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Original Article

Timing of Intrauterine Manipulator Insertion During Minimally Invasive Surgical Staging and Results of Pelvic Cytology in Endometrial Cancer

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ABSTRACT **Study Objective:** Considering the hypothetical concern of retrograde tumor spread to the peritoneal cavity by insertion of an intrauterine manipulator, we examined the correlation between the timing of manipulator insertion and the results of pelvic cytology during total laparoscopic hysterectomy (TLH) in endometrial cancer.

Design: Case-control study (Canadian Task Force classification II-2).

Setting: University-based hospitals.

Patients: Stage I to IV endometrial cancer patients who underwent TLH in which an intrauterine manipulator was used. Medical records were reviewed for patient demographics, surgical details, and tumor characteristics.

Interventions: Archived medical record review.

Measurements and Main Results: A total of 333 patients was identified. Cases were divided into those with intrauterine manipulator insertion after pelvic cytology sampling (Group 1, n = 103) and those with intrauterine manipulator insertion before pelvic cytology sampling (Group 2, n = 230). Types of intrauterine manipulator were similar across the 2 groups (p = .77). There was no statistical difference in the results of pelvic cytology between the 2 groups: Group 1 versus 2, atypical cells 2.9% versus 4.8% and malignant cells 5.8% versus 9.6% (p = .36). Uterine perforation related to intrauterine manipulator insertion was seen in 1.0% and .4% of each group (p = .52). In a multivariate analysis controlling for demographics and tumor characteristics, advanced-stage disease remained an independent risk factor associated with increased risk of atypical and malignant cells (adjusted odds ratio, 10.3; 95% confidence interval, 4.44–23.8; p < .001).

Conclusion: Our study suggested that the timing of intrauterine manipulator insertion during TLH for endometrial cancer is not associated with the results of pelvic cytology. Journal of Minimally Invasive Gynecology (2016) 23, 234–241 © 2016 AAGL. All rights reserved.

Keywords: Cytology; Endometrial cancer; Minimal invasive surgery; Uterine manipulator

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Endometrial cancer is the most prevalent gynecologic malignancy in the United States, with an estimated 54 870 new cases and 10 170 deaths identified in 2014 [1]. Some 67.5% of patients are diagnosed with localized endometrial cancer and are surgically staged with hysterectomy, bilateral salpingo-oophorectomy, and possible lymphadenectomy [2]. The treatment of endometrial cancer has seen a paradigm shift toward minimally invasive surgery, which serves

as an alternative to standard laparotomy for surgical management [3]. Randomized control trials comparing laparoscopy with laparotomy in the surgical management of early-stage endometrial cancer have shown that the laparoscopic approach had similar rates of overall and disease-free survival and similar rates of severe postoperative morbidity. The laparoscopic approach has also been shown to be associated with reduced operative morbidity and length of hospital stay [4–7]. Consequently, the use of this approach is increasing. According to a Nationwide Inpatient Sample database 38% of endometrial cancer patients underwent minimally invasive surgery in 2010 [8].

Most gynecologic surgeons recognize the advantage of uterine manipulators during hysterectomy. Nevertheless, some surgeons avoid their use with endometrial cancer for fear of iatrogenic spillage, uterine perforation, and the potential risk of pushing cancer cells into the peritoneal cavity or lymphatic spaces. However, the clinical significance of positive pelvic cytology with endometrial cancer confined to the uterus is controversial [9–11]. A recent study suggested that minimally invasive hysterectomy-based surgical staging for endometrial cancer with the use of an intrauterine manipulator is associated with increased risk of atypical cells in pelvic cytology compared with conventional abdominal hysterectomy [12]. However, a weakness of this study was that the timing of intrauterine manipulator insertion was not clearly defined for each candidate.

Concerns remain regarding whether the use of an intrauterine manipulator is associated with an increased risk of disease spread. The aim of our study was to evaluate the influence of the timing of intrauterine manipulator placement on the histopathologic outcomes in women undergoing minimally invasive surgery for the management of endometrial cancer.

Methods

Study Design and Eligibility

After Institutional Review Board approval was obtained at the University of Southern California, an institutional surgical pathology database was used to identify cases. Eligibility criteria for the study included patients with a diagnosis of endometrial cancer and those who were treated via conventional laparoscopic hysterectomy, laparoscopic radical hysterectomy, or robot-assisted hysterectomy at Los Angeles County Medical Center and Keck Medical Center of University of Southern California between January 1, 2000 and August 31, 2015. Cases were excluded if the following criteria were met: (1) the patient did not undergo minimally invasive surgery, (2) use of intrauterine manipulator was absent, (3) inadequate information about intrauterine manipulator insertion was provided, and (4) timing of pelvic cytology or performance of cytology was not defined.

Eligible cases were divided into 2 groups: patients having undergone pelvic cytology followed by intrauterine manipulator during surgery (Group 1) and control groups in which insertion of the intrauterine manipulator was followed by cytology (Group 2). The decision as to the timing of intrauterine manipulator insertion was at the discretion of the surgeon. All cases were performed or supervised by a faculty member of the division of gynecologic oncology at the University of Southern California. The Strengthening the Reporting of Observational studies in Epidemiology guidelines were consulted for reporting in a case-control study [13]. Some of the patients in this study were within the context of our previous studies [14].

Clinical Information

Among eligible cases, medical records were examined to abstract patient demographics at the time of surgery, surgical outcomes, and histopathology results for hysterectomy and pelvic cytology during the surgery. Patient demographics included age, ethnicity, body mass index (BMI), presence of medical comorbidities (hypertension, diabetes mellitus, and hypercholesterolemia), and past history of fallopian tubal ligation. Diagnostic procedures were based on endometrial biopsy within 3 months of surgical staging, whereas other cases were diagnosed by other procedures: hysteroscopy, uterine curettage, and vacuum curettage by Vabra (Sterylab, Milan, Italy). Surgical demographics included estimated blood loss (EBL, in mL), details regarding surgical staging (type of hysterectomy, salpingo-oophorectomy, and lymphadenectomy), use of intraoperative fallopian tube coagulation, intraoperative complications (laparotomic conversion, uterine perforation), and institution at which the surgical procedure was performed. Histopathology results included uterine weight (g), histologic subtype, grade, stage, depth of myometrial tumor invasion, presence of lymphovascular space invasion (LVSI), cervical involvement, and classification of pelvic cytology during surgery.

Definition

Cancer stage was evaluated based on the 2009 International Federation of Gynecology and Obstetrics system. In our study, histologic subtypes were grouped as endometrioid, serous, clear cell, or other adenocarcinoma. Tumor grade was grouped into low-grade versus high-grade. Grade 1 and 2 endometrioid tumors were categorized as low grade. Grade 3 endometrioid, serous, and clear cell tumors were categorized as high grade. Deep myometrial tumor invasion was defined as the presence of tumor in the outer half of the myometrial layer ($\geq$50%). Cervical involvement was defined as the tumor existing within the cervical glands or stroma. Intrauterine manipulator was defined as a uterine manipulator device (VCare [Conmed, Utica, NY], RUMI/Koh [Cooper Surgical, Inc, Trumbull, CT], and HUMI [Medline Industries, Inc, Mundelein, IL]) inserted into the uterine cavity.

Pelvic cytology was performed by infusion of saline into the pelvis and followed by aspiration of the peritoneal washing. Pelvic cytology was classified as negative, atypical or malignant. Cytology was considered “atypical” when pathologists could not provide a definitive diagnosis for malignancy [15]. Laparotomy conversion was defined as conversion from laparoscopic to abdominal hysterectomy caused by complication or mini-laparotomy to deliver the specimen. The co-investigators performed the data entry into the identified database, and the principal investigator of the study examined the database for accuracy, consistency, and quality.

Statistical Analysis

The primary interest of analysis was to identify independent predictors for the presence of positive pelvic cytology in laparoscopic surgery for endometrial cancer and to evaluate the risk of using intrauterine manipulators. Continuous variables were examined for normality by the Kolmogorov-Smirnov test and expressed