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Original article

Endometrial histology in severely obese bariatric surgery candidates: an exploratory analysis

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Abstract

Background: Endometrial pathology risk has been linked to obesity; however, little is known of its prevalence in severely obese women not seeking care for endometrial pathology associated symptoms. This pilot study was designed to explore the frequency and risk factors associated with endometrial pathology in cancer-free, severely obese, bariatric surgery candidates using the Pipelle endometrial sampling technique (SureFlex Preferred Curette, Bioteque America, Inc, New Taipei City, Taiwan).

Methods: Twenty-nine severely obese bariatric surgery candidates with intact uteruses and no history of endometrial cancer or endometrial ablation were included in this subanalysis from a larger cohort of 47. Endometrial samples were obtained using a Pipelle endometrial suction curette at a single time point before surgery. Logistic regression was used to assess the relationship between body mass index and endometrial pathology when adjusting for age and race.

Results: Of the 29 successful biopsies, 8 (27.6%) were classified as abnormal endometrium: 1 was classified as complex atypical hyperplasia, 1 was classified as hyperplasia without atypia, 4 samples were identified with endometrial polyps, and 2 samples were identified with metaplasia. None presented with cancer. Increasing body mass index was significantly associated with higher risk of abnormal endometrium (OR = 1.19, 95% CI [1.03–1.36], $P = .01$).

Conclusions: The findings in this sample suggest that obesity may be associated with increased risk of having undiagnosed endometrial pathology. More thorough examination of relationships between levels of obesity and endometrial pathology are needed to better characterize high cancer risk groups who may benefit from introducing new screening measures. (Surg Obes Relat Dis 2015;▮:00–00.)

Keywords: Bariatric surgery; Endometrial cancer; Endometrial hyperplasia; Endometrial polyps; Obesity; Pipelle sampling

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Endometrial cancer (EC) incidence has been increasing since 2007 and is the most common gynecologic cancer in the United States [1–3]. The American Cancer Society estimates that at least 52,630 new cases of EC will be diagnosed in 2014 [4]. Risk factors for EC, as well as its

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precursor, endometrial hyperplasia (EH), include high levels of unopposed estrogen, low physical activity [5], and obesity [6,7]. A large, retrospective cohort study exploring the association between EC risk and specific body mass index (BMI) found that for every 1 kg/m^2 increase in BMI, there was an 11% increase in the likelihood of EC diagnosis [8]. A meta-analysis of BMI and incident EC revealed an overall risk ratio of 1.6 for every 5 units of BMI increase [9].

EH, particularly complex hyperplasia with atypia, is a well-known precursor for EC [6,10]. Risk factors for EH are similar to those for EC, including increased BMI [11]. Compared with women with normal BMI, previously published work suggests that obese women (BMI 30–39.9) had a 4.6-fold increase in risk of complex hyperplasia (95% CI: 2.1, 10.3) and a 3.7-fold increase in risk of hyperplasia with atypia (95% CI: 1.0, 13.8) [12]. Morbidly obese women (BMI $\geq$40) had a 23-fold increase in risk of complex hyperplasia (95% CI: 6.6, 79.8) and a 13-fold increase in risk of hyperplasia with atypia (95% CI: 1.9, 86.9) [12]. Approximately 30% of women with untreated complex hyperplasia with atypia progress to carcinoma, so timely diagnosis of EH is crucial [13]. In addition to hyperplasia, it is important to know the prevalence of endometrial polyps and metaplasia in the general population of obese women, because those conditions have been associated with EC in previous research [14,15]. Although asymptomatic women generally are not screened for EC, endometrial Pipelle sampling can potentially be used as a routine screening tool in the outpatient setting for identifying endometrial pathologies [16,17]. Because previous literature has shown endometrial Pipelle sampling to be successful in obtaining sufficient tissue [18] and because the sampling can be done on outpatient basis without the use of anesthetics, Pipelle biopsy has been used in this population.

In previous studies of untreated, asymptomatic, severely obese women (BMI $>$35), Argenta et al. found that the prevalence of endometrial hyperplasia is approximately 6.8% [19,20]. Viola et al. found endometrial cancer or hyperplasia in 8.9% of asymptomatic overweight or obese women, both pre -and post- menopausal, undergoing Pipelle biopsy [21]. Although previous studies provided important information on the prevalence of hyperplasia and cancer in asymptomatic women, they did not report information on the prevalence of other pathologies (such as polyps and metaplasia) and they were also limited by the inclusion of asymptomatic women only. The primary objective of the present study was to describe the prevalence of a wide spectrum of endometrial pathologies in a general cohort of cancer-free, severely obese women considering bariatric surgery.

Materials and methods

Study participants

Severely obese (BMI $\geq$35), female bariatric surgery candidates were recruited from Magee-Women's Hospital of the University of Pittsburgh Medical Center Health System (UPMC). Patients were considered eligible to participate in this investigation if they were at least 29 years old (because of a suspected lower prevalence of endometrial pathologies in the younger age group), enrolled in a bariatric surgery program, and expected to undergo bariatric surgery (Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding, or sleeve gastrectomy) within 6 months of recruitment. Exclusion criteria included prior endometrial ablation or hysterectomy, severe inflammatory or autoimmune diseases (as these samples were collected from larger study investigating inflammatory biomarkers), or refusal to consent to endometrial biopsy. Patients were not excluded on the basis of gynecologic symptoms such as abnormal menstrual bleeding; however, most patients were asymptomatic. This subanalysis was restricted to women with successful/sufficient endometrial biopsies (biopsies yielding sufficient endometrial tissue for pathology analysis). To justify the focus on participants with successful biopsies, these patients (n = 29) were compared with those without successful biopsies (n = 18) using Wilcoxon tests for continuous variables and χ^2 tests for categorical variables to ensure that there was no substantial difference between the groups.

All study-related procedures were performed at the Clinical and Translational Research Center of Magee-Women's Hospital of UPMC by trained clinical and/or research staff. The University of Pittsburgh Institutional Review Board approved this study, and all patients provided written, informed consent (Protocol #PRO08080042).

Measurements

Two experienced clinical staff members (a gynecologic oncologist and a physician assistant) obtained endometrial samples using a Pipelle endometrial suction curette in accordance with the manufacturer's instructions. Cervical ripening agents were not administered before biopsies. Acquired specimens were formalin-fixed, embedded in paraffin, sectioned, and stained using standard hematoxylin and eosin stain preparation, then evaluated by 2 independent pathologists with expertise in gynecologic pathology, who were blinded to the patients' health histories, age, BMI, and identifying characteristics. A third (senior) pathologist addressed any discrepancies between the findings of the 2 pathologists. Patients who evidenced pathology were referred to a gynecologist or gynecologic oncologist (as appropriate) for follow-up care.

A research registered nurse collected anthropometric measurements, during which participants wore light clothing and no shoes. Waist and hip circumferences were measured to the nearest centimeter using a nonstretchable tape. Height was recorded to the nearest inch by a standardized wall-mounted stadiometer. A Tanita body