GYNECOLOGY

The effect of a uterine manipulator on the recurrence and mortality of endometrial cancer: a multi-centric study by the Italian Society of Gynecological Endoscopy

Stefano Uccella, MD, PhD; Matteo Bonzini, MD; Mario Malzoni, MD; Francesco Fanfani, MD; Stefano Palomba, MD; Giovanni Aletti, MD; Giacomo Corrado, MD; Marcello Ceccaroni, MD; Renato Seracchioli, MD; Fevzi Shakir, MD; Annamaria Ferrero, MD; Roberto Berretta, MD; Raffaele Tinelli, MD; Enrico Vizza, MD; Giovanni Roviglione, MD; Lucia Casarella, MD; Eugenio Volpi, MD; Ettore Cicinelli, MD; Giovanni Scambia, MD; Fabio Ghezzi, MD

BACKGROUND: Although widely adopted, the use of a uterine manipulator during laparoscopic treatment of endometrial cancer represents a debated issue, and some authors hypothesize that it potentially may cause an increased risk of relapse, particularly at specific sites.

OBJECTIVE: Our aim was to evaluate the risk and site of disease recurrence, overall survival, and disease-specific survival in women who had laparoscopic surgery with and without the use of a uterine manipulator.

STUDY DESIGN: Data were reviewed from consecutive patients who had laparoscopic surgery for endometrial cancer staging in 7 Italian centers. Subjects were stratified according to whether a uterine manipulator was used during surgery; if so, the type of manipulator was identified. Multivariable analysis to correct for possible confounders and propensity score that matched the minimize selection bias were utilized. The primary outcome was the risk of disease recurrence. Secondary outcomes were disease-specific and overall survival and the site of recurrence, according to the use or no use of the uterine manipulator and to the different types of manipulators used.

RESULTS: We included 951 patients: 579 patients in the manipulator group and 372 patients in the no manipulator group. After a median follow-up period of 46 months (range,12−163 months), the rate of recurrence was 13.5% and 11.6% in the manipulator and no manipulator groups, respectively (P=.37). Positive lymph nodes and myometrial invasion of >50% were associated independently with the risk of recurrence after adjustment for possible confounders. The use of a uterine manipulator did not affect the risk of recurrence, both at univariate (odds ratio, 1.18; 95% confidence interval, 0.80−1.77) and multivariable analysis (odds ratio, 1.00; 95% confidence interval, 0.60−1.70). Disease-free, disease-specific, and overall survivals were similar between groups. Propensity-matched analysis confirmed these findings. The site of recurrence was comparable between groups. In addition, the type of uterine manipulator and the presence or not of a balloon at the tip of the device were not associated significantly with the risk of recurrence.

CONCLUSION: The use of a uterine manipulator during laparoscopic surgery does not affect the risk of recurrence and has no impact on disease-specific or overall survival and on the site of recurrence in women affected by endometrial cancer.

Key words: endometrial cancer, laparoscopy, oncological safety, prognosis, recurrence, uterine manipulator

Although skepticism had been raised for many years regarding the application of minimally invasive surgery to gynecologic oncology, laparoscopy is now widely accepted for the surgical treatment of endometrial cancer. Results of 2 large randomized trials recently have shown that the endoscopic approach is associated with improved perioperative outcomes and short-term quality of life compared with traditional open surgery, without impairing safety in patients who are affected by endometrial cancer.[1-3]

However, when laparoscopic surgery for this malignancy is performed, there are crucial technical aspects that still remain controversial. Among them, the use of a uterine manipulator represents a big dilemma for oncologic surgeons. Most surgeons claim that the use of an intrauterine device to mobilize the uterus during laparoscopic hysterectomy allows better exposure of the spaces and, consequently, a faster and safer procedure.[4] On the other hand, several concerns have been raised around its use, because of the possible risk of disruption of the tumor mass, spread of malignant cells, and seeding of the disease, particularly at the level of the vaginal cuff or peritoneum.[5-9] Several reports have analyzed this issue; some of them have suggested that the risk of positive cytologic evidence increases when the uterine manipulator is positioned[5,6]; others have observed that lymph vascular space invasion is more common among those patients in whom the device is utilized[7,8] or even that the use of intrauterine probes may cause tumor dissemination in the fallopian tubes.[9] Conversely, several studies have questioned these observations by demonstrating that the risk of positive peritoneal washings, lymphovascular space invasion, and nodal micrometastases are not different when a uterine manipulator is used compared with when it is not.[10-13] Unfortunately, all these studies could not provide definitive conclusions on this issue, because they had a small sample size. Moreover, the main question regarding long-term oncologic outcomes were not addressed.

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TABLE 1
Demographic characteristics of the 2 groups

Characteristics	Manipulator (n=579)	No manipulator (n=372)	*P* value
Age, y[a]	60.8±11.4	61.2±10.9	.47
Body mass index, kg/m^2[a]	27.9±5.4	28.9±6.4	.01
Obese, n (%)	178 (30.7)	159 (42.7)	.02
No vaginal birth, n (%)	187 (32.3)	138 (37)	.14
Previous cesarean delivery, n (%)	60 (10.4)	40 (10.8)	.92
Charlson Comorbidity Index, n (%)			.29
0	301 (52)	213 (57.3)	
1-2	239 (41.3)	133 (35.8)	
≥3	39 (6.7)	26 (6.9)	
American Society of Anesthesiologists score≥ 3, n (%)	86 (14.8)	42 (11.3)	.12

[a] Values are expressed as mean±standard deviation.

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Two recent articles have tried to analyze survival after laparoscopic treatment of endometrial cancer with a uterine manipulator.[14,15] Unfortunately, they are largely underpowered to investigate prognostic outcomes (<70 patients included per group). As a consequence, the surgeon's decision about whether to use or not use the uterine manipulator during laparoscopic surgery for endometrial cancer relies only on speculations, personal opinions, and prejudices, rather than on scientific evidence.

Using a multicentric database that has been endorsed by the Italian Society of Gynecological Endoscopy, we decided to design the present study with the aim of investigating the long-term oncologic safety of the use of a uterine manipulator during laparoscopic surgery for endometrial cancer.

Materials and Methods

The present investigation is a multi-institutional cohort study of patients with primary, histologically confirmed endometrial carcinoma. Seven Italian institutions were involved in the collection of data. Demographics, surgical procedures, intra-/postoperative details, pathology reports, and follow-up evaluations were collected routinely from each institution in specifically designed research-quality databases that were reviewed retrospectively. This is in line with previously published studies.[16,17] The protocol for this study was in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

All consecutive patients who received surgical treatment for endometrial cancer by laparoscopy in the period between January 2000 and March 2013 were included. Subjects with clinical stage >I disease (ie, evidence of extrauterine spread of disease and frank cervical involvement) and those with a postoperative oncologic follow up of <12 months were excluded. None of the operations was performed by robotic surgery.

Some patients in this study have been included in 2 previous publications by the same research team.[16,17] Subjects were divided in 2 groups (manipulator [M] group vs no-manipulator [NoM] group) according to the use or not of a uterine manipulator to mobilize the uterus at the time of hysterectomy. The decision as to whether to use the uterine manipulator was based on surgeons' attitude towards this instrument and the type of procedure. In the NoM group, the vagina was filled with gauzes to delineate the fornices and to prevent loss of pneumoperitoneum at the time of colpotomy.

All patients had peritoneal washing taken, total laparoscopic hysterectomy and bilateral salpingo-oophorectomy with or without pelvic/paraaortic lymphadenectomy was performed. The decision to perform pelvic/paraaortic lymphadenectomy was based on preoperative and intraoperative uterine risk factors and the expected anesthesia risk. Details of the surgical technique used for both laparoscopic and open approach have been published previously.[18,19] During the study period, routine coagulation of the tubes at the beginning of the procedure to avoid possible intraperitoneal spread of disease was not performed. All the procedures were accomplished by 14 surgeons who have been performing surgery for a minimum of 5 years, with at least 200 minimally invasive and 30 oncologic surgical interventions per year.

In all participating centers, institutional review board approval was not required because the study involved the analysis of existing data. A written informed consent was obtained from all patients for the anonymized insertion of the data regarding their treatment and oncologic outcome in our research databases, and the Ethics Committee at each institution approved the collection of data for research purposes.

Preoperative assessment of the expected anesthesiologic risk was based on the American Society of Anesthesiology (ASA) score.[20] Moreover, the presence and relevance of comorbidities were assessed using the Charlson Comorbidity Index (CCI), which predicts the 10-year mortality rate because of comorbid conditions.[21]

International Federation of Gynecology and Obstetrics (FIGO) surgical stage,[22] tumor grade, myometrial invasion, and histopathologic type were recorded for each patient. After surgery, patients were examined every 3 months for 2 years, then every 6 months for the next 3 years, and yearly thereafter.

Adjuvant pelvic radiation therapy (50.5 Gy of external-beam radiation with