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RESEARCH ARTICLE

Choosing the most appropriate minimally invasive approach to treat gynecologic cancers in the context of an enhanced recovery program: Insights from a comprehensive cancer center

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Abstract

Objective

The aim of the study was to compare the characteristics of procedures for gynecologic cancers conducted with conventional laparoscopy (CL) or robotically assisted laparoscopy (RAL) in the context of an enhanced recovery program (ERP).

Methods

This is a secondary analysis of prospectively collected data from a cohort study conducted between 2016 (when the ERP was first implemented at the Institut Paoli-Calmettes, a comprehensive cancer center in France) and 2018. We included patients who had undergone minimally invasive surgery for gynecological cancers and followed our ERP. The endpoints were the analysis of postoperative complications, the length of postoperative hospitalization (LPO), and the proportion of combined procedures depending on the approach (RAL or CL). Combined procedures were defined by the association of at least two of the following operative items: hysterectomy, pelvic lymphadenectomy, and para-aortic lymphadenectomy.

Results

A total of 362 women underwent either CL (n = 187) or RAL (n = 175) for gynecologic cancers and followed our ERP. The proportion of combined procedures performed by RAL was significantly higher (85/175 [48.6%]) than that performed by CL (23/187 [12.3%]; p < 0.001). The proportions of postoperative complications were similar between the two groups (19.4% versus 17.1%; p = 0.59). Logistic regression analysis revealed a statistically

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insignificant trend in the association of RAL with a reduced likelihood of an LPO > 3 days after adjusting for predictors of prolonged hospitalization (adjusted OR = 0.573 [0.236–1.388]; p = 0.217).

Conclusion

Experts from our cancer center preferentially choose RAL to perform gynecologic oncological procedures that present elements of complexity. More studies are needed to determine whether this strategy is efficient in managing complex procedures in the framework of an ERP.

Introduction

Over the past two decades, the implementation of enhanced recovery programs (ERPs) worldwide has allowed physicians to re-evaluate and improve the management of patients who undergo surgery [1,2]. The main goal of an ERP is to create an optimal, standardized environment for surgery to improve patient recovery. Decreasing hospitalization length without increasing the complication and readmission rates is the primary goal of this improvement [1,3]. The benefit of ERPs is well established for many types of surgeries [2], including gynecologic oncological surgery [4–6].

Minimally invasive surgery (MIS) has been the most important surgical innovation in the past three decades. Its widespread implementation has allowed drastic reductions in length of stay and postoperative morbidity compared with that of open surgery for many procedures, including those related to gynecologic cancers [7–9]. Robotic-assisted laparoscopy (RAL) enables a greater adoption of MIS by supporting the ability to perform complex procedures that were previously restricted to surgeons with advanced laparoscopic skills. However, the benefits of RAL in improving surgical quality and patient health in comparison to conventional laparoscopy (CL) are still debated for most procedures [9]. In addition, RAL generates higher costs, and many MIS expert centers are still compelled to use both CL and RAL to manage hospital expenditures. There are no studies in the scientific literature that specifically assess the value of RAL in comparison to CL in the context of an ERP.

In a previous study, we determined predictors of successful early hospital discharge in the context of our ERP [10]. Combined procedures (e.g., the association of at least two procedures) and overweight were found to be associated with a prolonged length of postoperative hospitalization (LPO). The aim of the present study was to describe and compare the characteristics of procedures for gynecologic cancers that were performed with either CL or RAL in our unit in the context of an ERP.

Materials and methods

Study design

This was a secondary analysis of prospectively collected data from a cohort study conducted between January 2016 (when the ERP was first implemented at the Institut Paoli-Calmettes, a comprehensive cancer center in France) and September 2018. All women over 18 years of age who required gynecologic surgery at the Institut Paoli-Calmette during the study period followed our ERP. They were informed of the study during their first consultation and were asked to provide written consent for the storage and use of their data. The study was approved

by our ethical committee (Paoli-Calmettes Institute's review board, RAAC-IPC-2016-011/ NCT03950011). All data were prospectively and anonymously collected in the Database for Data Collection in the Context of an Enhanced Recovery After Surgery Program in Oncology Surgery (BDD RAAC).

Our institutional ERP was published in 2017 [4] and is in accordance with the latest published recommendations [5,11–14]. The main pathways of the ERP are summarized in Fig 1. Consecutive patients undergoing minimally invasive procedures (hysterectomy and/or pelvic or para-aortic lymphadenectomy) either by RAL or CL for gynecologic cancers (cervical, endometrial or ovarian cancer) were identified. We excluded patients who underwent surgery for benign indications and patients for whom a laparotomy was indicated. RALs were performed either with a da Vinci Xi® or a da Vinci Si® surgical system (Intuitive Surgical Inc. Sunnyvale, California, United States), and CLs were performed with a basic IMAGE1 S™ set (Karl Storz Endoskope SE & Co. KG, Tuttlingen, Germany).

All procedures were performed by four senior surgeons. In the context of the ERP, the choice of MIS was determined for each case according to what was feasible with consideration of the type of cancer, tumor stage and patient's comorbidities. As access to the robotic platform was limited, the choice between RAL and CL also took into consideration the availability of the platform.

The following parameters were analyzed: age, BMI, American Society of Anesthesiologists (ASA) score, Charlson Comorbidity Index score [15], oncological indication, surgical procedure, surgical approaches and LPO (defined as nights spent at hospital after surgery, excluding the night before the surgery). The exclusion criteria were surgery for benign indications and open surgery procedures. After discharge, a postoperative nurse coordinator conducted phone call interviews on days 1, 7 and 30 to record all occurrences of readmission to other hospitals and/or long-term postoperative complications. Per- and postoperative complications were collected according to the Clavien-Dindo classification [16].

All procedures in this study involving human participants were performed in accordance with the French ethical standards and with the 2008 Helsinki declaration. All included patients provided written informed consent before surgery. This work was approved by the institutional review board of the hospital (Institut Paoli-Calmettes Comité d'Orientation Stratégique).

Statistical analysis

Categorical variables are described using counts and frequencies, and quantitative variables are described using medians and 95% confidence intervals (95% CIs). The characteristics of patients who underwent CL or RAL were compared using χ^2 tests for discrete variables and two-sample t-tests for continuous variables. To compare the likelihood of a prolonged hospitalization (LPO $>$ 3 days) between the RAL and CL procedures, we conducted a logistic regression analysis, integrating predictors that were previously established by our team [10]: age $>$ 70 years, overweight and obesity, ASA score $>$ 2, combined procedures and radical hysterectomies. The results were reported as adjusted odds ratios (ORs) with 95% confident intervals (95% CIs) and p values.

Procedures were categorized as 'isolated' (hysterectomy [± omentectomy] or pelvic lymphadenectomy or para-aortic lymphadenectomy) or 'combined' (association of two or more different procedures).

The level of statistical significance was set at $\alpha = 0.05$. Statistical analyses were carried out using SPSS® software version 24. We followed the reporting recommendations specified in

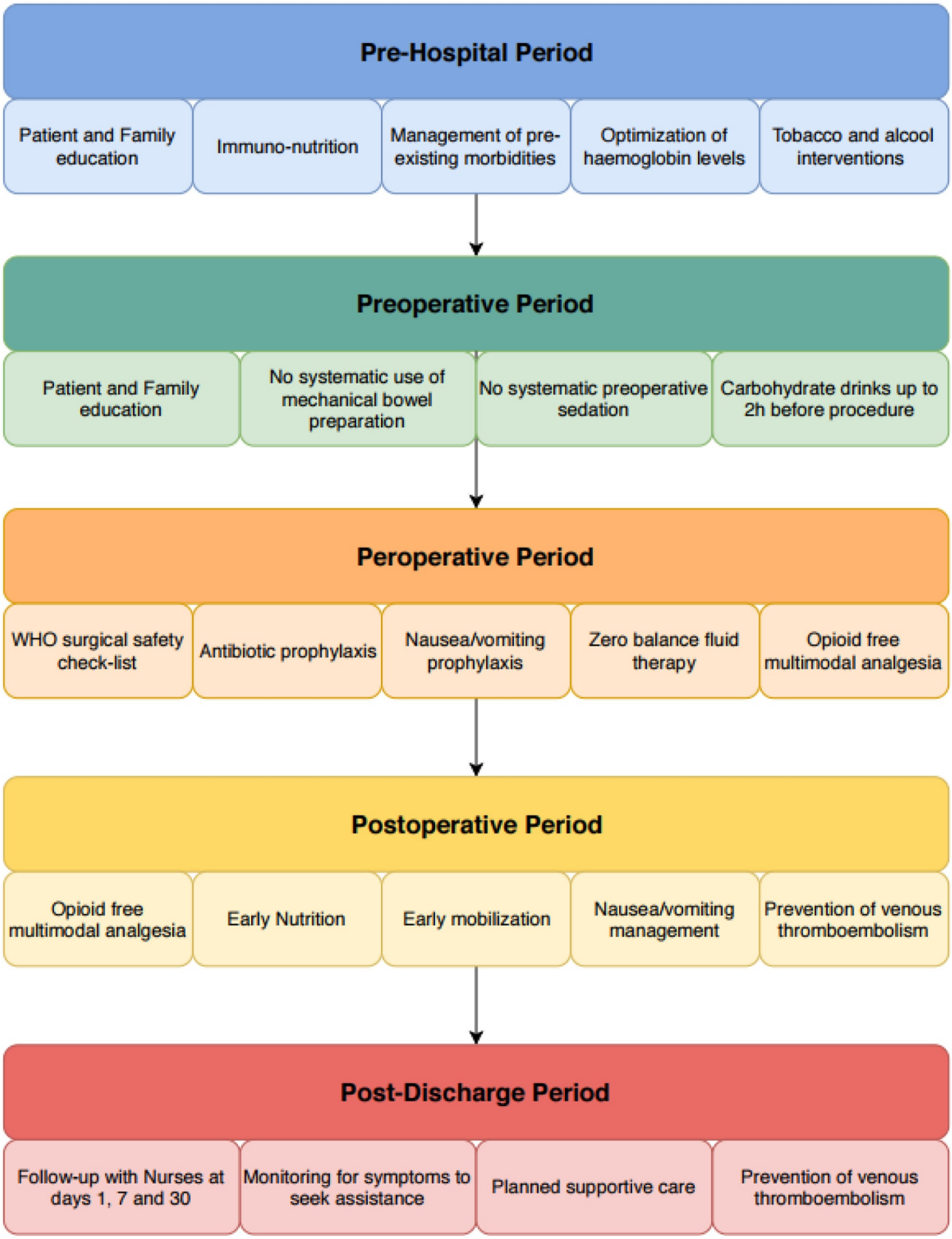


Fig 1. Summary of the Institut Paoli-Calmettes enhanced recovery program.

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the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) Statement.

Results

Characteristics of the study population

A total of 540 patients underwent surgery and followed our ERP during the study period (Fig 2). We excluded 178 patients who either underwent laparotomy (n = 97, including 12 for benign indications) and/or had surgery for benign indications (n = 93). Thus, a total of 362 patients were included in the final analysis (that is, 362/447 [81%] of patients with malignant indications underwent MIS). A total of 187 patients underwent CL, and 175 patients underwent RAL. The percentage of procedures performed using RAL over time is presented in Fig 3. Baseline characteristics are summarized in Table 1. The overall compliance rate with the ERP criteria was 90% (previously published data [4]). The populations of patients who underwent CL and RAL were comparable in terms of Charlson Comorbidity Index score (p = 0.126), ASA score (p = 0.216) and oncological indication (p = 0.216). Patients who underwent RAL were significantly older (61.0 years [58.7–62.9] vs. 57 years [54.8–58.8]; p = 0.006) and had a higher median BMI (25.0 kg/m^2 [25.9–28.1] vs. 24.1 kg/m^2 [24.6–26.4]; p = 0.044) than patients who underwent CL. The proportion of combined procedures performed by RAL was significantly higher than that performed by CL (RAL: 85/175 [48.6%]; CL: 23/187 [12.3%]; $p < 0.001$).

Peri- and postoperative outcomes

The median operative time was longer for RAL (163 minutes [95% CI 170.9–193.5]) than for CL (137 minutes [140.2–161.6]; $p < 0.001$). The overall proportion of perioperative complications was 0.8% and was similar for both surgical approaches (p = 0.612) (Table 2). The rate of conversions to laparotomy was similar for the two approaches (1.1% for RAL vs. 4.3% for CL; p = 0.069). The median LPO was higher after RAL (2.0 days [1.8–2.2]) than after CL (1.0 day [1.4–1.9]; p = 0.027).

Operative time

The operative time analyzed according to subgroups of procedures is shown in Table 3. Combined procedures were performed faster with RAL than with CL (229.0 minutes [213.2–245.3] vs. 269.0 minutes [234.2–331.4]; p = 0.008). The operative times were similar for isolated procedures for the two approaches (131.0 minutes [128.8–146.7] for RAL vs. 130.0 minutes [125.9–138.9] for CL; p = 0.338). There was no statistically significant difference for any of the procedures when analyzed individually.

Length of postoperative hospitalization

The LPO analyzed according to subgroups of procedures is shown in Table 4. For combined procedures, the median LPOs were similar for both approaches (2.0 days [1.7–5.0] for CL vs. 2.0 days [1.9–2.5] for RAL; p = 0.114). For isolated procedures (i.e., total hysterectomy, pelvic lymphadenectomy or para-aortic lymphadenectomy), the median LPO was significantly higher for RAL (2.0 days [1.6–2.1]) compared with CL (1.0 day [1.3–1.7]; p = 0.045). The median LPOs were similar in both groups for total hysterectomies (p = 0.391), pelvic lymphadenectomies (p = 0.105) and para-aortic lymphadenectomies (p = 0.661). For total hysterectomies with pelvic lymphadenectomies, LPO was significantly lower in the RAL group (2.0 days [1.4–1.9]) than in the CL group (2.0 days [1.3–4.0]; p = 0.007). The number of observations for the other combined procedures was too low to allow any reliable comparison of the LPO.

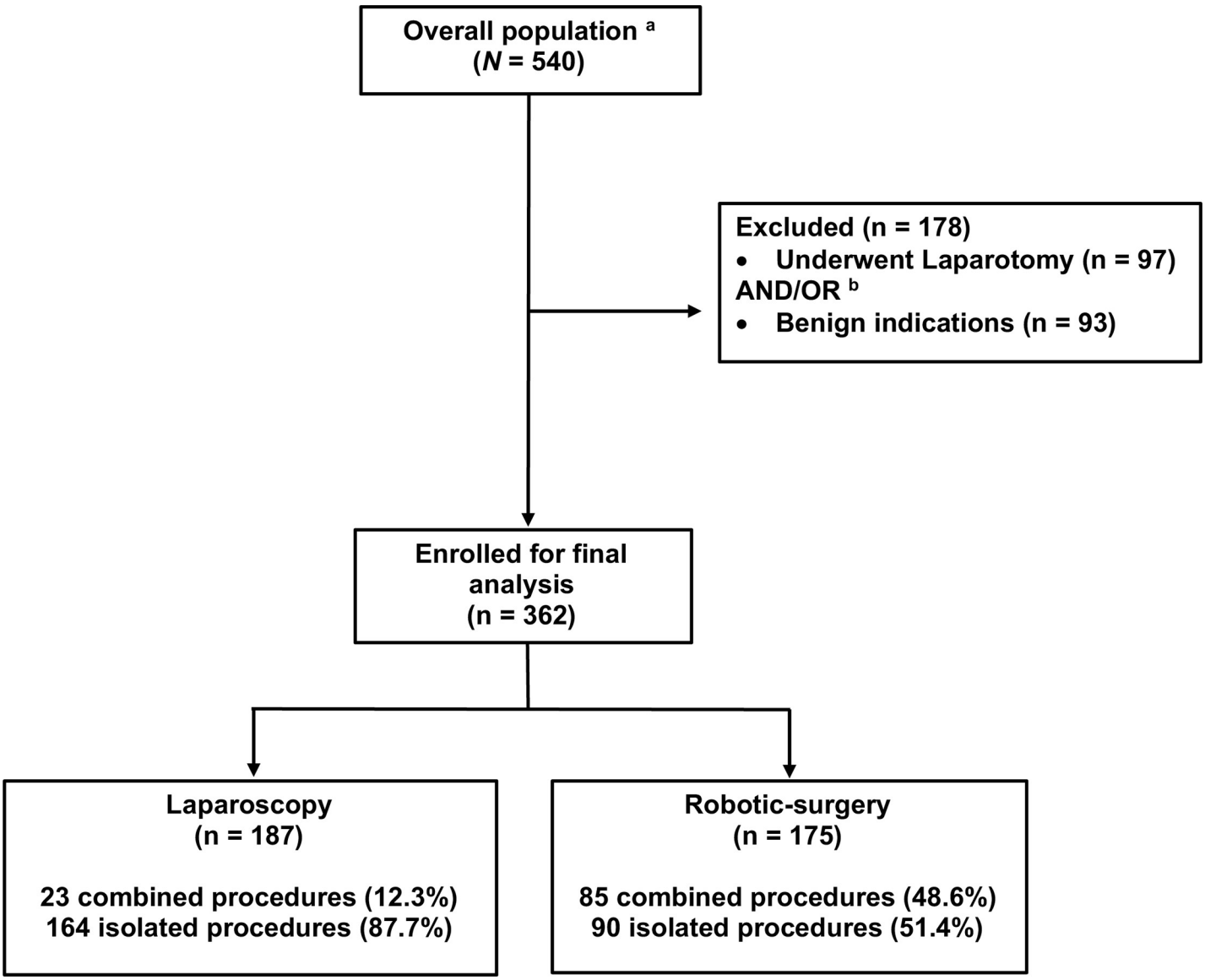


Fig 2. Subject disposition (CONSORT flow diagram). [a] Overall population was represented by those women who followed the enhanced recovery program between January 2016 and September 2018 [b] 12 Women underwent laparotomy for benign indications.

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Logistic regression analysis showed a statistically insignificant trend of RAL reducing the likelihood of an LPO > 3 days after adjusting for predictors of prolonged hospitalization (age > 70 years, overweight and obesity, ASA score > 2, combined versus isolated procedures and radical hysterectomies) (adjusted OR = 0.573 [0.236–1.388]; p = 0.217).

Discussion

In a previous study, we determined predictors of increased hospital stay in the context of an ERP [10]. The present study describes and compares the procedures that were performed by CL or by RAL over three years in our unit after the implementation of our ERP. Our results show that when expert surgeons from our unit have to choose between CL and RAL to treat gynecological cancers, they more frequently choose RAL to perform procedures that present

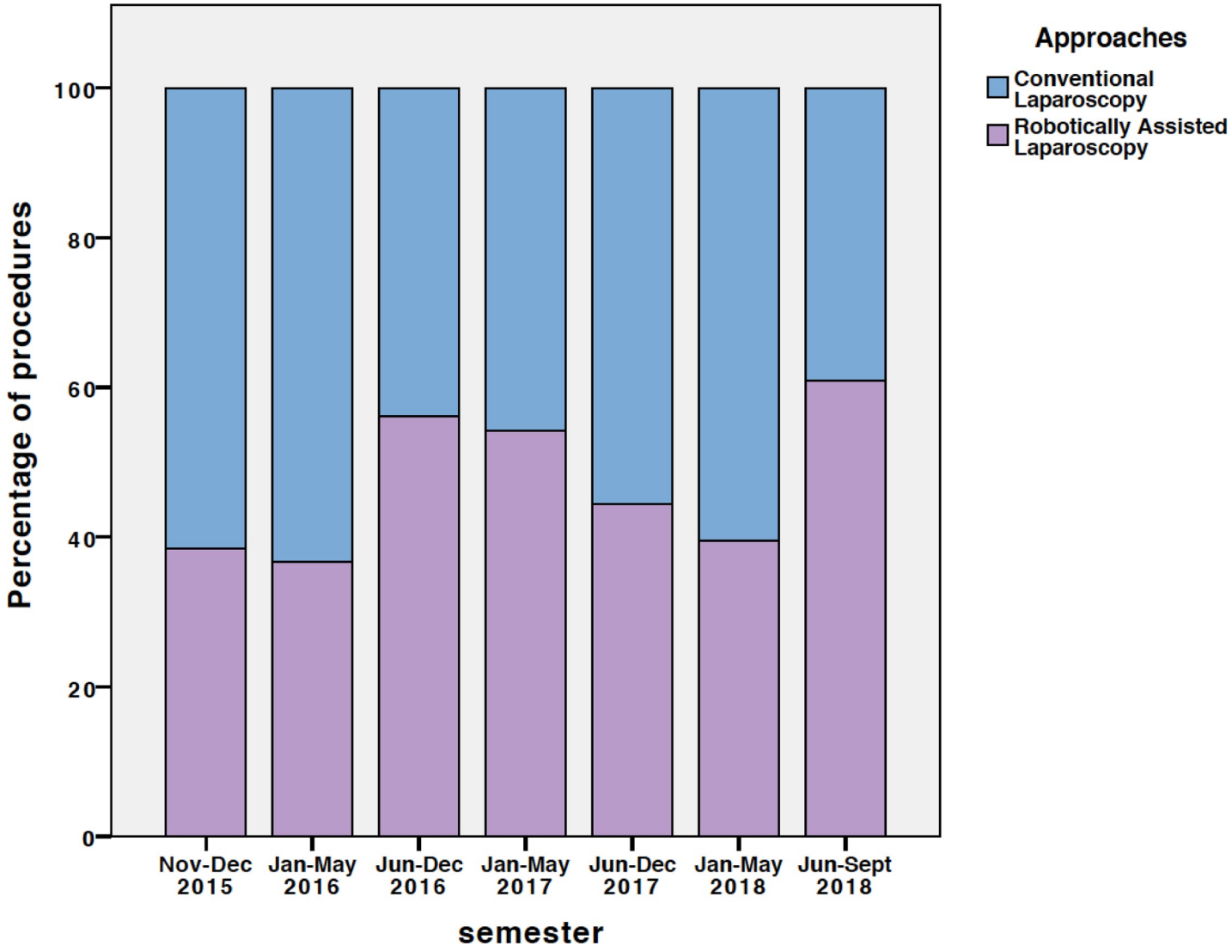


Fig 3. Percentage of minimally invasive procedures performed by conventional laparoscopy and robotically assisted laparoscopy over time.

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elements of complexity (i.e., higher age, higher BMI and/or combined procedures). Consequently, the two groups (RAL and CL) are too different to allow a reliable comparison. This prevents us from firmly forming a conclusion on the effect of this strategy of choosing the surgical route on the LPO. Despite this major impediment, our study provides a hint on the value of RAL in managing complex patients and procedures. Indeed, the results of the logistic regression analysis, which took into account predictors of prolonged hospitalization, showed a statistically insignificant trend in the association of RAL with a reduced likelihood of an LPO greater than 3 days. Without statistical adjustment, the only subgroup that showed a significant reduction in the LPO for RAL compared to that for CL was the total hysterectomies with pelvic lymphadenectomies subgroup. The number of observations for the other combined procedures was too low to draw any reliable conclusions. Conversely, when used for isolated procedures, RAL seems to be significantly associated with an increased LPO compared to CL. These results, while broadly limited by the weak comparability of the groups, seem to support the idea that RAL is more profitable when used for more complex procedures and patients. The

Table 1. Patient characteristics at baseline and surgical procedures.

Characteristics	Total N = 362	Conventional Laparoscopy N = 187	Robotically assisted laparoscopy N = 175	p-value
Age, years, median (95% CI)	59.0 (57.3–60.2)	57.0 (54.8–58.8)	61.0 (58.7–62.9)	0.006**
BMI, kg/m^2, median (95% CI)	24.6 (25.5–27.0)	24.1 (24.6–26.4)	25.0 (25.9–28.1)	0.044*
ASA score, median (95% CI)	2.0 (1.9–2.0)	2.0 (1.8–2.0)	2.0 (1.9–2.0)	0.216
Charlson score, median (95% CI)	0.0 (0.3–0.5)	0.0 (0.2–0.5)	0.0 (0.3–0.7)	0.126
Isolated procedures, n (%)	254 (70.2%)	164 (87.7%)	90 (51.4%)	< 0.001**
Total Hysterectomy (± omentectomy)	133 (36.7%)	71 (38.0%)	62 (35.4%)	0.663
Pelvic lymphadenectomy	24 (6.6%)	15 (8.0%)	9 (5.1%)	0.187
Para-aortic lymphadenectomy	97 (26.8%)	78 (41.7%)	19 (10.9%)	<0.001**
Combined procedures[a], n (%)	108 (29.8%)	23 (12.3%)	85 (48.6%)	< 0.001**
Total hysterectomy and pelvic lymphadenectomy	55 (15.2%)	10 (5.3%)	45 (25.7%)	< 0.001**
Radical hysterectomy and pelvic lymphadenectomy	13 (3.6%)	1 (0.5%)	12 (6.9%)	0.001**
Pelvic and para-aortic lymphadenectomy	6 (1.7%)	2 (1.1%)	4 (2.3%)	0.312
Hysterectomy, pelvic and para-aortic lymphadenectomy	9 (2.5%)	1 (0.5%)	8 (4.6%)	0.014*
Hysterectomy, pelvic and para-aortic lymphadenectomy and omentectomy	25 (6.9%)	9 (4.8%)	16 (9.1%)	0.078
Oncological indication, n (%)				0.216
Cervical cancer	176 (49.0%)	99 (53.5%)	77 (44.3%)	0.055
Endometrial cancer	153 (42.6%)	69 (37.3%)	84 (48.3%)	0.021
Ovarian cancer	28 (7.8%)	16 (8.6%)	12 (6.9%)	0.343
Uterine sarcoma	2 (0.6%)	1 (0.5%)	1 (0.6%)	0.743

*p-value<0.05

**p-value<0.01

[a]Combined procedures: association among two or more different procedures.

Abbreviations: BMI = Body Mass Index; ASA = American Society of Anesthesiologists; 95% CI = 95% Confidence Interval

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interpretation of the operative time is subject to the same limitations since we cannot take into account all the possible confounders related to the differences between the two populations. The operative time was decreased for combined procedures performed by RAL. For isolated procedures, however, the operative time was similar between the two approaches, suggesting that the increased LPO in patients that underwent isolated procedures could be attributable to other features of RAL (such as the number and width of incisions), or to other confounders (age, BMI).

Over three years, 81% of the gynecologic oncological procedures at our center were performed by minimally invasive techniques. Maintaining this high proportion of procedures performed by MIS is one of the key objectives of our ERP, as it allows drastic reductions in LPO. As with many MIS expert centers, we are compelled to use both CL and RAL to address both hospital expenditures and surgical equipment availability. Therefore, for each procedure, the surgical approach has to be carefully determined to safely reduce length of stay and morbidity and improve return to the intended oncological treatment.

There is abundant literature comparing RAL and CL for the management of gynecologic cancer [17]. However, the vast majority of studies are retrospective or historical control studies and report on a limited number of observations. The most robust evidence in favor of RAL

Table 2. Operative time, length of hospitalization, complications and readmissions.

Characteristics	Total N = 362	Conventional Laparoscopy N = 187	Robotically assisted laparoscopy N = 175	p-value
Operative time, minutes, median (95% CI)	150.0 (158.2–173.9)	137.0 (140.2–161.6)	163.0 (170.9–193.5)	< 0.001**
Conversions to laparotomy, n (%)	10 (2.8%)	8 (4.3%)	2 (1.1%)	0.069
Perioperative complications, n (%)	3 (0.8%)	1 (0.5%)	2 (1.1%)	0.612
Length of hospitalization after the operation, days, median (95% CI)	1.0 (1.7–2.0)	1.0 (1.4–1.9)	2.0 (1.8–2.2)	0.027*
Intensive care unit hospitalizations, n (%)	5 (1.4%)	2 (1.1%)	3 (1.7%)	0.676
Postoperative complications, n (%)	66 (18.2%)	32 (17.1%)	34 (19.4%)	0.588
Hospital Readmissions	30 (8.3%)	15 (8.0%)	15 (8.6%)	0.851
Complication severity (Clavien-Dindo classification), n (%)				0.577
Stage I	15 (22.7%)	8 (25.0%)	7 (20.6%)	-
Stage II	27 (40.9%)	11 (34.4%)	16 (47.1%)	-
Stage III	23 (34.8%)	12 (37.5%)	11 (32.4%)	-
Stage IV	1 (1.5%)	1 (3.1%)	0 (0.0%)	-
Type of complication, n (%)				0.411
Infectious	10 (15.2%)	3 (9.4%)	7 (20.6%)	-
Scar complications	2 (3.0%)	2 (6.3%)	0 (0.0%)	-
Digestive	6 (9.1%)	2 (6.3%)	4 (11.8%)	-
Bleeding	10 (15.2%)	4 (12.5%)	6 (17.6%)	-
Lymphatic	25 (37.9%)	15 (46.9%)	10 (29.4%)	-
Neurologic	3 (4.5%)	1 (2.9%)	2 (6.3%)	-
Urinary	7 (10.6%)	2 (6.3%)	5 (14.7%)	-
Thromboembolic	1 (1.5%)	1 (3.1%)	0 (0.0%)	-
Others	2 (3.0%)	1 (3.1%)	1 (2.9%)	-

95% CI = 95% Confidence Interval

* p-value < 0.05

** p-value < 0.01

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concerns the surgical treatment of endometrial cancers, with several meta-analyses showing reduced rates of conversion to laparotomy and estimated blood loss but overall similar lengths of stay, operative times, complications and oncologic outcomes [18]. One randomized controlled trial with 101 patients compared RAL to CL for surgery related to endometrial cancer and found reduced operative time and rate of conversions to laparotomy with RAL. Length of stay and postoperative pain were similar between the two groups [19]. Studies investigating the surgical treatments of cervical and ovarian cancers are less consistent and have not demonstrated the superiority of RAL over CL [20–22]. Overall, the only consensus with regard to the management of gynecologic cancers using MIS is that MIS is superior to open surgery for peri- and early postoperative outcomes, although the noninferiority of MIS has recently been questioned with regard to long-term oncological outcomes, in particular for early-stage cervical cancers [23]. Furthermore, the literature tends to show that RAL can increase the utilization of MIS by improving learning curves compared with CL but is more costly than CL or open surgery [17,24–26].

Table 3. Operative time (minutes, median (95% CI)), analyzed by subgroups of procedures.

	Conventional laparoscopy	Robotically assisted laparoscopy	p-value
Isolated procedures	130.0 (125.9–138.9)	131.0 (128.8–146.7)	0.338
Total hysterectomy	117.0 (115.9–136.0)	131.0 (124.3–147.3)	0.197
Pelvic lymphadenectomy	130.0 (116.9–157.9)	147.0 (130.0–191.5)	0.160
Para-aortic lymphadenectomy	139.0 (127.8–147.0)	129.0 (117.7–148.7)	0.689
Combined procedures[a]	269.0 (234.2–331.4)	229.0 (213.2–245.3)	0.008**
Total hysterectomy and pelvic lymphadenectomy	190.5 (158.7–246.9)	186.0 (177.1–210.2)	0.644
Radical hysterectomy and pelvic lymphadenectomy	534.0	250.5 (236.8–277.1)	NS
Pelvic and para-aortic lymphadenectomy	237.0	259.0 (175.0–342.0)	NS
Hysterectomy, pelvic and para-aortic lymphadenectomy	248.0	236.5 (148.7–279.5)	NS
Hysterectomy, pelvic and para-aortic lymphadenectomy and omentectomy	353.0 (291.6–424.2)	282.5 (266.3–351.3)	0.165

* p-value < 0.05

** p-value < 0.01

[a] Combined procedures: association among two or more different procedures. NS = Not statistically significant

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The current literature evidence is weak, and randomized controlled studies should be conducted to set recommendations on the profitability of RAL for gynecologic oncological procedures.

The main strengths of our study are its prospective data collection, the standardized ERP that assures similar management for every patient, the thorough reporting of postoperative complications and the subgroup analysis by type of procedure rather than by type of cancer.

Our primary objective was to describe and compare the characteristics of procedures for gynecologic cancers that were performed with either CL or RAL in our unit. Although we determined that surgeons from our unit preferentially choose to use RAL to perform complex procedures, two major impediments prevented us from concluding whether this strategy is effective in reducing LPO. First, surgical approaches are clearly chosen by surgeons with the a priori belief of a better profitability of RAL for more complex procedures and patients. Consequently, we obtained two groups with very different features, which makes it difficult to compare outcomes. We attempted to overcome this bias by conducting a subgroup analysis and a

Table 4. Length of postoperative hospitalization (median (95% CI)), analyzed by subgroups of procedures.

	Conventional laparoscopy	Robotically assisted laparoscopy	p-value
Isolated procedures	1.0 (1.3–1.7)	2.0 (1.6–2.1)	0.045*
Total hysterectomy	1.0 (1.4–2.0)	2.0 (1.5–2.2)	0.391
Pelvic lymphadenectomy	1.0 (1.2–1.9)	2.0 (0.9–3.9)	0.105
Para-aortic lymphadenectomy	1.0 (1.0–1.7)	1.0 (1.2–1.7)	0.661
Combined procedures[a]	2.0 (1.7–5.0)	2.0 (1.9–2.5)	0.114
Total hysterectomy and pelvic lymphadenectomy	2.0 (1.3–4.0)	2.0 (1.4–1.9)	0.007**
Radical hysterectomy and pelvic lymphadenectomy	2.0	2.0 (1.9–3.2)	NS
Pelvic and para-aortic lymphadenectomy	1.5	2.5 (1.2–4.3)	NS
Hysterectomy, pelvic and para-aortic lymphadenectomy	2.0	1.5 (0.9–3.1)	NS
Hysterectomy, pelvic and para-aortic lymphadenectomy and omentectomy	2.0 (0.7–6.4)	2.0 (2.0–4.7)	0.886

* p-value < 0.05

[a] Combined procedures: association among two or more different procedures. 95% CI = 95% confidence interval; NS = non-statistically significant.

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logistic regression analysis. These analyses must be interpreted with the utmost precaution and cannot provide sufficient evidence for the recommendation of one surgical approach over the other regardless of complexity. Second, our study population presents with a high degree of heterogeneity since it includes patients suffering from different gynecological cancers. We chose to conduct our subgroup analysis by regrouping patients who underwent similar procedures rather than those with the same cancer localization. Although this method is suitable for analyzing the surgical complexity, it does not account for the specific difficulties associated with the surgical treatment of each cancer. Furthermore, our study focused mainly on the LPO, which is the easiest way to assess the efficiency of an ERP. However, it does not render the whole complexity of the treatment of gynecological cancers. Indeed, we did not reported data on oncological outcomes, such as relapse-free survival. The long-term quality of life is also missing from our reported data. In particular, we did not report any data on fertility preservation, which is strongly linked to the well-being of young patients suffering from gynecological cancers [27–31]. Thus, we cannot formally make conclusions on the profitability of each surgical approach and can only describe the elements that we used to decide which MIS technique will be used. Finally, the reproducibility of our findings is limited to MIS expert centers where surgeons have advanced skills in both RAL and CL.

In conclusion, experts from our cancer center preferentially choose RAL to perform gynecologic oncological procedures that present elements of complexity. With regard to technical and financial concerns, these results may suggest a dedicated role for RAL and CL in these clinical pathways. Additional studies are needed to confirm the value of this approach.

Supporting information

S1 Dataset. Clinical and surgical data.
(XLSX)

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