Robotically Assisted Para-aortic Lymphadenectomy: Surgical Results

A Cohort Study of 487 Patients

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Objectives: The aim of this study was to evaluate perioperative outcomes of robotic-assisted laparoscopic para-aortic lymphadenectomy (PAL) in patients with gynecologic cancers during the learning phases of robotic surgery programs and to compare results of extraperitoneal versus transperitoneal approaches of PAL.

Materials and Methods: This study is a retrospective multicentric study of patients who underwent robotically assisted laparoscopic PAL (N = 487). Eleven European centers and 1 US center participated in the study. Abstracted data included age, body mass index, indication, type of surgical approach (transperitoneal or extraperitoneal), associated surgical procedures, operative time, estimated blood loss, lymph node count, hospital length of stay (LOS), and complications. Para-aortic lymphadenectomy was performed by an extraperitoneal approach in 58 cases (12%) and transperitoneal in 429 cases (88%).

Results: The mean (SD) para-aortic lymph node count was 12.6 (8.1), operative time was 217 (85) minutes, estimated blood loss was 105 (110) mL, and LOS was 2.8 (3.2) days. Four (0.8%) conversions to open and 2 (0.4%) conversions to laparoscopy were described. There were 32 lymphocysts (6.6%), 3 deep venous thromboses (0.6%), and 10 transfusions (2.1%). For transperitoneal approach, the average number of lymph nodes removed was higher in isolated PAL group than the hysterectomy combined group (report node counts 95% confidence interval, -7.29 to -3.52, $P = 1.5 \times 10^{-6}$). For isolated PAL, the LOS was shorter in the extraperitoneal group than in the transperitoneal group (report data 95% CI, -1.35 to -0.35, $P = 0.001$).

Conclusions: Robotic-assisted PAL seems safe and feasible. More lymph nodes were removed during an isolated transperitoneal PAL dissection compared with a combined procedure with hysterectomy. Extraperitoneal approach seems attractive relative to transperitoneal dissection, but the superiority of one or the other way is not demonstrated by our study.

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Para-aortic lymphadenectomy (PAL) is the cornerstone in the management of many gynecological malignancies. Para-aortic lymphadenectomy is often recommended in the surgical staging of advanced cervical cancers before radiation to determine the extent of the fields. It is also used in the therapeutic management of type 2 and high-risk type 1 endometrial cancers. Para-aortic lymphadenectomy specifically including dissection of the infrarenal lymph nodes remains a standard of care for the accurate staging and debulking of ovarian cancer.

Minimally invasive surgery procedures such as traditional laparoscopy (transperitoneal or extraperitoneal), single-port laparoscopy, and robotic-assisted laparoscopic surgeries are used more frequently to decrease postoperative morbidity. Currently, the use of robotic-assisted laparoscopic surgery as an alternative to traditional laparoscopy or open surgery has been adopted in many centers.[1] Robotic-assisted PAL has been described by several authors, with transperitoneal[2,3] or extraperitoneal[4] approaches.

The primary aim of this multicenter study was to evaluate the safety and feasibility of robotic-assisted laparoscopic PAL and to compare our results with the reported peer-reviewed literature in regards to different surgical approaches. The second objective was to compare the extraperitoneal and transperitoneal approach and the results of isolated PAL versus combined with another surgical gesture.

MATERIALS AND METHODS

Patient Population

The study analyzed clinical outcomes data on 487 patients who underwent PAL between November 2004 and March 2012 at 11 centers across Europe and one from the United States (Orlando, FL). Cases were from the European centers made up to 54%, with the remaining cases being from the United States. All cases represent serially collected from each institution, beginning from near the initiation of their respective robotic surgery programs. Our data were contemporaneously abstracted during the study period at respective institutions as part of the surgical database and were approved by the local institutional review boards.

Surgical Management

Robotic-assisted PAL was performed for the following cancers: endometrial, cervical, ovarian, and fallopian tube. When PAL was performed as the only surgical procedure, it is referred to as "isolated," and when PAL was associated with hysterectomy, pelvic lymphadenectomy, or omentectomy, it is described to as "combined." Isolated PAL was performed for lymph node staging before concomitant chemoradiation for locally advanced cervical cancer. Combined PAL was carried out in the context of complete surgery for endometrial cancer or ovarian cancer. Para-aortic lymphadenectomy was conducted by either transperitoneal or extraperitoneal approaches in this study. For transperitoneal surgery, the robotic platform was center-docked between the patient's legs. For extraperitoneal PAL, the robot was docked either perpendicular on the patient's right side or obliquely over the patient's right shoulder.

The anatomic landmarks for aortic dissections varied among the institutions and by diagnosis. Para-aortic lymphadenectomy was performed from the aortic bifurcation (including common iliac area) up to the left renal vein and the gonadal pedicles bilaterally to their respective venous insertions. In several cases, particularly for patients with endometrial cancer, PAL was performed up to the inferior mesenteric artery only.

All surgeons who participated in the study were skilled in laparoscopic surgery and/or robotically assisted laparoscopic surgery. Most PAL cases described in the study were the first robotically assisted laparoscopy PAL done by these experienced surgeons.

Data Comparison and Statistical Analysis

The following data characteristics were described: age, body mass index (BMI), surgical indications, surgical/pathological factors with operative time (OT), estimated blood loss (EBL), number of lymph nodes retrieved, and hospital length of stay (LOS). The OT was defined as the time from the skin incision to skin closure. Variables with normal distribution were expressed as mean (SD). The Student t test, χ^2 test, or Fisher exact test was used to compare the different groups. Multivariate analyses were performed using multiple linear regressions. All analyses were performed using R package with rms libraries (http://lib.stat.cmu.edu//R/CRAN/). A P value less than 0.05 was considered as statistically significant.

RESULTS

Between November 2004 and March 2012, 487 robotic-assisted PAL cases were performed at the investigators institutions, and their perioperative clinical data were abstracted by each investigator for inclusion in this pooled database. Indications for performance of PAL were endometrial cancer (52.8%), cervical cancer (32.2%), ovarian and tubal cancers (13.1%), and other indications (1.8%), including recurrence of cancer disease. The median

TABLE 1. Characteristics of 487 patients with various gynecologic malignancies

	Total Population (N = 487)	Isolated PAL		Combined PAL	
		Transperitoneal	Extraperitoneal	Transperitoneal	Extraperitoneal
		72 (14.8%)	49 (10.1%)	357 (73.3%)	9 (1.8%)
Age, mean (range), y	57 (15–89)	49 (23–79)	52 (27–74)	58 (15–89)	62 (26–74)
BMI, mean (range), kg/m^2	25.4 (16–50)	22.5 (16.63–35)	25 (19–48.83)	26.6 (16.2–50)	26.6 (20.82–33.2)
Indications, n (%)					
Cervical cancer stage	**157 (32.2)**	**61 (84.7)**	**47 (95.9)**	**46 (12.9)**	**3 (33.3)**
IA1	1 (0.6)			1	
IA2	1 (0.6)			1	
IB1	33 (21)	2		30	1
IB2	25 (15.9)	13	8	4	
IIA	10 (6.4)	2	6	2	
IIB	66 (42)	32	26	7	1
IIIA	8 (5.1)	4	4		
IIIB	6 (3.8)	3	2	1	
IVA	5 (3.2)	3	1		1
Unknown	2 (1.3)	2			
Endometrial cancer stage	**257 (52.8)**	**5 (6.9)**		**248 (69.5)**	**4 (44.4)**
IA	61 (23.7)	2		57	2
IB	115 (44.7)	2		113	
II	18 (7)			18	
IIIA	23 (8.9)			23	
IIIC	34 (13.2)	1		31	2
IV	4 (1.6)			4	
Unknown	2 (0.8)			2	
Ovarian and tubal cancer	**64 (13.1)**	**6 (8.3)**	**2 (4.1)**	**54 (15.1)**	**2 (22.2)**
Other	**9 (1.8)**			**9 (2.5)**	

PAL, para-aortic lymphadenectomy.

age was 57 years (range, 15–89 years), and the median BMI was 25.4 kg/m^2 (range, 16–50 kg/m^2). Procedures were isolated in 121 patients (24.9%) and combined in 366 patients (72.2%). The transperitoneal approach has been performed in 429 (88.1%) patients, and 58 (11.9%) cases underwent an extraperitoneal PAL procedure. Demographic

TABLE 2. Surgical outcomes of 487 patients who underwent robotic-assisted laparoscopic PAL

	OT, min	EBL, mL	LOS, d	Lymph Nodes Retrieved
Total population (N = 487)	**217.6 (85.1)**	**105.4 (109.9)**	**2.8 (3.2)**	**12.6 (8.1)**
Transperitoneal PAL (n = 429)				
Combined procedures (n = 357)	225.6 (89.2)	100.2 (104.1)	2.6 (3.3)	10.9 (6.9)
Isolated procedures (n = 72)	200.4 (66)	149.8 (118.8)	3.5 (1.9)	16.6 (8.9)
	***P* = 0.007**	***P* = 0.053**	***P* = 0.0007**	***P* = 1.5 × 10^{-06}**
Isolated PAL (n = 121)				
Transperitoneal access (n = 72)	200.4 (66)	149.8 (118.8)	3.5 (1.9)	16.6 (8.9)
Extraperitoneal access (n = 49)	177.1 (62.7)	113.5 (132.8)	2.7 (0.8)	18.3 (9.4)
	***P* = 0.054**	***P* = 0.28**	***P* = 0.001**	***P* = 0.32**

Data are presented as mean (SD).
d, days; EBL, estimated blood loss; OT, operative time; LOS, hospital length of stay; PAL, para-aortic lymphadenectomy.

characteristics and distribution of the different groups of cases are summarized in Table 1.

The mean (SD) OT for the entire cohort was 217.6 (85.1) minutes, and the mean (SD) EBL was 105.4 (109.9) mL. The mean (SD) lymph node count was 12.6 (8.1), and the mean (SD) hospital LOS was 2.8 (3.2) days (Table 2). As expected, the OT for transperitoneal PAL combined procedures exceeded that for isolated PAL dissections ($P = 0.007$, Table 2). Although the EBL was not statistically different for the combined and isolated dissections, the hospital LOS was longer in the isolated PAL cases ($P < 0.001$). The number of resected para-aortic lymph nodes was higher in isolated PAL than combined procedures (mean 16.0 vs 10.9 para-aortic nodes, $P < 0.001$). The number of retrieved lymph nodes was higher in the isolated PAL group, regardless of the patients' age, BMI, and indication ($P = 0.029$; odds ratio, 2.22; 95% confidence interval, 1.2–4.5).

Isolated PAL dissections were performed in 121 patients (24.8%), the vast majority of whom underwent staging procedures for advanced cervical cancer before radiation therapy (Table 1). A comparison of transperitoneal versus extraperitoneal dissections for patients undergoing isolated PAL procedures was performed (Table 2). The OT, EBL, and number of lymph nodes retrieved were not statistically different between the 2 surgical approaches. Transperitoneal isolated PAL had a longer hospital LOS than the extraperitoneal isolated PAL ($P = 0.001$). This observation is also confirmed by the multivariate analysis regardless of the patients' age and/or BMI ($P = 0.016$) with an odds ratio of 4.35 and a 95% confidence interval of 1.3 to 14.4.

Only 4 (0.8%) and 2 (0.4%) cases were converted to laparotomy or laparoscopy, respectively (Table 3). The 4 laparotomy conversions were observed in transperitoneal procedures (4/429, 0.9%); 2 were for vascular injuries, one for bowel injury, and one for difficult exposure related to adhesions. Two conversions to transperitoneal laparoscopy resulted from vascular injuries during extraperitoneal PAL (2/58, 3.4%). There was no difference statistically between transperitoneal and extraperitoneal approach for conversion to open ($P = 0.39$). There were 11 intraoperative complications (2.7%) including 7 vascular injuries (1.4%), 3 bladder injuries (0.6%), and 1 bowel injury (0.2%). Ten patients (2.1%) received blood transfusions in this cohort. There was no perioperative deaths observed in this study.

Postoperative complications were graded according to the Dindo et al[5] classification. Only complications requiring medical, radiological, or surgical management were collected (Table 3). Lymphatic complications were the most frequent with 32 patients affected (6.6%), and only symptomatic lymphocysts were recorded. For total complications, there were no differences between access transperitoneal and extraperitoneal ($P = 0.31$). Symptomatic lymphocysts were found for 32 patients, 25 (5.8%) in transperitoneal group and 7 (12%) in extraperitoneal group, without difference statistically ($P = 0.06$).

Lymphocysts were managed radiologically in 31 cases (6.4%), a drain was placed by interventional radiology, and 1 case (0.2%) required a surgical drainage. The majority of grade II complications were urinary tract infections, dysesthesia, or symptomatic lymphedema. Concerning deep venous thrombosis (DVT) and pulmonary embolism, 3 DVTs (0.6%) are described, and no pulmonary embolism occurred. Grade III complications were mostly symptomatic lymphocysts managed mainly with radiological drainage, and there were only 2 ureteral complications (0.4%) (one each for hydronephrosis and fistula).

DISCUSSION

This collaborative task has no equivalent in the current gynecologic literature and constitutes one of the most relevant data collections concerning this advanced surgical procedure

TABLE 3. Conversions and complications for 487 who underwent robotic-assisted laparoscopic PAL

Conversions or Complications	Results for Total Population (N = 487)
Conversion	
Conversion to open	**4 (0.8%)**
Vascular injury	2 (0.4%)
Bowel injury	1 (0.2%)
Difficulty of exposure	1 (0.2%)
Conversion to laparoscopy	**2 (0.4%)**
Vascular injury	2 (0.4%)
Complications	
Intraoperative complications	**21 (4.3%)**
Vascular injury	7 (1.4%)
Transfusion	10 (2.1%)
Bladder injury	3 (0.6%)
Bowel injury	1 (0.2%)
Postoperative complications (Clavien and Dindo classification)	**108 (22.2%)**
Grade I	Data not collected
Grade II	66 (13.6%)
DVT	3 (0.6%)
Grade III	42 (8.6%)
Lymphocyst	32 (6.6%)
Grade IIIA	**35 (7.2%)**
Radiological management	
For lymphocyst	31 (6.4%)
For wall abscess	1 (0.2%)
For pelvic collection	2 (0.4%)
For hydronephrosis	1 (0.2%)
Grade IIIB	**7 (1.4%)**
Laparoscopy management	
For port-site hernia	3 (0.6%)
For ureteral fistula	1 (0.2%)
For pelvic peritonitis	2 (0.4%)
For suspected adhesions and lymphocyst	1 (0.2%)

PAL, para-aortic lymphadenectomy.

TABLE 4. Robot-assisted PAL: comparison of published studies in the peer-reviewed literature

Author(s)	Year	No. Patients	Tumor Type	Transperitoneal or Extraperitoneal Access	Age, y	BMI, kg/m^2	OT, min	EBL, mL	LOS, d	Lymph Nodes Retrieved
Fader et al[13]	2012	**125**	Endometrial cancer	Transperitoneal	65.4	30.1	**193**	**NR**	**1**	**15**
Lambaudie et al[3]	2012	**53**	Cervical/ endometrial/ ovarian cancers	Transperitoneal (n = 38) or extraperitoneal (n = 15)	47.8	22.2	**197**	**500**	**3.9**	**12.2**
Holloway and Ahmad[2]	2012	**162**	Endometrial cancer	Transperitoneal	63.8	31.7	**148**	**79**	**1.36**	**11**
Tinelli et al[12]	2011	**5**	Cervical cancer	Transperitoneal	43.1	28	**323**	**157**	**3**	**10.2**
Escobar et al[11]	2012	**7**	Endometrial cancer	Transperitoneal	59.7	31.4	**174**	**75**	**1.4**	**3.5**
Narducci et al[4]	2009	**6**	Cervical/vaginal/ testicular cancers	Extraperitoneal	47.8	26	**200**	**133**	**NR**	**12.2**
Magrina et al[10]	2009	**1**	Cervical cancer	Extraperitoneal	32	27	**103**	**30**	**2**	**10**
Fastrez et al[9]	2009	**8**	Cervical cancer	Transperitoneal	58	24.3	**137.5**	**NR**	**4.5**	**1–38**
Seamon et al[8]	2009	**79**	Endometrial cancer	Transperitoneal	59	34.2	**241**	**188**	**1**	**10**
Boggess et al[7]	2008	**103**	Endometrial cancer	Transperitoneal	61.9	32.9	**191.2**	**74.5**	**1**	**12**
Vergote et al[6]	2008	**5**	Cervical cancer	Extraperitoneal	49.6	23.8	**83.8**	**NR**	**2.2**	**9.2**
Our study	2014	**487**	Cervical/ endometrial/ 1ovarian cancers	Transperitoneal (n = 429) or extraperitoneal (n = 121)	57	25.4	**218**	**105**	**2.8**	**12.6**

BMI, body mass index; d, days; EBL, estimated blood loss; NR, not reported; OT, operative time; LOS, hospital length of stay; PAL, paraaortic lymphadenectomy; y, years.

using robotic assistance. Our results confirm the feasibility and safety of robotic-assisted surgery for PAL. Several single institutional database analyses of robotic surgeries including PAL have been published in recent years.[2–4,6–13] These series were largely collected during the initial "learning" phases of their respective institutions. The results of our pooled population analysis are comparable with those of smaller case series (Table 4). Robotic-assisted PAL seems to have a relatively low incidence of perioperative morbidity. The postoperative complication rate (22.2%) and intraoperative rate (4.4%) are comparable to other published series. No complication did require major intervention. Moreover, few intraoperative complications required conversion to laparotomy (0.8%), and grade IIIB postoperative complications (1.4%) requiring a second operative intervention were rather infrequent. The lymphocyst rate is comparable to other laparoscopic approaches. By comparison, in a series of 342 laparoscopic extraperitoneal PAL,[14] 38 symptomatic lymphocysts (11%) were reported compared with 6.6% in this cohort analysis. The rate of thromboembolic complications in this multicenter study is comparable to the published data, that is, 2 (0.4%) of 471 DVTs after robotic staging for endometrial cancer.[15]

PAL Robotic-Assisted Transperitoneal Versus Extraperitoneal Access

Concerning the isolated PAL procedures, extraperitoneal and transperitoneal approaches were seemingly equivalent, other than the hospital LOS that was shorter for extraperitoneal cases. Given the relatively smaller number of isolated PAL cases and the large number of institutions contributing data to this study, it is difficult to draw clinically relevant conclusions from the LOS finding. However, the extraperitoneal PAL average of 2.7 days LOS is comparable to LOS data from laparoscopic extraperitoneal access studies. Since the year 2000, the extraperitoneal approach for PAL has been described by many investigators.[16–30]

Based on a Cochrane review[37] about the surgical paraaortic lymph node assessment in locally advanced cervical cancer, laparoscopy should be preferred to laparotomy. The extraperitoneal dissection reduces postoperative adhesions

TABLE 5. PAL: conventional laparoscopy, transperitoneal and extraperitoneal approach (comparison of published studies in the peer-reviewed literature)

Author(s)	Year	No. Patients	Tumor Type	Age, y	BMI, kg/m^2	OT, min	EBL, mL	LOS, d	Lymph Nodes Retrieved
Transperitoneal									
Fader et al[13]	2012	66	Endometrial cancer	65.4	30.1	**193**	**NR**	**1**	**15**
Escobar et al[11]	2012	11	Endometrial cancer	61.9	31.3	**155**	**100**	**1.2**	**6**
Seamon et al[8]	2009	55	Endometrial cancer	57	28.7	**287**	**200**	**2**	**11**
Boggess et al[7]	2008	81	Endometrial cancer	62	29	**213.4**	**145.8**	**1.2**	**6.3**
Cartron et al[22]	2005	154	Cervix, endometrial, ovarian cancer	45	23	**NR**	**NR**	**1.9**	**17**
Extraperitoneal									
Benito et al[33]	2012	30	Cervix cancer	47.6	23.6	**118.7**	**75**	**1.9**	**14.2**
Gil-Moreno et al[32]	2012	88	Cervix cancer	50	26.3	**NR**	**NR**	**NR**	**15.9**
Uzan et al[31]	2011	89	Cervix cancer	45	23	**185**	**NR**	**3**	**13**
Ramirez et al[30]	2011	60	Cervix cancer	48	NR	**140**	**22.5**	**1**	**11**
Estrade et al[29]	2010	37	Cervix cancer	56	24.5	**142**	**NR**	**NR**	**14**
Dowdy et al[28]	2008	38	Endometrial cancer	68	33.3	**69**	**NR**	**2**	**16.5**
Gil-Moreno et al[27]	2008	69	Cervix cancer	51	27	**140**	**100**	**2**	**15.2**
Fichez et al[25]	2007	81	Cervix, endometrial, ovarian cancer	50	22	**109**	**NR**	**3**	**14**
Tillmanns and Lowe[24]	2007	18	Cervix cancer	49	29	**108**	**25**	**NR**	**10**
Nagao et al[23]	2006	76	Cervix, endometrial cancer	51	NR	**75**	**5**	**NR**	**4**
Cartron et al[22]	2005	234	Cervix, endometrial, ovarian cancer	46	23.5	**175**	**NR**	**1.2**	**21**
Mehra et al[21]	2004	32	Cervix, endometrial, ovarian	58		**80**		**2**	**12**
Burnett et al[20]	2004	46	Cervix, endometrial, ovarian	53	27.1	**135**	**100**	**1.6**	**14**
Sonoda et al[19]	2003	111	Cervix	46	24	**157**	**100**	**2**	**19**
Vergote et al[18]	2002	21	Cervix	51		**55**	**78**		**6**
Schlaerth et al[17]	2002	40	Cervix	41.2	23	**209**		**6.3**	**12.1**
Dargent et al[16]	2000	21	Cervix	50	23	**119**			**15**

BMI, body mass index; d, days; EBL, estimated blood loss; NR, not reported; OT, operative time; LOS, hospital length of stay; PAL, para-aortic lymphadenectomy; y, years.

compared with the transperitoneal dissection.[38] However, the laparoscopic extraperitoneal and transperitoneal approaches are not seemingly different in terms of overall survival, disease-free survival, EBL, OT, or severe complications,[37,39] but these concepts must obviously be confirmed by prospective studies with larger number of cases.

PAL Robotic-Assisted Combined Versus Isolated Procedures

Concerning the transperitoneal PAL, the OT was found to be longer in combined procedure as expected. However, the LOS was actually shorter in combined procedures. This parameter can likely be explained by the proportion of patients managed in the United States in this cohort (45.8%), with a significantly shorter hospital LOS than in Europe. In addition, the number of lymph nodes retrieved during the combined procedures was statistically lower than in isolated procedures. This result can be explained first by the biases inherent in our study. Indeed, the multicenter retrospective nature creates potential inclusion bias, a lack of harmonization in the landmark of lymph node dissection. In addition, data collected includes the first procedures used to the learning curve of each team, which perhaps changes some of the results. However, on the isolated procedure versus combined, a hypothesis can be proposed: a dedicated docking would improve the quality of lymph node sampling.

As previously described,[40] only 1 position is used for the robot (between patient's legs, most of the time) when PAL is

associated to a pelvic procedure. This technique avoids the surgeon to change the robot's position during the procedure. But with one robot's position surgical landmarks are modified and if it was easy to reach the inferior mesenteric artery, it was rather more difficult to reach the left renal vein because it has been established in a previous multicentric study,[3] particularly in patients with higher BMI. This issue may in part explain the significant difference concerning the lymph node counts between the isolated PAL and combined PAL procedures with only single docking.

Moreover, the results of our study are comparable to those with laparoscopic approach. Table 5 compares the peer-reviewed published data for the results of PAL using conventional laparoscopy for transperitoneal and extraperitoneal lymphadenectomy. In our study, the mean lymph nodes retrieved was 10.9 and 16.6 for combined and isolated procedures with transperitoneal approach against the mean between 6 and 17 for literature data. Concerning extraperitoneal approach, the median was 18.3 in our study and between 4 and 21 in others studies. The OT, EBL, and LOS in published data are also equivalent with our results.

In conclusion, this collaborative task has no equivalent in the current gynecologic literature and constitutes one of the most relevant data collections concerning this advanced surgical procedure using robotic assistance. Our multi-institutional database review demonstrates the feasibility and the overall safety of robotic-assisted laparoscopic PAL, even in the early phases of individual institutional robotic surgery programs. Concerning isolated PAL, our results suggest interest of extraperitoneal approach compared with the transperitoneal dissection; superiority of either of them remains to be demonstrated. In regards to the combined PAL, aortic lymph nodes retrieved were lower than in the isolated procedures. Beyond this bias of the multicenter study with indications and behavior, perhaps we must adapt our technique to the characteristics of robotic-assisted laparoscopic surgery using double docking so as to increase the lymph node retrieval. Thus, in ways, minimally invasive surgery is presently preferred to laparotomy, and the robot can be a logical alternative for the trained surgeon in laparoscopic approach.

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