Original Article

Incidence and Factors Associated with Inadequate Endometrial Tissue for Pathological Evaluation from Uterine Curettage in Abnormal Uterine Bleeding at Udon Thani Hospital

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Objective: To study the incidence and factors associated with inadequate endometrial tissue for pathological evaluation from uterine curettage in patients with abnormal uterine bleeding (AUB) at Udon Thani Hospital.

Materials and Methods: The electronic medical records of women aged 35 years and older with AUB that underwent endometrial curettage in a regional hospital between October 2018 and November 2019 were retrospectively reviewed. The incidence of inadequate endometrial tissue for pathological evaluation was studied. Multiple logistic regression analysis was performed to determine the factors associated with inadequate curettage.

Results: Three hundred fifty-two patients with AUB that underwent endometrial tissue curettage and had complete medical records were included in the present study. The mean age was 48.09±8.01 years. The incidence of inadequate endometrial tissue for pathological evaluation was 23.30% (95% CI 18.98 to 28.07). Postmenopausal status (adjusted OR 3.80, 95% CI 1.93 to 7.50), the low experience of the clinician (adjusted OR 2.20, 95% CI 1.15 to 3.87), and the uterine cavity length measured by uterine sound (adjusted OR 0.66 for each 1 cm increment, 95% CI 0.54 to 0.80) were significant factors associated with inadequate tissue for pathological evaluation.

Conclusion: The incidence of inadequate endometrial tissue for pathological evaluation from endometrial curettage was one-quarter of all cases. The associated factors of inadequate endometrial tissue included postmenopausal status, inexperience operators, and shorter uterine length.

Keywords: Endometrial tissue curettage; Insufficient endometrial tissue; Sampling adequacy; Endometrial carcinoma; Abnormal uterine bleeding

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Abnormal uterine bleeding (AUB) refers to abnormal in quantity, duration, or schedule in menstrual bleeding. It is a common symptom accounting for one-third of gynecological outpatient visits[1]. Endometrial curettage is one of the standard methods for AUB investigation in women older than 40 years with the goal of excluding malignancy[2]. According to the ACOG guidelines (2013), endometrial sampling should be performed on patients older than 45 years or younger than 45 years old with a history of unopposed estrogen exposure, failed medication, and persistent AUB[3]. In the present study center, women aged 35 years and older with AUB were advised for inpatient endometrial pathological evaluation[4]. Unfortunately, from the previous studies, the endometrial pathology could not be obtained in 2.01% to 29.82% cases due to inadequate tissue for diagnosis[5-13]. Therefore, this causes the need for subsequent management and the anxiety of the patients. The factors associated with inadequate tissue from endometrial curettage included postmenopausal status, and endometrial thickness[4,7,14,15].

Subsequent management of women with inadequate tissue for pathological evaluation include fractional curettage, hysterectomy, ultrasound scan follow-up, and no further investigation[5,11,16]. The subsequent investigations found that 4.32% to 9.51% of the women had a malignant result[9,11,16].

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In the present study, the authors evaluated the incidence and factors associated with inadequate tissue from endometrial curettage in women with AUB treated in Udon Thani Hospital, Thailand. Subsequent management of women with inadequate tissue for pathological evaluation were also studied.

Materials and Methods

The present study was approved by the Udon Thani Hospital Research Ethics Committee for research with human subjects, Udon Thani Hospital (No. 64/2562). The authors reviewed the electronic medical records of patients. The inclusion criteria were the patients that underwent endometrial curettage between October 2018 and November 2019 at the Department of Obstetrics and Gynecology, Udon Thani Hospital, Thailand. The exclusion criteria were the cases with no pathological data. The present study was conducted according to the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines.

Gynecologists, residents, interns or externs, performed all endometrial tissue samples. Pathology and endometrial thickness evaluated by transabdominal or transvaginal ultrasonography before the sampling were recorded. In cases of repeated curettage from the previous procedures which resulted in inadequate tissue sampling, both initial and repeated curettage were included in the present study. The endometrial tissue was obtained by fractional curettage. In Udon Thani Hospital, women's aged 35 years or older with AUB were advised for inpatient endometrial pathological evaluation[4]. The curettage procedure was done under intravenous analgesia, without ultrasound guidance. A tenaculum was used for cervical grasping, endocervical curettage was done then a uterine sound was inserted for uterine cavity measurement before the endometrial curettage was performed. The endocervical and endometrial tissues were fixed by formaldehyde and were sent for pathological examination.

The pathological slides were examined and interpreted by a pathologist. In general, there was no consensus criteria of inadequate or suboptimal tissue. A report of an inadequate tissue meant suboptimal, or no malignancy features seen in a scanty specimen tissue[17]. In the present study, the inadequate tissue for pathological diagnosis was a lack of any intact tissue fragments containing both glands and stroma.

Statistical analysis

The sample size was calculated using the formula for the descriptive study. The proportion of inadequate endometrial sampling was 0.29[6] and a 0.05 acceptable error was used for the calculation. The value of α was 0.05 and the power was 80%. The calculated sample size was 317 cases. Three hundred fifty-two cases between October 2018 and November 2019 were used.

The patients' characteristics were presented as number, percentage, range, or mean ± standard deviation. The patients with adequate and inadequate tissue sampling groups were compared using a linear regression analysis for continuous variables. Logistic regression analysis was used for categorical variables. The odds ratio and adjusted odds ratio (OR) with a 95% confidence interval (CI) were calculated for the magnitude of effect. A p-value ≤0.1 from bivariable analysis was used for variable selection to multivariable model. Statistical analysis was performed using Stata, version 13 (StataCorp LP, College Station, TX, USA). A p-value of less than 0.05 was considered statistically significant.

Results

The electronic medical records of 352 women that underwent endometrial curettage were reviewed. Overall, the mean age of the patients was 48.09±8.01 years. The postmenopausal status was about one-fifth or 72 of the 352 women. All patients were evaluated for associated conditions by ultrasonography before uterine curettage. Myoma uteri and adenomyosis were detected in 38.35% and 7.10% of the cases, respectively. Endometrial thickness, by ultrasonography, was recorded in 101 women (28.69%) and uterine sound measurement before the procedure was recorded in 319 women (90.63%).

Inadequate endometrial tissue for pathological evaluation was noted in 82 women (23.30%, 95% CI 18.98 to 28.07). The results of bivariate analysis, to assess for association between individual clinical characteristics and inadequate endometrium for pathological evaluation, are given in Table 1. The women in the inadequate tissue group were significantly older (mean 51.79±8.45 vs. 46.97±7.54, $p<0.01$) and had a shorter uterine cavity length determined by uterine sound (mean 6.81±2.28 vs. 8.08±1.55, $p<0.01$) than in the other group. Inadequate endometrial tissue was found in 17.86% of premenopause and 44.44% of postmenopause ($p<0.01$).

From the bivariate analysis, age (OR 1.07, 95% CI 1.04 to 1.11, $p<0.01$) and postmenopausal status (OR 3.68, 95% CI 2.11 to 6.42, $p<0.01$) were

Table 1. Baseline characteristics

Variables	Total (n=352)	Adequate tissue sampling (n=270)	Inadequate tissue sampling (n=82)	p-value
Age (year); mean±SD	48.09±8.01	46.97±7.54	51.79±8.45	<0.01*
BMI (kg/m^2); mean±SD	25.84±4.84	25.80±5.03	25.97±4.84	0.77
Previous vaginal birth; n (%)				0.94
No	89	68 (76.40)	21 (23.60)	
Yes	263	202 (76.81)	61 (23.19)	
Menopausal status; n (%)				<0.01*
Premenopause	280	230 (82.14)	50 (17.86)	
Postmenopause	72	40 (55.56)	32 (44.44)	
Previous uterine scar; n (%)				0.28
No	277	216 (77.98)	61 (22.02)	
Yes	75	54 (72.00)	21 (28.00)	
History of inadequate tissue (repeated curettage); n (%)				0.15
No	333	258 (77.48)	75 (22.52)	
Yes	19	12 (63.16)	7 (36.84)	
Associated conditions with AUB; n (%)				
No	192	140 (72.92)	52 (27.08)	Reference
Myoma uteri	135	109 (80.74)	26 (19.26)	0.10
Adenomyosis	25	21 (84.00)	4 (16.00)	0.24
Endometrial thickness (cm); mean±SD	1.19±0.76 (n=101)	1.24±0.82 (n=77)	1.04±0.51 (n=24)	0.27
Operator; n (%)				0.06
Staff & resident	203	163 (80.30)	40 (19.70)	
Intern & extern	149	107 (71.81)	42 (28.19)	
Uterine cavity length (cm); mean±SD	7.80±1.81 (n=319)	8.08±1.55 (n=249)	6.81±2.28 (n=70)	<0.01*

BMI=body mass index; AUB=abnormal uterine bleeding

* Statistically significant (p<0.05)

associated with increased risk of inadequate tissue sample by endometrial curettage. An increasing uterine cavity sound length measurement decreased the likelihood of inadequate tissue sampling (OR 0.61, 95% CI 0.51 to 0.74, p<0.01).

Multivariable analysis revealed postmenopausal status (adjusted OR 3.80, 95% CI 1.93 to 7.50), the experience of the medical clinician (adjusted OR 2.20, 95% CI 1.18 to 4.08), and uterine cavity length (adjusted OR 0.66, 95% CI 0.54 to 0.80 per each 1 cm increment) were significantly associated with inadequate tissue results. Bivariable and multivariable logistic regression analysis are presented in Table 2.

The histologic results were normal endometrium with proliferative and secretory phase, benign endometrial pathology with polyp, atrophy, and disordered, endometrial hyperplasia without atypia, premalignancy, malignancy, and inadequate tissue in 178 (50.57%), 67 (19.03%), 3 (0.85%), 4 (1.14%), 18 (5.11%), and 82 (23.30%) cases, respectively. The pathologies of the premalignancy were endometrial hyperplasia with atypia in three cases and CIN 3 in one case, while the pathologies of malignancy were adenocarcinoma in 15 cases, squamous cell carcinoma in two cases, and clear cell carcinoma in one case.

Subsequent management of women with inadequate tissue for pathological evaluation were repeat fractional curettage in six cases, hysterectomy in 20 cases, hysteroscopy in two cases, ultrasound scan follow-up in 27 cases, and no further investigation in 25 cases. Two patients did not come for follow up treatment. The histological results from the repeated investigation, which was repeat factional curettage, hysterectomy, and hysteroscopy, were normal endometrium, benign endometrial pathology, malignancy (endometriod type grade 2) and inadequate tissue in 11 (39.28%), 15 (53.57%), 1 (3.57%), and 1 (3.57%) case, respectively.

Discussion

In the present study, 23.30% of 352 women that underwent endometrial curettage had inadequate

Table 2. Bivariable and multivariable logistic regression analysis to identify factors associated with inadequate tissue sampling

Variables	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Age (year)	1.07 (1.04 to 1.11)	NA
BMI (kg/m^2)	1.00 (0.96 to 1.06)	NA
Previous vaginal birth	0.98 (0.56 to 1.72)	NA
Postmenopause	3.68 (2.11 to 6.42)	3.80 (1.93 to 7.50)
History of inadequate tissue (repeated curettage)	2.01 (0.76 to 5.28)	NA
Previous uterine scar	1.38 (0.77 to 2.46)	NA
Operator		
Staff & resident	Reference	Reference
Intern & extern	1.60 (0.97 to 2.63)	2.20 (1.18 to 4.08)
Uterine cavity length by uterine sound (cm)	0.61 (0.51 to 0.74)	0.66 (0.54 to 0.80)

BMI=body mass index; CI=confidence interval; NA=not applicable

Adjusted for postmenopause, conditions related with abnormal uterine bleeding, operator, endometrial thickness, uterine cavity length by uterine sound. Age was not included in the adjusted model because of multicollinearity.

tissue for a definitive pathological diagnosis. The present study result is similar to the previous published studies[6,9,10,18] that reported the rate of inadequate tissue sampling as being between 21.30% and 29.80%, although other studies reported the lower range as between 2.01% and 8.70%[5,7,11-13]. The wide variance of inadequate tissue rates may be the result of different study sample sizes. The small sample size caused the wide confidence interval in the incidence of inadequate endometrial tissue sample.

Since the rate of inadequate tissue sampling is high in the authors center, a revision of curettage technique and collection method should be conducted. Moreover, ultrasonographic monitoring of canula tip during operation might be used in the case of patients deemed to be at a high risk of inadequate tissue sampling, such as postmenopausal status, short uterine length measured by uterine sound, or difficult operation, to ensure the correct position of canula for endometrial sampling.

The present study found that postmenopausal status was associated with an increased risk of inadequate tissue (adjusted OR 3.80, 95% CI 1.93 to 7.50), which is in accordance with other studies (OR 3.60, 95% CI 1.84 to 7.05 and OR 4.49, 95% CI 2.49 to 8.09, p=0.001)[6,14]. The higher rate of inadequate tissue in postmenopausal status might be due to atrophic endometrium having only minimal tissue, mucous, or blood clot on endometrial biopsy[19]. The age of the patient from bivariate analysis was also significant, which was different from a prior study[14], but the age was not included in the multivariate analysis due to the multicollinearity problem with the menopause.

The present study results demonstrated that short uterine cavity length measured by uterine sound was an independent factor associated with an increased risk of inadequate tissue sampling. The reason might be that a representative endometrial tissue should be sampled from the fundus to the endocervical canal. A shorter uterine cavity length, which was associated with the cesarean section scar defect, extreme uterine flexion, or an intracavitary fibroid[20], can obstruct the cavity and mislead the operator about the cavity length. Therefore, the shorter device insertion into the uterine cavity, the higher the rate of inadequate tissue is expected.

In the current study, obtained tissue by intern and extern was at a significantly higher rate of being inadequate than when gynecologic staff and resident performed the same procedure (adjusted OR 2.20, 95% CI 1.18 to 4.08). Concordant with Gordon and Westgate (1999), they reported that the chance of success at obtaining an adequate tissue in senior house officers was better than general practitioners (p=0.02)[15]. Furthermore, Adambekov et al[21] reported that the expertise of provider was a significant factor of failure rate in endometrial sampling procedure (OR 9.15, 95% CI 2.49 to 33.69). Because of the surgical skills training program, such as workshop and their experience from training requirement, gynecologic staff and resident had better skills and technical expertise[22]. Although another study suggested that the chance of inadequate tissue sampling was not related to the clinician's experience (adjusted OR 1.57, 95% CI 0.90 to 2.77, p=0.11)[9].

The main limitation of the present study was its retrospective nature; thus, data were not recorded. Another limitation might be that information bias could have occurred because the pathological slides

were examined and interpreted by three boarded pathologists. However Breijer et al (2016) reported that a structured reassessment of endometrial biopsy samples classified as inconclusive due to insufficient material did not change the conclusion[23]. Therefore, the present study pathological results should be reliable.

Conclusion

The incidence of inadequate endometrial tissue for pathological evaluation from endometrial curettage was approximately one-quarter of all cases. The associated factors of inadequate endometrial tissue were postmenopausal status, inexperience operators, and shorter uterine length.

What is already known on this topic?

Inadequate endometrial tissue for pathological evaluation from uterine curettage in AUB is a frequent problem that causes difficulties in the diagnosis and treatment.

What this study adds?

The incidence of inadequate endometrial tissue for pathological evaluation from endometrial curettage was one-quarter of all cases. These were associated with postmenopausal status, operator experience, and shorter uterine cavity length measured by uterine sound during procedure.

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Availability of data and material

All available anonymized data can be obtained by contacting the corresponding author until five years after publication.

Conflicts of interest

None of the authors has any conflict of interest relative to this work.

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