

Laparoscopic Versus Abdominal Approach to Endometrial Cancer

A 10-Year Retrospective Multicenter Analysis

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Objective: The objective of this study was to give a reality-based picture of the use of laparoscopic surgery for staging endometrial cancer patients out of the experimental setting.

Methods: Consecutive data of patients with endometrial cancer who underwent laparoscopic or abdominal surgical staging in 6 Italian centers were recorded. Baseline patients and tumors characteristics, surgery performed, and safety data were collected and analyzed.

Results: A total of 1012 subjects (403 and 609 treated by laparoscopy and laparotomy, respectively) who received surgical stadiation for endometrial cancer were included in the final analysis. The laparoscopic approach to endometrial cancer was more commonly performed in younger and nonobese patients who had received less previous surgeries, whereas the abdominal approach was preferred for the advanced stages and rare histotypes. Irrespectively to stage, the operative time was higher for the laparoscopy than laparotomy, whereas blood loss and postoperative complications were lower in the laparoscopy group than in the laparotomy group. No difference between surgical approaches was observed in complication rates in stage I endometrial cancers, whereas they were worst in higher stages. The site, but not the incidence, of recurrences differed only for advanced stage endometrial cancers. No differences in overall, disease-free, and cancer-related survival rates were also observed.

Conclusions: In the clinical practice, heterogeneous criteria are adopted to recur to laparoscopy for staging endometrial cancer. The safety and the feasibility of the laparoscopy are confirmed for stage I endometrial cancers, whereas they appear suboptimal for the advanced stages.

Key Words: Endometrial cancer, Laparoscopy, Laparotomy, Surgery, Uterine cancer

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Endometrial cancer is the most common gynecologic malignancy. The traditional approach for staging and treating endometrial cancer includes peritoneal washing and surgical removal of the uterus, tubes, and ovaries. Pelvic lymphadenectomy and eventual extension to para-aortic sites are also procedures to combine in several centers, even if their effectiveness is not universally recognized.¹⁻³

The efficacy and safety of the laparoscopic approach to endometrial cancer have been clearly established by multiple publications, including randomized controlled studies⁴⁻¹¹ and meta-analyses.^{12,13} Almost all these data were obtained in the most prestigious oncologic centers with historical expertise in the endoscopic field⁴⁻¹¹ and/or were limited to the treatment of early-stage endometrial cancer.^{5,6,7-11} To date, international guidelines of gynecologic oncology (http://www.gfmer.ch/Guidelines/Female_genital_neoplasms/Endometrial_cancer.htm) did not give specific indication to laparoscopy, either in early stages or in advanced stages.

Considering the discrepancy between the evidence from the literature and clinical guidelines, to date the behavior regarding the endometrial cancer staging by surgeons in general practice is controversial.^{14,15} As a consequence, some surgeons have baseless skepticism for laparoscopy in oncologic patients. On the contrary, for others, laparoscopy is routinely used in their surgical practice for staging endometrial cancer, also for the advanced stages.

Based on these considerations, the aim of the current multicenter study was to give a reality-based picture of the use of laparoscopic surgery for staging endometrial cancer patients out of the experimental setting.

MATERIALS AND METHODS

We retrospectively studied data recorded of consecutive patients who had undergone a laparoscopic or open surgery for staging endometrial cancer between January 2000 and May 2010 in 6 Italian centers, that is, 3 academic departments of obstetrics and gynecology (Universities of Catanzaro, Insubria, and Verona), 2 cancer centers (Aviano and Catanzaro), and 1 general hospital (Reggio Emilia).

Inclusion criteria were as follows: the presence of histologically confirmed endometrial cancer treated with standard surgical staging consisting in peritoneal washing and total hysterectomy (including both totally laparoscopic/abdominal approach and laparoscopically assisted vaginal approach) with bilateral salpingo-oophorectomy and/or pelvic/para-aortic lymphadenectomy. Pelvic lymphadenectomy consisted of the removal of the lymphatic tissue overlying the external, internal, and common iliac veins and arteries and the fossa obturatoria above the obturator nerve, whereas para-aortic lymphadenectomy consisted of the excision of the lymphatic tissue overlying the right upper common iliac artery, aorta, and vena cava to a level just below the renal vein.

Exclusion criteria were the absence of clear and complete clinical and histological data and having not undergone a hysterectomy.

Patient data were distinguished in the 2 groups on the basis of surgical treatment received, that is, laparoscopy (laparoscopy group) or laparotomy (laparotomy group). Baseline

characteristics and oncologic, efficacy, and recurrence data were recorded for each patient.

Baseline characteristics included age, body mass index, parity, previous major open surgery, menopausal state, and concurrent medical diseases.

Oncologic data collected consisted of the International Federation of Gynecology and Obstetrics (FIGO) surgical stage (based on preoperative imaging data, ie, whole-body magnetic resonance or computed tomography with the use of a contrast medium to enhance the details seen in an organ scan), tumor grade, and histopathologic type.

Surgical data collected were as follows: pelvic and/or para-aortic node dissection performed, number of pelvic and para-aortic lymph nodes yielded, total operative time, blood loss, conversion to laparotomy, type of complications, and time when they occurred. The complications were classified in intraoperative and postoperative (adverse events occurring within 30 days of surgery as a result of the procedure) complications and graded according to standardized criteria.¹⁶

Efficacy data were obtained from the follow-up clinical charts. In particular, we evaluated the time and the number and the site of recurrence. Recurrences were defined as loco-regional (vaginal and/or pelvic recurrences) and distant (para-aortic node metastases, abdominal relapses, liver, lung, bone and brain metastases, and diffuse metastatic disease) failures. Treatment of each recurrence and characteristic of the adjuvant therapy, including type and dose, were also recorded.

Finally, overall recurrence-free and cancer-related survival rates, from surgery to death or last follow-up visit, were noted for each patient and calculated for both groups.

The institutional review board approval was not required because data were retrospectively collected and did not include any personally identifiable information.

Statistical Analysis

Continuous variables were expressed as median and interquartile range (IQR) and analyzed using Mann-Whitney *U* test or Wilcoxon signed rank test for 2 independent or related samples, respectively. For categorical variables, the Pearson χ^2 test, the exact method, and the Fisher exact test were applied as required.

The analysis was performed by stratifying patients according to the FIGO surgical stages. Data were also analyzed with the use of general linear model univariate procedure that provides regression analysis and analysis of variance (ANOVA) for 1 dependent variable by 1 factor. Analysis of variance is robust to departures from normality, although the data should be symmetric. The model included as dependent variable the overall survival, and as between-subjects factor, which divided the population into groups as fixed factors, the investigational centers involved.

Statistical analysis was performed using the SPSS 11.0 (SPSS Inc, Chicago, IL) package. A *P* < 0.05 value was considered as statistically significant.

RESULTS

A total of 1743 clinical charts were examined, and after inclusion/exclusion criteria were applied, 731 patients were

TABLE 1. Surgical stage, grade, and histology of the endometrial cancers

Group	Laparoscopy (n = 403)	Laparotomy (n = 609)
FIGO stage, n (%)		
IA	52 (12.9)	68 (11.2)
IB	248 (61.5)	257 (42.2)
IC	70 (17.4)	135 (22.2)
IIA	12 (3.0)	37 (6.1)
IIB	5 (1.2)	29 (4.8)
IIIA	6 (1.5)	19 (3.1)
IIIB	1 (0.2)	5 (0.8)
IIIC	8 (2.0)	44 (7.2)
IVA	0 (0.0)	1 (0.1)
IVB	1 (0.2)	14 (2.3)
Grade, n (%)		
G1	191 (47.4)	289 (47.4)
Stage I	177 (43.9)	260 (42.7)
Stage II	9 (2.2)	22 (3.6)
Stage III	5 (1.2)	5 (0.8)
Stage IV	0 (0.0)	2 (0.3)
G2	142 (35.2)	224 (36.8)
Stage I	134 (33.3)	168 (27.6)
Stage II	5 (1.2)	29 (4.8)
Stage III	3 (0.7)	23 (3.8)
Stage IV	0 (0.0)	4 (0.7)
G3	70 (17.4)	96 (15.8)
Stage I	59 (14.6)	32 (5.3)
Stage II	3 (0.7)	15 (2.5)
Stage III	7 (1.7)	40 (6.6)
Stage IV	1 (0.2)	9 (1.5)
Histology, n (%)		
Endometrioid	347 (86.1)	449 (73.8)
Stage I	338 (83.9)	410 (67.3)
Stage II	9 (2.2)	39 (6.4)
Papillary serous	16 (4.0)	64 (10.5)*
Stage II	2 (0.5)	13 (2.1)
Stage III	13 (3.2)	51 (8.4)
Stage IV	1 (0.2)	0 (0.0)
Adenosquamous	30 (7.4)	48 (7.9)
Stage I	25 (6.2)	44 (7.2)
Stage II	5 (1.2)	4 (0.7)
Clear cell	0 (0.0)	16 (2.6)
Stage III	0 (0.0)	8 (1.3)
Stage IV	0 (0.0)	8 (1.3)
Adenocanthoma	0 (0.0)	16 (2.6)
Stage I	0 (0.0)	6 (1.0)
Stage II	0 (0.0)	10 (1.6)

TABLE 1. (Continued)

Group	Laparoscopy (n = 403)	Laparotomy (n = 609)
Mucinous	10 (2.5)	0 (0.0)
Stage I	7 (1.7)	0 (0.0)
Stage II	1 (0.2)	0 (0.0)
Stage III	2 (0.5)	0 (0.0)
Small cell	0 (0.0)	16 (2.6)
Stage III	0 (0.0)	9 (1.5)
Stage IV	0 (0.0)	7 (1.1)

**P* < 0.05 versus laparoscopy group.

excluded. Thus, a total of 1012 subjects who received surgical stadiation for endometrial cancer were included in the final analysis. In particular, 403 patients underwent laparoscopy, whereas 609 patients underwent laparotomy.

The contribution in patients' enrolment by the 6 oncologic centers is shown in the Supplementary Table (see Supplementary Table, <http://links.lww.com/IGC/A78>). Throughout the time, a significant increase in the laparoscopies/laparotomies ratio in each center was observed (see Supplementary Figure, <http://links.lww.com/IGC/A78>).

Patients' ages (mean, 53 [SD, 12] years [IQR, 30–62 range years] vs 58 [SD, 9] years [IQR, 32–93 years], respectively) and body mass index (mean, 27.4 [SD, 5] kg/m² [IQR, 15.6–41.0 kg/m²] vs 30.2 [SD, 7] kg/m² [IQR, 18–51 kg/m²], respectively) were significantly (*P* < 0.05) lower in the laparoscopy than in the laparotomy group. The rate of patients with more than 2 previous operations (8/403 [2.0%] vs 42/609 [6.9%]), respectively) was significantly (*P* < 0.05) lower in the laparoscopy than in the laparotomy group. These differences were maintained also after stratification for FIGO stage (data not shown).

Table 1 shows the FIGO surgical stage for both groups, and the grade and the histology in patients with endometrial cancers subgrouped according to the FIGO stage. In 370 (91.8%) of 403 and 460 (75.5%) of 609 patients for laparoscopy and laparotomy groups, respectively, a stage I endometrial cancer was diagnosed (*P* = 0.0001). On the other hand, patients with stage II (4.2% vs 10.8%, respectively), stage III (3.7% vs 11.2%, respectively), and stage IV (0.2% vs 2.5%, respectively) endometrial cancers were more likely to receive open surgery (*P* < 0.05). The rate of patients with papillary serous histology in the general population and the distribution of both grade 3 and papillary serous histology among stages were significantly (*P* < 0.05) different between the laparoscopy and laparotomy groups.

In 350 (86.8%) of 403 cases, the laparoscopic procedure was successfully completed, whereas in 53 (13.2%) of 403 patients, the laparoscopy was converted to laparotomy. The conversion rate was significantly (*P* < 0.001) lower in patients with stage I (36 [10.3%] of 350) and stage II (2 [11.7%] of 17) endometrial cancers than in patients with stage III (14 [93.3%] of 15) or stage IV (1 [100.0%] of 1) endometrial cancers.

The distribution of patients who underwent Piver-Rutledge class I (365 [90.6%] of 403 vs 423 [69.4%] of 609, respectively) and class II (38 [9.4%] of 403 vs 186 [30.5%] of 609, respectively) hysterectomies differed significantly ($P = 0.032$) between the laparoscopy and laparotomy groups.

In overall population, no difference in the rate of pelvic (192 [47.6%] of 403 and 312 [51.2%] of 609 patients from the laparoscopy and laparotomy groups, respectively) and para-aortic (41 [10.2%] of 403 and 64 [10.5%] of 609 patients from the laparoscopy and laparotomy groups, respectively) lymphadenectomies was noted between the 2 groups. After stratification for the surgical stage, no significant difference in the distribution of patients who received a pelvic lymphadenectomy was again observed between groups (data not shown). On the contrary, the distribution of patients subclassified according to surgical stage who received a para-aortic lymphadenectomy was significantly ($P < 0.05$) different between the 2 groups. In particular, in the laparoscopy and laparotomy groups, para-aortic lymphadenectomy was performed, respectively, in 41 (11.1) of 370 versus 64 (10.5%) of 609 patients with stage I endometrial cancer, in 2 (11.7%) of 17 versus 8 (12.1%) of 66 patients with stage II, in none (0.0%) of 403 versus 6 (8.8%) of 68 patients with stage III, and in none (0.0%) of 1 versus 2 (13.3%) of 15 patients with stage IV.

The numbers of pelvic (16 [SD, 6.0] [IQR, 0–41] vs 18 [SD, 9.0] [IQR, 0–62], respectively) and para-aortic (5 [SD,

3.0] [IQR, 0–21] vs 5.5 [SD, 2.5] [IQR, 0–24], respectively) lymph nodes removed were similar between the laparoscopy and laparotomy groups.

Surgical data, in the overall population and in the population subgrouped according to the surgical stage, are shown in Table 2.

For the overall population and for subgroups in each FIGO stage, the global operative times were significantly ($P < 0.05$) longer in the laparoscopy than in the laparotomy group, whereas the intraoperative blood loss was significantly ($P < 0.05$) lower in the laparoscopy than in the laparotomy group.

Significant ($P < 0.05$) difference was observed between groups in the distribution of the complications' grade (Fig. 1), without any change observed after stratification for the surgical stage (data not shown). No significant difference in intraoperative complications was observed between groups in the overall population and in subpopulations with stages I and II; whereas intraoperative complications were significantly ($P < 0.05$) higher in the laparoscopy than in the laparotomy group for patients with stages III and IV endometrial cancers. The postoperative complications were significantly ($P < 0.05$) lower in the laparoscopy than in the laparotomy group for the overall populations and for patients with stage I endometrial cancer; no difference was observed among women with stages II and IV, whereas in patients with stage III

TABLE 2. Surgical data of the laparoscopy and laparotomy groups in overall population and after stratification for stage

Group	Laparoscopy	Laparotomy
Operative time, (min)	199 (32, 150–310)	135 (26, 105–160)*
Stage I	181 (30, 150–280)	130 (27, 105–155)*
Stage II	203 (33, 173–290)	140 (27, 132–154)*
Stage III	207 (30, 180–345)	147 (24, 135–157)*
Stage IV	206 (31, 173–340)	150 (25, 139–160)*
Blood loss, (mL)	200 (45, 50–850)	550 (50, 150–1800)*
Stage I	194 (46, 50–750)	530 (46, 150–1500)*
Stage II	200 (43, 80–800)	550 (53, 300–1700)*
Stage III	210 (44, 85–750)	550 (50, 450–1700)*
Stage IV	250 (49, 100–850)	580 (52, 500–1800)*
Intraoperative complications	33/403 (8.2)	42/609 (6.9)
Stage I	11/370 (3.0)	15/460 (3.3)
Stage II	7/17 (41.2)	11/66 (16.7)
Stage III	14/15 (93.3)	12/68 (17.6)*
Stage IV	1/1 (100.0)	6/15 (40.0)*
Postoperative complications	101/403 (25.1)	334/609 (54.8)*
Stage I	75/370 (20.3)	255/460 (55.4)*
Stage II	13/17 (76.5)	37/66 (56.0)
Stage III	12/15 (80.0)	34/68 (50.0)*
Stage IV	1/1 (100.0)	8/15 (53.3)

Data expressed as median (IQR, range) or as number (%).

* $P < 0.05$ versus laparoscopy group.

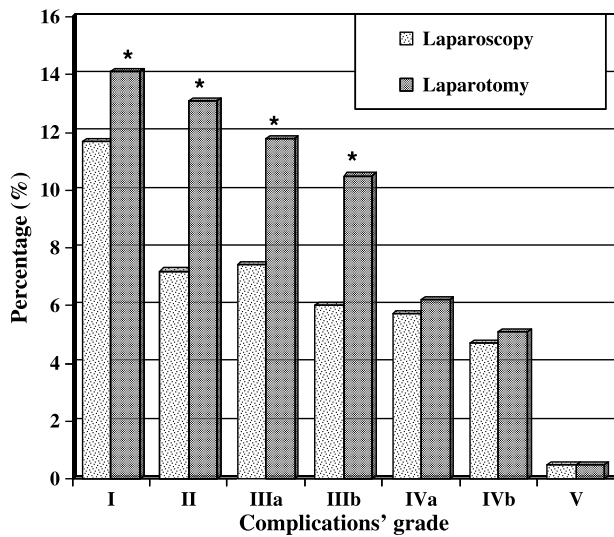


FIGURE 1. Complications' grades according to the scale of Dindo et al¹⁶ for each stage of endometrial cancer. Grade I: any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions; grade II: complications requiring specific pharmacological treatments including blood transfusions and total parenteral nutrition; grade III: complications requiring surgical, endoscopic, or radiological intervention without (IIIa) or with (IIIb) general anesthesia; grade IV: life-threatening complication due to single (IVa) or multiorgan dysfunction (IVb); grade V: death of a patient. * $P < 0.05$ vs laparoscopy group.

postoperative complications were significantly ($P < 0.05$) higher in the laparoscopy than in the laparotomy group.

In Table 3, the characteristics of the adjuvant therapy in the overall population and in the population subgrouped according to the surgical stage are shown.

One hundred twenty-five (31.0%) of 403 and 153 (25.1%) of 609 patients for the laparoscopy and the laparotomy groups, respectively, received adjuvant therapy after surgeons' and multidisciplinary opinion according to the patients' characteristics and the cancer stage, grade, and histotype. It consisted of chemotherapy (CT) (5% vs 5.1, respectively), external beam radiotherapy (EBR) (6.9% vs 9.0%, respectively), vaginal brachytherapy (VB) (6.5% vs 1.5%, respectively), and the following combinations: VB/CT (0.5% vs 0.3%, respectively), EBR/CT (3.0% vs 2.8%, respectively), VB/EBR (7.7% vs 2.6, respectively), and VB/EBR/CT (1.5% vs 3.8%, respectively). The rates of patients who received VB alone or the combinations VB/EBR and VB/EBR/CT were significantly ($P < 0.05$) higher in the laparoscopy than in the laparotomy group.

After subcategorization for surgical stage, the rates of patients with stage I endometrial cancer who received CT, VB, and VB/EBR were significantly ($P < 0.05$) higher after laparoscopy. On the other hand, in patients with stage III

endometrial cancer, the rate of subjects who underwent EBR and VB/EBR/CT was significantly ($P < 0.05$) different between groups.

The oncologic safety data in the overall population and in the population subgrouped according to the surgical stage are shown in Table 4. After a median of 49 (23, 144-471) and 66 (30, 144-509) months for the laparoscopy and laparotomy groups, respectively, the overall survival, the disease-free and

TABLE 3. Adjuvant therapy characteristics of the laparoscopy and laparotomy groups in overall population and after stratification for stage

Group	Laparoscopy	Laparotomy
CT, n (%)	20/403 (5.0)	31/609 (5.1)
Stage I	11/370 (3.0)	4/460 (0.9)*
Stage II	4/17 (23.5)	8/66 (12.1)
Stage III	4/15 (26.7)	9/68 (13.2)
Stage IV	1/1 (100.0)	10/15 (66.7)
EBR, n (%)	28/403 (6.9)	55/609 (9.0)
Stage I	14/370 (3.8)	12/460 (2.6)
Stage II	6/17 (35.2)	27/66 (40.9)
Stage III	8/15 (53.3)	11/68 (16.2)*
Stage IV	0/1 (0.0)	5/15 (33.3)
VB, n (%)	26/403 (6.5)	9/609 (1.5)*
Stage I	26/370 (7.0)	9/460 (2.0)*
Stage II	0/17 (0.0)	0/66 (0.0)
Stage III	0/15 (0.0)	0/68 (0.0)
Stage IV	0/1 (0.0)	0/15 (0.0)
VB and CT, n (%)	2/403 (0.5)	2/609 (0.3)
Stage I	0/370 (0.0)	0/460 (0.0)
Stage II	0/17 (0.0)	1/66 (1.5)
Stage III	2/15 (13.3)	1/68 (1.5)
Stage IV	0/1 (0.0)	0/15 (0.0)
EBR and CT, n (%)	12/403 (3.0)	17/609 (2.8)
Stage I	7/370 (1.9)	2/460 (0.4)
Stage II	4/17 (23.5)	13/66 (19.7)
Stage III	1/15 (6.7)	2/68 (2.9)
Stage IV	0/1 (0.0)	0/15 (0.0)
VB and EBR, n (%)	31/403 (7.7)	16/609 (2.6)*
Stage I	30/370 (8.1)	4/460 (0.9)*
Stage II	1/17 (5.9)	8/66 (12.1)
Stage III	0/15 (0.0)	12/68 (17.6)
Stage IV	0/1 (0.0)	0/15 (0.0)
VB and EBR and CT, n (%)	6/403 (1.5)	23/609 (3.8)*
Stage I	4/370 (1.1)	2/460 (0.4)
Stage II	2/17 (11.8)	9/66 (13.6)
Stage III	0/15 (0.0)	21/68 (30.9)*
Stage IV	0/1 (0.0)	0/15 (0.0)

* $P < 0.05$ versus laparoscopy group.

TABLE 4. Oncologic safety data of the laparoscopy and laparotomy group in overall population and after stratification for stage

Group	Laparoscopy	Laparotomy
Overall survival, n (%)	314/403 (77.9)	484/609 (79.5)
Stage I	297/370 (80.3)	389/460 (84.6)
Stage II	11/17 (64.7)	50/66 (75.8)
Stage III	6/15 (40.0)	43/68 (63.2)
Stage IV	0/1 (0.0)	2/15 (13.3)
Disease-free survival, n (%)	295/403 (73.2)	450/609 (73.9)
Stage I	285/370 (77.0)	385/460 (83.7)
Stage II	6/17 (35.3)	35/66 (53.0)
Stage III	4/15 (26.7)	29/68 (42.6)
Stage IV	0/1 (0.0)	1/15 (6.7)
Cancer-related survival, n (%)	19/403 (4.7)	34/609 (5.6)
Stage I	12/370 (3.2)	4/460 (0.9)*
Stage II	5/17 (29.4)	15/66 (22.7)
Stage III	2/15 (13.3)	14/68 (20.6)
Stage IV	0/1 (0.0)	1/15 (6.7)

* $P = 0.027$

cancer-related survival rates were not significantly different between groups. Similarly, the survival outcomes were similar between the laparoscopy and laparotomy groups for each endometrial cancer stage with the exception of the cancer-related survival that resulted significantly higher in laparotomy group of stage I endometrial cancer (Table 4).

Recurrence data in the overall population and in the population subgrouped according to the surgical stage are shown in Table 5. In the overall population, no significant difference between groups was observed in the recurrence rate, number of recurrences, site of recurrence, time to first recurrence, and treatment for recurrences. On the contrary, in patients with stages II and III endometrial cancers, the rates of local recurrence were significantly ($P < 0.05$) higher in the laparoscopy than in the laparotomy group; similarly, in patients with stage IV endometrial cancer, distant recurrences were significantly ($P < 0.05$) more frequent after laparoscopy than after laparotomy (Table 5). In no case was port site or incisional site recurrence was observed.

Using the univariate ANOVA, overall survival was not significantly ($P = 0.378$) influenced by the investigational center, independently from surgical procedure.

In the laparoscopy group alone, a significant ($P < 0.05$) interaction of time on the rate of para-aortic dissections, on the number of para-aortic nodes removed, and on the rate of surgery for endometrial cancer higher than stage I was noted.

DISCUSSION

The current multicenter study is probably the widest retrospective analysis aimed to show the clinical use of lap-

aroscopic surgery for staging endometrial cancer out of the experimental setting and the standard indication, by analyzing the clinical experiences of 6 Italian centers with experience and expertise in gynecological oncology and advanced laparoscopy. We analyzed data collected during a period of 10 years including 1012 consecutive patients who had undergone surgical staging of endometrial cancer through laparoscopy or laparotomy. Four hundred three and 609 laparoscopies and laparotomies, respectively, were analyzed showing the unequal distribution of type of surgery in the general practice, even if the frequency of the laparotomies/laparoscopies ratio was not constant during the years and among the involved centers. In particular, throughout the time, a significant increase in the laparoscopies/laparotomies ratio in each center was observed.

TABLE 5. Recurrences data

Group	Laparoscopy	Laparotomy
Recurrence rate, n (%)	83/403 (20.6)	154/609 (25.3)
Stage I	33/83 (39.8)	57/154 (37.0)
Stage II	26/83 (31.3)	32/154 (20.8)
Stage III	22/83 (26.5)	51/154 (33.1)
Stage IV	2/83 (2.4)	14/154 (9.1)
No. recurrences, n (%)		
1	62/403 (15.4)	100/609 (16.4)
2	9/403 (2.2)	24/609 (3.9)
≥3	1/403 (0.2)	2/609 (0.3)
Site of recurrence, n (%)		
Local	52/403 (12.9)	65/609 (10.7)
Stage I	23/370 (6.2)	31/460 (6.7)
Stage II	13/17 (76.5)	8/66 (12.1)*
Stage III	14/15 (93.3)	16/68 (23.5)*
Stage IV	2/1 (100.0)	10/15 (66.7)
Distant recurrence	31/403 (7.7)	89/609 (14.6)
Stage I	10/370 (2.7)	26/460 (5.7)
Stage II	12/17 (70.6)	24/66 (36.4)
Stage III	8/15 (53.3)	35/68 (51.5)
Stage IV	0/1 (0.0)	4/15 (26.7)*
Time to first recurrence, mo (mo)	18 (4, 1–69)	24 (6, 1–74)
Treatment for recurrence, n (%)		
CT	4/403 (1.0)	14/609 (2.3)
VB	13/403 (3.2)	5/609 (0.8)
Surgery followed by EBR	36/403 (8.9)	61/609 (10.0)
Surgery followed by VB	21/403 (5.2)	57/609 (9.4)
Surgery followed by VB plus EBR	9/403 (2.2)	17/609 (2.8)

* $P < 0.05$ versus laparoscopy group.

The analysis of basal anthropometric and clinical data of subjects included furnished information regarding the attitude to choose a laparoscopic or an open surgery in the general practice. Even if the feasibility and safety of laparoscopy in treating endometrial cancer were demonstrated also in obese and elderly patients,^{17–23} populations that could really have the best benefits from this minimally invasive surgical technique, our data demonstrate that the laparoscopic approach is preferred for younger and leaner subjects. In addition, laparoscopy seemed to be frequently avoided in patients who had had previous abdominal surgeries (>2 operations).

Interesting data were obtained by the analysis of the FIGO surgical stage and histotype of cancers as classified by international guidelines (National Comprehensive Cancer Network. NCCN Practice Guidelines in Oncology. Uterine neoplasms. V.2.2010. Available at: www.nccn.org). In fact, although these parameters seemed to drive the choice of the surgeon toward a specific approach, no restriction in general practice was imposed for the laparoscopy use in advanced stages, such as in rare histotypes. The rates of G3 endometrial cancers and papillary serous histology were lower in patients treated with laparoscopy than in those treated with laparotomy, suggesting that the grade and the histotype could draw the indication for the surgical approach.

As expected, in the current analysis, patients with endometrial cancer higher than stage I were more likely to undergo laparotomy. However, in about 8% of endometrial cancers higher than stage I, the laparoscopy was performed, and in about 50% of them, it was successfully concluded without conversion.

Our data confirmed^{12,13} the safety of laparoscopy for stage I endometrial cancers and extended its indication, probably also to stage II. In fact, in women with stage II endometrial cancers, a higher complication rate was detected for the laparoscopic approach, but it resulted in no statistical difference when compared with laparotomy. On the contrary, the role of laparoscopy in endometrial cancer stages higher than stage II is still flawed, as demonstrated by the higher intraoperative complications after laparoscopy in these cases. Furthermore, well-designed studies are needed to evaluate the surgical safety and feasibility of the laparoscopy in stages III and IV endometrial cancers and to identify predictors of complication and/or conversion to laparotomy.

The current study confirmed¹² a longer operative time and less intraoperative blood loss for the laparoscopic procedure, also in the population subgrouped according to the surgical stage.

The rate of postoperative complications was relatively high for both surgical procedures (25.0% and 54.8%, respectively) and likely reflects the heterogeneous sample studied. However, our findings on the safety were in agreement with previous data,^{4–13} showing less postoperative complications after laparoscopy. This figure was probably related to stage I endometrial cancer; the advantages (ie, less postoperative complications) of the laparoscopic approach were lost in patients with stages II and IV (only 1 subject), whereas in patients with stage III, more postoperative complications were found after laparoscopy than after laparotomy. In regard of the complications' severity, not only the complication graded 1

and 2, but also grade 3 complications that include requirement of surgical, endoscopic, or radiological intervention¹⁶ were less frequent for laparoscopy. Moreover, no difference was observed between the 2 surgical approaches in grade 4 to 5 complications.

In our series, even if no standard indication was followed to perform a lymph node (pelvic and para-aortic) excision, pelvic and para-aortic lymphadenectomy was performed in about 50% and 10% of cases, respectively, without difference between the 2 approaches in the general population. After analyzing data on node excision by surgical stage, no difference between groups was observed in pelvic lymphadenectomies, whereas the distribution of patients who received para-aortic lymphadenectomy differed between laparoscopy and laparotomy (ie, patients with stages I and II endometrial cancers underwent para-aortic lymphadenectomy in a comparable percentage of cases, whereas para-aortic lymphadenectomy was performed only through laparotomy in patients with stages III and IV). However, the number of pelvic and para-aortic lymph nodes removed was comparable between the 2 surgical approaches.

In this regard, a recent meta-analysis³ from 2 randomized controlled trials^{1,2} found no evidence that pelvic node dissection decreases the risk of death or disease recurrence compared with no lymphadenectomy in women with presumed stage I disease, whereas women who receive pelvic lymphadenectomy are more likely to experience surgically related systemic morbidity or lymphedema/lymphocyst formation.²⁴ However, no data evaluating the effects of combination pelvic and para-aortic node dissection are at the moment available in literature.

The indication for adjuvant therapies was generally given after a multidisciplinary counseling in all centers included in the current study, considering the patients' characteristics and the cancer stage, grade, and histotype. Even if no difference between the 2 approaches was detected in the number of patients who received adjuvant therapies, the evaluation of the specific postsurgical treatments varied after laparoscopy or laparotomy. In particular, in the general population, the indication for VB, VB/EBR, and VB/EBR/CT was more frequently recommended to women who underwent laparoscopy. Moreover, the distribution of patients who had received different adjuvant therapies after laparoscopy or laparotomy differed among subgroups of surgical stages.

The difference observed in adjuvant therapy highlighted the different perceptions of surgical safety due to oncologic radicality of the laparoscopic intervention. However, in our analysis, the rate of patients who underwent Piver-Rutledge class II hysterectomy during laparoscopy was lower than those who underwent laparotomy. To this regard, a recent study²⁵ demonstrated that in stage I endometrial cancer there was no difference between Piver-Rutledge class II and class I (extrafascial) hysterectomy. Moreover, the authors concluded that in the presence of technical problems with potential excision of insufficient vaginal cuff, the class II radical hysterectomy is the appropriate approach to guarantee an adequate locoregional control of the disease.²⁵ On the other hand, even if the use of Piver-Rutledge class II hysterectomy gives a theoretically good support for stage II endometrial cancers, the

role of cervical extension in predicting parametrial spread remained poor because other factors, such as histopathology, seemed to be involved.^{26,27}

Recurrence data on general population were similar between the 2 approaches, and the site of recurrence was influenced by the surgical procedure. Furthermore, confirming the fear of an increased rate of local recurrences after laparoscopy,^{11,28} here we found that local recurrences occurred more frequently after laparoscopy in stages II and III endometrial cancers. On the contrary, distant recurrences seemed to occur more frequently in patients with stage IV endometrial cancer, probably for the initial distribution of tumors characteristics among stages in both groups, although the analysis included only 1 case in the laparoscopic group but converted to open surgery.

The oncologic safety of the laparoscopic approach was confirmed^{12,13,23} also in this multicenter clinical study reporting reassuring data in terms of overall, disease-free, and cancer-related survival rates, also when the surgeries are performed out of an experimental setting. In addition, the oncologic safety of the laparoscopic surgery was shown also in advanced stages.

Finally, by the univariate ANOVA, we did not find any influence of the investigational centers involved in the current multicenter analysis on the overall survival, independently from the surgical procedure performed. This finding suggested the oncologic long-term efficacy of surgical staging of endometrial cancer in general practice, independently from the surgical approach and from different settings.

In conclusion, current data show that in the clinical practice heterogeneous criteria are adopted to recur to laparoscopy for staging endometrial cancer, and there are different attitudes to prescribe adjuvant treatments in subjects who receive laparoscopy. The safety and the feasibility of the laparoscopic staging of stage I endometrial cancer are confirmed. It seems to be also highly feasible and with a discrete safety also in patients with stage II endometrial cancer, whereas in patients with a higher stage, it should be used with caution and only in experimental setting.

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