

Diagnostic Accuracy of Hysteroscopic Scoring System in Predicting Endometrial Malignancy and Atypical Endometrial Hyperplasia

Bhukya Harika, Murali Subbaiah, Dilip Kumar Maurya

Department of Obstetrics and Gynaecology, JIPMER, Puducherry, India

ABSTRACT

Aims and Objectives: The aim of this study was to determine the diagnostic accuracy of a hysteroscopic scoring system in predicting endometrial cancer and endometrial hyperplasia with atypia. **Materials and Methods:** This is a prospective study involving 95 peri and postmenopausal women with abnormal uterine bleeding who underwent hysteroscopic-guided endometrial biopsy. After the calculation of hysteroscopic score, biopsy was obtained and sent for histopathological examination. Hysteroscopic diagnosis of carcinoma endometrium was made when the total score was ≥ 16 and a score ≥ 7 supported a diagnosis of endometrial hyperplasia with atypia. **Results:** Out of the 95 women, 46 (48.4%) women had postmenopausal bleeding. The mean age of women was 50.4 ± 10.3 years. Eight women were diagnosed to have endometrial cancer and eight had endometrial hyperplasia with atypia on histopathological examination. Using a hysteroscopy score ≥ 16 , the sensitivity and specificity were found to be 62.5% and 90.8%, respectively, for diagnosing endometrial cancer. Hysteroscopy score ≥ 9 was found to be a better cutoff for diagnosing endometrial cancer using Youden index. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for diagnosing endometrial cancer with score ≥ 9 was 100%, 67.8%, 22.2%, and 100%, respectively. The sensitivity, specificity, PPV, and NPV for diagnosing endometrial hyperplasia with atypia with score ≥ 7 was found to be 75%, 58.6%, 14.3%, and 96.2%, respectively. **Conclusion:** The hysteroscopic scoring system has a good diagnostic performance when a cutoff score ≥ 9 is used in predicting endometrial cancer. However, the scoring system has lower diagnostic accuracy in predicting endometrial hyperplasia with atypia.

KEYWORDS: *Diagnostic hysteroscopy, endometrial cancer, endometrial hyperplasia with atypia, hysteroscopic scoring*

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INTRODUCTION

Endometrial malignancy is one of the major causes of cancer-related mortality and morbidity in women.^[1] Although it predominantly affects postmenopausal women, up to 15%–20% of cases may be detected in premenopausal women.^[2] Hysteroscopic-guided endometrial biopsy is currently considered the gold standard in diagnosing endometrial pathology.^[3] It is considered superior to blind dilation and curettage, which can miss focal lesions in the endometrium.^[4]

Endometrial cancer can be suspected based on hysteroscopic appearance of the lesions.^[5,6] Hysteroscopic

appearances of endometrial malignancy and hyperplasia have been described in several studies.^[7-10] As hysteroscopy is a subjective diagnostic test, its accuracy depends on the experience of the physician performing it.^[11] A hysteroscopy-based scoring system has been recently described by Ianieri *et al.*^[12] This scoring system may be particularly useful to less experienced physicians

Address for correspondence: Dr. Murali Subbaiah, Department of Obstetrics and Gynaecology, WCH Block, JIPMER, D. Nagar, Puducherry - 605 006, India.
E-mail: muralidraiims@gmail.com

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in diagnosing endometrial cancer and hyperplasia. This scoring system has not been evaluated in any prospective study. The aim of this prospective study was to evaluate the diagnostic accuracy of this scoring system in predicting endometrial cancer and endometrial hyperplasia with atypia.

MATERIALS AND METHODS

This is a prospective study conducted in the Department of Obstetrics and Gynecology at a Tertiary Care Hospital in India from January 2018 to July 2020. The study was approved by the Institute Ethics Committee for human studies (JIP/IEC/2018/0146). Informed consent was obtained from all the patients. Women ≥ 18 years with abnormal uterine bleeding (AUB) who required endometrial biopsy were included in the study. Exclusion criteria of the study were pregnancy, acute pelvic inflammatory disease, and diagnosis of pyometra on transvaginal ultrasound. Diagnostic hysteroscopy was done in the operation theater using a 2.9 mm rigid hysteroscope (Karl Storz, Germany) without any anesthesia. Vaginoscopic approach was used, and intrauterine pressure was maintained under 80 mmHg using a hysteromat. Vaginal misoprostol (200 μg) was instilled 2 h before the procedure. All the procedures were performed by an experienced consultant (with experience of diagnostic hysteroscopy in more than 500 women with AUB)^[13] who was blinded to the imaging findings including endometrial thickness. Hysteroscopic findings were documented, and the hysteroscopic score was calculated as described by Ianieri *et al.*^[12] The scoring system includes eight components: atypical vessels (score 7), widespread and irregular endometrial thickening (score 2), dilated glandular orifices (score 2), crumbling of endometrial neoplasm (score 6), multiple endometrial polyps (score 2), irregular aspect of the polyp (score 3), growth of cerebroid and arborescent aspects (score 14), and irregular endometrial color (score 4). The total score was calculated by adding all these scores. Hysteroscopic-guided biopsy was subsequently obtained using a 5F hysteroscopic biopsy forceps and sent for histopathological examination. Hysteroscopic diagnosis of carcinoma endometrium was made when the total score was ≥ 16 and a score ≥ 7 supported a diagnosis of endometrial hyperplasia with atypia.^[12]

Statistical analysis

Statistical testing was performed using STATA software version 13.1 (STATA Corp., Texas USA). Continuous variables are presented as mean with the standard deviation and categorical variables as percentages. The diagnostic ability was assessed by calculating the sensitivity, specificity, positive predictive value (PPV),

and negative predictive value (NPV). The area under the curve was assessed by receiver operating characteristic curve analysis, to test the ability of hysteroscopic scoring in identifying women with endometrial cancer and atypical endometrial hyperplasia.

Sample size

Assuming an α error of 5% with 95% confidence interval and expecting a sensitivity of 95% for diagnosing carcinoma endometrium with an absolute precision of 10%, the minimal sample size was calculated to be 95. This was with an assumption of the incidence of carcinoma endometrium to be 10% in the study population.

RESULTS

A total of 98 women with AUB were assessed for eligibility and included in the study. Three women were excluded because of imaging findings of pyometra. The mean age of women who underwent hysteroscopy was 50.4 ± 10.3 years. Ninety-three (97.9%) of them had a parity ≥ 2 . The mean BMI was 24.1 ± 2.9 kg/m². Forty-six (48.4%) women had postmenopausal bleeding. The rest were premenopausal with AUB. The mean endometrial thickness in postmenopausal women was 9.49 ± 8.13 mm. There were no complications during hysteroscopy in any patient. Forty-two women (44.2%) had a score ≥ 7 and were suspected to have atypical endometrial hyperplasia; 13 women (13.7%) had a hysteroscopic score ≥ 16 and were suspected to have endometrial cancer. The final histopathological findings in the 95 women who underwent hysteroscopy are given in Table 1. Eight women (8.4%) were diagnosed to have endometrioid adenocarcinoma (Grade 1 in 5; Grade 3 in 3 women).

Using a cutoff ≥ 16 for diagnosing endometrial cancer, the sensitivity, specificity, PPV, and NPV of hysteroscopic scoring were found to be 62.5%, 90.8%, 38.5%, and 96.3%, respectively. Because of low sensitivity with this cutoff, Youden index was calculated to determine a better cutoff for diagnosing endometrial carcinoma. A cutoff score ≥ 9 had high sensitivity, with relatively good

Table 1: Histopathological findings in 95 women who underwent hysteroscopic guided biopsy

Histopathological report	n=95, n (%)
Atrophic endometrium	6 (6.3)
Proliferative endometrium	44 (46.3)
Secretory endometrium	14 (14.7)
Nonatypical endometrial hyperplasia	13 (13.7)
Atypical endometrial hyperplasia	8 (8.4)
Endometrial cancer	8 (8.4)
Endometrial polyp	2 (2.1)

specificity when compared to other scores as given in Table 2. The Youden index J (0.678) for this cutoff was the highest. The diagnostic accuracy of hysteroscopic scoring in detecting endometrial cancer using a cutoff score ≥ 9 is given in Table 3. The diagnostic accuracy of hysteroscopic scoring in diagnosing atypical endometrial hyperplasia is also given in Table 3.

DISCUSSION

In this study, a hysteroscopic scoring system was prospectively evaluated in 95 women with AUB. The sensitivity, specificity, PPV, and NPV for diagnosing endometrial cancer with score ≥ 9 were 100%, 67.8%, 22.2%, and 100%, respectively. Using score ≥ 16 for diagnosing endometrial cancer resulted in poor sensitivity (62.5%). The sensitivity, specificity, PPV, and NPV for diagnosing endometrial hyperplasia with atypia (score ≥ 7) were found to be 75%, 58.6%, 14.3%, and 96.2%, respectively.

Taking endometrial biopsy under hysteroscopic view has advantages over blind biopsy. Dilation and curettage done blindly can miss focal lesions. On the other hand, hysteroscopic appearance permits an accurate macroscopic diagnosis of lesions and directed biopsy. A careful analysis of surface, color, vascular arrangement, and general appearance allows estimating the risk of malignancy and identifying sites for taking biopsies.

The hysteroscopic scoring system used in this study was developed to diagnose endometrial hyperplasia, atypical endometrial hyperplasia, and endometrial carcinoma.^[12] The authors retrospectively reviewed the videos of diagnostic hysteroscopies done in patients with normal endometrium, endometrial hyperplasia, and carcinoma. They evaluated several variables and developed this scoring system using an ordinal multivariate analysis. They hypothesized the scoring system to have a sensitivity and specificity of 95.4% and 98.2%, respectively, for endometrial carcinoma using a cutoff of score ≥ 16 . The sensitivity and specificity were predicted to be 63.3% and 90.4%, respectively, for detecting atypical endometrial hyperplasia with a cutoff of score ≥ 7 . The results of our prospective study indicate that this scoring system has a higher sensitivity (75%) but lower specificity (58.6%) in diagnosing atypical endometrial hyperplasia. However, the sensitivity of the scoring system (62.5%) with score ≥ 16 was found to be very low in our study for diagnosing endometrial carcinoma. A lower cutoff (Score ≥ 9) was found to have better diagnostic accuracy with 100% sensitivity and NPV for diagnosing endometrial carcinoma. However, at this cutoff, the specificity (67.8%) was lower.

Table 2: Accuracy of hysteroscopic score at various cut off values using Youden index for diagnosing endometrial cancer

Hysteroscopic score cut off \geq	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio
2	100	36.8	1.5	0
4	100	54.0	2.17	0
7	100	60.9	2.55	0
8	100	62.1	2.6	0
9	100	67.8	3.1	0
11	87.5	77.0	3.8	0.16
12	75	79.3	3.6	0.31
13	62.5	82.8	4.3	0.30
14	62.5	86.2	4.5	0.43
15	62.5	89.7	6.0	0.41
16	62.5	90.8	6.7	0.41
19	62.5	94.3	10.8	0.39
20	62.5	97.7	27.1	0.38
22	62.5	98.9	54.37	0.37
24	50.0	98.9	43.4	0.50
26	50.0	100	1	0.50

Table 3: Diagnostic accuracy of hysteroscopic scoring in detecting endometrial cancer and atypical endometrial hyperplasia

	Percentage	95% CI	
		Lower	Upper
Diagnostic accuracy in detecting endometrial cancer with hysteroscopy score ≥ 9			
Sensitivity	100	63.1	100
Specificity	67.8	56.9	77.4
PPV	22.2	10.1	39.2
NPV	100	93.9	100
Positive likelihood ratio	3.1	2.29	4.22
Negative likelihood ratio	0		
ROC (AUC)	0.92	0.83	1
Diagnostic accuracy in detecting atypical endometrial hyperplasia with hysteroscopy score ≥ 7			
Sensitivity	75	34.9	96.8
Specificity	58.6	47.6	69.1
PPV	14.3	5.4	28.5
NPV	96.2	87	99.5
Positive likelihood ratio	1.8	1.13	2.9
Negative likelihood ratio	0.43	0.13	1.42
ROC (AUC)	0.67	0.52	0.81

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

We found that two components of the hysteroscopic scoring system with the highest scores (growth of cerebroid and arborescent aspects – score 14; crumbling of endometrial neoplasm score 6) were normal in many

women with early-stage endometrial carcinoma. This could explain the low sensitivity to diagnose endometrial carcinoma with score ≥ 16 .

Endometrial hyperplasia is one of the common causes of AUB and can lead to endometrial carcinoma if left untreated. In 2014, the WHO suggested a new classification of endometrial hyperplasia: (1) nonatypical endometrial hyperplasia and (2) atypical endometrial hyperplasia or endometrial intraepithelial neoplasia.^[14] Up to 59% of patients with atypical endometrial hyperplasia may have coexistent invasive endometrial carcinoma.^[15] Hysteroscopic scoring system was found to have good sensitivity (75%) and NPV (96.2%) in detecting atypical endometrial hyperplasia in our study. Ianieri *et al.* have suggested a hysteroscopy score ≥ 2 to diagnose nonatypical endometrial hyperplasia with a predicted sensitivity of 48.7%.^[12] Because of this poor sensitivity, we did not use this scoring system to diagnose nonatypical endometrial hyperplasia in this study. Further, they have a very low risk of coexistent invasive carcinoma and will regress once the endocrine milieu has been normalized.^[14]

Dueholm *et al.* developed another hysteroscopic scoring system for use in women with postmenopausal bleeding.^[16] They evaluated visual patterns in hysteroscopy in women with postmenopausal bleeding who had an endometrium thickness >5 mm and developed a hysteroscopic cancer scoring using multivariate logistic regression. It includes seven components: irregular surface, papillary projections, “candy floss” necrosis, surface necrosis, white hyperintense spots, irregular distribution of irregular vessels, and irregular branching vessels. A score of 1 is given for each component. A total score ≥ 3 suggests a diagnosis of endometrial cancer with a sensitivity of 89% with a specificity of 92%. No prospective studies have evaluated this scoring system. We did not use this scoring system in our study as we had both premenopausal and postmenopausal women in our cohort.

Strengths of the study

This is the first prospective study to evaluate a hysteroscopic scoring system. To eliminate observer bias, the consultant who did hysteroscopy was blinded to imaging findings such as endometrial thickness.

Limitations of the study

The demerit of the study is its relatively small sample size. Further, the reproducibility of the score and interobserver bias was not assessed. This could have been done by video recording of the procedure and calculation of hysteroscopic score by another consultant.

CONCLUSION

The hysteroscopic scoring system displayed a good diagnostic performance when a cutoff score ≥ 9 was used in predicting endometrial malignancy. However, the scoring system had lower diagnostic accuracy in predicting atypical endometrial hyperplasia.

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Conflicts of interest

There are no conflicts of interest.

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