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Accuracy of preoperative endometrial sampling diagnosis for predicting the final pathology grading in uterine endometrioid carcinoma

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Abstract

Purpose: To explore the accuracy of preoperative endometrial sampling diagnosis for predicting the final pathology grading in endometrial cancer.

Methods: A cross-sectional study was carried out on patients who underwent surgical treatment for clinically early-stage endometrioid carcinoma of uterus at our Centers from March, 1991 to June, 2012. The agreement levels for the histological grading between the preoperative endometrial sampling diagnosis and the final surgical pathology were analyzed by the Kappa (κ) statistics with 95% confidence intervals (CI). The statistical analyses were also based on frequency data and diagnostic agreement of the procedures.

Results: We retrospectively selected 79 patients that fit the criteria of this analysis. The overall level of agreement between preoperative and postoperative grading was "fair" according to Kappa (κ) statistics ($\kappa = 0.221$; 95%CI = 0.389–0.053; $p = 0.01$). Accordingly, the overall concordance was 48/79 (60.75%)–39/58 (67.24%) for G1, 7/16 (43.75%) for G2, and 2/5 (40%) for G3 tumors. The preoperative grade 1 diagnosis was upgraded to grade 2 (n = 6) or 3 (n = 1) in 15.2% of patients after hysterectomy. Sensitivity, specificity, NPV, PPV, and accuracy of preoperative endometrial sampling diagnosis to predict grade 1 at the final surgical pathology was 67.2%, 66.7%, 42.4%, 84.8% and 67.1%, respectively.

Conclusions: Preoperative endometrial sampling was found to be only a modest overall predictor of postoperative histological grading. A selective staging policy based on predictive models to avoid lymph node dissections in endometrial cancer should take into account additional parameters.

Keywords: Endometrial neoplasm; Lymphadenectomy; Neoplasm staging; Surgical pathology; Dilatation and curettage; Hysteroscopy

Introduction

Endometrial cancer is the most frequent gynecological malignancy in developed countries and is the second most common in developing countries.[1] However, the majority of patients suffering of this tumor are diagnosed at an early-stage, which fortunately results in overall high cancer-specific survival rates after a surgical treatment.[1,2] In these settings, simple total hysterectomy (TH) plus bilateral salpingo-oophorectomy (BSO) remains a cornerstone for the management of endometrial cancer,[2] whereas the value of systematic lymph node dissection is a matter of great debate.[3–5]

Due to the lack of benefit of systematic lymphadenectomy for women with clinically early-stage endometrial cancer at low risk of lymph node metastasis,[6–8] the preoperative identification of these patients emerged as key for the proper surgical management of this malignancy.[9] Accordingly, several models have been proposed to predict

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nodal metastasis taking into account preoperative parameters,[10–13] whereas the histology and grade of endometrial cancer are well-know predictors of nodal involvement. Thus, the assessment of endometrial sampling as a predictor of final surgical pathology in endometrial cancer is an important point to be scrutinized, since the surgical staging decisions are often based on a preoperative biopsy in most of oncological centers.[12,14,15]

This current study aimed to explore the accuracy of preoperative endometrial sampling diagnosis for predicting the final pathology grading on endometrial cancer patients from two Northeast Brazilian Centers.

Materials and methods

A cross-sectional study was carried out on patients who underwent surgical treatment for endometrial cancer at the Hospital de Câncer de Pernambuco – HCP and Instituto de Medicina Integral Professor Fernando Figueira – IMIP from March 1991 to June 2012. Using a prospectively maintained authors' database, we selected patients underwent TH plus BSO due to a malignant uterine diagnosis histologically verified by preoperative endometrial sampling. We limited our study to adults (≥18 years) with clinically early-stage disease and endometrioid subtype histology, and excluded those cases without the main medical records. The study protocol was reviewed by our *Ethics Research Committee* (CAAE: 25422913.3.0000.5569).

We re-explore clinicopathological prognostic factors such as age, lymph node dissection, histological grade, myometrium invasion, cervical involvement, lymph node metastasis, and the use of adjuvant chemo or radiation therapies. The post-operative pathological exams were also reviewed in order to up-date the pathological stage to the current version (TNM, 2010). Hysterectomy specimens were fixed and processed by the pathology department of each Center, and usually involved standard *H&E* staining without additional immunostaining methods.

Continuous variables were summarized as medians (interquartile range) and categorical variables as frequencies (percent). The statistical analysis was based on frequency data and diagnostic agreement of the procedures. We determined sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and the diagnostic accuracy was the proportion of accurate predispositions. The agreement levels for histological grading between the preoperative endometrial sampling diagnosis and the final surgical pathology were also analyzed by the Kappa (κ) statistics with 95% confidence intervals (CI).

Descriptive analyses were performed using the STATISTICA Data Analysis Software System, Version 8.0 (Statsoft, Inc., Tulsa, OK, USA), and the Kappa statistics were develop by a free on-line calculator system available at http://www.lee.dante.br/pesquisa/kappa/index.html. The general (conventional) consensus scheme for strength of agreement by κ-values was used in the evaluation as follows: <0, no agreement; 0–0.19, poor; 0.2–0.39, fair; 0.4–0.59, moderate; 0.6–0.79, substantial; 0.8–1, excellent.[16] The analyses considered a statistically significant two-tailed p-value of 0.05.

Results

From our own database of 166 patients who underwent surgical treatment for endometrial cancer, we selected 79 of them with clinically early-stage endometrioid carcinomas that fit the criteria of this analysis. Patients excluded from this analysis involved those with a diagnosis other than endometrioid adenocarcinoma in the sampling procedure (n = 7) or hysterectomy specimens (n = 1), gross extra-uterine disease at laparotomy (n = 12), and unknown grade on preoperative biopsy (n = 63) or final pathology (n = 4). Patients in this sample underwent TH plus BSO without any lymph nodes dissection (48/79, 60.75%) or with a sampling dissection alone (31/79, 39.25%). Their baseline characteristics are summarized in Table 1.

Among patients with a preoperative non-endometrioid histology, the diagnosis of papillary serous (n = 2) changed to grade 3 endometrioid adenocarcinoma in one case, whereas both cases reported as clear cell carcinoma were confirmed on exam of hysterectomy specimens. Additionally, the report of endometrioid histology on sampling diagnosis was replaced to adenosquamous type in one case, and another one reported as adenosquamous was replaced to endometrioid histology after hysterectomy. Both case with atypical hyperplasia changed to grade 1 endometrioid adenocarcinoma at the final pathology.

Our survival outcomes were previously explored and reported.[14] In summary, over the 12.2-year follow-up

Table 1
Baseline characteristics.

Variables	n (%) or median (Q_{25}–Q_{75})
Age (years)	63 (56–70)
Sampling method	
Hysteroscopy	32 (40.51)
Curettage	30 (37.98)
Others	10 (12.65)
Missed	7 (8.86)
Preoperative histological grade	
G1	46 (58.23)
G2	24 (30.37)
G3	9 (11.40)
Postoperative histological grade	
G1	58 (73.42)
G2	16 (20.25)
G3	5 (6.33)
pTNM Stage	
I	56 (70.89)
II	19 (24.05)
III	4 (5.06)

G1, well differentiated; G2, moderately differentiated; G3, poorly differentiated.