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Mucinous differentiation does not impact stage or risk of recurrence among patients with grade 1, endometrioid type, endometrial carcinoma

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HIGHLIGHTS

- Among grade 1 endometrial type lesions, the incidence of mucinous differentiation was 20.9%.
- Mucinous differentiation was more common among older patients.
- Mucinous differentiation did not affect FIGO stage or the risk of recurrence.

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ABSTRACT

Objective. To evaluate whether the presence of mucinous differentiation influences histopathologic findings, stage distribution, or rate of recurrence among women with grade 1, endometrioid type, endometrial carcinoma.

Methods. This was a retrospective cohort study of all patients with grade 1, endometrioid type, endometrial carcinoma between January 2005 and December 2012. Patients were separated by the presence or absence of mucinous differentiation and then compared.

Results. Of 655 patients, mucinous differentiation was present in 137 (20.9%) and absent in 518 (79.1%) patients. Compared to the group without mucinous differentiation, the group containing mucinous differentiation was older at diagnosis (mean: 61.1 vs. 58.5 years, OR, 95% CI; 1.03, 1.01–1.05) and more likely to have myometrial invasion (61.3% vs. 51.5%, OR, 95% CI; 1.49, 1.01–2.19). Additional histopathologic findings including: tumor size, cervical stromal invasion, adnexal involvement, LVI and/or the presence of positive lymph nodes were similar between groups. Mucinous differentiation did not affect stage distribution, as most patients were stage 1A (85.4% vs. 86.3%). The median PFS for the entire group has yet to be reached. The mean PFS for the entire study sample was 94.7 months. There was no difference in mean PFS when comparing the group with mucinous differentiation to the group without mucinous differentiation (98 vs. 93.4 months, $p = 0.07$).

Conclusions. In the setting of grade 1, endometrioid type, endometrial carcinoma, mucinous differentiation is more common in older patients and is associated with an increased likelihood of myometrial invasion. However, stage distribution and risk of recurrence are not affected.

Introduction

Endometrial cancer is the most common gynecologic malignancy in the United States and it is estimated that in 2014, greater than 50,000 women will be newly diagnosed with this disease [1]. Previous studies have shown that 30% of newly diagnosed cases of endometrial cancer will be of grade 1, endometrioid type, histology and have estimated the 5-year crude survival at 87% [2]. While most patients will present with disease confined to the uterine corpus, 10–15% of patients will have extra-uterine spread [3–5]. Factors associated with extra-uterine spread, risk of recurrence and risk of death have been identified and include: myometrial invasion, presence of lymph-vascular space invasion (LVI) and regional lymph node metastases [4–6].

Endometrial cancers may often show patchy changes in differentiation and grade 1, endometrioid type, lesions can often be associated with areas of mucinous, squamous, or tubal differentiation [7]. Pure mucinous type, endometrial cancers are rare and represent less than 10% of all cases of endometrial cancer [8–11]. Recent reports have

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compared pure mucinous endometrial cancers with those of endometrioid histology and have shown that patients with pure mucinous lesions more frequently have pelvic lymph node metastases and advanced stage disease [12,13]. However, the significance of mucinous differentiation among grade 1, endometrioid type, endometrial cancers has yet to be evaluated. The primary objective of the current study was to evaluate whether the presence of mucinous differentiation influences histopathologic findings, stage distribution, or the rate of recurrence among women with grade 1, endometrioid type, endometrial carcinoma.

Materials and methods

After obtaining institutional review board (IRB) approval, we conducted a retrospective chart review of all patients diagnosed with grade 1, endometrioid type, endometrial carcinoma between January 2005 and December 2012. The extent of surgical staging (i.e. pelvic and/or para-aortic lymphadenectomy) was left at the discretion of the surgeon. Patients with deep (≥50%) myometrial invasion on frozen section evaluation were more likely to undergo pelvic and/or para-aortic lymphadenectomy. All procedures consisted of at least a total hysterectomy and bilateral salpingo-oophorectomy (if the adnexa had not been previously removed).

Adjuvant therapies were tailored to pathologic findings, patient preference and physician discretion. Adjuvant radiation therapy (RT) consisted of external beam, whole pelvic RT and/or vaginal brachytherapy. Adjuvant chemotherapy varied over the years but was predominantly platinum-based. Postoperative therapy was typically administered in women with documented extrauterine disease or high-risk early stage disease.

Patients were categorized by the presence or absence of mucinous differentiation. The presence or absence of mucinous differentiation was based upon the presence of cells (or areas of cells) associated with the primary malignancy, that contained intracellular mucin. Groups were compared with respect to patient characteristics, histopathologic findings and the development of recurrent disease. Patients were staged according to the 2009 classification of the International Federation of Gynecology and Obstetrics (FIGO).

Patients were excluded from the final analysis based on the presence of any of the following: incomplete medical records, synchronous primary malignancy at the time of endometrial carcinoma diagnosis, neoadjuvant chemotherapy or non-grade 1, endometrioid type histology. We performed univariate logistic regression analyses with mucinous differentiation as the outcome. Continuous variables were modeled categorically and continuously. Associations are shown as odds ratios (OR) and 95% confidence intervals (CI). A survival curve was generated by the Kaplan–Meier method. The SPSS version 20.0 statistical package was used for all statistical analyses. A p-value of less than 0.05 was considered to be statistically significant.

Results

Of a total of 655 patients available for analysis, mucinous differentiation was present in 137 (20.9%) and absent in 518 (79.1%) patients. As shown in Table 1, compared to patients without mucinous differentiation, those with mucinous differentiation were diagnosed with endometrial cancer at a slightly older age (61.1 vs. 58.5 years, OR, 95% CI; 1.03, 1.01–1.05). However, there was no significant difference between groups with respect to preoperative body mass index (BMI) or race (Table 1).

Table 2 shows a comparison between those with and without mucinous differentiation with respect to histopathologic characteristics and surgical stage distribution. In summary, myometrial invasion was more common within the group with mucinous differentiation (61.3% vs. 51.5%, OR, 95% CI; 1.49, 1.01–2.19). However, the frequency of deep myometrial invasion (≥50%) was similar between groups (12.4% vs. 10%, OR, 95% CI; 1.27, 0.71–2.28). Additional histopathologic findings including: tumor size, cervical stromal invasion, adnexal involvement, LVI and/or the presence of positive lymph nodes were similar between groups. Furthermore, mucinous differentiation did not affect FIGO stage distribution, as the majority of patients were stage 1A (85.4% vs. 86.3%) (data not shown).

The majority of patients in both groups required no adjuvant therapy and underwent clinical observation following surgical intervention (86.1% vs. 87.8%). Using those that underwent observation as the reference group, there were no differences between those with and without mucinous differentiation with respect to postoperative treatment strategies after logistic regression analyses. Additional treatment strategies utilized included: vaginal brachytherapy (4.4% vs. 6%, OR, 95% CI; 0.75, 0.30–1.83), external beam radiation (4.4% vs. 3.5%, OR, 95% CI; 1.29, 0.50–3.31) and chemotherapy ± radiation (5.1% vs. 2.7%, OR, 95% CI; 1.93, 0.76–4.89).

Of the 137 patients with mucinous differentiation, there were 2 recurrences (1.5%) and among the 518 patients without mucinous differentiation, there were 23 recurrences (4.4%). The median PFS for the entire group has yet to be reached. The mean PFS for the entire study sample was 94.7 months and there was no difference in mean PFS when comparing the group with mucinous differentiation to the group without mucinous differentiation (98 vs. 93.4 months, $p = 0.07$) (Fig. 1).

Discussion

The current study represents the first evaluation of the oncologic impact of the presence of mucinous differentiation among patients with grade 1, endometrioid type, endometrial cancer. Overall, the incidence of mucinous differentiation within our patient sample was 20.9%. In undertaking this study, we hypothesized that the presence of mucinous differentiation could be associated with negative prognostic factors

Table 1
Comparison of patient characteristics among patients with grade 1, endometrioid type, endometrial cancer with and without mucinous differentiation.[a]

	Mucinous differentiation present N = 137	Mucinous differentiation absent N = 518	OR (95% CI)	p-Value
Age at diagnosis (years)				
Mean (SD)	**61.1 (8.7)**	**58.5 (10.5)**	**1.03 (1.01–1.05)**	**0.009**
Age ≥ 60	**73 (53.3)**	**226 (43.6)**	**1.47 (1.01–2.15)**	**0.04**
Race				
Caucasian	121 (89.6)	460 (90.6)	1.00	–
African-American	7 (5.2)	24 (4.7)	1.84 (0.41–8.21)	0.42
Hispanic	5 (3.7)	10 (2)	2.04 (0.37–11.22)	0.41
Other	2 (1.5)	14 (2.8)	3.50 (0.56–21.81)	0.18
Body mass index (kg/m^2)				
Mean (SD)	32.9 (9.1)	33.7 (9.5)	0.99 (0.97–1.01)	0.44
Body mass index ≥ 30	57 (57.6)	253 (60.1)	0.90 (0.58–1.41)	0.65

[a] Values displayed represent number and percentage unless otherwise specified. Percentages displayed were calculated after excluding missing entries.