

Original Article

Analysis of ultrasonic imaging changes and factors related to malignant transformation in postmenopausal patients with endometrial polyps

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Abstract: Objective: To examine the ultrasonic changes in postmenopausal endometrial polyps and analyze factors related to their malignant transformation. Methods: This retrospective study analyzed clinical data from 200 postmenopausal patients with endometrial polyps treated at Jinan Maternity and Child Care Hospital and Pingyin Hospital of Traditional Chinese Medicine from December 2020 to December 2023. All patients underwent pathological biopsies to diagnose the nature of the endometrial polyps. This study compared the clinical and ultrasonic imaging features of these patients and analyzed factors influencing the malignant transformation of postmenopausal endometrial polyps. Results: Pathological findings classified 160 patients (80.00%) into the benign group and 40 patients (20.00%) into the malignant group. Significant differences were noted in endometrial thickness, polyp diameter, heterogeneity of lesion echogenicity, and vascularization between the groups (all $P < 0.05$). The malignant group exhibited notably higher blood flow (Grade II+III constituted 70.00% compared to 29.38% in the benign group, $P < 0.05$). The time average velocity (TAV), pulse index (PI), and resistance index (RI) were significantly lower in the malignant group (all $P < 0.05$). The area under curve (AUC) values for TAV, PI, and RI in diagnosing malignant endometrial polyps were 0.754, 0.713, and 0.771, respectively. Increased body mass index (BMI), irregular premenopausal menstruation, and ≥ 2 occurrences of postmenopausal bleeding were identified as risk factors for malignant transformation (all $P < 0.05$). These six indicators were used to create a predictive model for malignant transformation, achieving an AUC of 0.942. Conclusion: Malignancy in postmenopausal endometrial polyps is uncommon, yet distinct differences exist in the transvaginal color Doppler ultrasound characteristics between benign and malignant cases. Factors such as increased BMI, irregular premenopausal menstruation, and ≥ 2 occurrences of postmenopausal bleeding significantly contribute to the risk of malignant transformation. These findings, combined with ultrasound features, provide a robust basis for screening and monitoring these patients.

Keywords: Endometrial polyps, ultrasonic characteristics, postmenopausal, endometrial carcinoma, high risk factors

Introduction

Endometrial polyps are formed by the focal proliferation of endometrial glands and stroma [1, 2]. Although most endometrial polyps are asymptomatic and benign, the likelihood of malignant transformation in postmenopausal endometrial polyps into endometrial cancer and other malignancies are as high as 20% [3]. Thus, early differential diagnosis and proactive treatment interventions are critical to prevent misdiagnosis and mistreatment that could neg-

atively impact patient outcomes. Currently, the clinical diagnosis of malignant endometrial polyps primarily relies on diagnostic curettage or hysteroscopic endometrial biopsy. However, these methods are invasive and can be particularly challenging and painful for postmenopausal women [4, 5].

Transvaginal Doppler ultrasound is a non-invasive alternative that can detect microvascular changes and utilize color blood flow histograms to minimize subjective judgment errors. It is

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easy to operate and serves as a critical tool for differential diagnosis based on specific ultrasound image characteristics [6, 7]. It is acknowledged that predicting endometrial cancer based solely on endometrial thickness has limitations, especially for type II endometrial cancers, which may result in missed diagnoses [8]. To enhance the understanding of color Doppler ultrasound characteristics in postmenopausal endometrial polyps and refine the use of transvaginal color Doppler ultrasound in differential diagnosis, we analyzed the clinical and ultrasound image characteristics of postmenopausal endometrial polyps and discussed factors related to their malignant transformation. This study aims to provide valuable insights for further clinical evaluation and treatment planning.

Materials and methods

Patients

The clinical data of 200 postmenopausal patients with endometrial polyps treated at Jinan Maternity and Child Care Hospital and Pingyin Hospital of Traditional Chinese Medicine from December 2020 to December 2023 were retrospectively analyzed. All patients underwent pathological biopsies to diagnose endometrial polyps. This study received approval from the ethics committees of Jinan Maternity and Child Care Hospital and Pingyin Hospital of Traditional Chinese Medicine.

Inclusion criteria

Patients eligible for this study met the following criteria: diagnosed with endometrial polyps through surgical, hysteroscopic pathological examination, or endometrial curettage [9]; natural menopause for more than one year; presence of abnormal vaginal bleeding or discharge; and no prior or post-onset treatment with estrogen and progesterone drugs.

Exclusion criteria

Patients were excluded from the study if they had infectious diseases, metabolic diseases, prior use of tamoxifen or non-steroidal anti-inflammatory drugs, or missing clinical or pathological data.

Ultrasonic examination

A color Doppler ultrasound diagnostic apparatus (Voluson E8, GE, USA) with a probe frequency of 4-9 MHz was utilized. Two experienced ultrasonic doctors conducted the examinations, and their results were reviewed and recorded. Prior to the examination, patients were asked to empty their bladders, assume a lithotomy position, and expose the vulva fully. The vaginal probe was coated with a coupling agent and covered with a sterile condom before insertion into the posterior fornix of the vagina. The uterus and bilateral adnexa were examined from multiple angles, assessing the position, size, shape, and echoes of the myometrium and endometrium. Special attention was paid to the endometrial thickness, location, number, size, morphology, and echogenicity of lesions, as well as their relationship to the surrounding endometrium. Endometrial lesions' blood flow resistance indices and classifications were observed using color Doppler flow imaging, with patients instructed to slow their respiratory rate. Pulse Doppler mode was used to further explore the blood flow spectrum of endometrial lesions, measuring detailed indices including time-average velocity (TAV), pulsatility index (PI), and resistance index (RI).

Observation indicators

General patient information such as age, body mass index (BMI), pregnancy and childbirth history, and the occurrence of postmenopausal bleeding were collected through the electronic medical record system.

Endometrial blood flow grading criteria

Grade 0: No blood flow signal in the endometrium. Grade I: Only 1-2 punctuate blood flow signals visible. Grade II: Either 3-4 small blood flows or one main vessel visible. Grade III: Three or more vessels with rich blood flow visible, interwoven into a network.

Statistical analysis

SPSS 22.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Measurement data underwent tests for normality and homogeneity of variance. All measurement data conformed to a normal distribution and showed homogeneity of variance, expressed as mean \pm stan-

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Table 1. Comparison of ultrasonic imaging characteristics between the two groups

Project	Benign group (n=160)	Malignant group (n=40)	P value
Intimal thickness (mm)	4.16±1.38	10.15±2.96	<0.001
Polyp diameter (mm)	9.31±1.24	16.83±1.34	<0.001
Lesion echo			<0.001
Well-distributed	89 (55.63%)	8 (20.00%)	
Inhomogeneous	71 (44.37%)	32 (80.00%)	
Abundant blood flow			<0.001
Yes	34 (21.25%)	37 (92.50%)	
No	126 (78.75%)	3 (7.50%)	

dard deviation (SD), and count data were expressed as n (%). t-tests were used for pairwise comparisons of measurement data between groups, and χ^2 tests for count data. Logistic regression was employed to analyze independent factors affecting the malignant transformation of postmenopausal endometrial polyps. The significance level was set at $\alpha=0.05$, with $P<0.05$ indicating statistical significance.

Results

Comparison of ultrasonic imaging characteristics

Based on pathological findings, 200 patients with endometrial polyps were classified into a benign group (160 patients, 80.00%) and a malignant group (40 patients, 20.00%). Significant differences were observed between the groups in terms of endometrial thickness, polyp diameter, heterogeneity of lesion echo, and the proportion of rich blood flow, with higher values in the malignant group (all $P<0.05$) (**Table 1**). A typical case of benign group can be seen in **Figure 1A**. A 64-year-old patient, who had been pregnant four times and given birth twice, was menopausal for 9 years. She had regular premenopausal menstruation and no familial history of malignant tumors. She was admitted to the hospital after a physical examination revealed endometrial thickening. Diagnostic curettage was performed, and the postoperative pathology confirmed endometrial polyps. Ultrasonic examination revealed an endometrial thickness of 9 mm, polyp diameter of 13 mm, uniform lesion echo, non-rich blood flow signal, and a clear boundary between the endometrium and myometrium.

Figure 1B reveal a typical case of malignant group. A 66-year-old patient, who had been pregnant four times and given birth once, was menopausal for 8 years. She experienced irregular premenopausal menstruation and had no familial history of malignant tumors. She was admitted to the hospital following multiple episodes of postmenopausal vaginal bleeding. Diagnostic curettage was performed, and the postoperative pathology revealed endometrial cancer. Ultrasonic examination

showed an endometrial thickness of 16 mm, polyp diameter of 19 mm, uneven lesion echo, rich blood flow signal, and an unclear boundary between the endometrium and muscularis.

Comparison of lesion blood flow grade

Lesions in the malignant group exhibited more abundant blood flow, with Grades II+III accounting for 70.00%, significantly higher than the 29.38% observed in the benign group ($P<0.05$) (**Table 2**).

Comparison of TAV, PI and RI

The TAV, PI and RI in the malignant group were significantly lower than those in the benign group (all $P<0.05$) (**Table 3**).

Diagnostic value of ultrasonic indexes in malignant lesions of endometrial polyps

The diagnostic efficacy of TAV, PI, and RI for malignant lesions of endometrial polyps was analyzed, revealing that the AUCs were 0.754, 0.713, and 0.771, respectively (**Figure 2**). The cutoff values, sensitivity, and specificity are detailed in **Table 4**.

Comparison of clinical characteristics

No significant differences were observed in age, age at menopause, number of pregnancies, parity, estradiol levels, or family history of malignant tumors between the groups (all $P>0.05$). However, differences in BMI, diabetes, hypertension, regularity of premenopausal menstruation, and occurrence of postmenopausal bleeding ≥ 2 times were significant (all $P<0.05$) (**Table 5**).

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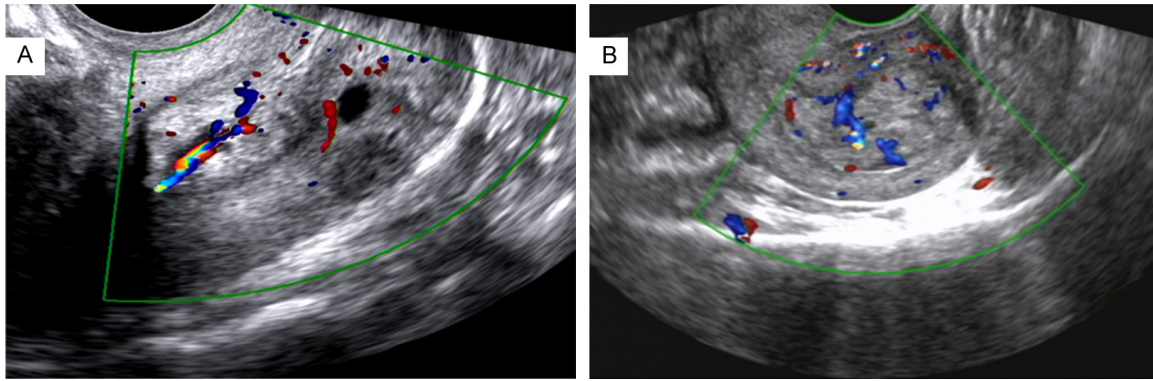


Figure 1. Typical ultrasonic images of benign and malignant groups. A: Benign Endometrial Polyps - The ultrasonic image displays endometrial thickening with a uniform echo of the lesion and a clear boundary between the endometrium and the myometrium. The area of interest is highlighted in a green box. B: Malignant Endometrial Carcinoma - The ultrasound features include abnormal thickening of the endometrium, uneven echo of the lesions, and an unclear boundary between the endometrium and myometrium. The typical area is marked in a green box.

Table 2. Comparison of lesion blood flow grades between the two groups

Group	Grade 0	Grade I	Grade II	Grade III	Grade II+III
Benign group (n=160)	29 (18.13%)	84 (52.50%)	30 (18.75%)	17 (10.63%)	47 (29.38%)
Malignant group (n=40)	0 (0.00%)	12 (30.00%)	17 (42.50%)	11 (27.50%)	28 (70.00%)
<i>P</i> value					<0.001

Table 3. Comparison of TAV, PI and RI between the two groups

Group	TAV (cm/s)	PI	RI
Benign group (n=160)	13.78±4.38	1.72±0.55	1.69±0.31
Malignant group (n=40)	6.31±1.66	0.64±0.18	0.38±0.12
<i>P</i> value	<0.001	<0.001	<0.001

Notes: TAV: time average velocity; PI: pulse index; RI: resistance index.

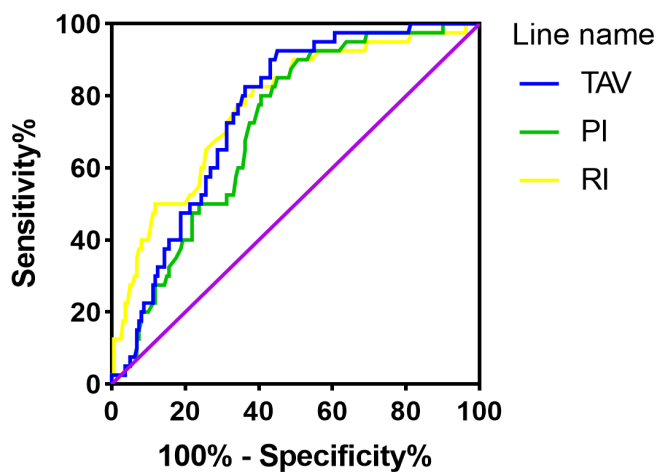


Figure 2. ROC curve of TAV, PI and RI in diagnosing malignant lesions of endometrial polyps. Notes: TAV: time average velocity; PI: pulse index; RI: resistance index; ROC: receiver operating characteristic curve.

Analysis of high-risk factors for malignant transformation of postmenopausal endometrial polyps

Elevated BMI, irregular premenopausal menstruation and occurrence of postmenopausal bleeding ≥ 2 times were identified as risk factors for the malignant transformation of postmenopausal endometrial polyps (all $P < 0.05$) (Table 6).

Establishment of predictive model for malignant transformation of postmenopausal endometrial polyps

A predictive model for the malignant transformation of postmenopausal endometrial polyps was developed using six indices: TAV, PI, RI, BMI, irregular premenopausal menstruation, and ≥ 2 occurrences of postmenopausal bleeding. The model's calibration was assessed using the Hosmer-Lemeshow test, yielding a χ^2 value of 1.514 with a P -value of 0.959 (> 0.05), indicating good calibration. Additionally, the model's effectiveness was evaluated by drawing the receiver operating characteristic (ROC)

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Table 4. Comparison of diagnostic value of TAV, PI and RI in malignant lesions of endometrial polyps

Project	AUC	95% CI		Sensitivity	Specificity	Youden's index	Truncated value
		Lower limit	Upper limit				
TAV	0.754	0.683	0.825	77.5	65.6	0.431	>10.54 cm/s
PI	0.713	0.635	0.791	72.5	62.5	0.350	>1.18
RI	0.771	0.690	0.851	80.0	63.8	0.438	>1.06

Notes: TAV: time average velocity; PI: pulse index; RI: resistance index; AUC: area under curve.

Table 5. Comparison of clinical features between the two groups

Project	Benign group (n=160)	Malignant group (n=40)	P value
Age (years)	59.44±2.94	60.15±3.34	0.186
BMI (kg/m ²)	22.64±1.29	23.32±1.74	0.006
Menopause (years)	4.89±1.25	4.65±1.37	0.288
Number of pregnancies (times)	2.88±0.48	3.03±0.36	0.066
Number of births (times)	1.24±0.43	1.38±0.54	0.083
Diabetes			<0.001
Yes	11 (6.88%)	13 (32.50%)	
No	149 (93.13%)	27 (67.50%)	
Hypertension			0.024
Yes	36 (22.50%)	16 (40.00%)	
No	124 (77.50%)	24 (60.00%)	
Family history of malignant tumor			0.766
Yes	10 (6.25%)	2 (5.00%)	
No	150 (93.75%)	38 (95.00%)	
Premenopausal menstruation regularity			0.001
Yes	93 (58.13%)	11 (27.50%)	
No	67 (41.88%)	29 (72.50%)	
Occurrence of postmenopausal bleeding ≥2 times			0.039
Yes	105 (65.63%)	33 (82.50%)	
No	55 (34.38%)	7 (17.50%)	

Note: BMI: body mass index.

Table 6. Analysis of multiple factors affecting postmenopausal endometrial polyposis

Project	β	SE	Wald	P value	Exp (B)	95% CI	
						Lower limit	Upper limit
BMI	2.441	0.541	20.359	0.016	11.489	3.978	13.177
Diabetes	2.727	0.633	18.593	1.618	15.293	4.427	52.830
Hypertension	1.086	0.473	5.275	0.216	2.962	1.173	7.480
Premenopausal menstruation regularity	-1.637	0.489	11.214	0.001	0.195	0.075	0.507
Occurrence of postmenopausal bleeding ≥2 times	1.769	0.576	9.438	0.002	5.865	1.897	18.131

Note: BMI: body mass index.

curve, which showed an area under the curve (AUC) of 0.942. An AUC greater than 0.8 indicates that the model is effective (**Figure 3**).

Discussion

Historically, endometrial polyps were believed to result from inflammation and mechanical

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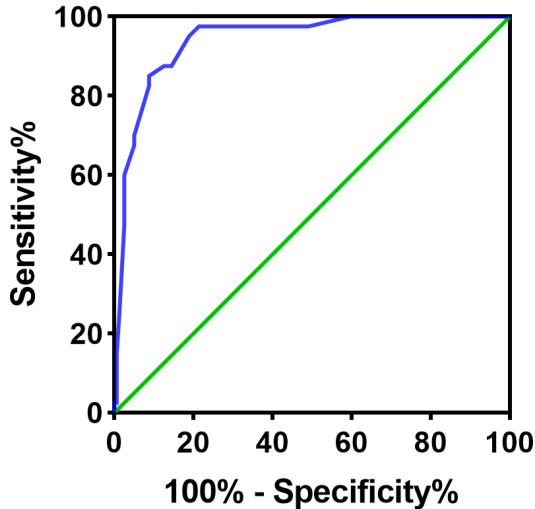


Figure 3. ROC curve of prediction model for malignant transformation of postmenopausal endometrial polyps. Note: ROC: receiver operating characteristic.

injury; however, recent theories suggest they are linked to estrogen stimulation, localized overgrowth of the endometrium, and neoplastic proliferation of stromal cells [10]. Conventionally, patients suspected of malignant transformation of endometrial polyps are diagnosed through invasive procedures such as diagnostic curettage and hysteroscopy, which carry surgical risks [11]. Therefore, initial triage screening for patients suspected of having endometrial polyps should ideally be non-invasive, cost-effective, simple, and repeatable.

In recent years, transvaginal ultrasound has emerged as a crucial tool for screening endometrial disorders. Three-dimensional power Doppler ultrasound, which displays blood flow status and evaluates abnormally proliferated vessels, addresses the limitations of two-dimensional ultrasound and is used in the diagnosis of suspected tumors and assessment of endometrial lesions [12, 13]. This study found that endometrial thickness, polyp diameter, uneven echo ratio, and rich blood flow ratio were significantly higher in the malignant group compared to the benign group. As endometrial lesions progress, the endometrium thickens and echoes become uneven. Endometrial cancer is typically characterized by thickening of the endometrium, uneven echoes, and scattered dark fluid areas with unclear boundaries with the muscularis [14]. Previous research has

highlighted that features such as endometrial thickening, non-uniform echo within the polyp, and indistinct boundaries between the polyp and muscular layer are critical ultrasonic imaging indicators of malignant transformation [15, 16]. Nevertheless, a meta-analysis has shown that endometrial thickening alone cannot serve as a solitary marker for screening for endometrial cancer and atypical hyperplasia in postmenopausal patients with endometrial polyps [17].

Uniform endometrial thickening may not suffice for the diagnosis of malignant endometrial lesions, but the presence of non-uniformly thickened endometrium alongside endometrial polyps exhibiting rich blood flow signals should raise high suspicion of potential malignant transformation [18, 19]. The study indicated that lesions in the malignant group displayed richer blood flow, with ultrasound blood flow parameters such as TAV, PI and RI showing significant differences compared to the benign group. Further analysis revealed that the AUC for TAV, PI, and RI in diagnosing malignant lesions of endometrial polyps are 0.754, 0.713, and 0.771, respectively. Malignant transformation of the endometrium occurs when endometrial epithelial cells deviate from their normal growth and proliferation patterns due to various factors, becoming cancerous. Concurrently, cancer development is accompanied by abnormal vascular proliferation, with an increase in the number and thickness of blood vessels to support the growth, invasion, and metastasis of tumors. Consequently, ultrasound imaging typically shows characteristics of low resistance and high velocity [20, 21]. However, transvaginal color Doppler ultrasound can also present a certain misdiagnosis rate in differentiating between endometrial cancer and endometrial polyps. Studies indicate that if the endometrial cancer lesion is too small, there is a higher likelihood of a false-negative diagnosis [22].

The decline in estrogen levels in postmenopausal women somewhat restricts the formation of endometrial polyps [23]. However, previous studies indicate that endometrial polyps can develop into malignant lesions, including a 40% probability of patients with atypical hyperplasia of the endometrium progressing to endometrial cancer, and an 8% probability of devel-

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oping cancer within five years [24]. Further analysis in this study revealed that increased BMI, irregular menstruation before menopause, and occurrence of postmenopausal bleeding ≥ 2 times are all risk factors for the malignant transformation of postmenopausal endometrial polyps. Aune et al. demonstrated a dose-response relationship between obesity and endometrial cancer, with an 81% increased risk for every five-unit increase in BMI in adult women [25]. Irregular menstruation before menopause may be linked to long-term irregular estrogen stimulation of the endometrium, which can lead to polyp formation. Postmenopausal vaginal bleeding is often the first clinical symptom of many endometrial lesions, and numerous studies suggest that endometrial polyps associated with vaginal bleeding are likely to be endometrial carcinoma [26, 27]. Additionally, studies have shown that conditions like hypertension and diabetes can promote endometrial hyperplasia and increase estrogen stimulation on the endometrium, thereby promoting the formation of endometrial polyps [28]. However, this study did not identify hypertension and diabetes as independent risk factors for endometrial polyps, which may be due to the limited sample size of malignant transformations in this study, preventing the achievement of expected results.

In this study, a prediction model for malignant lesions of endometrial polyps was established using ultrasound indices such as TAV, PI, RI, along with clinical indices including BMI, irregular premenopausal menstruation, and postmenopausal bleeding episodes ≥ 2 times. The AUC was 0.942, indicating that the model possesses strong predictive value for the occurrence of malignant lesions in patients with endometrial polyps. Seckin et al. [8] observed that patients presenting with clinical symptoms such as vaginal bleeding are more likely to be diagnosed with endometrial cancer when endometrial thickness is ≥ 8 mm, which aligns with the findings of this study.

Clinically, the risk of malignant lesions in patients with endometrial polyps can be assessed, and ultrasound examination can be conducted simultaneously. If the risk of malignancy is low, there is no significant endometrial thickening observed on ultrasound, the ultrasound indices are low, and other systemic dis-

eases are ruled out, then invasive procedures such as diagnostic curettage and hysteroscopy biopsy may be deferred, although close monitoring is required. However, for patients at high risk of malignancy and with high ultrasound indices, diagnostic curettage or hysteroscopy biopsy should be considered for further diagnosis [29].

The limitations of this study include a small sample size of malignant transformations, which may affect the accuracy of the evaluation criteria. Continued accumulation of positive samples is necessary. Additionally, subjective factors in ultrasound examination and the varying expertise of examining doctors may influence the accuracy of the results. Future studies should aim to identify more ultrasound predictors for further investigation.

In summary, while the rate of malignant lesions in postmenopausal endometrial polyps is low, significant differences exist in the ultrasonic characteristics observed in transvaginal color Doppler ultrasound. Factors such as increased BMI, irregular premenopausal menstruation, and frequent postmenopausal bleeding are significant risk factors for the malignant transformation of endometrial polyps. The combination of BMI and ultrasound features serves as an effective reference for screening and monitoring patients.

Disclosure of conflict of interest

None.

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