Role of Dilatation and Curettage for Diagnosing Uterine Tumors: A University Hospital Experience

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Abstract

Background and Aims: Endometrial cancer is a common gynecological malignancy, with a chief complaint of vaginal bleeding. Dilation and curettage (D&C) prior to performing definite surgical procedure is the gold standard pre-operative diagnostic method. This is a retrospective comparative study that aims is to determine the accuracy rate of D&C in diagnosing cancer at our institution.

Materials and Methods: Endometrial cancers with pre-operative D&C diagnosed and underwent definite surgical procedures at our institution during the last 10 years were included. Corresponding slides for pre-operative D&C and final post surgical diagnosis were reviewed for histopathological characteristics. Any pre-operative cervical smears within one year of diagnosis were also reviewed.

Results: 54cases of endometrial cancer were studied. Mean age =62.5 years. 79.6% of patients were menopausal. 32 had available follow up(mean period = 16.5 months). Most common histopathological types were endometrioid carcinoma (74%); followed by serous carcinoma (11%) and 4carcinosarcoma (7.4%). Accuracy rate of D&C was 87 %. Cases with discrepancy were 3 endometrioid cancers, and one each of serous carcinoma, leiomyosarcoma, endometrial stromal sarcoma, and placental site trophoblastic tumor.

Conclusions: accuracy rate of D&C in detecting endometrial epithelial cancers is high; but is low for sarcomas. Potential factors that reduce accuracy include interpretation errors, sampling issues, and lack of ancillary immunohistochemistry.

Keywords: Dilatation and Curettage; Endometrium; Endometrial cancer.

Introduction

Endometrial cancer (EC) is the second most common gynecological malignancy worldwide, the commonest in developed countries, and the fourth most common among Jordanian females according to most recent cancer statistics[1,2]. The disease prevails among postmenopausal women with an average age of 60 years[1]. It is significantly associated with metabolic abnormalities including hypertension, hyperglycemia and increased BMI in addition to reproductive risk factors[3].

Patients most commonly present with a chief complaint of vaginal bleeding. Pre-operative investigations aim to obtain endometrial tissue

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diagnostic of cancer prior to performing definite surgical procedure as determined by tumor histologic type, stage, preoperative imaging results and the patient's desire to keep fertility, among other factors[4]. D&C remains the gold standard for the diagnosis of endometrial carcinoma[5].

Till date, no standard screening test for early detection of EC is proposed, on the contrary to the successful and validated cervical Pap test for premalignant and malignant lesions of uterine cervix. Exfoliated endometrial cells can be seen in pap smears and warrant further clinical evaluation to exclude an endometrial pathology. However, cervical Pap test is not as sensitive or specific as tissue biopsy in detecting EC[6].

In the literature there are many similar articles of the same purpose, however this one reflects our institution experience in this regards. This study is a retrospective comparative analysis of histological type, grade, preoperative endometrial sampling and Pap test results of patients diagnosed with uterine cancer at the department of pathology atour institution. The aim is to determine the accuracy rate of D&C in the preoperative diagnosis of such tumors, and any factors that affect such accuracy.

Materials and Methods. Institutional Review Board approval was obtained. Cases of EC diagnosed on hysterectomy specimens in Histopathology between Jan-2007 and Dec-2017 were identified and retrieved from hospital database records. Patient`s clinical follow up (FU) notes were also retrieved. FU tests included abdomino-pelvic imaging and vaginal vault smear biopsies. Only cases with an in-house pre-operative D&C were included in this study. All included cases underwent definite surgical procedures comprising a total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), pelvic lymph node

dissection and peritoneal washing. We reviewed corresponding tumor slides for each case and identified tumor histologic type, grade, depth of myometrial invasion, cervical stromal invasion, lymph-vascular invasion (LVI), spread to adjacent organs and omental metastasis. Endometrial Endometrioid cancers (EEC) were graded according to the International Federation of Gynecology and Obstetrics (FIGO) grading system into grades I, II and III. This grading system does not apply to serous carcinoma (ESC), clear cell carcinoma (CCC), or carcinosarcomas /malignant mixed mullerian tumors (MMMT) which are all by definition high-grade tumors.

For each case, we reviewed pre-operative D&C histopathology reports and H&E microscopic slides. Preoperative cervical Pap smear reports and slides within 1 year prior to diagnosis were also reviewed.

Agreements and discordance between preoperative and postoperative diagnoses were then noted and analyzed in respect to patient's demographics including age, menopausal status and available follow-up clinical data. The accuracy rate of D&C in the diagnosis of uterine cancer was then calculated.

Results. A total of 54E Ccases were included. Time intervals between diagnostic D&C and definite surgical procedures ranged from one week to 20 months (mean= 2.6 months). 13 patients had undergone a cervical Pap test within one year prior to hysterectomy. Patients age at diagnosis ranged from 37 to 80 years old (median = 62.5 years).With respect to menopausal status, 43 patients were postmenopausal (79.6%) and 11 were premenopausal (20.3%). 32 cases had available FU data with FU periods ranging from 1 month to 8 years (mean= 16.5 months). 24 cases had no recurrence of their malignancy (75% of FU cases). The remaining 8 patients had

recurrences (25%) as early as 6 months and as late as 36 months post-diagnosis. We reviewed tumor slides for those patients looking for lymphovascular invasion (LVI), thickness of myometrial invasion and cervical stromal invasion. Of those 7 cases, all showed more than 50% myometrial invasion, three were found to have LVI, two had cervical stromal invasion and one had right adnexal involvement.

The histopathological types of EC on hysterectomy specimens included: 40 endometrioid carcinoma (EEC) (74%); 6 endometrial serous carcinoma (ESC) (11%); 4carcinosarcoma(MMMT) (7.4%), one clear cell carcinoma (CCC) (1.9%), one placental site trophoblastic nodule (1.9%), one leiomyosarcoma (1.9%) and one low grade endometrial stromal sarcoma (ESS) (1.9%).Within EEC cases, 28/ 40 cases of EC were FIGO grade 1 (70%), 11 were grade 2 (27.5%) and one was grade 3. The histopathological findings of the study sample are summarized in Table I.

All D&C diagnoses were concordant with hysterectomy diagnoses except for seven cases(≈13%).Of these, three cases were diagnosed as disordered proliferative endometrium (DPE) on D&C. Later, EEC was identified on hysterectomy. One revealed necrotic tissue on preoperative D&C, but on hysterectomy viable tumor tissue was identified and diagnosed as placental site trophoblastic tumor. Another D&C was reported as "endometrial tissue, negative for hyperplasia or malignancy". 3 months later, she underwent hysterectomy for persistent vaginal bleeding and was found to have a low grade ESS .The sixth case was diagnosed as moderately differentiated EEC on D&C while after hysterectomy, ESC was detected (Figure 1). The last case was reported as proliferative endometrium on D&C. since the imaging study was suspicious for a uterine mass, hysterectomy was performed and histopathology revealed leiomyosarcoma. Details for discrepant cases are summarized in Table 2.

Regarding cervical Pap smear results, as stated above, only 13 cases were found to have a test within a year of diagnosis. 11 of which were reported as negative for intraepithelial lesion or malignancy. The remaining two cases were reported as atypical glandular cells of undetermined significance. Preoperative tissue biopsy and hysterectomy specimens then revealed ESC in one case and EECFIGO grade I in the other.

Table I. histopathological characteristics of the study sample on hysterectomy specimens.

Histopathological variant (no.)		LVI (%)	Confined to Endometrium (%)	with Myometrial Invasion	
				< 50%	>50%
EEC (40)	Grade 1 (28)	4/28 (14.3%)	6/28 (21.4%)	8/28 (28.5%)	14/28 (50%)
	Grade 2 (11)	3/11 (27.3%)	---	7/11 (63.6%)	4/11 (36.4%)
	Grade 3 (1)	No	---	1/1(100%)	---
ESC(6)		3/6 (50%)	---	3/6 (50%)	3/6 (50%)
MMMT (4)		1/4 (25%)	---	---	4/4 (100%)
CCC (1)		No	---	1/1 (100%)	---
ULMS (1)		No	---	---	1/1 (100%)
PSTT(1)		Yes	---	---	1/1 (100%)
ESS (1)		Yes	---	---	1/1 (100%)

Abbreviations: EEC: endometrioid carcinoma; ESC: endometrial serous carcinoma; MMMT: carcinosarcoma; CCC: clear cell carcinoma ;ULMS: uterine leiomyosarcoma; PSTT: placental site trophoblastic tumor; ESS: endometrial stromal sarcoma; LVI: lymphovascular invasion.

Table II. Clinicopathological details for cases with discrepant diagnosis.

Final diagnosis	No. (%)	with discrepancy (%)	D&C diagnosis	Time lag (wk)	Age	D&C Tissue (mm)	IHC on D&C	FIGO stage	Recurrence
EEC*	40/54 (74.1%)	3/40 (7.5%)	DPE	88	57	2	No	IB	No
			DPE	10	59	10	No	IA	No
			DPE	37	78	25	No	IB	No
ESC	6/54 (11.1%)	1/6 (16.7%)	EEC	4	64	25	No	IIA	No
LMS	1/54 (1.8%)	1/1 (100%)	PE	5	51	10	No	IB	No
PSTT	1/54 (1.8%)	1/1 (100%)	Necrotic tissue	7	24	30	No	IV	No
ESS	1/54 (1.8%)	1/1 (100%)	PE	15	59	15	No	IB	No

Abbreviations: EEC: endometrial endometrioid carcinoma; ESC: endometrial serous carcinoma; LMS: leiomyosarcoma; PSTT: placental site trophoblastic tumor; ESS: endometrial stromal sarcoma; D&C: dilatation and curettage; wk: weeks; DPE: disordered proliferative endometrium; PE: proliferative endometrium; mm: amount of D&C tissue in millimeters; IHC: immunohistochemistry.

Discussion

The role of preoperative diagnosis in suspected EC cannot be over-emphasized. Variable options exist for endometrial sampling, but well-established screening tests are still not available. The accuracy rate, sensitivity and specificity of D&C and cervical Pap smears in preoperative diagnosis of EC had been reported by many authors[5,7-10], and in the literature there are many similar articles of the same purpose, however this one reflects our institution experience in this regards. Our study is the first among Jordanian patients which aims to determine the accuracy rate of endometrial D&C in pre-operative diagnosis of EC.

D&C has been the standard method of choice for the detection of EC for years. In our study, we found that the accuracy rate of D&C

in the preoperative diagnosis of EC is 87%. Literature review revealed that sensitivity in diagnosing endometrial pathology including EC ranges between 46% and 100% according to many authors[8-10]. It is the method of choice in postmenopausal women with a non-diagnostic office endometrial sample and worrisome transvaginal ultrasound[11]. However, as reported by some authors, disadvantages of D&C include inadequate sampling of endometrial cavity in a large percentage of cases, especially with focal lesions[12,13].

Alternatively, an outpatient Pipelle biopsy is a low-cost method requiring no analgesia with relatively good sensitivity and specificity in detecting EC in postmenopausal women[7,13]. However, limitations to this procedure exist. A systematic quantitative review reported an

average failure rate of 7% and an inadequacy rate of 15%, rendering a negative/non-specific result unhelpful in excluding endometrial pathology, especially among high risk postmenopausal patients in whom the performance of hysteroscopy, D&C on the other hand remains the gold standard for the diagnosis of EC [5].

In the current study, three cases with FIGO grade 1 EEC were diagnosed as disordered proliferative endometrium (DPE) on D&C. In all 3 cases, the diagnostic criteria of EC were not met in submitted curettage. This may be the result of poor sampling which could represent an inherent characteristic of the procedure itself as stated above or the focality of the lesion. Another patient was diagnosed preoperatively to have moderately differentiated EEC, without any diagnostic ancillary tests. Later, post hysterectomy diagnosis was issued as ESC. We retrospectively performed immunohistochemistry (IHC) test for p53 on the paraffin embedded D&C specimen, which showed typical strong and diffuse nuclear stain of ESC. Although someone might argue that this is not an actual discrepancy as both are ECs, it is significant to emphasize the impact on the appropriate surgical procedure that must include adequate staging, omental and peritoneal sampling in ESC.

Problematic cases as such are encountered, and the morphologic spectrum of both types is wide in a sense that even low grade EEC can have a papillary architecture or an entirely glandular tumor can turn out to be ESC. Keeping ESC in the differential diagnosis of is essential in cases with compatible patient demographics, background endometrium and the presence of endometrial serous intraepithelial carcinoma[14]. The use of IHC for p53, B-catenin, estrogen receptor (ER), progesterone receptor (PR) and testing for PTEN loss has shown to aid in such cases [14,15]. In our

case, IHC was not applied to the preoperative biopsy at the time of diagnosis. Obviously, the accuracy of D&C can definitely be improved by adding the role of immunohistochemistry in increasing the sensitivity of D & C in diagnosis and further subtyping.

Data regarding the role of D&C in the preoperative diagnosis of uterine leiomyosarcomas (ULMS), endometrial stromal sarcoma (ESS), or gestational tumors are limited. The largest cohort up to date reported a sensitivity of 35.3% of preoperative endometrial sampling in detecting ULMS. The percentage was reported to rise to 51.5 % with postmenopausal patients having persistent vaginal bleeding and suspicious biopsies for ULMS due to the presence of atypical spindle cells or atypical stromal cells[16]. In our patient with ULMS, the preoperative D&C was reported as benign endometrial tissue. We reviewed corresponding D&C slides and no myometrial tissue was identified making the diagnosis impossible. However; because the imaging studies were alarming, hysterectomy was performed anyway. This emphasizes the supreme importance of clinicopathological correlation and high index of suspicion when dealing with such scenarios. The same applies to ESS. Bansal et al and others concluded that D&C has a low predictive value in preoperative diagnosis of uterine sarcomas[17]. In fact, most ESS cases included in a case series of uterine sarcomas were identified as being sarcomas by postoperative examination of uteri excised for leiomyoma[18]. In our ESS case, review of the D&C slides revealed a fragment of stromal proliferation that was missed. 3 months post-D&C, the patient underwent hysterectomy due to uterine enlargement and persistent menorrhagia which then revealed low grade ESS. It is well understood how difficult it can

be to diagnose endometrial stromal lesions as nodule versus sarcoma based on D&C because invasion cannot be assessed; however, the practicing pathologist should make a comment that this proliferation may be a "stromal neoplasm" if endometrial stroma is present without glands[17].

While cervical smears have been successfully used for decades in detecting premalignant and malignant cervical lesions, their role in detecting EC is very limited due to their low sensitivity[6]. A recent paper by Lai et al found out that only 38% of pre- operative Pap smears of EC revealed positive findings. They concluded that more effective detection of EC could be achieved by adding new criteria to routine screening[6]. Another study published by Sams et AL retrospectively reviewed 69 liquid based Pap smears for patients who were later diagnosed with EC. After rescreening, the sensitivity rose to 59.3% from an original of 31.9%. They attributed this to poor specimen quality and cognitive failure[19].

In our study, only 13 patients had undergone preoperative Pap test within one year of their EC, a small sample size that doesn't allow for statistical analysis. However; all had negative cytology except two whom their smears revealed atypical glandular cells without specific designation. The FUD&C showed EEC in one patient and ESC in the other. We do not know if the abnormal Pap result was the only reason for these two patients to undergo further evaluation or if it resulted in delayed diagnosis. Nevertheless, the presence of atypical glandular cells in cervical smears is an alarming clue to clinicians to further investigate the possibility of endometrial pathology[20].

Analysis of the available patient's FU data revealed that patients with EC recurrences had higher T stage and LVI at time of diagnosis.

Unfortunately, the small sample size, lack of FU data for some patients as well as the wide range of FU periods impede our ability to derive statistically significant associations. However; it is established that higher tumor grade, increased depth of myometrial invasion and involvement of regional lymph nodes are well characterized factors associated with increased risk of recurrence[4,21]. Regarding LVI, it is considered by many as an independent prognostic factor in predicting nodal disease, poor outcome and tumor relapse[22].

Our study had some limitations including its retrospective design and small sample size compared to the disease burden in Jordan. The studied group represents only those with a previous D&C result at our hospital. We did not include patients with an outside preoperative result which could have increased the sample size as well as affected the calculated accuracy rate. Because of the retrospective nature of the study, we did not perform IHC on all cases. Obviously, the accuracy of D&C could have been improved by adding immunohistochemistry to increase the sensitivity of D & C in diagnosis and further subtyping.

In conclusion, this study is the first to determine the accuracy rate of D&C in the preoperative diagnosis of EC among a subset of Jordanian patients. The findings in our study are in accordance with the previously reported in literature. The study illustrates a high accuracy rate of D&C. it also emphasizes that accuracy can be improved by the use of ancillary tests like IHC, adequate endometrial sampling, as well as the importance of correlation between clinico-radiological findings and histopathology in the diagnosis of uterine tumors.

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PSTT(1)	Yes	---	---	1/1 (100%)
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Discussion

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In conclusion, this study is the first to determine the accuracy rate of D&C in the preoperative diagnosis of EC among a subset of Jordanian patients. The findings in our study are in accordance with the previously reported in literature. The study illustrates a high accuracy rate of D&C. it also emphasizes that accuracy can be improved by the use of ancillary tests like IHC, adequate endometrial sampling, as well as the importance of correlation between clinico-radiological findings and histopathology in the diagnosis of uterine tumors.

Figure 1. A case with diagnostic discrepancy. A)Dilatation &Curettage diagnosed as endometrioid carcinoma (H&E; x 40). B) Hysterectomy specimen diagnosed as serous carcinoma (H&E; x 40). C) Strong and diffuse p53 nuclear staining performed retrospectively on D&C specimen (p53; x 100).
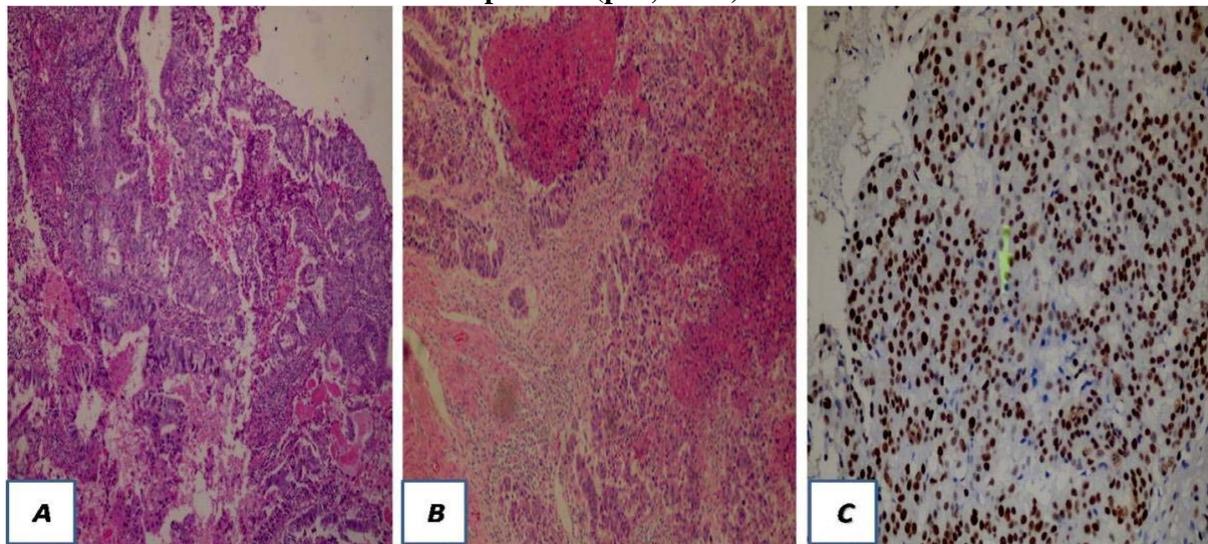
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مقارنة الدقة التشخيصية لعينات خزعة بطانة الرحم في مريضات سرطانات الرحم: خبرة مستشفى جامعي

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الملخص

يعد سرطان الرحم من أكثر السرطانات انتشارا في الدول النامية وهو الرابع في المملكة الأردنية الهاشمية حسب إحصائيات وزارة الصحة. أعراض المرض لأغلب الحالات هو نزيف غير طبيعي من المهبل، وعوامل الخطر تشمل بلوغ سن اليأس، ارتفاع ضغط الدم، مرض السكري وازدياد مؤشر كتلة الجسم بالإضافة لعوامل اخرى. ويتم تشخيص المرض عن طريق مجموعة من الفحوصات المخبرية والنسيجية وتشمل فحص تنظير الرحم وأخذ خزعة من انسجة الورم وذلك للكشف عما إذاكان هناك خلايا سرطانية لفحصها مجهريا ومن ثم تحديد نوعها ودرجتها. الدراسة الحالية اجريت على مجموعة من العينات النسيجية لمريضات تم تشخيص اصابتهن بسرطان الرحم في مستشفى الجامعة الاردنية خلال الفترة (2007–2017)، وهي دراسة تحليلية لنوع الورم ودرجته ومقارنته بتشخيصات الفحوصات التي اجريت لهؤلاء المريضات قبل خضوعهن لعملية استئصال الرحم حيث ضمت الدراسة نتائج فحصي خزعة بطانة الرحم و مسحة عنق الرحم. الهدف من هذه الدراسة هو تقييم معدل دقة التشخيص في خزعات بطانة الرحم ومسحات عنق الرحم ومقارنتها بالتشخيص المعطى لعينات استئصال الرحم، وكذلك تفصيل الخصائص النسيجية لتلك الاورام، بالإضافة الى مقارنة نتائجنا مع الدراسات العالمية.

الكلمات الدّالة: التوسعة والتجريف، بطانة الرحم، سرطان الرحم.