Case series

Pelvic exenteration by robotically-assisted laparoscopy: A feasibility series of 6 cases

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A B S T R A C T

After concomitant chemo-radiation therapy, 20 to 30% of advanced cervical cancers recur in irradiated territory. Pelvic exenteration remains a therapeutic option for selected patients. However, this procedure remains complex because of tissue fragility after radiotherapy and their associated co-morbidities. Minimally invasive surgery such as robotically assisted laparoscopy may overcome these surgical challenges. The objective of this study was to evaluate the feasibility of pelvic exenteration with robotically assisted laparoscopy.

Patients who underwent this procedure between 2015 and 2016 were included. Patients characteristics, treatment indication, intraoperative events, immediate and late complications, and histological outcomes were recorded.

The data of 6 patients were analyzed. The primary cancer staging ranged from IB1 to IIB. All cases were loco-regional recurrence and 2 cases presented with with vesico-vaginal fistula. All patients had a history of pelvic irradiation. The mean operative time was 6.7 h. No complications occurred during surgery. The average hospital stay was 11.5 days. Immediate complications were mostly represented by urinary tract infections (4/5). Histological margins were clear in 67% (4/6), and a focal involvement was found in 33% (2/6) of cases. Late complications occurred within 82 days on average and included stenosis of ileal anastomosis, wound infection, acute renal failure, and pulmonary embolism. Revision surgery was necessary in 2 cases. There were 3 local recurrences occurring within an average of 215 days.

In the light of these results, pelvic exenteration by robotically assisted laparoscopy may represent a valuable treatment modality of recurrent cervical cancer with low immediate postoperative morbidity.

1. Introduction

Cervical cancer is the third leading cause of cancer in women worldwide after breast and colon cancer, with an incidence rate of 6.7 per 100,000 women (Globocan 2012) (Fact Sheets by Population [Internet], n.d). In France, the incidence rate ranked at the 9th position. In 2012, 3028 new cases were diagnosed, with almost 1100 deaths per year. The incidence of cervical cancer is almost non-existent before the age of 25 and reaches a peak between 40 and 50 years old amounting to 20 cases per 100,000 women. Cervical cancer screening allows for early diagnosis and management.

Recurrences occur within 18 to 24 months of initial treatment and its frequency is related to initial stage. The risk is 10% for stage IB and 17% for stage IIA. Twenty to 30% of locally advanced cervical cancers recur in previously irradiated area. After concomitant radio-chemotherapy recurrences occur in 23% for stage IIB, 42% for stage III and 74% for stage IV (Sardain et al., 2016).

In case of recurrence, chemotherapy associated with bevacizumab is now available (NCCN Guidelines®), but currently, the only curative treatment is surgery. Pelvic exenteration (anterior, middle, posterior or total) is the corner stone of the surgical approach. However, surgical challenges, increased by previous irradiation, need for urinary re-construction and a high peri-operative complication rate represent the most common limitations.

The first total laparoscopic pelvic exenteration was performed in 2003 by Pomel et al. (2003), but the use of this technique remains

limited, probably due to the difficulty of laparoscopic urinary reconstruction. Robotically-assisted laparoscopy may help overcome these limitations. This technique allows to combine the advantages of a micro-surgical approach with laparoscopy with accurate gestures of laparotomy. The objective of this study was to assess the feasibility of pelvic exenterations by a robotically-assisted laparoscopic approach in local recurrences of advanced cervical cancers.

1.1. Patient and methods

A retrospective analysis was carried out including all patients who underwent pelvic exenterations between 2015 and 2016 in the gynecological surgery department of "Hôpital Européen Georges Pompidou". Information was collected from patient's electronic health record. Data including age, weight, height, medical and surgical history, alcohol and tobacco use, medical treatments such as anti-platelet aggregation or anticoagulant therapy were collected from anesthesia records. Operator's name, type of intervention, operative time, as well as procedures carried out intraoperatively were recorded along with the histological type, staging and initial treatment.

Details pertaining the postoperative stay including drainage, intensive care unit stay (ICU), transfusion need, prophylaxis of venous thromboembolic diseases, use of level 3 analgesics (morphine-based drugs), duration of hospitalization were captured. Immediate and late complications were reviewed. Early complications were defined as any complications occurring within 30 days postoperatively and late complications were those occuring after 30 days. Early and late complications were reported with an analysis of the onset of first complication symptom and their management. Histological findings were also analyzed, including resection margins. Finally, recurrences after pelvic exenteration and their management were reported.

2. Results

Between 2015 and 2016, 6 patients underwent pelvic exenteration by robotically-assisted laparoscopy. The average age of these patients was 58.5 years (39–75 years). Mean body mass index was 24.5 kg/m^2. Two patients had cardiovascular risk factors, none smoked, and none had anti-coagulant or anti-platelet aggregation therapy. Most of the patients (83.3% (5/6), were treated for cervical squamous cell carcinoma and one patient had a cervical adenocarcinoma. Initial staging of the disease ranged from Ib1 to IIB. A radical hysterectomy was initially performed in 3 patients followed by concomitant chemo-radiotherapy (RCC) followed by brachytherapy. Two had exclusive RCC treatment. The patient with cervical adenocarcinoma was initially treated with RCC followed by completion hysterectomy (Table 1).

Recurrences occurred after an average of 5 years (1–15 years). There were 3 recurrences involving the vaginal fundus, two of which were associated with a vesico-vaginal fistula. There were also two local

recurrences (cervix) and one involving the centro-pelvic and digestive area. These recurrences were managed by anterior pelvic exenteration with Bricker type derivation in 2 cases. One posterior pelvic exenteration with stomy was performed and another one with anastomosis. Finally, a total pelvic exenteration was performed for the last patient. Mean operating time was 402 min (180–480 min). One patient required intraoperative transfusion. No intraoperative complication occurred and no conversion to laparotomy was necessary (Table 2).

2.1. Immediate complications (≤ 30 days)

Postoperatively, no patient was admitted in the ICU. One patient needed 2 red blood cell transfusions. Prophylactic anticoagulation was implemented for 28 days. Normal bowel function resumed after an average of 5.5 days (2–8 days). The bladder catheter was removed after an average of 3.7 days (1–5 days). Four patients required level 3 analgesia for an average of 6.8 days. There were 4 urinary tract infections treated with antibiotics and one sepsis with no etiology found and diagnosed with positive blood culture. Average length of stay was 11.5 days (5–15 days). (Table 3).

2.2. Histological findings

The histologic analysis revealed the initial typing in 5 cases and some inflammatory cells in the remaining case. Margins were free in 4 cases and focal lesion was found in 2 cases. (Table 3).

2.3. Late complications (> 30 days)

Late complications occurred in 5 patients. Two required surgical management, because of a stenosis of anastomosis after ileostomy closure and obstructive renal failure. The 3 other complications were medically managed: a vaginal scar disunion, postoperative dysuria and a pulmonary embolism. The mean onset time of the first complication symptom was 82.4 days (6–247 days).

During follow-up, 3 recurrences were reported: vaginal fundus and lymph node. These recurrences occurred after an average of 7 months and were all treated with chemotherapy.

Long-term complications were represented by recto-vaginal fistula for 2 patients and ilio-ureteral fistula for one patient. The onset time of these complications was approximately one year.

One patient died after 10 months of hemorrhagic shock due to vaginal bleeding. (Table 3).

3. Discussion

Pelvic exenteration is a complex surgical procedure and remains the only cure for local recurrence of advanced cervical cancers that have been irradiated. Laparotomy remains the standard procedure for

Table 1
Patients characteristics.

Case	Age (year)	BMI (kg/m^2)	Histological type	Initial stage	Initial treatment	Recurrence localization	Time to recurrence (year)
1	56	19.6	Squamous cell carcinoma	NM	RH, RCC and brachytherapy	Vaginal fundus + vesico-vaginal fistula	15
2	39	18.2	Squamous cell carcinoma	IIB	RCC	Cervix	2
3	70	21.4	Adénocarcinoma	IIB	RH, RCC and brachytherapy	Vaginal fundus + bladder	2
4	75	26	Squamous cell carcinoma	IIB	RCC and brachytherapy	Cervix and proximal parametrium	1
5	53	34.7	Squamous cell carcinoma	IB1	RH and brachytherapy	Centro-pelvic + digestive	4
6	58	27.1	Squamous cell carcinoma	NM	RH, RCC and brachytherapy	Vaginal fundus + vesico-vaginal fistula	6

RH: total non conservative hysterectomy.
RCC: concomittant radiochemotherapy.
NM: not mentioned.

Table 2
Peroperative data.

Case	Procedure	Operating time (min)	Peroperative complication	Peroperative transfusion	Reconstruction method	Histological findings/Resection margins
1	Anterior pelvic exenteration	480	0	0	Bricker	Squamous cell carcinoma Free, no LVI
2	Radical hysterectomy + posterior pelvic exenteration	480	0	0	Rectal resection, colo-rectal anastomosis	Squamous cell carcinoma Free, one LVI
3	Anterior pelvic exenteration	480	0	3 UPC	Bricker	Adenocarcinoma free, no LVI
4	Radical hysterectomy	180	0	0	–	Squamous cell carcinoma focal positive margin, LVI
5	Posterior pelvic exenteration	390	0	0	Left colectomy, colo-rectal anastomosis	Inflammatory cells
6	Anterior and posterior pelvic exenteration	NR	0	0	Bricker, rectal resection	Squamous cell carcinoma Focal positive margin, no LVI

UPC: unit packed cells.
LVI: lymphovascular invasion.

Table 3
Postoperative complications.

Case	Early complications (≤30 days)	Late complications (>30 days)	Recurrence	Time to recurrence (month)	Treatment of recurrence
1	Urinary tract infection	Vaginal scar disunion	Vaginal fundus, peritoneal carcinosis, lymph node metastasis	6,5	Cisplatine Topotecan Bevacizumab
2	Sepsis	Anastomosis stenosis after ileostomy closure	Vaginal fundus, lymph node and bone metastasis	7,3	Cisplatine Bevacizumab
3	Urinary tract infection	Acute obstructive renal failure	Pelvic lymph node metastasis	7,7	Carboplatine Taxol Bevacizumab
4	Dysuria (self-sounding) and urinary tract infection	0	0		
5	Pulmonary embolism	0	0		
6	Urinary tract infection	0	0		

exenterations, but several teams have demonstrated its feasibility by laparoscopy with good histological results (Pomel et al., 2003; Iavazzo and Gkegkes, 2014; Lambaudie et al., 2010).

The advantage of robotically-assisted surgery is to offer 3-dimensional vision, better precision of operative gestures by increasing degrees of freedom of the hand and by reducing tremors (Ngô et al., 2016). The learning curve is also reduced using robotically-assisted surgery. In the literature, few is known about pelvic exenteration by robot-assisted laparoscopy in cervical cancer recurrence. A series of 7 patients operated for cervical cancer recurrence by robotic-assisted laparoscopy was published by Jauffret et al., (2011). However, they included only 2 anterior exenterations. The other procedure were anterior colpectomies. Postoperative complications observed in this series were fistulas and severe sepsis with acute obstructive renal failure. Our study has the advantage of describing six cases of pelvic exenterations for cervical cancer recurrence.

A recent review listed and compared 8 cases of pelvic exenterations performed by robotically-assisted laparoscopy in cervical cancer recurrences (Iavazzo and Gkegkes, 2014). Initial staging of cancer ranged from IB2 to IVA. An anterior exenteration was performed in 7 cases, the last patient underwent a total exenteration. Operating time ranged from 375 to 600 min. Two patients had postoperative complications including a perineal abscess, Miami pouch fistula, and ureteral stenosis. Results of this review compared to the present series are presented in Table 4.

In our series, immediate postoperative complications were mostly grade II and IIIb, according to Clavien-Dindo classification.

The rate of early complications (≤30 days postoperative) after pelvic exenterations, varies between 16 and 71% depending on series (Sardain et al., 2016; Chiantera et al., 2014a). These complications are mostly represented by digestive fistulas, ureteral anastomosis leakage

and thromboembolic complications. Risk factors described for these complications were tissue sequelae due to radiotherapy and operating time above 7 h (Ferron and Martel, 2003). In our series, there were 3 early complications, as pulmonary embolism, vaginal scar disunion, and postoperative dysuria requiring self-sounding learning.

Late postoperative complications (>30 days postoperatively) vary between 36 and 61% in the literature and are represented by enterocutaneous and vaginal fistulas, ureteric obstructions, digestive occlusions and pyelonephritis. Risk factors found were postoperative adhesions, self-sounding and tumor recurrences (Yoo et al., 2012). Our series agree with these findings. There were 3 fistulas (2 recto-vaginal fistulas and 1 urethral fistula) after local recurrences and ureteral stenosis requiring percutaneous nephrostomy and a mono-J-probe. Mortality in relation to post-operative complications is estimated between 0 and 12% according to the series (Yoo et al., 2012; Kaur et al., 2012; Chiantera et al., 2014b; Tanaka et al., 2014; Schmidt et al., 2012). In our series, a patient died at 10 months of pelvic exenteration, after haemorrhagic shock secondary to vaginal bleeding related to local recurrence. This recurrence occurred at 7 months of the operation and was treated with cisplatin and bevacizumab. Our results are therefore comparable to those observed previously in laparotomy series. Assisted robot approach aims to reduce peri-operative morbidity and mortality but do not alter the course of disease.

Based on previously published data, the median recurrence period ranged from 6 to 50 months. Recurrences were local in 35 to 60% of cases and distant metastasis in 20 to 40% of cases (Sardain et al., 2016; Yoo et al., 2012). In our series, median occurrence of recurrence was 3 years (1 to 15 years).

Our histological findings showed a positive resection margins in 33.3% of cases, which is in agreement with the literature reporting 70% of free margins after pelvic exenterations, in all types of interventions

Table 4
Comparison of our series to Lavazzo et al. review (Iavazzo and Gkegkes, 2014).

Series	Age	Histologic type	Type of operation performed	Procedure duration	Complications	Postoperative stay
Jauffret et al., 2011	67	Squamous cell carcinoma	Anterior pelvic exenteration, lymphadenectomy	480	None	3
	59	Squamous cell carcinoma	Anterior pelvic exenteration	480	None	24
Davis et al., 2010	50	Squamous cell carcinoma	Anterior pelvic exenteration	Mean, 540	NM	8
	58	NM	Anterior pelvic exenteration		NM	NM
Lambaudie et al., 2010	65	Squamous cell carcinoma	Anterior pelvic exenteration	480	Perineal abcess, miami pouch fistula	53
	60			480	Ureteral stenosis	25
	43			600	None	30
Lim et al., 2009	57	Squamous cell carcinoma	Total pelvic exenteration	375	None	10
Our series 1	56	Squamous cell carcinoma	Anterior exenteration	480	Vaginal suturing	14
2	39	Squamous cell carcinoma	Extended colpohysterectomy, posterior exenteration	480	Anastomosis stenosis after ileostomy closure	14
3	70	Adenocarcinoma	Anterior exenteration	480	Acute obstructive renale failure	15
4	75	Squamous cell carcinoma	Extended colpohysterectomy	180	Immediate dysuria	12
5	53	Squamous cell carcinoma	Posterior exenteration	390	Immediate pulmonary embolism	5
6	58	Squamous cell carcinoma	Total pelvic exenteration	NM	Immediate urinary tract infection	9

(Pomel et al., 2003). This criterion is essential for patient prognosis. Indeed, pelvic exenterations are performed with curative goal and are no longer palliative. It has been reported that positive margins after pelvic exenterations considerably decreases survival with 55.2% survival at 2 years if margins are free and 10.2% if they are not (Sardain et al., 2016; Marnitz et al., 2006).

The other reported prognostic factors for pelvic recurrence were size of recurrence (above 3–5 cm, risk of failure of in sano resection was high), delay between initial treatment and recurrence, histological type of recurrence, and initial pelvic and lombo-aortic lymph node involvement. Postoperatively, prognostic histological criteria included nodal mesorectal involvement (earlier recurrence: 2.4 months vs. 7.3 months, p = 0.005), presence of vascular emboli, and positive resection margins (Yoo et al., 2012; Chiantera et al., 2014b).

4. Conclusion

Pelvic exenteration by robotically-assisted laparoscopy can be implemented in cervical cancer recurrence. Morbidity and mortality are acceptable and not superior to standard laparoscopy and laparotomy. Robotic-assisted laparoscopic surgery is associated with shorter hospital stay, less postoperative pain, and less intraoperative blood loss. This robotically-assisted approach offers increased ergonomic and technical comfort to the surgeon during difficult and time-consuming surgical procedures. Histological results are positive and encouraging but remain to be confirmed with long-term follow-up. Based on careful patient selection, this minimally invasive surgery can represent an interesting treatment alternative to laparotomy in recurrence of pelvic cancers in irradiated area.

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