Comparison between Adenocarcinoma in both Endocervical and Endometrial Specimens from Fractional Curettage and Pathologic Findings in Subsequent Hysterectomy Specimens

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Objective: *To evaluate the hysterectomy specimen findings in the patients who underwent fractional curettage (F&C) with presence of adenocarcinoma in both endocervical and endometrial specimens.*
Material and Method: *Forty-one patients who had adenocarcinoma in both endocervical and endometrial specimens from F&C and underwent subsequent hysterectomy for surgical staging without pre-operative radiotherapy or chemotherapy at King Chulalongkorn Memorial Hospital between 1999 and 2007 were evaluated. Histologic slides from both F&C and hysterectomy specimens were reviewed and assessed. All cases of endometrial adenocarcinoma with cervical involvement (stage 2) in hysterectomy specimens were also assessed and compared to the results in F&C specimens.*
Results: *Fifteen patients (36.6%) with both positive endocervical and endometrial specimens from F&C were diagnosed as endometrial adenocarcinoma within uterine cavity with lower uterine segment involvement. Only 34.1% of cases were endometrial carcinomas with cervical involvement. In the 35 cases with endometrial carcinoma stage 2, 60% had adenocarcinoma in both endocervical and endometrial specimens from F&C.*
Conclusion: *In the patients who had adenocarcinoma in both endocervical and endometrial specimens from fractional curettage, the most common final pathological diagnosis from hysterectomy specimens was endometrial adenocarcinoma within uterine cavity with lower uterine segment involvement. Therefore, only 60% of endometrial carcinoma stage 2 revealed positive adenocarcinoma in both endocervical and endometrial specimens from fractional curettage.*

Keywords: *Endometrial adenocarcinoma, Fractional curettage*

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Endometrial carcinoma is the most common invasive neoplasm of the female genital tract in the United States and is the 5th most common cancer of women in worldwide[1].Approximately 90% of women with endometrial carcinoma have vaginal bleeding or discharge as the presenting symptom. To evaluate the patients with abnormal uterine bleeding or suspected endometrial pathology, office endometrial biopsy tests or fractional curettage is commonly used. Fractional curettage (F&C), consisting of endocervical and endometrial curettage, is a classic standard procedure to diagnose endometrial carcinoma preoperatively. Recently, several highly efficient and less traumatic alternative methods have been used to diagnose endometrial lesions, but they did not show more significant superiority than fractional curettage[2]. In the past, the clinical staging system was used, which was based on pelvic examination, imaging tests and pathological findings[3]. Although the staging system of endometrial carcinoma is changing from clinical to

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surgical system by the national Federal of Obstetrics and Gynecology (FIGO), the preoperative evaluation remains as an important factor to determine the most appropriate procedure for the patients. Assessment of cervical involvement may be necessary to guide therapy. It appears that cervical involvement is an important factor because prognosis for women with cervical involvement (stage 2) is much worse than prognosis for earlier lesions[4].

The aim of the present study was to evaluate the hysterectomy specimen findings in the patients who underwent fractional curettage with presence of adenocarcinoma in both endocervical and endometrial specimens.

Material and Method

Of all cases of fractional curettage retrieved from surgical pathology files of Division of Gynecologic Pathology, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, from January 1999 to June 2007; patients who had adenocarcinoma in both endocervical and endometrial specimens and underwent subsequent hysterectomy for surgical staging without pre-operative radiotherapy or chemotherapy were included in the present study. From a retrospective review of medical records, the patient's demographic and surgical data were collected. The microscopic slides of the curettage specimens were reviewed to confirm the histological diagnosis and assessed pathological features. The histologic slides of the surgical staging including hysterectomy specimens were reviewed and assessed. The authors also assessed all cases of endometrial adenocarcinoma with cervical involvement (stage 2) in hysterectomy specimens, which were diagnosed between January 1999 and June 2007, compared to the prior results from fractional curettage in each case.

Statistical analyses were performed with the SPSS for Windows software (version 13; SPSS Inc, Chicago, IL, USA). Data were evaluated as descriptive statistics. The correlation between variables was assessed with the Chi-square and Fisher's exact tests. Statistical significance was defined as a probability value (p-value) < 0.05.

Results

The present study included 41 cases with adenocarcinoma in both endocervical and endometrial specimens from fractional curettage. The mean age ($\pm$ SD) was 53.63 ± 10.69 years (range 29-76 years). All patients presented with abnormal vaginal bleeding. According to hysterectomy pathologic examination, 5 groups of cases were observed, 1) endometrial adenocarcinoma within uterine cavity, 2) endometrial adenocarcinoma within uterine cavity with lower uterine segment involvement, 3) endometrial adenocarcinoma within uterine cavity with cervical involvement, 4) cervical carcinoma with endometrial involvement and 5) cervical carcinoma with no endometrial involvement. The detail of each group is shown in Table 1. The most common finding was endometrial adenocarcinoma within uterine cavity with lower uterine segment involvement (36.6%), followed by endometrial adenocarcinoma within uterine cavity with cervical involvement (34.1%). One case showed no evidence of residual tumor in hysterectomy specimen, but the preoperative fractional curettage confirmed grade 3 endometrial adenocarcinoma in both endocervical and endometrial specimens.

Out of 41 cases which were diagnosed as endometrial adenocarcinoma with cervical involvement (stage 2); only 35 cases had available slides of fractional curettage specimens to review. The mean age ($\pm$ SD) was 54.25 ± 10.53 years (range 31-72 years). Most of the cases were well differentiated and demonstrated cervical stromal invasion. In the 35 cases with available fractional curettage specimens, 21 cases (60%) revealed adenocarcinoma in both endocervical and endometrial specimens from fractional curettage. The authors also compared the fractional curettage sample grade with

Table 1. Final pathologic diagnosis in hysterectomy specimens (total 41 cases)

Diagnosis	Number	Percent
Endometrial adenocarcinoma within uterine cavity	5	12.2%
Endometrial adenocarcinoma within uterine cavity with lower uterine segment involvement	15	36.6%
Endometrial adenocarcinoma within uterine cavity with cervical involvement	14	34.1%
Cervical carcinoma with endometrial involvement	3	7.3%
Cervical carcinoma with no endometrial involvement	3	7.3%
No evidence of residual tumor	1	2.5%

Table 2. Comparison of tumor grade between fractional curettage and hysterectomy specimens in endometrial carcinoma stage 2 (total 35 cases)

F&C	Hysterectomy			Total
	Grade 1	Grade 2	Grade 3	
Grade 1	15	3	3	21 (60%)
Grade 2	2	4	1	7 (20%)
Grade 3	1	1	5	7 (20%)
Total	18 (51.4%)	8 (22.9%)	9 (25.7%)	35 (100%)

hysterectomy grade as shown in Table 2. The overall concordance rate was 68.6% with the rate of 83.3% for grade 1, 50% for grade 2, and 55.6% for grade 3.

Discussion

Among diagnostic methods used in patients with endometrial carcinomas, fractional curettage is considered as a gold-standard procedure in preoperative evaluation and may guide the following management[5]. Although many recent studies recommended using other less traumatic alternative methods to preoperative evaluate in cases of endometrial carcinomas[2,4,6,7], fractional curettage is still used widely, especially in developing countries. According to FIGO 2000 recommendation in treatment of patients with endometrial carcinoma stage 2, radical hysterectomy with bilateral pelvic lymphadenectomy and selective node dissection should be performed in the cases with clinically overt cervical involvement[8]. A commonly found problem in management is the presence of adenocarcinoma in both endocervical and endometrial specimens from fractional curettage with no obvious clinically cervical lesion as some surgeons prefer to do more extensive surgery in such cases. In general, when a tumor was found in both endocervical and endometrial curettage specimens, the systematic reviews from tissue admission to microscopic reevaluation, including academic meeting for further management were necessary. Some histologic features and immunohistochemical study may help to discriminate the tumor origin. However, tissue in most curettage specimens was very small and quite hard to evaluate. In the present study, the authors found that the most common final pathological diagnosis from hysterectomy specimens in the patients who had adenocarcinoma in both endocervical and endometrial specimens from fractional curettage was endometrial adenocarcinoma within uterine cavity with lower uterine segment involvement. Only 14 cases (34.1%) had endometrial carcinoma with cervical involvement. These findings may be due to deep insertion of the curette into the lower uterine segment while doing the endocervical curettage. However, tumor involving the lower uterine segment was also suggested as a poor prognostic factor. Location of the tumor within the endometrial cavity is considered as an important factor in further treatment because a tumor low in the cavity can be expected to involve the cervix earlier than fundal lesions. The patients with disease of the lower uterine segment have a higher incidence of pelvic and periaortic lymph node metastases[4].

Frauenhoffer et al[9] studied the accuracy of endocervical curettage (ECC) in predicting cervical involvement by endometrial adenocarcinoma and found that 3 out of 5 women (60%) with tumor clearly present within the endocervical tissue of the ECC had cervical involvement in the hysterectomy specimens. They also reported that 13 out of 41 women (32%) with a tumor present but not contiguous with endocervical tissue within the ECC had a tumor in the cervix in hysterectomy specimens. In summary of all cases with a tumor present in ECC specimens regardless of definite tumor present within endocervical tissue or not, 34.78% (16 out of 46 cases) had cervical involvement in the hysterectomy specimens. The authors also found a similar result in the present study as 14 out of 41 cases (34.1%) with tumor in endocervical curettage specimens showed cervical involvement in subsequent hysterectomy specimens. The authors did not separate cases as obvious endocervical invasion and floaters because, according to the authors experience, the main problem in diagnosis and management was in the cases that had tumor floaters in endocervical specimen with no obvious endocervical tissue invasion. In addition, endocervical tissue involvement was clearly demonstrated in only small numbers of cases. Interestingly, when the authors conversely reviewed in hysterectomy cases that were diagnosed as endometrial adenocarcinoma with cervical involvement (stage 2), 21 out of 35 cases

(60%) revealed adenocarcinoma in both endocervical and endometrial specimens from fractional curettage. In contrast, Morimura et al[2] evaluated the value of pre-operative diagnostic procedures for cervical involvement in uterine corpus carcinoma and reported that endocervical curettage showed high sensitivity (90.9%) and specificity (88.9%). Based on the present study, only one-third of cases with a tumor in both endocervical and endometrial tissue from curettage actually revealed cervical involvement in the subsequent hysterectomy specimens. This result may reflect the worth of radical hysterectomy, which was commonly performed in such cases. However, further well-controlled prospective studies were needed to evaluate the role of radical hysterectomy. In the authors' opinion, fractional curettage was still a good and practical procedure to evaluate the cervical involvement, but the operators should be well-trained and pay attention to the steps of the procedure to decrease the chance of tissue contamination in both specimens.

In evaluation of cases with endometrial carcinoma stage 2, the authors found a rather high discrepancy rate (31.4%) in grades between F&C and hysterectomy specimens. Grade 1 had the highest concordance rate when compared with grade 2 and grade 3, but there was no statistical significance ($p = 0.646$). Previous published studies of the accuracy of tumor grades of endometrial cancer by curettage were varied in the association of concordance rate and tumor grade[10-15]. Obermair et al[10] reported the concordance rate of 78.8% for grade 1, while Wang et al[15] demonstrated only 20% concordance rate for grade 1 tumor. The discrepancy in grades between curettage and hysterectomy specimens may be associated with the amount of the tissue. The criteria of grading endometrial cancer were based on the proportion of solid growth area. In grade 2 and 3 tumor grading, the overall solid areas needed to be evaluated. In addition, some invasive grade 2 or 3 tumors had well differentiation on the superficial portions in the uterine cavity. If curettage mainly got these superficial parts, the diagnosis would be downgraded[14]. As hysterectomy specimens provided more amount of tissue to examine than curettage specimens, the discrepancy in grades were most likely to be high in tumor grade 2 and 3.

In conclusion, the most common final pathological diagnosis from hysterectomy specimens in the cases with adenocarcinoma in both endocervical and endometrial specimens from fractional curettage was endometrial adenocarcinoma within the uterine cavity with lower uterine segment involvement. Only 34.1% were endometrial carcinoma with cervical involvement. However, 60% of cases with endometrial carcinoma stage 2 revealed positive adenocarcinoma in both endocervical and endometrial specimens from fractional curettage.

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การศึกษาเปรียบเทียบผลทางพยาธิวิทยาระหว่างชิ้นเนื้อมะเร็งเยื่อบุที่ได้จากการขูดมดลูกและจากการผ่าตัดมดลูก

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วัตถุประสงค์*: เพื่อประเมินผลทางพยาธิวิทยาของชิ้นเนื้อที่ได้จากการผ่าตัดมดลูกในผู้ป่วยที่ได้รับการขูดมดลูกและพบมะเร็งเยื่อบุทั้งในชิ้นเนื้อที่ได้จากการขูดภายในปากมดลูกและโพรงมดลูก*

วัสดุและวิธีการ*: ทำการศึกษาในผู้ป่วย 41 ราย ที่ได้รับการขูดมดลูก และพบมะเร็งเยื่อบุทั้งในชิ้นเนื้อที่ได้จากการขูดภายในปากมดลูกและโพรงมดลูก จากนั้นได้รับการรักษาต่อด้วยการตัดมดลูก โดยไม่ได้รับการรักษาทางรังสีวิทยาหรือ เคมีบำบัด ก่อนผ่าตัดที่โรงพยาบาลจุฬาลงกรณ์ในช่วงปีพ.ศ. 2542-2550 โดยทบทวนและประเมินผลทางพยาธิวิทยาของชิ้นเนื้อทั้งที่ได้จากการขูดมดลูกและผ่าตัดมดลูก นอกจากนี้ยังได้ประเมินในรายที่วินิจฉัยเป็นมะเร็งเยื่อบุโพรงมดลูกระยะที่ 2 จากชิ้นเนื้อที่ได้จากการผ่าตัดมดลูก เปรียบเทียบกับผลทางพยาธิวิทยาที่ได้จากการขูดมดลูกจำนวน 35 ราย*

ผลการศึกษา*: ผู้ป่วยจำนวน 15 รายจากทั้งหมด 41 ราย (ร้อยละ 36.6) ที่ได้รับการขูดมดลูกและพบมะเร็งเยื่อบุทั้งในชิ้นเนื้อที่ได้จากการขูดภายในปากมดลูกและโพรงมดลูก ได้รับการวินิจฉัยจากการผ่าตัดมดลูกเป็นมะเร็งเยื่อบุโพรงมดลูกที่ลุกลามมายังโพรงมดลูกส่วนล่าง มีเพียงร้อยละ 34.1 เท่านั้น ที่เป็นมะเร็งเยื่อบุโพรงมดลูกที่ลุกลามมายังปากมดลูก ส่วนในรายที่วินิจฉัยเป็นมะเร็งเยื่อบุโพรงมดลูกระยะที่ 2 จากชิ้นเนื้อที่ได้จากการผ่าตัดมดลูกจำนวน 35 ราย พบว่าร้อยละ 60 ของผู้ป่วยพบมะเร็งเยื่อบุทั้งในชิ้นเนื้อ ที่ได้จากการขูด ภายในปากมดลูกและโพรงมดลูก*

สรุป*: ส่วนใหญ่ของผู้ป่วยที่พบมะเร็งเยื่อบุทั้งในชิ้นเนื้อที่ได้จากการขูดภายในปากมดลูกและโพรงมดลูกจะได้รับการวินิจฉัยจากการผ่าตัดมดลูกเป็นมะเร็งเยื่อบุโพรงมดลูกที่ลุกลามมายังโพรงมดลูกส่วนล่าง นอกจากนี้มีเพียงร้อยละ 60 ของผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกระยะที่ 2 ที่พบมะเร็งเยื่อบุทั้งในชิ้นเนื้อที่ได้จากการขูดภายในปากมดลูกและโพรงมดลูกจากการขูดมดลูกก่อนผ่าตัด*