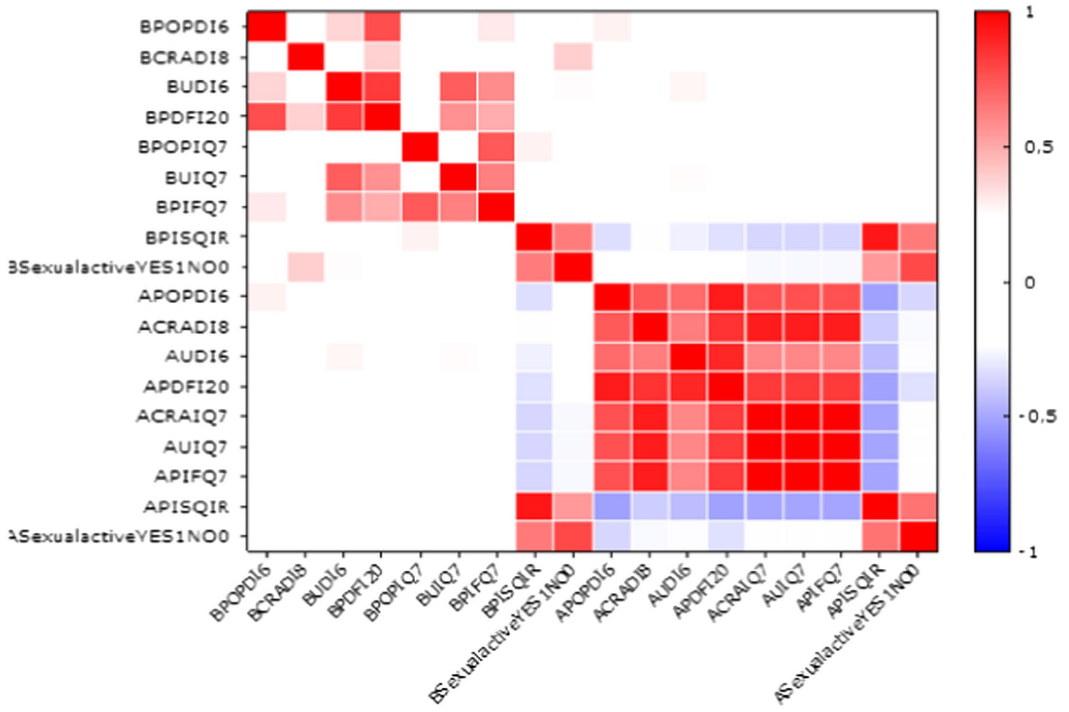

FIGURE 2
Correlation between sexual activity and symptomatic domains of questionnaire (red colors represent positive correlations, while blue colors denote negative correlations, the darker or more saturated the color—the stronger the relationship).

those with anal incontinence, and creating a universally applicable instrument for international use (67). These objectives have been successfully achieved with the development of the PISQ-IR, a revised and enhanced version of the original questionnaire.

PISQ-IR includes new ways of evaluating the inherent diversity of women who suffer from pelvic floor disorders (PFDs). Notably, the questionnaire incorporates gender-neutral items to evaluate the impact of a partner on sexual function. Although PISQ-IR enhances the ability to assess outcomes in women who are not sexually active and in women with anal incontinence. Importantly, this questionnaire was designed as an instrument that was directed toward international usage. The PISQ-IR questionnaire has undergone translation and validation in 11 different languages, including Polish (67).

The main focus of our study was the treatment of apical vaginal wall prolapse. There are various surgical techniques for treating apical vaginal prolapse, including open, laparoscopic, and vaginal approaches. These surgical procedures for PFD are associated with a range of side effects, some of which can be successfully avoided by selecting an appropriate method. The gold standard to treat apical prolapse is sacrocolpopexy (SCP) (10, 48). Recent research has confirmed that laparoscopic lateral suspension (LLS) is a valid and effective alternative to sacrocolpopexy (SCP) for apical pelvic organ prolapse (POP) repair. There is no significant difference in apical prolapse cure rates between LLS and SCP, indicating that LLS can achieve comparable outcomes to the SCP. The LLS seems preferable in terms of the Female Sexual Function Index, Pelvic Organ Prolapse Symptom Score, reoperation, and complications (68).

In our study those patients who were sexually active had sexual intercourse regardless of the POP. However, the improvement of anatomical conditions after surgery reduced the feeling of discomfort. Although before surgery, the majority of respondents in the group of SA women reported that POP did not affect their sexual life.

The vast majority associated the quality of sex life with a good relationship with their partner. Like other authors, we did not find any changes in the behavioral-emotional domain after surgical treatment, which assesses sexual desire and arousal, frequency of sexual activity, and the feeling of orgasm. One year after the surgery, the percentage of women with reduced sexual desire before the surgery did not change significantly after the surgery. Patients who did not have sexual intercourse before surgery mentioned age-related decreased sexual drive as the reason for this. The next cause was the POP. Surgical treatment did not improve these feelings, only the patients' psychological comfort. It is worth emphasizing the fact that in the group of patients who did not have intercourse, some of them returned to sexual activity. This was due to the improvement in the quality of life in the range of experienced symptoms of POP and the return of the desire to have intercourse with a partner.

Numerous studies compare the postoperative results of patients who underwent LSC and anterior vaginal mesh (AVM), including impact on sexual activity or function. For example, vaginal length was greater following LSC-Cx compared to AVM. However, it is essential to note that vaginal length does not have a significant impact on female sexuality either preoperatively or postoperatively, the most important factors were "having a partner" for sexual activity and dyspareunia for sexual function (69). The persistence of dyspareunia was found to be higher after AVM (70, 71). Besides, transvaginal procedures have an

increased risk of vaginal erosion, which can occur in up to 20% of patients who undergo transvaginal surgery for POP repair (72). We did not observe any cases of mesh erosion in any of the groups.

According to the available data, surgical management of POP usually results in improved or unchanged scores in sexual function, regardless of the type of procedure used.

None of the patients reported any deterioration in the quality of sexual life after both procedures. We did not observe dyspareunia after both surgeries. There were no women who became sexually inactive due to the surgery.

Our results showed that laparoscopic surgery can improve the quality of women's sex lives by reducing symptoms associated with POP. The improvement in satisfaction with sexual life resulted from getting rid of the main problem, which was POP and the associated discomfort. Patients who had their uterine corpus removed during urogynecological surgery considered it an element that did not affect their quality of life, including sexual life. This is extremely important in the current discussion on leaving the uterine body during surgery for static disorders.

The data and results collected in this study can serve as a reference for future follow-up on the same cohort with the same tool, namely the PISQ+IR questionnaire. Including the same questionnaire in future studies containing different surgical techniques for POP repair will allow for objective and valid comparison between the operative techniques (73).

This study has several limitations. Considering the potential long-term complications associated with vaginal mesh observed in clinical practice, further investigations are warranted. Factors contributing to these complications include the inherent complexity of pelvic floor disorders, which remain inadequately understood; the biomechanical properties of the mesh, which may not be suitable for pelvic floor applications; variations in surgical techniques and the use of different modifications in operational practices across hospitals; and deficiencies in the regulatory processes for monitoring implantable medical devices. Standardization of surgical procedures is also needed.

The follow-up period is 12 months after the surgery. A longer follow-up is required to evaluate functional status for the long-term results and potential complications such as postoperative incontinence, other voiding dysfunctions, pudendal neuralgia. This study though, as mentioned, can be an initial reference point for any future follow-up. On the other hand, 12 months after surgery is an adequate period to assess POP surgeries efficacy. Our study presents important information regarding the success of laparoscopic lateral suspension pelvic organ prolapse reconstructive surgery.

Data availability statement

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

Author contributions

EM-J: Conceptualization, Investigation, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft. AS: Supervision, Writing – review & editing. MM: Data curation, Resources, Writing – review & editing. DF: Project administration, Writing – review & editing. DO: Project administration, Writing – review & editing. JD: Supervision, Writing – original draft.

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Conflict of interest

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

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