



Lomboaortic Lymphadenectomy in Gynecological Oncology: Laparotomy, Laparoscopy or Robot-Assisted Laparoscopy?

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ABSTRACT

Background. The outcomes of paraaortic lymphadenectomy were compared for the treatment of gynecological malignancies to identify the most appropriate surgical approach.

Methods. Our retrospective, multicentric study included 1304 patients who underwent paraaortic lymphadenectomy for gynecological malignancies. The patients were categorized into the following five groups based on treatment type: transperitoneal laparoscopy (group A, $n = 198$), extraperitoneal laparoscopy (group B, $n = 681$), robot-assisted transperitoneal laparoscopy (group C, $n = 135$), robot-assisted extraperitoneal laparoscopy (group D, $n = 44$), and laparotomy (group E, $n = 246$).

Results. The prevalence of cancer types differed according to the surgical approach: there were more ovarian cancers in group E and more cervical cancers in groups B and D ($p < 0.001$). Estimated blood loss was higher in group E (844.2 mL) than in groups treated with minimally invasive interventions (115.8–141.5 mL, $p < 0.005$). For infrarenal dissection, fewer nodes were removed in group C compared with the other approaches (16 vs. 21 nodes, respectively, $p < 0.05$). The average operative time ranged

from 169 min for group A to 247 min for group E ($p < 0.001$). Length of hospital stay was 14 days for group E versus 3.5 days for minimally invasive procedures ($p < 0.05$). The early postoperative grade 3 and superior Dindo–Clavien complications occurred in 9–10% of the patients in groups B–D, 15% of the patients in group E, and only 3% and 4% for groups A and C, respectively. The most common complication was lymphocele.

Conclusions. Laparotomy increases preoperative and postoperative morbidity. The robot-assisted transperitoneal approach demonstrated a poorer lymph node yield than laparotomy and extraperitoneal approaches.

Paraaortic lymphadenectomy (PAL) is a routine procedure for staging or therapeutic purposes of gynecological malignancies. The purpose of conventional interventions in cervical cancers and advanced vaginal cancers is to guide the fields of radiation and for therapeutic benefits.^{1,2} In endometrial cancer, PAL is therapeutic; however in high-risk endometrial cancers, PAL also acts to guide the irradiation.³ In adnexal cancers, PAL is performed for therapeutic purposes, although recent data may call into question some of its interests.

Historically, PAL was systematically performed by laparotomy, and this is still the first route of choice, especially in ovarian cancers. Nevertheless, for several decades, transperitoneal and retroperitoneal laparoscopy also have been used to perform this procedure. More recently, robot-assisted PAL has been introduced. The development of minimally invasive surgery, particularly with respect to lymphadenectomy, meets the need to

perform adjuvant treatments as soon as possible after surgery. In this context, the interest of laparoscopy (transperitoneal or extraperitoneal) is demonstrated.⁴⁻⁶

Studies show that lymphadenectomy procedures by robot-assisted laparoscopy have good feasibility but are not superior to the laparoscopic approach alone. Each of these approaches has its own advantages and limitations, and the utility of each procedure is dependent on the type of cancer, the stage of the disease and the patient concerned. Thus, our objective is to evaluate the outcomes of PAL for the treatment of gynecological malignancies according to the surgical approach.

METHODS

This retrospective study involved multiple centers across France and Belgium. The six participating cancer surgery centers were: The Oscar Lambret Center, Lille; University Hospital of Liège, Liège; Institut Paoli-Calmettes, Marseille; Hospital Européen Georges Pompidou, Paris; University Hospital of Tours; and Citadelle Hospital, Liège. All centers were included for their specificities regarding type of surgical procedures.

This study included patients who had PAL for the treatment of gynecological cancer between 2006 and 2015. The PAL was performed in each center according to five different modalities: transperitoneal laparoscopy, extraperitoneal laparoscopy, robot-assisted transperitoneal laparoscopy, robot-assisted extraperitoneal laparoscopy, and laparotomy. Robotic procedures were performed after 2010. The extraperitoneal approach was used at the beginning of the data collection (2006). Patients who had received debulking procedures (adenectomy) were excluded from the study. The clinical decision for PAL was made for the treatment of one of the following gynecological conditions: cancer of the endometrium, ovary, cervix, and vagina. The included patients presented cancers of different stages and various pathological characteristics.

The clinical indications for PAL in cervical cancer were: IB1 FIGO stage carcinoma in cases of pelvic lymph node involvement, and cervical cancer of stage IB2 or higher. For endometrial cancers, PAL was performed for the first time in cases of high risk and high/intermediate risk. PAL also was performed a second time when the severity of the case was initially underestimated. PAL was performed for the treatment of adnexal cancers with a higher stage than FIGO IC.

The choice of surgical approach was decided in a multidisciplinary consultation meeting, in agreement with the surgeon referring the patient. PAL was systematically performed up to the level of the left renal vein (IR), except in some patients with cervical cancer (since 2013), in

which case the upper limit was the inferior mesenteric artery (IMA). The data collected were: body mass index (BMI), age, surgical approach, dissection level, number of lymph nodes, marsupialization, blood loss, skin-to-skin operative time, peri- and postoperative complications, and length of stay in the hospital. The classification of Dindo-Clavien⁷ for postoperative complications was used: grades I and II were considered minor, whereas grades III or higher were major. All surgeries were performed by surgeons with experience in minimally invasive surgery and robot-assisted laparoscopy. In some patients, other procedures were performed concomitantly, such as hysterectomy with bilateral salpingo-oophorectomy, omentectomy, appendicectomy, and pelvic lymphadenectomy. The characteristics of the patients are presented using the standard methods of descriptive statistics: frequencies and percentage for categorical variables; medians, extreme values, means and standard deviations for continuous variables. The difference between the proportions of the first pathways (such as age, BMI, and blood loss, depending on the pathway) is analyzed using the Chi square test or the Fisher exact test (if the theoretical size is less than 5). For the prognostic factor analysis, logistic regression analysis is used. The software used for statistical analysis was Stata v13.1 (StataCorp, 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP).

RESULTS

Our retrospective, multicenter study included 1304 patients who received PAL for gynecological cancers. The patients were divided into the following five groups, depending on their treatment type: transperitoneal laparoscopy (group A, $n = 198$), extraperitoneal laparoscopy (group B, $n = 681$), transperitoneal robotic laparoscopy (group C, $n = 135$), robot-assisted extraperitoneal laparoscopy (group D, $n = 44$) and laparotomy (group E, $n = 246$). Table 1 describe the distribution of procedure in the different centers. The distribution of type of cancer differed according to the surgical approach; there were more ovarian cancers in group E and more cervical cancers in groups B and D, $p < 0.001$. Only 15% of our patients, especially those operated on after 2013, received an inframesenteric artery dissection. Most patients received a complete infra-renal dissection. The transperitoneal robotic laparoscopy was mainly performed in two centers and using simple docking technique. No differences were found in BMI between groups, but the proportion of patients with $BMI \geq 30 \text{ kg/m}^2$ was significantly higher in extraperitoneal groups (Table 2). No differences were observed in age between groups, but there were significantly more patients younger than age 60 years in the minimally

TABLE 1 Details of operations per centers

Centers	Group A: transperitoneal laparoscopic approach		Group B: extraperitoneal laparoscopic approach		Group C: transperitoneal robotic approach		Group D: extraperitoneal robotic approach		Group E: laparotomy		Total	
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%
Citadelle Hospital, Liège	0	0.00	0	0.00	38	28.10	0	0.00	14	5.70	52	4.00
University Hospital of Tours	0	0.00	47	6.90	4	3.00	0	0.00	0	0.00	51	4.00
University Hospital of Liège	76	38.40	13	1.90	0	0.00	0	0.00	0	0.00	89	6.80
Oscar Lambret Center, Lille	122	61.60	571	83.80	11	8.10	32	72.70	232	94.30	967	74.15
Hopital Européen Georges Pompidou, Paris	0	0.00	50	7.30	0	0.00	12	27.30	0	0.00	62	4.70
Institut Paoli-Calmettes, Marseille	0	0.00	0	0.00	82	60.70	0	0.00	0	0.00	82	6.30
Total	198		681		135		44		246		1304	

TABLE 2 Characteristics of patient population

	Group A: transperitoneal laparoscopic approach	Group B: extraperitoneal laparoscopic approach	Group C: transperitoneal robotic approach	Group D: extraperitoneal robotic approach	Group E: laparotomy	<i>p</i>
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	
<i>Age (year)</i>						
< 60	145 (74.7)	527 (79)	87 (66.4)	31 (70)	112 (46.1)	< 0.002
≥ 60	49 (25.3)	140 (20)	44 (33.6)	13 (30)	131 (53.9)	
<i>BMI (kg/m²)</i>						
< 30	161 (88)	491 (80.5)	115 (90.6)	31 (70)	154 (71.3)	< 0.02
≥ 30	22 (12)	119 (19.5)	12 (9.4)	13 (30)	62 (28.7)	
<i>Localization</i>						
Cervix	104 (56.5)	572 (85.5)	78 (59.5)	37 (84)	0 (0)	< 0.001
Endometrium	41 (22.3)	41 (6.1)	35 (26.7)	7 (16)	80 (32.5)	
Ovary	39 (21.2)	54 (8.1)	18 (13.7)	0 (0)	166 (67.5)	
Vagina	0 (0)	2 (0.1)	0 (0)	0 (0)	0 (0)	
<i>Level of dissection</i>						
IMA	82 (42.3)	79 (11.8)	41 (40.2)	6 (13.6)	0 (0)	
IR	112 (57.7)	592 (88.2)	61 (59.8)	38 (86.4)	233 (100)	

BMI body mass index, *IMA* inframesenteric artery, *IR* infrarenal

invasive groups. The mean estimated blood loss was higher in group E (844.2 mL) compared with the minimally invasive groups (115.8–141.5 mL, $p < 0.005$). The mean operative time ranged from 169 min in group A to 247 min in group E ($p < 0.001$). The operative time was significantly lower in extraperitoneal groups. The duration of stay was 14 days for group E versus 3.5 days for minimally invasive procedures ($p < 0.05$; Table 3). During infrarenal dissection, fewer lymph nodes were removed in group C compared with the other groups (16 vs. 21 nodes, respectively, $p < 0.05$).

Complications with postoperative grade 3 and higher (classified using the Clavien–Dindo system) occurred in 9–10% and 15% of patients in groups B–D and group E, respectively, and in only 3% and 4% of groups A and C, respectively. Acute morbidity (grades 1–3 of the Clavien–Dindo classification) was more common in extraperitoneal groups and laparotomy than for transperitoneal groups. On the other hand, severe morbidity (grades 4–5) is higher for the laparotomy group than for the minimally invasive groups (Table 4). The most common complication was lymphocele. A univariate logistic regression analysis

TABLE 3 Details of operations

	Group A: transperitoneal laparoscopic approach	Group B: extraperitoneal laparoscopic approach	Group C: transperitoneal robotic approach	Group D: extraperitoneal robotic approach	Group E: laparotomy	<i>p</i>
Operative time (<i>n</i> = 653)	103	381	60	43	66	
Mean	214.6 ^{a,b}	207.1 ^{c,d}	257.1	220.2 ^e	250.5	
SD	88.3	73.4	117.1	63.9	70.1	
Blood loss (<i>n</i> = 223)	0	74 ^{f,g}	92 ^h	31 ⁱ	26	
Mean	NA	116.9	141.5	115.8	844.2	
SD	NA	407.9	265.7	134.5	965.1	
Hospital stay (<i>n</i> = 700)	178	338	77	43	64	0.0001
Median	3 ^j	3 ^k	3	3	9	
Range	1–24	1–41	1–19	1–16	4–84	
Lymph nodes (<i>n</i> = 1207)	180	645	108	41	233	< 0.02
Median	14	18	13	20	19	
Range	1–51	1–53	0–49	3–50	1–84	

^aGroup 1 compared with group 2, *p* = 0.04

^bGroup 1 compared with group 5, *p* = 0.002

^cGroup 2 compared with group 3, *p* = 0.004

^dGroup 2 compared with group 5, *p* = 0.0001

^eGroup 4 compared with group 5, *p* = 0.005

^fGroup 2 compared with group 3, *p* = 0.0004

^gGroup 2 compared with group 5, *p* = 0.0001

^hGroup 3 compared with group 5, *p* = 0.0001

ⁱGroup 4 compared with group 5, *p* = 0.0001

^jGroup 1 compared with group 2, *p* = 0.0001

^kGroup 2 compared with group 3, *p* = 0.0004

TABLE 4 Complications resulting from paraaortic lymphadenectomy (*n* = 159)

Dindo–Clavien classification	Group A: transperitoneal laparoscopic approach	Group B: extraperitoneal laparoscopic approach	Group C: transperitoneal robotic approach	Group D: extraperitoneal robotic approach	Group E: laparotomy
Grade 1–2, <i>n</i> (%)	8 (4)	8 (1.2)	1 (0.7)	1 (2.3)	9 (3.7)
Grade 3, <i>n</i> (%)	14 (7.1)	75 (11)	5 (3.7)	6 (13.6)	25 (10.2)
Grade 4, <i>n</i> (%)	1 (0.5)	1 (0.1)	0 (0)	0 (0)	1 (0.4)
Grade 5, <i>n</i> (%)	0 (0)	2 (0.3)	0 (0)	0 (0)	2 (0.8)

allowed us to identify the following as prognostic factors: the appearance of symptomatic lymphoceles; obesity (BMI > 30); age younger than 60 years; the number of lymph nodes removed; and the use of the extraperitoneal approach. Marsupialization reduced the number of lymphoceles in the extraperitoneal groups (Table 5).

DISCUSSION

The number of lymph nodes removed showed no significant differences between groups, with the exception of the transperitoneal robot-assisted laparoscopy group. These results are in agreement with the literature.⁸ Parkish et al. compared the transperitoneal and extraperitoneal approaches performed by laparoscopy and robot-assisted laparoscopy for the treatment of endometrial cancer. The

TABLE 5 Predictive factors of lymphocele

Factors	Events/total	OR (IC 95%)	<i>p</i>
BMI			
< 30	52/618	1	0.004
≥ 30	25/153	2.17 (1.30–3.63)	
Age (year)			
< 60	65/578	1	0.01
≥ 60	13/226	0.48 (0.26–0.89)	
Upper limit of dissection			
IR	88/1036	4.34	0.02
IMA	9/207	8.49	
Number of lymph nodes harvested		1.03 (1.01–1.05)	0.08
Localization			
Cervix	77/789	1	0.005
Endometrium	7/204	0.33 (0.15–0.72)	
Ovary	10/266	0.36 (0.18–0.71)	
Others	1/14	0.71 (0.09–5.51)	
Surgical approach			
Minimally invasive transperitoneal	5/144	1	< 0.0001
Minimally invasive extraperitoneal	66/476	3.51 (1.38–8.92)	
Laparotomy	9/233	0.88 (0.29–2.68)	
Marsupialization			
No	30/145	1	0.01
Yes	19/177	0.46 (0.25–0.86)	

BMI body mass index, *IMA* inframesenteric artery, *IR* infrarenal

number of lymph nodes removed was significantly lower in the transperitoneal approach, regardless of BMI. Nevertheless, there was no significant difference between the laparoscopic transperitoneal approach and the robot-assisted laparoscopy, unlike the findings of our study.

The first explanation for this inconsistency between studies is that, in a large number of robotic transperitoneal procedures in our study, double docking was not achieved, thus preventing a more extensive lymph node dissection.⁹ Lymph node dissection rate also could be influenced by the fact that some of the robotic procedures were performed with the older generation of the Da Vinci S robot (Intuitive Inc, Sunnyvale, CA).¹⁰ Second, in our study, there were more patients with BMI ≥ 30 kg/m² in the extraperitoneal groups. With increased BMI, transperitoneal lymphadenectomy may not have been sufficient to adequately collect the lymph nodes of the renal vessels because of poor visualization, due to increased intraabdominal adipose tissue. Ponce et al.¹¹ suggested that a learning curve of 20 cases was necessary to manage properly the surgical technique. In our study, mainly two centers performed this procedure routinely. In the other centers, the learning curve of 20 cases was not achieved. The extraperitoneal approach provides an alternative means for complete lymphadenectomy in this patient population. An ongoing, randomized

trial (STELLA Trial: Transperitoneal vs. Extraperitoneal Approach for Laparoscopic Staging of Endometrial Cancer and Ovarian Cancer [NCT01810874]) will clarify the potential benefits of extraperitoneal PAL compared with the transperitoneal approach.

The extraperitoneal approach was associated with several advantages over the transperitoneal approach: namely shorter operative time and shorter hospital stay. Therefore, when possible, this approach may be the most appropriate route of PAL. Nonetheless, an increased number of mild complications was observed in the extraperitoneal groups. Most of these complications were percutaneous drainages for symptomatic lymphoceles (grade 3a). These findings are in agreement with previous studies investigating the role of extraperitoneal laparoscopic PAL in gynecologic malignancies, which have shown that this procedure is both safe and feasible.^{12–14}

As mentioned above, the most common delayed complication in our study was lymphocele. The prognostic factors for the onset of symptomatic lymphocele were obesity (BMI > 30), age younger than 60 years, an increased number of lymph nodes removed, and use of the extraperitoneal approach. Regarding the extraperitoneal approach, it became obvious that marsupialization was a protective factor against lymphoceles. Thus,

marsupialization was initiated in patients who had been operated on more recently. This helps to explain why so few patients have benefited from the extraperitoneal approach. Nevertheless, it is likely that the difference in complications would have been more significant with a greater number of study participants. Systematic marsupialization at the end of the extraperitoneal procedure has not yet been evaluated prospectively. Therefore, data in the literature to corroborate or invalidate our result are limited, except for one study published by our team.¹⁵

Only one published study compares the laparoscopic robot-assisted approach to the laparoscopic approach.¹⁶ Diaz-Feijoo et al. compared the results of 17 and 83 patients undergoing extraperitoneal lymphadenectomy by robot-assisted laparoscopy and laparoscopic surgery, respectively. The authors observed that the operative time, the duration of hospitalization, and the rate complications were similar between the two approaches. However, robot-assisted laparoscopy was associated with decreased blood loss [20 mL, (range, 5–350) vs. 90 mL (range, 10–260)] and a greater number of lymph nodes [17 (range, 10–31) vs. 14 (range, 4–62)] compared with conventional laparoscopy ($p < 0.05$). The data from our study support these findings, except for the findings regarding increased lymph node dissection. This could be explained by a lack of participants in the robotic group.

Our study was retrospective, which means that bias could have affected the choice of the surgical approach. Due to the modalities of data collection, there are numerous missing information on perioperative data (Table 3) that could possibly influence our results. Furthermore, it was not possible to assess the patients' quality of life, or information on patients' preferences for cosmetic results after the various surgical approaches. Other weaknesses include our inability to evaluate the data based on the surgeon's learning curve and the team's experience. This would be particularly interesting to assess how the growing experience of robotic surgery influences docking and operative time. Another limitation is the lack of standardized follow-up in different studies. In fact, it is possible that long-term events (late complications) occurred after publication. We did not perform a cost analysis between the groups.

CONCLUSIONS

Mild morbidity is higher in the groups who underwent laparotomy and extraperitoneal approaches. On the other hand, serious morbidity is higher in the group who underwent laparotomy. Marsupialization and IMA

dissection is an effective way to reduce the risk of post-operative lymphocele. Randomized trials are required to confirm the benefit of the extraperitoneal and robot-assisted routes.

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