Incisional Recurrences After Endometrial Cancer Surgery

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Abstract. *Aim: The aim of the present study was to estimate the incisional recurrence (IR) rate after endometrial cancer (EC) staging surgery and analyze characteristics of affected patients. Patients and Methods: We retrospectively searched for patients with EC at 2 institutions and analyzed the occurrence of IR after open, laparoscopic, or robotic surgery. Additionally, a review of the literature was performed. Results: Out of 2,636 patients with EC, 1,732 (65.7%), 461 (17.5%), and 443 (16.8%) had open, laparoscopic, and robotic surgery, respectively. Only 3 patients (0.11%) had IR, all after open surgery. Additionally, 38 cases of IR were identified from the literature. Patients with non-isolated IR had worse overall survival than patients with isolated IR (p=0.04). Among this latter group, combined treatments may be associated with improved survival outcome. Conclusion: IR after EC surgery is rare and may occur after minimally-invasive or open operations. Combination of local and systemic treatments may provide favorable outcomes for patients with isolated IR.*

Endometrial cancer (EC) is the most prevalent gynecologic cancer in developed countries (1). In 2014, the number of estimated new EC cases in the United States was more than 52,000, with an estimated 8,590 cancer-related deaths due to EC (2). The 5-year relative survival rate for cancer of the uterine corpus is more than 80%. This good prognosis is related to an early stage of diagnosis in most EC patients (1). In fact, most patients with tumor limited to the uterus at-diagnosis have a low risk of recurrence (2-15%) (3, 4). Recurrence associated with EC has 4 main routes of dissemination: vaginal (local), lymphatic (locoregional), peritoneal (distant), or hematogenous (distant) (4).

Recently, great interest has been attributed on recurrence at the site of surgical incision, because of the concern that minimally-invasive treatment can be a risk factor (5). Although many articles have been published, the real magnitude of incisional recurrence (IR) and its clinical course remain obscure (5-32). Several studies report minimally-invasive surgery as being responsible for tumor seeding into the incision (11, 33). IR at the site of the open abdominal wound, although rare, has been described since 1986 (6).

No consensus exists regarding the incidence of risk factors for and management of IR in patients with EC. Therefore, the aim of this study was to estimate the incidence of IR in a large cohort of patients undergoing open abdominal, laparoscopic, and robotically-assisted surgery for EC. Moreover, through a systematic review of the medical literature, we sought to identify characteristics of, risk factors for, and prognosis of IR.

Patients and Methods

Patients. We retrospectively searched for the medical records of consecutive women who underwent treatment for EC at 2 gynecologic oncology units (Division of Gynecologic Surgery, Mayo Clinic, Rochester, Minnesota, and Gynecologic Oncology Unit, University of Insubria, Varese, Italy) from January 1, 1999, through December 31, 2012. Institutional review board approval for this study was obtained from both institutions. Patients gave written consent for the use of personal records for health research.

Surgical procedures. Detailed description of surgical guidelines for both institutions are reported elsewhere (3, 34). Data concerning the type of surgical procedures, intraoperative and postoperative details, adjuvant therapy, and follow-up evaluations were prospectively recorded in the computerized oncology database of both units. Patients who had only a vaginal approach were excluded from the study; patients who had vaginal hysterectomy followed by other staging procedure (*e.g.*, lymphadenectomy, omentectomy) via open abdominal, laparoscopic, or robotic surgery were included in the study.

Open abdominal, laparoscopic, and robotically-assisted surgical procedures have been described in detail elsewhere (34-36). Women undergoing laparoscopic staging had type IV E total laparoscopic

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hysterectomy (according to the American Association of Gynecologic Laparoscopists classification) (34). An intrauterine manipulator (RUMI System; Cooper Surgical, Inc. Trumbull, CT, USA) in conjunction with a Koh Cup (Koh Colpotomizer System; Cooper Surgical, Inc. Trumbull, CT, USA) was inserted (34). A CO_2 pneumoperitoneum was created using a Veress needle, followed by introduction of a (3- to 10-mm) 0° operative laparoscope at the umbilical site. Three 3- to 12-mm ancillary trocars (1 suprapubic and 2 lateral to the epigastric arteries) were inserted with direct visualization in the left and right lower abdominal quadrants, respectively. The operation was then performed laparoscopically according to patient and disease characteristics (34). The laparoscopic patient group also included those who had undergone vaginal hysterectomy followed by laparoscopic procedures (e.g., pelvic and/or para-aortic lymphadenectomy), as previously described (36).

Robotically-assisted surgery was performed using the da Vinci Surgical System (Intuitive Surgical, Inc. Sunnyvale, CA, USA). A 12-mm trocar was placed through the umbilicus. A Veress needle was used per surgeon preference. Two ancillary trocars (8 mm) were introduced bilaterally in the abdomen, lateral to the midclavicular line, a few centimeters above the 12-mm trocar. An adjunctive third 8-mm trocar was introduced on the left side. Additionally, an ancillary laparoscopic assistant port (12 mm) was placed in the right upper abdominal quadrant. An Apple Vaginal Probe (AFS Medical, Teesdorf, Austria) was generally used to identify the vagina for bladder dissection and colpotomy (35). The RUMI uterine manipulator was used in selected patients, per surgeon preference (34). Intra-abdominal pressure was set at 10 to 12 mm Hg. The uterus was extracted from the vagina. If the uterus was too large for vaginal extraction, the surgical specimen was usually retrieved through a minilaparotomy incision. No power morcellators were used. All other surgical specimens (e.g., lymph nodes, omentum, spleen) were delivered vaginally. It was not our practice to morcellate surgical specimens. Trocar irrigation was performed per surgeon preference. Fascial closure was performed at the site of the 12-mm trocars, and skin incisions were sutured using resorbable stitches.

Patients were considered in the open rather than minimally-invasive group according to the intention-to-treat principle; hence, for the statistical analysis, laparoscopic and robotic operations that were converted to open surgery were included in the laparoscopic and robotic groups, respectively.

Follow-up. Follow-up evaluations were planned every 3 to 6 months for the first 3 years [according to National Comprehensive Cancer Network guidelines if the patient was at high or low risk for recurrence (37)] and annually thereafter. Follow-up visits included pelvic examination. Imaging studies were generally performed at the discretion of the treating physician, but no routine imaging studies are generally suggested. If IR was identified by physical examination, imaging studies were performed to identify other possible synchronous sites of recurrence. IR was defined as subcutaneous tumors, histologically documented, at the site of the surgical scar. The presence of other synchronous site(s) of recurrence was documented.

Systemic review. To provide greater insight on the rate of, risk factors for, and prognosis of IR, we reviewed the English-language literature. MEDLINE (PubMed) was searched for records from January 1, 1980, to August 10, 2013, using the terms "endometrial cancer," "port site metastasis," "incisional recurrence," "scar relapse," and "incision metastases," alone or in combination. The reference lists of the articles retrieved were then checked manually to identify additional relevant references. Abstracts, letters, and comments not presenting original data were excluded. Articles reporting inadequate information about IR and those including cases that were subsequently reported in larger studies were excluded. Skin metastases at different sites of surgical scars were not considered in the present study. Since most of the investigations reporting IR were case reports, it was not possible to perform a heterogeneity test between different studies included in our review.

Statistical analysis. Statistical analysis was performed with GraphPad Prism version 6.00 for Mac (GraphPad Software Inc. La Jolla, CA, USA) and IBM-SPSS (version 20.0) for Mac. Incidence of events among the groups was analyzed for statistical significance with the Fisher's exact test. Normality testing (D'Agostino and Pearson test) was performed to determine whether data were sampled from a Gaussian distribution. Patient characteristics were compared between groups (minimally-invasive vs open; isolated vs non-isolated IR) using the Fisher's exact test for categorical variables, the 2-sample *t*-test for age, and the Mann-Whitney *U*-test for the time from primary surgery to IR. Because it is not possible to estimate incidence from case reports, the rate of IR after different surgical approaches was evaluated considering only studies reporting more than 100 patients undergoing EC surgery. Survival after IR was estimated using the Kaplan-Meier method. Patient characteristics were assessed for their association with death by fitting univariate Cox proportional hazards models, and associations were summarized using hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). All calculated *p*-values were 2-sided, and $p < 0.05$ was considered statistically significant.

Results

During the 14-year study period, 2,842 patients underwent surgery for EC, out of whom 206 underwent vaginal hysterectomy and were excluded, thus leaving 2,636 patients for the analysis. Among these, 1,732 (65.7%), 461 (17.5%), and 443 (16.8%) patients underwent the open abdominal, laparoscopic, and robotic surgical approach, respectively. Out of 2,100 Mayo Clinic patients, the numbers for these procedures were 1,522 (72.5%), 135 (6.4%), and 443 (21.1%) patients with the open abdominal, laparoscopic, and robotically-assisted approach, respectively. From 1999 to 2008 at Mayo Clinic, 92% of cases used the open approach, compared to 41% from 2009 to 2012. The 536 patients at the University of Insubria had 210 open abdominal (39.2%), 326 laparoscopic (60.8%), and 0 robotically-assisted procedures.

Among all 2,636 patients, only 3 (0.11%) had IR: 2 out of 2,100 (0.10%) at Mayo Clinic and 1 out of 536 (0.19%) at the University of Insubria. All three IRs were diagnosed by physical examination. All IRs occurred after open abdominal surgery (3/1,732; 0.17%). The time from primary surgery to IR was 11, 13, and 24 months for these 3 patients. All three IRs were non-isolated: synchronous sites of recurrence were pelvis in 1 patient, inguinal lymph nodes in 1 patient, and vagina and spleen in 1 patient.

Our search for studies in the PubMed database describing IR in patients with EC surgery retrieved 28 studies reporting a total of 38 cases with IR (5-30). Overall, 41 cases (including our 3 cases) were included in the literature analysis: 17 (41%) occurred after open abdominal, 15 (37%) after laparoscopic, and 9 (22%) after robotic surgery. Table I summarizes the 41 cases. Median time to recurrence was 16.5 (range=1-166) months. Overall, 67% of patients with IR had uterine-confined disease (stage I-II), 78% had G1 and G2 tumors, and 69% had type I histology (endometrioid and adenosquamous).

The rates of IR after different surgical approaches, considering only studies reporting more than 100 patients undergoing surgery, are shown in Table II (5, 24, 26, 27, 30). The rates of IR were 0.11%, 0.20%, and 0.57% after open abdominal, laparoscopic, and robotically-assisted surgery, respectively (*p*=0.5).

Table III describes the differences between patients with IR after open abdominal (n=17, 41%) and minimally-invasive surgery (n=24, 59%). Patients undergoing minimally-invasive surgery were more likely to have extra-uterine disease at the time of primary diagnosis than those who underwent open surgery (*p*=0.01). No significant differences in age, International Federation of Gynecology and Obstetrics (FIGO) grade (G1 & G2 *vs*. G3), or histological sub-type (type I *vs*. type II) were observed. Events that may be considered as potential factors favoring the development of IR were described in 4 patients who had minimally-invasive surgery–port site hernia requiring reoperation (n=1), uterine perforation (n=2), and difficult uterine extraction (n=1) (15, 25, 28, 32); none of these events were reported for patients who underwent open surgery (*p*=0.13). Median (range) time from primary surgery to IR was significantly shorter after minimally-invasive surgery than open procedures [11 (1-48) months *vs*. 24 (6-166) months; *p*=0.02]. However, the route of primary surgery did not influence the proportion of surviving patients (HR=1.23; 95% CI,=0.30-5.05; *p*=.76) (Figure 1A).

Several factors influenced overall survival (Table IV). Patients with high-grade (FIGO grade 3) disease (HR=16.4; 95% CI=1.78-151.9; *p*=0.01) and non-isolated IR (HR=4.48; 95% CI=1.08-18.6; *p*=0.04 log-rank test, Figure 1B) had significantly worse overall survival. Overall, patients with non-isolated IR were more likely to have FIGO grade 3 EC than patients with isolated IR (Table V).

For the analysis of treatment modalities after IR, we focused on 13 of the 18 patients with isolated IR who had follow-up information after the IR (6, 9, 10, 13-16, 19, 23, 28, 29, 32). Patients undergoing combined local (*i.e.*, surgery and/or radiotherapy) plus systemic treatments (*i.e.*, chemotherapy and/or hormone therapy) had a lower recurrence rate (2/8, 25%) than patients undergoing local or systemic treatment as a single modality (4/5, 80%), although the difference did not reach statistical significance (odds ratio, 12.0; 95% CI=0.79-181.1; *p*=0.10). In addition, none of the 8 patients receiving a combined approach died of disease, compared to 2 of 5 patients (40%) receiving single-modality treatment (HR=9.0; 95% CI=0.55-146.7; *p*=0.12 log-rank test). Of note, no significant differences in measurable variables (*i.e.*, constitutional and disease characteristics) existed between patients undergoing different therapies.

Discussion

The current study reports a low rate of IR (0.11%) in a large series of patients with EC undergoing open abdominal, laparoscopic, and robotically-assisted surgery. Moreover, analysis of the data available in the literature shows that the route of primary surgery (*i.e.*, minimally-invasive *vs*. open surgery) did not affect the rate of IR or significantly influence survival. Isolated IR generally occurred in patients with FIGO grade 1 or 2 tumors. Patients with isolated IR had a better prognosis than those with other associated synchronous recurrences. Among patients with isolated IR, the use of aggressive treatments (local plus systemic therapy) seemed to provide a more favorable prognosis.

In the medical literature, data on IR in EC are limited. The few studies published on this issue show great heterogeneity among reported cases (5-32). Because of the rarity of IR, several biological and clinical features remain obscure. Multiple hypotheses have been proposed about the etiology of IR, such as spread of neoplastic cells through the lymphatic and blood vessels, implantation during surgical management (*e.g.*, contact of the instruments with the skin), seeding of neoplastic cells through the cervical canal or the fallopian tubes, the "chimney effect" due to the aerosolization of neoplastic cells during minimally-invasive surgery, or peritoneal immunologic reactions related to CO_2 (6-33, 38, 39). DerHagopian *et al*. (40) proposed the alternative theory of "inflammatory oncotaxis": implantation and growth outside the primary origin site are fostered by incisional repair mechanisms such as immunohistochemical and angiogenic processes. Therefore, according to this theory, manifestation of cancer at the abdominal wall, after surgery, should not always be considered the effect of iatrogenic spread (40).

During the past decade, some reports have stressed that IR is a complication of minimally-invasive surgery (11, 38). Because of the relatively small numbers and the inherent biases of retrospective reviews of the literature, we cannot clearly determine whether the route of surgery influences the risk of IR. We emphasize, however, that IR can occur after both minimally-invasive and open abdominal surgery. Furthermore, we speculate that the rate of IR is probably under-reported, especially during open surgery. Hence, it is

Table I. *IR after open abdominal and minimally-invasive endometrial cancer surgery.*

Study	Age, y[a]	Surgical approach	Lpty incision	Stage[b]	Grade	Histology	Primary therapy	DFS, mo	Synchronous recurrence	Survival outcome (mo)[c]
Isolated Recurrence										
Barter *et al*. 1986 (6)	64	Lpty	Mid	IB	1	NA	Surg	15	...	NED (18)
Curtis *et al*. 1994 (9)	50	Lpty	Mid	IIIA[d]	1	NA	Surg, RT, HT	18	...	AWD (24)
Kotwall *et al*. 1994 (10)	65	Lpty	Pfann	IB	1	Adenopapillary	Surg	84	...	NED (15)
Khalil *et al*. 1998 (13)	58	Lpty	Mid	IB	2	NA	Surg, RT	60	...	NED (48)
Muntz *et al*. 1999 (14)	58	Lscpy	...	IA	2	Endometrioid	Surg	21	...	DOD (42)
Faught *et al*. 1999 (15)[e]	84	Lscpy[f]	...	IC	3	Endometrioid	Surg, RT	7	...	DOD (5)
Macias *et al*. 2003 (16)	64	Lpty	Mid	IIIA[d]	2	Endometrioid	Surg, RT, CT	37	...	NED (11)
Joshi *et al*. 2003 (17)	45	Lpty	Para	II	NA	Papillary	Surg, RT, CT	21	...	NA
Lorenz *et al*. 2004 (18)	59	Lpty	Pfann	IA	2	Endometrioid	Surg, RT	166	...	NA
Chen *et al*. 2004 (19)	51	Lpty	Mayl	IB	2	Papillary	Surg	6	...	AWD (12)
Sanjuan *et al*. 2005 (21)	55	Lscpy	...	IIB	2	Endometrioid	Surg, RT	48	...	NA
Balbi *et al*. 2006 (23)	65	Lpty	Mid	IIB	1	Endometrioid	Surg, RT	24	...	AWD (12)
Maenpaa *et al*. 2009 (25)	68	Lscpy	...	IC	2	NA	Surg, RT	6	...	NA
Palomba *et al*. 2012 (28)	66	Lscpy	...	IB	2	Endometrioid	Surg, RT	24	...	NED (10)
Santeufemia *et al*. 2013 (29)	60	Lpty	Mid	IB	1	Endometrioid	Surg	120	...	NED (12)
Kilgore *et al*. 2013 (30)	NA	Robotic	...	NA	NA	NA	NA	NA	...	NA
Grabosch and Xynos 2013 (32)	56	Robotic	...	IB	1	NA	Surg	13	...	NED (13)
	54	Robotic	...	IIIA[d]	2	NA	Surg	4	...	NED (4)
Non-isolated Recurrence										
Chapman *et al*. 1988 (7)	65	Lpty	Mid	IB	2	Papillary	Surg, RT	88	Vaginal	NA
Nguyen *et al*. 2013 (31)[e]	78	Robotic[g]	...	IC	3	Endometrioid	Surg, VB	12	Vaginal cuff	NED (12)
Espinos *et al*. 1993 (8)	77	Lpty	Mid	IB	3	NA	Surg, RT	7	Lymph nodes	DOD (3)
Sanjuan *et al*. 2005 (21)	78	Lscpy	...	IIB	3	Serous	Surg, RT	39	Lymph nodes	NA
Wang *et al*. 1997 (12)[e]	56	Lscpy	...	IIIC	3	NA	Surg[h]	6	Peritoneal; perineum	DOD (13)
Baydar *et al*. 2005 (20)	58	Lpty	NA	IB	2	NA	Surg, RT	15	Thorax; vaginal cuff	NA
Gucer *et al*. 2005 (22)	62	Lpty	Mid	IB	1	Endometrioid	Surg	38	Small bowel	NED (24)
Zivanovic *et al*. 2008 (24)	NA	Lscpy	...	IIIC	NA	Serous	Surg, intra-peritoneal CT	14.7	Peritoneal	DOD (53)
Martinez *et al*. 2010 (5)	60	Lscpy	...	IIIA	NA	Serous	Surg, CT	6	Peritoneal	DOD (11)
Ndofor *et al*. 2011 (26)	50	Robotic	...	IIIA	1	NA	RT, CT, Surg	11	Peritoneal; lymphatic	NA
Kilgore *et al*. 2013 (30)	NA	Robotic	...	NA	NA	NA	NA	NA	Yes (NA)	NA
	NA	Robotic	...	NA	NA	NA	NA	NA	Yes (NA)	NA
	NA	Robotic	...	NA	NA	NA	NA	NA	Yes (NA)	NA
	NA	Robotic	...	NA	NA	NA	NA	NA	Yes (NA)	NA
Current study	75	Lpty	Mid	IB	1	Endometrioid	Surg, VB	13	Inguinal lymph node	DOD (25)
	68	Lpty	Mid	IB	3	Adenosquamous	Surg, RT	11	Pelvis	DOD (2)
	63	Lpty	Mid	IB	2	Endometrioid	Surg	24	Vaginal cuff; spleen	DOD (10)
Other Recurrence Information NA										
Kadar 1997 (11)[e]	68	Lscpy	...	IIIC	2	NA	Surg, RT	1	NA	NA
	72	Lscpy	...	IV	3	NA	Surg, RT, HT	1	NA	NA
Walker *et al*. 2012 (27)[i]	NA	Lscpy	...	IB	2	Endometrioid	Surg, NA	NA	NA	NA
	NA	Lscpy	...	IIIA	2	Endometrioid	Surg, NA	NA	NA	NA
	NA	Lscpy	...	IIIC	2	Endometrioid	Surg, NA	NA	NA	NA
	NA	Lscpy	...	IVB	NA	Carcinosarcoma	Surg, NA	NA	NA	NA

AWD, Alive with disease; CT, chemotherapy; DFS, disease-free survival between primary surgery and IR; DOD, died of disease; HT, hormonal therapy; IR, incisional recurrence; Lpty, laparotomy; Lscpy, laparoscopy; Mayl, Maylard; Mid, midline; mo, month; NA, not available; NED, no evidence of disease; Para, paramedian; Pfann, Pfannenstiel; RT, radiotherapy; Surg, surgery; VB, vaginal brachytherapy; y, year. [a]At initial surgery. [b]According to the 1988 International Federation of Gynecology and Obstetrics classification (8). [c]After IR. [d]Peritoneal washing positive for malignant cells. [e]Patients with 2 port site metastases. [f]Laparotomy was performed 10 days after surgery because of port site hernia. [g]Robotic staging was performed 2 months after open abdominal hysterectomy and bilateral salpingo-oophorectomy. [h]The patient refused adjuvant treatment. [i]None of the cases from Walker *et al*. (27) are confirmed. They reported 4 abdominal wall recurrences in the laparoscopic group, but there was no evidence that they occurred in incisional sites.

Table II. *Cohort studies with >100 cases reporting rate of IR after endometrial cancer surgery.*

	Rate of IR[a]			
Study	After laparoscopy	After robotic surgery	After open surgery	Overall
Zivanovic *et al*. (24)	1/547 (0.18%)	...	...	0.18%
Martinez *et al*. (5)	1/295 (0.33%)	...	...	0.33%
Ndofor *et al*. (26)	...	1/116 (0.86%)	...	0.86%
Walker *et al*. (27)b	4/1,696 (0.24%)	...	0/920 (0%)	0.15%
Kilgore *et al*. (30)	...	5/499 (1.0%)	...	1.0%
Current series	0/461 (0%)	0/443 (0%)	3/1,732 (0.17%)	0.11%
Overall	6/2,999 (0.20%)	6/1,058 (0.57%)	3/2,652 (0.11%)	0.22%

IR, Incisional recurrence. [a]Data are expressed as No. with IR/total No. of patients (rate). [b]Cases not confirmed. Walker *et al*. (27) reported 4 "abdominal wall recurrences" in the laparoscopic group (assumed to be trocar recurrence sites).

Table III. *Comparison of IR after minimally-invasive (laparoscopic or robotic) vs. open abdominal surgery (n=41)[a].*

	Surgery Type[b]		
Characteristic	Minimally-invasive (n=24)	Open abdominal (n=17)	*p*-Value
Age at primary surgery (years)	64.5 (2.8)	61.7 (1.9)	0.41
Isolated recurrence	8/18 (44.4)	10/17 (58.8)	0.50
Extrauterine disease at primary surgery	10/19 (52.6)	2/17 (11.8)	0.01
FIGO grade 3	5/16 (31.3)	2/16 (12.5)	0.39
Nonendometrioid histology	4/14 (28.6)	4/12 (33.3)	>0.99
Time from surgery to IR, mo	11 (1-48)	24 (6-166)	0.02
Progression of disease (including recurrence) after IR	7/11 (63.6)	8/14 (57.1)	>0.99

FIGO, International Federation of Gynecology and Obstetrics; IR, incisional recurrence. [a]The analysis is limited to women with specific information available. [b]Data are expressed as mean (SD), median (range), or No./No. with data available (%).

not possible to ascertain with adequate precision the true incidence of IR. Most of the available studies are case reports (6-10, 13-23, 25).

To the best of our knowledge, this is the first study to report the rate of IR after open surgery. Therefore, no comparison can be done with other studies. In contrast, the absence of port site IR in our series is corroborated by other investigations in the field of minimally-invasive surgery (34-36).

Unfortunately, the available information about IR is not consistent. In the largest published prospective study of minimally-invasive surgery in EC (the LAP2 study), Walker *et al*. (27) reported 4 cases of IR (0.24%). The authors reported that "the four abdominal wall recurrences were potentially trocar recurrence sites, because all were identified in patients undergoing laparoscopy," whereas no cases of IR after open abdominal staging were reported (27). Additionally, among studies reporting IR after robotically-assisted surgery, detailed information on the clinical characteristics of patients with recurrence was missing in 5 of the 9 patients described (30).

We highlight 3 points of our study. First, although our data suggest that the route of primary surgery did not influence survival outcomes after IR, the interval between surgery and IR was shorter in the minimally-invasive group. It is possible that IR is more likely to be diagnosed and reported after minimally-invasive surgery than after open abdominal surgery, or the more aggressive nature of the tumor in the minimally-invasive group, compared to the open-abdominal group (53% *vs*. 12% had extrauterine disease at the time of primary EC diagnosis; Table III) may account for the earlier presentation of port site metastases. Second, the worse prognosis of patients with non-isolated IR probably reflects the poor outcome of patients with lymphatic, peritoneal, or hematogenous recurrence. Due to the small sample size and the heterogeneity of the studies in the literature, it is difficult to determine the efficacy of different treatments. However, on the basis of the limited data available, a combination of local (*i.e*., wide local excision and adjuvant radiotherapy) and systemic (chemotherapy or hormonal therapy) treatments for isolated IR seems to represent a reasonable therapeutic option (32). In contrast, therapy for non-isolated IR should be tailored on the

Table IV. *Factors, at the time of primary surgery, influencing overall survival in patients with endometrial cancer and incisional recurrence.*

Characteristic	Cox model HR (95% CI)	p-Value
Age[a]	1.84 (0.81-4.21)	0.14
Extrauterine diasease[b]	0.82 (0.16-4.11)	0.81
FIGO grade 3	16.4 (1.78-151.9)	0.01
Nonendometrioid histology	0.40 (0.04-3.54)	0.41
Minimally-invasive approach	1.23 (0.30-5.05)	0.76

FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio. [a]HR per 10-year increase in age. [b]Includes stage III and IV disease.

basis of the associated synchronous site of recurrence and patients' characteristics, but the prognosis is generally poor.

We acknowledge certain limitations in our investigation. First, owing to the retrospective study design, the limited clinical information available from the literature, and rarity of the event, the present study is not powered to ascertain risk factors for IR after different surgical approaches (*i.e.*, minimally-invasive *vs.* open abdominal surgery). Second, our review is subject to publication bias (*e.g.*, because IR could be considered an iatrogenic complication, surgeons could be reluctant to publish series with a high rate of IR) and temporal bias (*e.g.*, it is possible that some IR occurred after the publication of the current article). Third, because minimally-invasive surgery was introduced in the most recent decade of our study, patients undergoing procedures *via* open abdominal surgery had longer follow-up time than patients undergoing minimally-invasive procedures. However, most IRs occurred during a relative short follow-up period. Fourth, the lack of standardization and details about surgeries and the different treatment methods (*e.g.*, adjuvant therapy administration) are also limitations. Nevertheless, the main strengths of the current study are represented by the large series of consecutive patients undergoing surgery for EC and the systematic review of the largest series of IR available to date in the medical literature.

In conclusion, IR is a rare event after EC surgery. Scar implantation of cancer cells is possible in both minimally-invasive and traditional open abdominal surgery. IR is usually characterized by poor prognosis when associated with other distant sites of synchronous recurrence. In contrast, isolated IR is generally observed in patients with FIGO grade 1 to 2 cancers and portends a more favorable outcome, especially when a combination of local and systemic treatments is used.

Conflicts of Interest

All Authors declare that there are no conflicts of interest associated with this work.
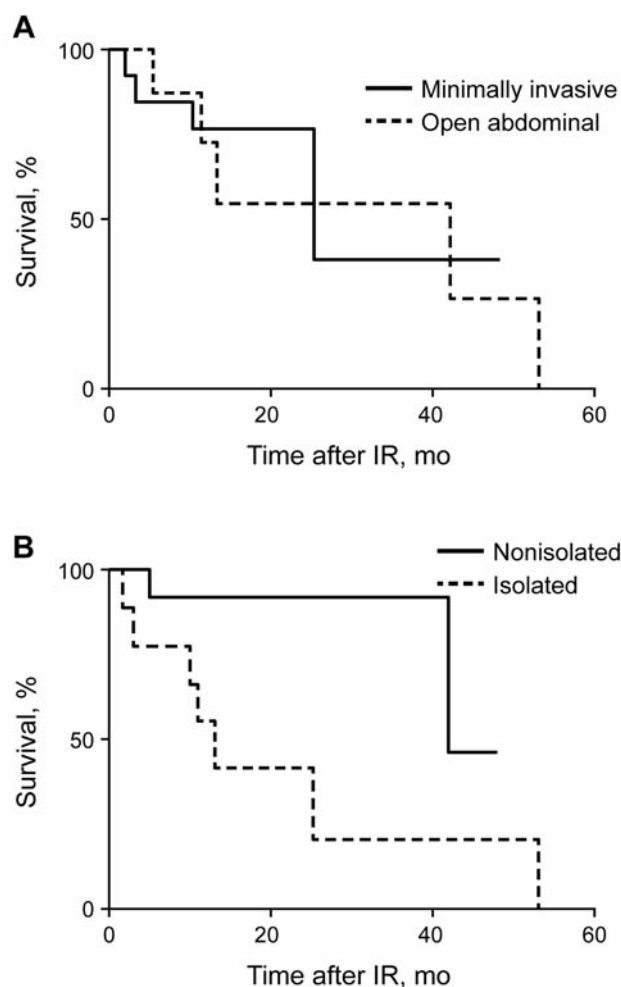

Figure 1. *Kaplan-Meier curves showing survival outcomes after incisional recurrence (IR). A, Overall survival after incisional recurrence in patients undergoing open abdominal (n=13) vs. minimally-invasive (n=9) surgery (p=0.76, log-rank test). B, Overall survival after isolated (n=13) vs. non-isolated (n=9) IR (p=0.04, log-rank test).*

Acknowledgements

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Table V. *Comparison of isolated vs. non-isolated IR (n=35)[a].*

Characteristic	Type of IR[b]		*p*-Value
	Isolated (n=18)	Non-isolated (n=17)	
Age at primary surgery (years)	59 (45-84)	64 (50-78)	0.13
Minimally-invasive approach[c]	8/18 (44.4)	10/17 (58.8)	0.50
Extrauterine disease at primary surgery	3/17 (17.6)	4/13 (30.8)	0.66
FIGO grade 3	1/16 (6.3)	5/11 (45.4)	0.02
Nonendometrioid histology	3/13 (23.1)	4/9 (44.4)	0.37
Time from surgery to IR, mo	24 (6-166)	13 (6-88)	0.17
Progression of disease (including recurrence) after IR	5/13 (38.5)	8/10 (80)	0.09

FIGO, International Federation of Gynecology and Obstetrics; IR, incisional recurrence. [a]The analysis is limited to women with specific information available. [b]Data are expressed as median (range) or No./No. with data available (%). [c]Laparoscopic or robotic.

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