Application of robot-assisted laparoscopic pelvic exenteration in treating gynecologic malignancies

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Introduction

Pelvic exenteration (PE) refers to the *en bloc* resection of the involved pelvic organs along with pelvic reconstruction so as to enhance the survival rate for tumor patients. First reported by Brunschwig in 1948,[1] PE has thereafter been utilized to treat rectal cancer, bladder cancer, prostate cancer, and cervical cancer as a curative or palliative treatment for advanced or recurrent malignancies. It is critical to carry out surgical resection of all the involved tumor lesions so as to prolong the overall survival (OS) of patients; nonetheless, such medical manipulation will induce various complications. For patients undergoing radiotherapy in the initial treatment, the increased tissue fragility, together with inflammation, has become trouble intraoperatively.[2]

Robot-assisted laparoscopic surgery is developed on the basis of traditional laparoscopy, which has completely inherited the superiorities of laparoscopic surgery. More importantly, it can achieve a more stereoscopic visual field as well as more precise operation through establishing the three-dimensional visual field, and using the inner wrist system as well as the tremor filtering system. Moreover, it can accurately return to the last operation area through the presetting and memory function of its system software, which can, thus, contribute to avoid miscarriage, further reduce intraoperative blood loss, and decrease the occurrence of intraoperative complications.[3,4] In 2009, Lim *et al*[5] had first performed the robot-assisted laparoscopic PE (RALPE) combined with ileal loop urinary diversion for a relapsed cervical cancer patient. The operation time was 375 min, the blood loss was about 375 mL, and no intra- or postoperative complications were observed. Thereafter, surgical teams from countries all over the world have continuously applied RALPE in treating gynecologic malignancies.

This study aimed to review the application of RALPE in treating gynecologic malignancies, including its indications, methods and feasibility, complications, and follow-up.

Indications for RALPE

Gynecologic malignancies have not only posed a severe threat to women's lives, but also caused various complications due to the invasion to surrounding tissues and organs, thus seriously affecting the quality of life of these patients. Surgery is not recommended in the guidelines to be the preferred choice for advanced cancer; in addition, surgical treatment has been generally recognized to be of limited value for patients developing distant metastasis.[6] As a result, physicians should carefully and strictly select the appropriate patients so as to ensure the safety and effectiveness of surgery. Specifically, factors including previous treatment history, size of recurrent tumors, distant metastasis, negative margin, the general condition of patients, economic conditions, and treatment intention should be evaluated preoperatively.

Over the last decades, the indication for PE has evolved from the classical indication of centrally persistent or recurrent cervical cancer to the locally advanced primary cancers or the recurrent endometrial, vulvar, vaginal, and ovarian cancers in selected cases; notably, pelvic sidewall recurrence is no longer an absolute contraindication.[2,7,8] In a recent monocentric cohort study carried out by Knight *et al*,[9] the frequency of PE performed during four successive periods had been evaluated, and it was concluded that the indications for PE had evolved toward the curative intents, though PE was initially developed to manage palliative situations with severe pelvic symptoms (such as fistulas, bleeding, visceral, and parietal pain) with no other therapeutic options. Typically, the increased success rate of curative PE can be attributed to the better selection of patients. However, it remains controversial regarding the importance of nodal involvement, though some studies have associated it with poor patient prognosis.[10,11] Meanwhile, some other studies do not identify that pelvic lymph or para-aortic lymph node metastasis and/or hydroureteronephrosis is a contraindication.[12-15]

Among the existing RALPE cases in the field of gynecologic oncology, only one case with advanced cervical cancer has selected RALPE as the initial treatment, while the rest have developed recurrent cervical or endometrial cancer. In addition, 17 out of those 22 recurrent cases have a radiotherapy history, while the remaining five have only received surgical treatment before, but these recurrent cases have been complicated with internal fistula or other contraindications of radiotherapy. Nevertheless, no detailed report is available for other gynecological malignancies, such as ovarian cancer and vulvar cancer, regarding the application of RALPE at present.

RALPE can reasonably expand the indications by providing minimally invasive surgery, better postoperative recovery, more flexible and precise manipulation for the elderly patients, obese patients, and patients with pelvic or aortic lymph node metastasis. Moreover, there is no large incision in the abdomen, which also facilitates the nursing care of the Ostomy Bag postoperatively.

Surgical Methods and Feasibility of RALPE

Surgical methods

Typically, the preparation process for robotic surgery is relatively more complex, including posture adjustment, Trocars insertion (five Trocars are routinely used), and mechanical arm docking. Specifically, the required time depends on the proficiency of the operation team, which is usually within 15 min by an experienced team. Notably, the main surgeon can start the operation in the operating area without hand washing and disinfection. For time-consuming multidisciplinary operations, such as PE, the robot system can provide a more comfortable and flexible operating platform for the main surgeon.

According to the resection extent (whether involving the bladder, rectum, or both), PE can be classified into anterior pelvic exenteration (APE), posterior pelvic exenteration (PPE), and total pelvic exenteration (TPE). Moreover, there are three basic methods for urinary reconstruction after radical cystectomy, including incontinent urinary diversion, as well as two types of continent urinary diversion, namely, controllable pouch and orthotopic neobladder. Of them, incontinent urinary diversion has become the most extensively applied surgery, thanks to its easy operation and few complications.[16] However, continent diversion has also been widely used in clinical practice, which can be ascribed to the improved surgical techniques as well as perioperative nursing. Studies have indicated no significant difference in the early mortality rate among these operation types.[17] Nonetheless, the long-term quality of life for patients receiving continent diversion is superior to that of those receiving an incontinent one, but the former is associated with a more complicated surgical procedure and a higher incidence of late postoperative complications.[18] On the other hand, gastrointestinal reconstruction includes coloanal anastomosis and colostomy.

Feasibility and safety of RALPE

Among the reported 23 RALPE cases, 17 have undergone APE, with the average operation time of 317.65 min (range: 180–600 min), the average blood loss of 229.41 mL (range: 110–550 mL), and the average postoperative length of stay of 11.6 days (range: 5–53 days). With regard to urinary reconstruction, five patients (29.41%) have received Miami pouch extracorporeally, while 12 had undergone ileal conduit.

In addition, TPE has been performed on six other patients, with the average operation time of 447.67 min (range: 240–700 min), the average blood loss of 490 mL (range: 300–1200 mL), and the average postoperative length of stay of 19.6 days (range: 10–37 days). As far as urinary reconstruction is concerned, two cases have received ureterocutaneostomy, three cases undergone ileal conduit, and one case received ureterosigmoidostomy. In terms of intestinal reconstruction, four cases were treated with end colostomy, while two cases have received coloanal anastomosis.

Generally, RALPE is safe and feasible, which leads to less blood loss and lower incidence of complications. However, due to sparse cases of robotic PE, few reliable prospective clinical trials are available at present to compare the surgical and oncologic outcomes among robot-assisted laparoscopy, traditional laparoscopy, and open surgery so as to perform PE. Martínez et al[19] had retrospectively compared the open with laparoscopic series of PE, and they had reported some encouraging results in the comparable margin status, operation time, length of stay, as well as short-term morbidity and survival. A meta-analysis, published by PelvEx Collaborative in 2018, had compared the minimally invasive PE with an open one, which suggested that operation time in the former was prolonged by 83 min, while the blood loss was reduced by 1750 mL, but no significant difference was observed in the negative rate of surgical margin between these two approaches.[20]

Postoperative complications

Lambaudie et al[21] had reported three cervical cancer patients who underwent robotic APE and received Miami Pouch urinary diversion; after the surgery, a 65-year-old patient had suffered from perineum abscess and Miami stoma fistula, while another 60-year-old patient had developed pyelonephritis and ureteral stenosis. Jauffret et al[22] had reported two cervical cancer patients who had undergone robotic APE combined with Miami Pouch urinary diversion, and both of them had suffered from Miami stoma fistula and septic shock, along with renal insufficiency, postoperatively. One cervical cancer patient had received robotic TPE in our department in 2018; in addition, the patient had also undergone coloanal anastomosis for intestinal reconstruction, and she got anastomotic fistula 8 days after surgery, which had well recovered after an emergency operation.[23]

Notably, no complications unique to laparoscopic surgery, such as subcutaneous emphysema, gas embolism, puncture injury, or electrothermal damage, have been reported from the existing reports of RALPE in gynecology. Our observation suggested that, for the 23 cases with gynecological tumors undergoing RALPE, the postopera-

tive complications were mainly associated with urinary reconstruction, which only occurred in patients (aged over 55 years) who received Miami Pouch urinary diversion, consistent with the previous reports.[17,18] It is recommended that continent urinary diversion should be performed by the experienced surgical team for younger patients, while for the elderly patients or those with ureteral obstruction-induced chronic kidney failure or renal insufficiency, incontinent urinary diversion (such as ureterocutaneostomy or ileal conduit) should be performed to reduce the incidence of postoperative complications (including ureteral stenosis and impaired renal function). As for gastrointestinal reconstruction, it is necessary to carefully evaluate whether coloanal anastomosis can be performed. Specifically, colostomy would be a better choice in the presence of a too low anastomotic site or an excessive anastomotic tension.

Follow-up conditions

In the early years, the survival rate following PE is unsatisfactory, which can be attributed to the large surgical wound, multiple involved organs, and numerous postoperative complications. Fortunately, the postoperative survival rate of PE has increased from 20% to 60% in recent years, thanks to the improved surgical techniques and perioperative nursing quality.[6] Among the 10 reports regarding the application of RALPE in gynecologic malignancies, four (involving a total of 14 cases) have described the surgical margin, with a negative rate of 92.86%. There are follow-up results of 16 cases, among which 31.25% of patients got recurrence or metastasis

after PE Moreover, Lambaudie et al[21] had reported three cervical cancer cases that underwent APE in 2010, including one receiving APE due to the relapsed IB2 cervical squamous cell carcinoma; specifically, central recurrence in the pelvic wall was discovered in this patient 9 months after PE, which was treated with chemotherapy. Jauffret et al[22] had reported two cervical cancer cases that underwent APE in 2011, of them one had a positive surgical margin and recurrence in perineum was detected 8 months after PE, while the other patient was detected with para-aortic lymph node metastasis 23 months postoperatively. Puntambekar et al[24] had reported in 2014 that, among the 10 patients undergoing APE, one had died of liver metastasis 7 months postoperatively, and another one was detected with para-aortic lymph node metastasis combined with liver metastasis 6 months after surgery, which was treated with postoperative complementary treatment [Table 1].

PE, regardless of its open or minimally invasive nature, is a risky and costly procedure for patients. To attain benefits from pelvic dissection for patients, it is suggested that preoperative positron emission tomography (PET) should be performed to exclude some existing metastasis in other parts of the body, in addition to local pelvic imaging evaluation, so as to reduce the probability of recurrence or metastasis in both the short and long term postoperatively.

Conclusion

RALPE remains relatively limited in terms of its application in treating gynecologic malignancies, which is mainly used for the re-treatment of recurrent cervical cancer. Moreover,

Table 1: Surgical outcomes and prognosis of RALPE in patients with gynecologic malignancies.

No.	PE	Reconstruction		OT (min)	EBL (mL)	Complications	Recurrence/ Metastasis
		DR	UR				
1[5]	TPE	End colostomy	Ileal loop urinary diversion	375	375	None	NM
2[21]	APE	–	Miami Pouch	480	200	Perineal abscess, Miami's stoma fistula	Recurrence
				480	400	Pyelonephritis, ureteral stenosis	None
				600	500	None	None
3[25]	APE	–	Ileal conduit	Average, 540	Average, 550	NM	NM
4[22]	APE	–	Miami Pouch	480	200	Miami's stoma fistula	Recurrence
				480	400	Septic shock, renal insufficiency	Recurrence
5[26]	TPE	Coloanal anastomosis	Uretero sigmoidostomy	240	300	None	NM
6[24]	APE	–	Ileal conduit	Average, 180	Average, 110	None	Metastasis (2/10)
7[4]	TPE	End colostomy	Pubic symphysis cystostomy	480	1200	None	NM
8[27]	TPE	End colostomy	Ileal conduit	641	400	NM	NM
9[23]	TPE	Coloanal anastomosis	Ileal conduit	700	300	Colonic anal anastomotic fistula	None
10[28]	TPE	End colostomy	Ureterocutaneostomy	250	365	None	NM

APE: anterior pelvic exenteration; DR: digestive reconstruction; EBL: estimated blood loss; NM: not mentioned in the relevant article; OT: operative time; PE: pelvic exenteration; RALPE: robot-assisted laparoscopic pelvic exenteration; TPE: total pelvic exenteration; UR: urinary reconstruction; –: No application.

relevant literature is mainly the case reports, which have preliminarily confirmed the safety and effectiveness of this surgery with low intraoperative blood loss, few postoperative complications, and fast recovery. Nonetheless, further prospective control trials are required to reach a more reliable conclusion. Importantly, patients should be comprehensively assessed before surgery, and it is recommended that all patients undergoing PE should be examined by preoperative PET-computed tomography (PET-CT) so as to exclude distant metastasis and to ensure the maximum benefit for patients. Notably, the experience of the surgical team and the general condition of the patient should be fully evaluated when reconstruction surgery is selected.

Conflicts of interest

None.

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