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The prevalence of occult endometrial cancer in women undergoing hysterectomy for benign indications

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ABSTRACT

Objective: To estimate the frequency of occult endometrial cancer in women undergoing hysterectomy for benign indications.
Study design: We performed a retrospective review of all patients undergoing hysterectomies for benign indications at our institution from 2006 to 2014. A departmental database was used to identify all hysterectomies performed, and institutional tumor registry was used to identify cases of endometrial carcinoma. Occult carcinomas were defined as cases with no suspicion preoperatively and histopathologic diagnosis of endometrial cancer postoperatively.
Results: A total of 6981 hysterectomies were performed for benign indications. Among these, thirteen patients (0.19%) were found to have occult endometrial cancer, with an overall rate of 1 in 537 patients (95% confidence interval 1:314–1:1008). Twelve patients had stage IA and one had stage IB disease. Median age of women found to have endometrial cancer was 50 years (range 35–72 years). The median BMI was 29.8 kg/m^2 (range 21.3–50.4 kg/m^2). The most common indications for hysterectomy were abnormal bleeding (47%), postmenopausal bleeding (15%), adnexal mass (15%), prolapse (15%), and endometrial hyperplasia without atypia (8%). Of the postmenopausal women that had bleeding, all patients underwent evaluation of the endometrium, however 75% of samples did not have adequate amount of endometrium to be evaluated and 25% were found to have hyperplasia.
Conclusion: This is one of the largest single institution cohorts to examine occult malignancy. Unexpected endometrial carcinomas were found to occur in 0.19% or 1:537 (95% confidence interval 1:314–1:1008) hysterectomies for benign indications in our population.
Précis: Occult endometrial carcinomas are found to occur in 1:537 (0.19%) hysterectomies for benign indications.

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Introduction

Uterine cancer is the most common gynecologic cancer in women in the United States, and the sixth leading cause of cancer deaths in women [1]. In 2014, after a well-publicized inquiry about concerns regarding the iatrogenic spread of occult malignant tissue during surgeries utilizing power morcellators, the Food and Drug Administration (FDA) issued a safety communication discouraging the use of laparoscopic power morcellation during a hysterectomy or myomectomy for uterine fibroids due to the risk of spreading occult cancerous tissue [2]. In response, the American Congress of Obstetricians and Gynecologists (ACOG) released a special report stating that physicians have the duty to select ideal surgical candidates for this procedure since it has been established that laparoscopic hysterectomies have decreased morbidity and mortality. They also urged physicians to discuss the benefits, risks, and alternatives to laparoscopic power morcellation so patients could make informed decisions [3]. In their analysis, the FDA quoted a risk of 1 in 350 women for occult uterine sarcoma in women undergoing a hysterectomy or myomectomy for the treatment of fibroids [2]. The Society of Gynecologic Oncology released a statement in July 2014 stating the risk calculated by the FDA was “questionable” for such a rare cancer since their analysis was based on retrospective cases series including patients from the

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1980s, where proper preoperative evaluations were not carried out, and a large number of patients were treated with abdominal hysterectomies, which made it unclear who was eligible for minimally invasive surgery [4].

Since then, there have been multiple studies that have published uterine sarcoma rates, ranging from 1 in 204 to 1 in 1124 [5–8]. However, uterine sarcomas account for less than 3% of all uterine cancers diagnosed annually. In 2017, there will be 61,380 new diagnoses and 10,920 deaths from uterine cancer [1]; the vast majority of these will be adenocarcinoma of the uterus. The most common symptom of endometrial carcinoma is abnormal or postmenopausal uterine bleeding and carcinoma of the uterus is usually diagnosed by office endometrial biopsy [5] or dilation and curettage (D&C) [9]. Given the relative frequency of adenocarcinomas, we sought to estimate the frequency of undetected endometrial cancer in women undergoing hysterectomies for benign indications.

Materials and methods

After approval from the University of Texas Southwestern (UTSW) Medical Center Institutional Review Board, all cases of hysterectomy performed for benign gynecologic indications from January 2006 to December 2014 at UTSW Medical Center and Parkland Memorial Hospital were identified from a prospectively maintained departmental billing database which includes all surgeries performed on our campus by UTSW faculty. The database is maintained with quality assurance by a database specialist and searchable through International Classification of Disease codes, Current Procedural Terminology, and faculty names. The database was queried by certified abstractors for all hysterectomies performed during this time period. Cases performed for obstetric purposes or for malignancies were excluded.

As a designated Academic Comprehensive Cancer Program by the American College of Surgeons' Commission on Cancer, we utilized the tumor registry of each hospital at UTSW to identify all cases of uterine cancer. The tumor registry was queried using the terms such as "adenocarcinoma," "endometrioid adenocarcinoma," "mixed cell adenocarcinoma," "papillary serous adenocarcinoma," "clear cell adenocarcinoma," or "carcinoma, not otherwise specified" of the endometrium or corpus uteri. Quality assurance for the abstraction of the data from these databases has 98% accuracy. Monthly reviews are done on random cases and there is software in the databases that helps maintain accuracy. Occult endometrial carcinomas were defined as cases where endometrial carcinoma was confirmed on surgical pathology, but there was no preoperative suspicion for malignancy. We excluded patients that had a preoperative diagnosis of complex atypical hyperplasia or surgeries performed by other specialties, for example urology. Patients that were included had preoperative pathology that was benign or simple hyperplasia with or without atypia, complex hyperplasia without atypia, or patients undergoing surgery for benign indications (such as urogynecologic procedures). Patient demographics, such as age, race, family history, preoperative evaluation, preoperative diagnosis, surgical specialty, intraoperative findings, pathology, postoperative treatment, and survival status were extracted from the medical records of the identified occult malignancy cases. Additional post-surgical staging was offered by gynecologic oncologists to the patients if they did not have a concurrent bilateral salpingo-oophorectomy or if they had intermediate/high risk features such as high grade histology, deep myometrial invasion, or lymph vascular space involvement. The staging of uterine cancer was based on International Federation of Gynecology and Obstetrics (FIGO) 2009 staging system. The exact Clopper-Pearson method was used to determine confidence intervals. The statistical analysis was performed with Prism version 7 (La Jolla, CA).

Results

A total of 6981 hysterectomies were performed for benign indications during this period. Thirteen patients (0.19%) were found to have occult endometrial cancer (Table 1), with an overall rate of 1 in 537 patients (95% confidence interval 1:314–1:1008). The median age of the women diagnosed with occult endometrial cancer was 50 years (range 35–72 years). Fifty-four percent (7/13) of the patients with occult cancer were postmenopausal. Of the patients diagnosed with occult endometrial cancer, 46% were Caucasian, 31% were African American, 15% were Hispanic, and 8% were Asian. The majority of the patients were parous (85%). The median BMI was 29.8 kg/m^2 (range 21.3–50.4 kg/m^2).

Other risk factors for endometrial cancer were determined for these patients. Sixty-two percent (8/13) of the patients were receiving hormone therapy with vaginal estrogen, progesterone, or combination hormones. Of the thirteen patients with occult uterine cancer, one patient was placed on vaginal estrogen treatment for pelvic prolapse. None of the patients had exposure to tamoxifen treatment. None of the patients had a family history of uterine cancer or known Lynch Syndrome. However, 46% (6/13) of the patients had a family history of cancer (breast, colon, or ovarian) and of those patients, 50% (3/6) of the patients had family members with both colon and breast cancer.

Each of the patients found to have occult uterine adenocarcinoma had preoperative imaging. The majority had an abdominal or pelvic ultrasound (92%; 12/13) and one patient had a computed tomography (CT) scan. In addition to the ultrasonography, 15% (2/13) had a CT and 8% (1/13) had a magnetic resonance imaging (MRI). Despite the majority of patients having a pelvic ultrasound, the endometrial stripe was unable to be evaluated through imaging 25% (3/12) of the time.

Twenty-three percent (3/13) of the patients found to have occult uterine cancer did not have endometrial sampling prior to proceeding to the operating room for hysterectomy. These three patients were all postmenopausal and did not have sampling prior to hysterectomy because their primary diagnosis was uterine prolapse/urinary incontinence (2 patients) or pelvic mass (1 patient) and none reported postmenopausal bleeding. Of note, each of these patients had preoperative imaging with a pelvic ultrasound, however 67% (2/3) of the patients' endometrial stripes were not able to be evaluated because it could not be visualized. One patient that did not have sampling was noted to have "focal areas of endometrial thickening" on ultrasound. Of the 10 patients who had preoperative endometrial sampling, 30% (3/10) had endometrial hyperplasia (20% complex hyperplasia without atypia and 10% simple hyperplasia without atypia), 40% (4/10) had normal or benign endometrial findings, and 30% (3/10) had scant/insufficient tissue during sampling. Two out of the three patients that had scant/insufficient tissue, underwent in office endometrial sampling with a pipelle, and did not undergo further follow up with dilation and curettage. Both of these patients had risk factors for endometrial carcinoma; one with class I obesity and abnormal uterine bleeding, the other was postmenopausal with class III obesity and a thickened endometrial stripe. This particular patient underwent 3 failed attempts at in-office endometrial sampling prior to proceeding with hysterectomy.

Of the 7 postmenopausal patients found to have occult endometrial carcinoma, 43% had postmenopausal bleeding with their preoperative endometrial sampling revealing benign endometrium (1/3), scant endometrial sample (1/3), and complex hyperplasia without atypia (1/3). Three (43%) had sonographic endometrial thickness which was measured, with a median value

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