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Association of endometrial thickness with lesions in postmenopausal asymptomatic women: risk factors and diagnostic thresholds

Wei Liu[1*] and Wenpei Bai[1]

Abstract

Purpose This study aimed to explore the relationship between endometrial thickness and lesions in asymptomatic postmenopausal women and identify diagnostic thresholds for lesions.

Methods A total of 279 postmenopausal asymptomatic women aged 40 years or older with endometrial thickness ≥ 4 mm were retrospectively selected in our hospital, from January 2018 to June 2023, there were 33 cases's operations which were failed due to the cervical stenosis, 8cases who used hormone replacement therapy within the past year, 7 cases with hysteromyoma that affect the shape of the uterine cavity line, and 5cases's hysteroscopic tissue acquisition were failed. Finally, A retrospective study was conducted on the endometrial thickness of 226 postmenopausal asymptomatic women measured by transvaginal ultrasound and those with thickening were subjected to hysteroscopy and pathological examination of endometrial biopsy tissues, and were divided into a normal group (80 cases), benign lesion group (143 cases), and malignant lesion group (3 cases) according to the pathology results. The endometrial thickness results measured by vaginal ultrasound were compared with the endometrial histopathologic results.

Results 1. There were 226 cases in all, including 117 cases of endometrial polyps (51.7%);2. BMI ≥ 25 kg/m^2 is a risk factor to postmenopausal asymptomatic women. OR = 1.132 $P < 0.05$,95%CI (1.039,1.234);3. endometrial thickness ≥ 4 mm is a risk factor to postmenopausal asymptomatic women. OR = 7.927 $P < 0.05$, 95%CI (3.015,20.839);4. The results of the Receiver Operating Characteristic (ROC) analysis of the subjects show that the optimal cut-off value for screening endometrial pathology by endometrial thickness in asymptomatic postmenopausal women is 5.65 mm, and its area under the curve for identifying endometrial lesion was 0.679.

Conclusion 1. The main cause of endometrial thickening after menopause was endometrial polyps (51.7%). 2. Overweight (BMI ≥ 25 kg/m^2) is a risk factor for asymptomatic endometrial thickening after menopause. 3. endometrial thickness ≥ 4 mm is a risk factor to postmenopausal asymptomatic women. 4. The appropriate diagnostic threshold of vaginal ultrasound diagnosis is 5.65 mm in asymptomatic postmenopausal women.

Keywords Menopause, Asymptomatic, Endometrial thickening, Endometrial lesions

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Cancer of the endometrium is the most common type of gynecologic cancer in developed country [1]. It prevalents among postmenopausal women. The classical symptom is that vaginal bleeding and thickening of the endometrium. In the year 2006, American Committee on Gynecologic (ACOG) Practice has proposed that the transvaginal ultrasonoscopy of endometrial thickness in postmenopausal women is Uniform, continuous, and the thickness is less than or equal to 4 mm. In the year 2018, ACOG draw a conclusion that vaginal bleeding is the presenting sign in more than 90% of postmenopausal women with endometrial carcinoma. Transvaginal ultrasonography is a reasonable alternative to endometrial sampling as a first approach in evaluating a postmenopausal woman with an initial episode of bleeding [2]. Aslo, Approximately 15% of postmenopausal women with endometrial carcinoma are asymptomatic. As health awareness and the use of transvaginal ultrasound increase, asymptomatic postmenopausal endometrial thickening is more frequently detected, but so far there is no consensus on the treatment of this disease. Based on the above situation, we conducted this study, hoping to provide a reference for clinical decision.

Data and methods

Subjects

A total of 279 postmenopausal asymptomatic women with endometrial thickness ≥ 4 mm were retrospectively selected from the gynecological outpatient department of our hospital from January 2018 to June 2023. A total of 226 cases were finally included in the study.

Inclusion criteria

① Age ≥ 40 years with primary amenorrhea for more than 1 year without a pharmacological explanation; ② No symptoms of postmenopausal bleeding; ③ Vaginal ultrasound showing a double-layer endometrial thickness ≥ 4 mm.

Exclusion criteria

① Use of hormone replacement therapy within the past year; ② Patients with hysteromyoma that affect the shape of the uterine cavity line; ③Hysteroscopic tissue acquisition failed.

Research methods

Vaginal ultrasound method of endometrial thickness

None of the vaginal ultrasound technicians knew the grouping beforehand. Endometrial thickness was measured by transvaginal ultrasound, measuring the distance between the basal layers of the anterior and posterior layers of the endometrium in the sagittal plane of the uterus. we provided to technicians to standardize measurements. The endometrial thickness was recorded in 1 mm increments.

Equipment and instruments

Hysteroscope and related equipment manufactured by Olympus (Japan) has been used in all patients enrolled in this study, with an outer sheath diameter of 4.5 mm for the diagnostic hysteroscope and 8.5 mm for the resectoscope. The uterine cavity was distended using 5% glucose solution (5% mannitol for diabetic patients). The uterine distension pressure was set to 80 mmHg, with an irrigation flow rate of 260–280 ml/min. The cutting output power was set to 80 W, and the coagulation (electrocautery) output power was set to 60 W. All data Settings are derived from《an atlas of hysteroscopy》3rd edition.

Hysteroscopy and endometrial biopsy method

After completing the vaginal ultrasound examination in the gynecological outpatient department, all patients with endometrial thickness ≥ 4 mm were admitted to the inpatient department, and the longest interval from ultrasound examination to hospitalization was 48 h. After admission, the medical history was collected by the resident doctor in detail, and the physical examination was carried out on admission, including height, weight, temperature, pulse, respiration, and blood pressure. After assessing no myocardial infarction, severe hepatorenal insufficiency, upper respiratory tract infection, allergy, asthma, hemophilia, and severe anemia contraindication for hysteroscopic, hysteroscopic preoperative preparation was performed. After sterilizing the vulvois, the speculum was opened, then disinfecting vagina for three times, and the uterine bougie was put in. If placement failed, the cervical surface was anesthetized with oxybuprocaine hydrochloride gel for 2 min instantly to loosen the cervix, and then a No. 14 catheter was placed 2 cm through the cervical canals into the uterine cavity, and the other end of it was retained in the vagina until the next day of surgery. Because oxybuprocaine hydrochloride gel is a lipid local anesthetic used primarily for surface anesthesia and has no potential impact on our final measurements. If replacement of the catheter fails, the patients will receive other forms of treatment, such as go to another hospital. A total of 33 patients had failed in the preoperative preparation phase.

The procedure was performed under general anesthesia and monitored by transabdominal ultrasound. A comprehensive evaluation of cervical canal shape, uterine cavity morphology, endometrial thickness, color, location and size of intrauterine lesions, presence of abnormal blood vessels, and lesion texture was performed. After hysteroscopy, cervical dilation was done until a No. 10.5 dilator passed smoothly, followed by insertion of a resectoscope for endometrial biopsy. If hysteroscopy detected

intrauterine lesions, a lesion resection was performed. Surgical complications occurred in 8 cases, of which 1 case was considered TURP (transurethral resection of the prostate) syndrome and improved after symptomatic treatment, 5 cases were cardio-cerebral syndrome, which improved after atropine treatment. After obtaining biopsy tissue, uterine perforation was found in 2 cases. The operation was stopped immediately, vital signs was monitored, and at the same time anti-inflammatory treatment was given for 3 days. The patients recovered from the hospital without discomfort.

Pathological examination

All biopsy specimens were evaluated by at least two pathologists. When the two pathologists disagreed on the interpretation of the findings, a third pathologist served as arbiter. None of the pathologists were aware of the treatment assignments. When all three pathologists disagreed, the diagnosis was determined by the gynecologist.

Disease diagnostic criteria

Endometrial thickening was defined as ultrasound measurements indicating. Hypertension was defined as a systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg (1 mm Hg = 0.133 kPa), or a history of hypertension, even if blood pressure was normal at the time of admission due to antihypertensive treatment. Diabetes was defined as fasting blood glucose ≥ 7.0 mmol/L and/or 2-hour postprandial blood glucose ≥ 11.1 mmol/L, or a history of diabetes, even if blood glucose was normal at admission due to treatment with hypoglycemic drugs or insulin. Obesity was defined by BMI, calculated as weight in kilograms divided by height in meters squared (kg/m²). A BMI of 18.5–25 kg/m² is normal, ≥ 25 kg/m² is overweight, ≥ 30 kg/m² is obese, and ≥ 35 kg/m² is morbidly obese with comorbidities, or ≥ 40 kg/m² without comorbidities.

Statistical analysis

Statistical analysis was performed using SPSS 24.0 and Medcalc software. Measurement data following a normal distribution were expressed as mean ± standard deviation (SD), and comparisons among multiple groups were conducted using analysis of variance (ANOVA). Measurement data that did not follow a normal distribution were expressed as median (M) and interquartile range (Q1, Q3), and comparisons among multiple groups were conducted using the Kruskal-Wallis H test. Categorical data were expressed as frequency (percentage), and comparisons between groups were made using the chi-square test or Fisher's exact test. To identify risk factors, we choose logistic regression analysis to calculate the correlation between risk factors and endometrial lesions. To determine the diagnostic threshold, we chooseROC curve analysis to assess the diagnostic value of endometrial thickness for endometrial lesions. A *P*-value of less than 0.05 was considered statistically significant.

Table 1 Comparison of general features of the patients with different pathologic types

Item	age (years)	BMI (kg/m²)	Diabetes (%)	Hypertension (%)
Normal group	67 (45, 79)	25.08 ± 3.42	4 (8.7%)	36 (45%)
Benign lesion group	59 (46,72)	25.10 ± 3.20	34 (15%)	99 (43.8%)
Malignant group	52 (51,62)	25.97 ± 3.43	1 (33%)	2 (66%)
H/F/ X^2	0.625	4.278	0.760	0.800
P	> 0.05	< 0.05	> 0.05	> 0.05

Results

Comparison of general data among the three groups

226 postmenopausal women ranged in age from 45 to 79 years, the median age was 57 years (43,72) years, the mean BMI was 25.38 ± 3.43 kg/m², 34 cases (15%) of diabetes, 99 cases (43.8%) of hypertension.

Pathological normal group 80 cases (35.40%); There were 143 cases in the benign lesion group, including 117 cases of endometrial polyps (51.7%), 8 cases of submucosal fibroids and 18 cases of endometrial hyperplasia without atypical cell hyperplasia. Malignant and precancerous lesions were 3 cases (1.32%). A conclusion can be drawn by comparison that the main cause of endometrial thickening lesions after menopause was endometrial polyps (51.7%).

In the normal group, the median age was 67 years (45, 79) years, the mean BMI was (25.08 ± 3.42) kg/m², 4 cases of diabetes and 36 cases of hypertension.

In the benign disease group, the median age was 59 years (46,72) years, the mean BMI was (25.1 ± 3.2) kg/m², 34 cases of diabetes and 99 cases of hypertension.

In the malignant and precancerous groups, the median age was 52 years (51,62) years, the mean BMI was 25.97 ± 3.43 kg/m², 1 case of diabetes and 2 cases of hypertension.

There were no significant differences in age, diabetes and hypertension among the three groups, but significant differences in BMI among the three groups ($P < 0.05$). See Table 1. Suggesting that there was a correlation between BMI and endometrial lesions in asymptomatic postmenopausal women.

Comparison of endometrial thickness among the three groups

The average endometrial thickness of 226 patients was (6.6 ± 4.4) mm. The average endometrial thickness in normal group was (4.8 ± 2.7) mm. The average endometrial

thickness of benign lesion group was (7.5 ± 4.8) mm. The endometrial thickness of malignant and precancerous lesion groups was 4 ~ 20 mm, with an average of (13 ± 8.2) mm. The endometrial thickness of malignant and precancerous lesion groups was significantly higher than that of normal and benign lesion groups ($P < 0.05$). The endometrial thickness of benign group was also higher than that of normal group, and the difference was significant ($P < 0.05$). See Table 2. logistic regression analysis was performed, and the result was OR = 7.927 $P < 0.05$, 95%CI (3.015,20.839), See Table 3. Suggesting that the prevalence rate of woman whose Endometrial thickness ≥ 4 mm is 7.927 higher than the others, and the prevalence rate of woman whose BMI ≥ 25 kg/m² is 1.132 higher than the others.

2.3 Taking the normal group as the reference population, ROC curve was drawn, and the optimal cut-off value of endometrial thickness was5.65 mm, which was used to identify endometrial lesions. The area under the curve was 0.679, diagnostic sensitivity was 0.555, specificity was 0.712, and Youden index was 0.267 (Fig. 1). Due to the limitations of the sample size, the diagnostic threshold of endometrial malignancy was not obtained. According to the area under the curve of 0.679, this AUC value represents poor diagnostic accuracy.

Table 2 Comparison of endometrial thickness in different pathological types

group	Number of cases in each group (n)	Endometrial thickness $\overset{?}{X} \pm S$ (mm)
Normal group	80	4.8 ± 2.7
Benign lesion group	143	7.5 ± 4.8
Endometrial polyps	117	
Submucosal fibroids	8	
Endometrial hyperplasia	18	
Malignant and precancerous lesion group	3	13 ± 8.2
Endometrial cancer	1	
Endometrial atypical hyperplasia	2	
H		21.267
P		< 0.05

Table 3 Univariate logistic regression analysis of endometrial lesions in asymptomatic postmenopausal women

Item	OR	P	CI	
			Lower limit	upper limit
BMI	1.132	<0.05	1.039	1.234
Endometrial thickness	7.927	< 0.05	3.015	20.839

Discussion

Our study find that the main reason of the endometrium thickening is endometrial polyp. YAO had conduct a study which embraces 188 cases, pathologically confirmed, they are 150 cases of benign endometrial lesions (79.8%), 30 cases of nonorganic lesions (15.9%), 8 cases of endometrial cancer and precancerous lesions (4.3%) [3]. It's also reported that postmenopausal patients with endometrial thickening without symptoms of vaginal bleeding are mainly characterized by benign endometrial lesions, and the most common pathological type is endometrial polyps, followed by uterine submucous myoma [4]. In our study, In the benign lesion group, there were 143 cases, of which 117 cases (51.7%) were endometrial polyps, the most common type, which was consistent with the above conclusion. Followed by endometrial hyperplasia in 18 cases (7.96%), submucosal myoma in 8 cases (3.53%). There were only 3 cases (1.32%) in malignant and precancerous lesion group. The incidence of malignant and precancerous lesions was the lowest. This is in line with ACOG [2].

By refering to the related thesis [8]. we found that Age, BMI, Diabetes, Hypertension are the risk factors for endometrial cancer of menopausal bleeding [5], So we choose these parameters as our study object. Because there are only one woman who has never pregnanted, so we don't consider this factor. In Table 1, according to the histopathological results of the endometrial tissue from hysteroscopic surgery, patients were divided into three groups: ① Normal group: Proliferative phase, atrophic endometrium, endometritis, adenomyomatoid polyps of uterus; ② Benign lesion group: Endometrial polyps, submucosal uterine fibroids, endometrial hyperplasia; ③ Malignant and precancerous lesion group: Endometrial carcinoma and endometrial atypical hyperplasia. Among them, the obesity value of the malignant lesion group was higher than that of the other two groups, and the difference was statistically significant. (OR = 1.132, $P < 0.05$), (1.039, 1.234). The risk of endometrial cancer is 2–3 times higher in overweight and obese women [6]. Maatela [7] analyzed the cases of asymptomatic endometrial thickening after menopause and found that the risk of pathological endometrial thickening increased when obesity (BMI > 26) was present. Similar to the conclusion of our study.

According to the Society of Obstetricians and Gynaecologists of Canada (SOGC) 2010 Guideline on asymptomatic endometrial thickening [8], if a patient presents with an endometrial thickness > 11 mm or any other positive ultrasonographic findings, such as increased vascularity, inhomogeneous endometrium, or particulate fluid, further investigations should be considered after accounting for various factors, such as age, obesity, diabetes, hypertension, hormone replacement therapy, tamoxifen, and late menopausal age. There is a slight

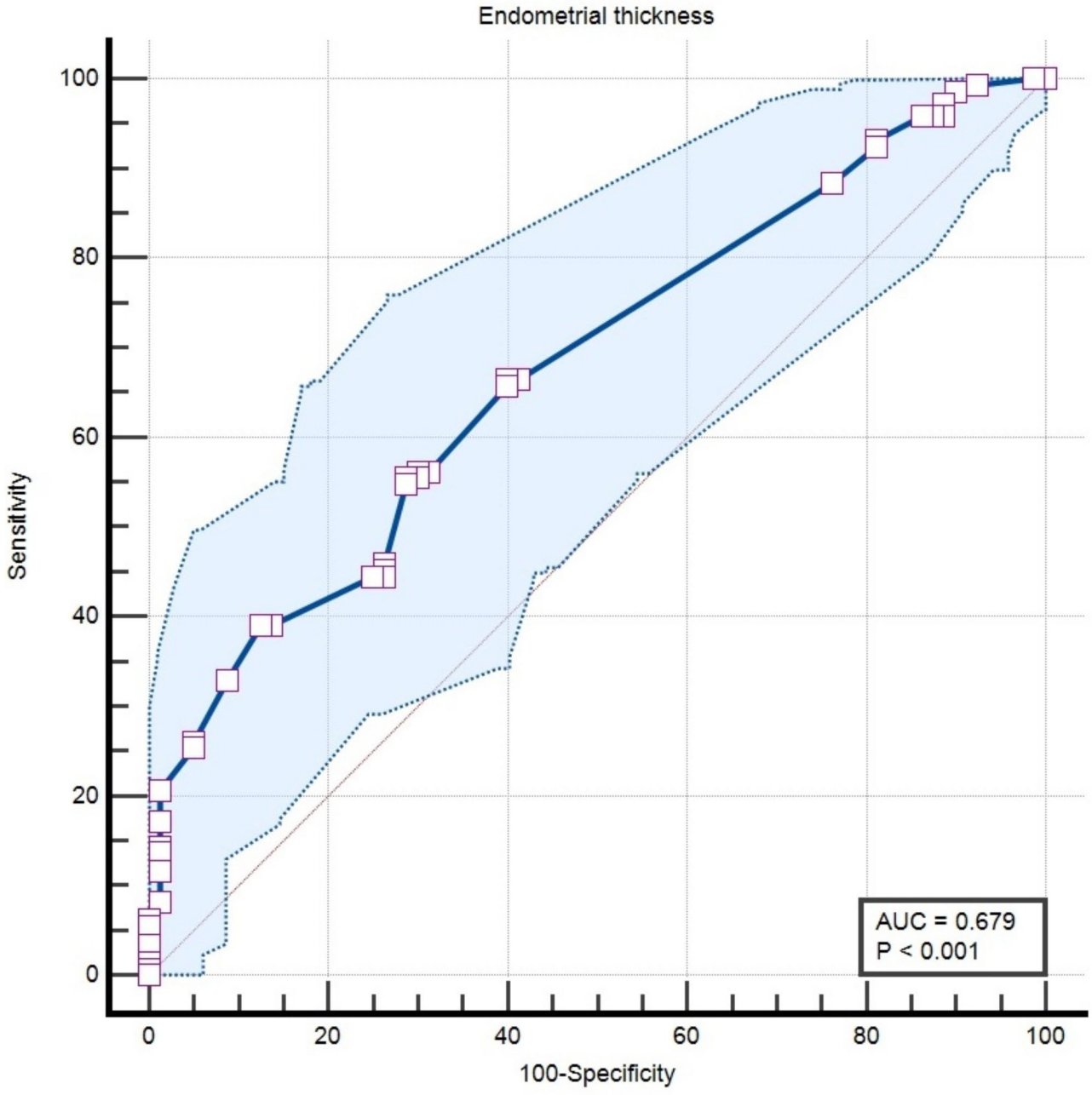

Fig. 1 ROC curve analysis showed that the optimal cut-off value of endometrial thickness for screening endometrial lesions in asymptomatic postmenopausal women was 5.65 mm, the area under the curve was 0.679, the sensitivity was 0.555, the specificity was 0.712, and Youden index was 0.267

difference, our study found that BMI was a risk factor among age, body mass index, hypertension and diabetes, and the prevalence rate of woman whose BMI ≥ 25 kg/m² is 1.132 higher than the others. This conclusion can help clinicians make clinic decisions.

Otherwise, we also found that endometrial thickness is another risk factor of endometrial lesion (OR = 7.927,$P < 0.05$), (3.015,20.839), the confidence level is wide, the reason may be that individual variation and sample size.

In a recent meta-analysis, which contains a total of 18 studies provided the data of 10,334 women, contrasting the low and high endometrial thickness thresholds, conclude that although using a 3.0 to 5.9 mm cutoff results in a lower specificity, the offsetting improvement in sensitivity may justify using this cutoff for further endometrial evaluation in patients with suspected endometrial malignancy [9].

In our study, due to the limitations of the sample size, the diagnostic threshold of cancer was not obtained, but

the diagnosis of benign lesions was obtained. the optimal threshold was5.65 mm, The most significance of our study is that women with endometrial thickness below this threshold can rule out the risk of endometrial disease without further examination, which not only saves medical resources, but most importantly relieves the psychological pressure of patients' anxiety and the pain caused by invasive operations.

In addition, a patient with endometrial atypical hyperplasia was found to have a endometrial thickness of 4 mm.

From this we infer the reason may be that a thin endometrial echo does not reliably exclude type II endometrial cancer (uterine papillary serous, mucinous, clear cell [10]), the relationship between type II endometrial cancer and Endometrial thickness is not study in our paper due to incomplete clinical data, and other studies are needed to further demonstrate.

In our study, there were 3 cases with adenomyomatoid polyps. After reviewing relevant literature, we found that the incidence of this type of polyp was 1.3% [11], so we classified it into the normal case group.

Our limitation is in the sample size, and there are 33 women's operations are failed, 8cases who use of hormone replacement therapy within the past year, 7 cases with hysteromyoma that affect the shape of the uterine cavity line, 5cases's hysteroscopic tissue acquisition failed. which may result in bias to our study. And there are 3 cases in the malignant and precancerous lesion group which may result in bias to our result.

In conclusion, through research we think that (1) The main cause of endometrial thickening after menopause was endometrial polyps (51.7%). (2) Overweight (BMI ≥ 25 kg/m²) is a risk factor for asymptomatic endometrial thickening after menopause. (3) endometrial thickness ≥ 4 mm is a risk factor to postmenopausal asymptomatic women. (4) The appropriate diagnostic thresholds of vaginal ultrasound diagnosis is 5.65 mm in asymptomatic postmenopausal women.

Abbreviations

BMI	Body mass index
ROC	Receiver Operating Characteristic
ACOG	American Committee on Gynecologic
TURP	Transurethral resection of the prostate
SOGC	Society of Obstetricians and Gynaecologists of Canada

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-025-03641-2.

Supplementary Material 1

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Author contributions
WeiLiu contributes to research design, literature review, data collection and analysis, and paper writing, WenPeiBai contributes to review of papers.

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Data availability
Data is provided within the supplementary information files.

Declarations

Ethics approval and consent to participate
Clinical Trial: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (The Ethics Committee of Shunyi District Hospital of Beijing) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for being included in the study. Ethics approval documents have been uploaded to related files.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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