

# The profile of patients with endometrial cancer: analysis of clinical and radiological signs

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## ABSTRACT

**Introduction:** Endometrial cancer (EC) ranks as the fourth most common neoplasm in women. Screening is not recommended, and investigation typically stems from complaints of abnormal uterine bleeding (AUB), with transvaginal ultrasound (TVUS) as the initial examination to assess endometrial thickening and determine the need for biopsy for diagnostic confirmation. **Objective:** Analysis of clinical signs and imaging changes leading to suspicion and diagnosis of EC. **Method:** A descriptive cross-sectional study conducted over 7 months, analyzing medical records of patients diagnosed with EC after video hysteroscopy. **Results:** The collected data allowed for profiling patients diagnosed with EC. Out of 4,129 records examined, 50 (1.2%) patients met the sampling criteria. Among them, 94% were aged over 54 years, 94% were in menopause, and 52% were overweight or obese. Regarding clinical presentation, 78% reported AUB as the main complaint. TVUS results indicated an average endometrial thickness of 14.85mm. However, it is crucial to note that in 6 cases (12%), the thickness was below 4mm. **Conclusion:** While most patients aligned with a risk profile for EC suspicion, some did not manifest all expected signs and symptoms. The study highlighted six cases with endometrial thickness below 4mm. According to various guidelines, this range would not require additional investigation with histopathology, potentially leading to negligence in the diagnostic flow, and depriving these patients of essential treatment.

**Keywords:** Endometrial neoplasms; Endometrial Cancer; Ultrasound; Endometrial hyperplasia.

## INTRODUCTION

Cancer in the uterine body can essentially arise in two regions: the endometrium and the myometrium, with the former being the most prevalent type, representing 75% to 80% of cases.<sup>5</sup> Endometrial cancer (EC) is not only the primary neoplasm of the uterine body but also the fourth most common neoplasm in women.<sup>7</sup> It is estimated that in 2018, 7,000 new cases emerged in Brazil, but this rate may be higher now due to the increase in obesity cases and population aging.<sup>6</sup>

Advanced age is an established risk factor for EC, with 90% of diagnoses occurring after the age of 50.<sup>1</sup> Additionally, obesity, along with other conditions that induce hyperestrogenism, such as diabetes and excessive fat consumption, are also predisposing factors for the development of EC, especially the endometrioid type.<sup>5</sup>

The endometrioid type, also known as type 1, is the most common histological type among the two subtypes of EC. It is generally related to estrogen and occurs in younger, obese, or perimenopausal women.<sup>20</sup> The pathophysiology is associated with structural modifications and changes in specialized endometrial cells in response to hormonal fluctuations during the menstrual cycle. When there is prolonged estrogen exposure without progesterone opposition, endometrial hyperplasia occurs, increasing the chances of developing atypia and, eventually, endometrial cancer<sup>1</sup>. Its histology is usually endometrioid, low-grade, and may be associated with genetic instabilities and mutations.<sup>4</sup>

Type 2 EC, or “non-endometrioid,” is a high-grade tumor with serous or clear cell histology, not associated with estrogen hyperstimulation, and does not have endometrial hyperplasia as a precursor lesion<sup>16</sup>. It represents up to 10% of cases and exhibits more aggressive and invasive behavior. Although the epidemiological profile of patients with type 2 disease is uncertain, it usually affects older women more frequently than type 1 and is more common in Black women<sup>3</sup>.

Currently, endometrial cancer screening is not recommended because no appropriate, economical, and acceptable test reduces mortality<sup>19</sup>. Diagnosis is usually made based on clinical suspicion in patients presenting postmenopausal bleeding or premenopausal or perimenopausal patients with intermenstrual bleeding or prolonged menstruation<sup>6</sup>. Women may also present with abnormal vaginal discharge or incidental findings of thickened endometrium on imaging, in addition to advanced disease symptoms: abdominopelvic pain, abdominal distension, early satiety, changes in bowel or bladder function, and pain during intercourse<sup>5</sup>.

When there is clinical suspicion, the initial requested exam is transvaginal ultrasound, due to its availability,

cost-benefit, and high sensitivity.<sup>17</sup> The aim is to determine if there is endometrial thickening. The ideal cut-off point for endometrial thickness is still uncertain, with the Brazilian Federation of Gynecology and Obstetrics Associations (FEBRASGO) suggesting investigation in postmenopausal women from 4mm thickness. Meta-analyses following a 5mm average cut-off for postmenopausal women obtained a post-test probability of 2.5% for endometrial cancer.<sup>8,3</sup> In premenopausal women, recommendations usually include a cut-off point of 16 mm or less.<sup>3</sup> It is worth noting that in all patients if bleeding persists despite a normal transvaginal ultrasound result, a tissue biopsy is necessary.<sup>7</sup>

Diagnosis is confirmed through histological evaluation of the endometrial tissue, which can initially be done outpatient with a Pipelle cannula, reported to have a diagnostic accuracy for EC of 91% in the general population.<sup>8,18</sup> However, hysteroscopic diagnosis is considered the gold standard, where direct visualization of the uterine cavity allows for material collection directed to the most suspicious portion.<sup>3,18</sup> Other exams, such as computed tomography, magnetic resonance imaging, or proton emission tomography, may be requested to assess the disease's extent once the diagnosis is established.<sup>5</sup>

Given the significant prevalence of EC in the population and the current absence of a screening protocol, since the diagnosis is mainly based on clinical suspicion, it becomes imperative to thoroughly investigate the profile of patients affected by this pathology. In this scenario, the main purpose of this study is to conduct a meticulous analysis, examining the clinical signs and imaging changes that culminated in the suspicion and subsequent diagnosis of EC. Additionally, it aims to identify possible discrepancies concerning the current medical literature, thus contributing to a more comprehensive understanding of this condition

and improvements in the early detection and treatment of EC.

## METHOD

### Study Design

This article is derived from a descriptive cross-sectional study conducted by medical students from Faculdade de Ciências Médicas de Minas Gerais (FCM-MG). The study was executed through the analysis of medical records from the University Hospital (UH) of the FCM-MG. The study began after the approval of the Institutional Scholarship and the Ethics and Research Committee (ERC), under the number CAAE 63297722.7.0000.5134, following the ethical principles of Resolution 466/12 of the National Health Council. Data from the anatomical pathology laboratory and medical records of patients from the postgraduate program in Minimally Invasive Gynecology and Video-Hysteroscopy Examination at the UH were used.

### Sample

The sample includes patients who are users of the Unified Health System (SUS) who attended the University Hospital (UH) and were diagnosed with endometrial cancer through an anatomical pathology examination following a video-hysteroscopic examination. The inclusion criteria adopted by the study were: (1) women over 18 years old, (2) medical indication for a video-hysteroscopic examination, and (3) diagnosis of EC by anatomical pathology examination. The exclusion criteria were: (1) underage women, (2) women who did not undergo video-hysteroscopy at the UH, and (3) women with medical records registered before 2008.

A convenience sample was employed in this study, selecting patients diagnosed with EC after video hysteroscopy from available records. This practical approach allowed for a comprehensive analysis of the

information necessary to achieve the research objectives, considering the availability and accessibility of medical records. However, it is important to note that this methodology may introduce a potential limitation in terms of the representativeness of the general population, as the selection was not random but based on the convenience of clinically available data.

### Analyzed Variables

The variables analyzed in the population were: age, BMI, presence of menopause, presence of previous comorbidities, clinical signs and symptoms reported by the patients, ultrasound alterations, and histological type of cancer.

### Instruments and Procedures

The research for this study was conducted in the following stages: initially, approval was requested from the Ethics and Research Committee (ERC) to start data collection. The data collection period took approximately 7 months, during which the medical records of SUS patients who participated in the postgraduate program in Minimally Invasive Gynecology and Video-Hysteroscopy Examination at the UH of FCM-MG were analyzed, following the medical referral of the patient for the video-hysteroscopic examination.

The postgraduate program provides patients with a questionnaire containing information such as age, obstetric history, comorbidities, allergies, use of regular medications, gynecological complaints, previous transvaginal ultrasound (TVUS) performance, and findings of this ultrasound. This information is recorded in the medical record along with the findings of the video-hysteroscopic examination performed. This examination involves the insertion of a hysteroscope through the patient's vagina and uterus, allowing the doctor to make a detailed evaluation of the uterine cavity through a real-time video monitor.

The data acquired in the medical records were tabulated in an Excel spreadsheet, and the research inclusion and exclusion criteria were subsequently applied. It is worth mentioning that the spreadsheet was exclusively filled out by the student authors of the study to minimize the risk of data leakage and undue exposure of participants' information. Subsequently, the acquired information underwent statistical analysis, data interpretation, and comparison with literature findings. Virtual Libraries, such as Bireme, SciElo, and Pubmed, were used to support the research.

## Statistical Analysis

After the data collection phase, statistical analysis and data interpretation were performed. For conducting association or difference tests between groups, the Chi-square test and Fisher's Exact Test were used for qualitative variables, along with the Kruskal-Wallis test for quantitative variables with fewer than three groups. The significance level used in the research was 0.05.

## RESULTS

The research collected data from 4,129 medical records, identifying a sample of 50 (1.2%) patients diagnosed with EC. The remaining 98.8% of the cases analyzed either had a negative anatomical patholo-

gy result or the medical records were incomplete and thus were not included in the sample.

Table 1 shows the characterization of the patients included in the sample.

Table 1 - Characterization of the Sample

Characteristics	N = 50
<b>Age</b>	
[50, 55)	3 (6%)
[55, 60)	8 (16%)
[60, 65)	12 (24%)
[65, 70)	13 (26%)
[70, 75)	6 (12%)
[75, 80)	6 (12%)
[80, 85)	2 (4%)
<b>BMI (Body Mass Index)</b>	
UNKNOWN	20 (40%)
Underweight	0 (0%)
Normal weight	6 (12%)
Overweight	11 (22%)
Obesity I	9 (18%)
Obesity II	3 (6%)
Obesity III	1 (2%)
<b>Menopause</b>	
UNKNOWN	1 (2%)
NO	2 (4%)
YES	47 (94%)
<b>Presence of Comorbidities</b>	
UNKNOWN	2 (4%)
YES	41 (82%)
NO	7 (14%)
<b>Diabetes</b>	
NO	32 (64%)
YES	16 (32%)
<b>Hypertension</b>	
NO	10 (20%)
YES	38 (76%)
<b>Dyslipidemia</b>	
NO	39 (78%)
YES	9 (18%)
<b>Hypothyroidism</b>	
NO	40 (80%)

YES	8 (16%)
<b>Other</b>	
NO	41 (82%)
YES	7 (14%)

In (%)

From this perspective, it was observed that among the 50 patients, 47 (94%) were aged  $\geq 55$  years, with a mean age of 66 years. The Body Mass Index (BMI) reveals that 52% of the patients are overweight or have some degree of obesity. Regarding menopause, 94% of the patients are in this stage. The analysis of comorbidities shows that 82% of the patients report having other medical conditions. Specifically, 32% have Diabetes Mellitus (DM), 76% have Hypertension, and 18% have Dyslipidemia.

The behavior for the variable “Patient Complaint” is evaluated in Table 2.

**Table 2 – Patient Complaint**

Characteristics	N = 50
UNKNOWN	3 (6%)
<b>Asymptomatic</b>	
NO	41 (82%)
YES	6 (12%)
<b>Pelvic Pain</b>	
NO	43 (86%)
YES	4 (8%)
<b>AUB</b>	
NO	8 (16%)
YES	39 (78%)

In (%)

AUB: Abnormal Uterine Bleeding

It was found that 6 participants (12%) did not have gynecological complaints, in contrast to 41 (82%) who presented at least one complaint. The prevalence

of abnormal uterine bleeding (AUB) stood out, being present in 39 (78%) participants.

The variable “endometrial thickness on TVUS” is evaluated in Table 3.

**Table 3 – Endometrial Thickness on TVUS**

Endometrial thickness (mm)	N=50
UNKNOWN	13 (26%)
[1,2)	2 (4%)
[2,3)	2 (4%)
[3,4)	2 (4%)
[4,5)	0 (0%)
[5,6)	1 (2%)
[6,7)	0 (2%)
[7,16)	14 (28%)
[16, 38)	16 (32%)

In (%)

Regarding endometrial thickening, 37 patients had recorded values in their medical records. The average thickening was 14.85 mm, with a median of 13 mm. Thickening greater than 4 mm was present in 64% of the patients.

The behavior for the variable “endometrial thickening  $\geq 4$ mm” in the subgroup of postmenopausal patients, with the respective simple frequencies and associated percentages, is presented in Table 4.

**Table 4 – Endometrial Thickening  $\geq 4$ mm in Postmenopausal Patients**

Endometrial thickness $> 4$ mm	Absolute Frequency	Relative Frequency (%)	Valid Frequency (%)
NO	6	12.7%	16,6%
YES	30	63.8%	83,3%
UNKNOWN	11	23.4%	-
TOTAL	47	100%	100%

%; percentage

Of the 36 postmenopausal patients who had their endometrial thickening levels recorded in their medical records, approximately 83.3% showed a thickness of

≥4mm on TVUS, while 16.6% had a lower value. The histological type of endometrial cancer is presented with the respective simple frequencies and associated percentages in Table 5.

Table 5 - Histological Type

Type	Absolute Frequency	Relative Frequency (%)	Valid Frequency (%)
I	29	58%	78,3%
II	8	16%	21.6%
UNKNOWN	13	23%	-
TOTAL	50	100%	100%

The medical records did not report the histological type in 23% of the patients. Among those with available data, approximately 78.3% were diagnosed with Type I and 21.6% with Type II.

## DISCUSSION

As reported in the literature, most cases of endometrial cancer occur in patients aged ≥ 55 years<sup>9</sup>. This finding is consistent with the results of the present study, in which 94% of the patients are aged ≥ 55 years. In addition to advanced age, other conditions leading to hyperestrogenism have been documented as risk factors for EC, especially for Type II<sup>3</sup>.

A meta-analysis involving 6 studies and 3132 cancer cases suggests that the strength of the association between obesity and cancer risk increases with increasing BMI: the Relative Risk (RR) for overweight is 1.32 (95% CI 1.16–1.50) and for obesity is 2.54 (95% CI 2.11–3.06)<sup>10</sup>. This association was present in our study, with 52% of patients being overweight or obese. The association between obesity and EC is notable, as excess adipose tissue is related to increased estrogen production.

Type II diabetes mellitus, present in 32% of the patients in the sample, has long been considered an independent risk factor for endometrial cancer, with literature suggesting an approximate doubling of risk (OR 2.1; 95% CI 1.40–3.41)<sup>10</sup>. However, the fact that people with Type II diabetes mellitus tend to be obese is a confounding factor and a recent epidemiological study in the United States questioned the independent role of Type II DM as a risk factor for endometrial cancer<sup>11</sup>.

Regarding the clinical complaint of the patients, our results confirm the predominance of abnormal uterine bleeding (AUB), present in 78% of the patients in the sample, as an important clinical suspicion. In a meta-analysis of observational studies, the pooled prevalence of postmenopausal bleeding among patients with endometrial cancer was 91% (95% CI 87-93), regardless of the tumor stage<sup>9</sup>. The pooled risk of endometrial cancer among patients with postmenopausal bleeding could not be assessed in the present study, however, the literature suggests it is 9% (95% CI 8-11), with estimates varying by use of hormone therapy and geographic region<sup>9</sup>.

Following clinical suspicion, transvaginal ultrasound is recommended as the first step in the diagnosis of endometrial cancer. According to FEBRASGO guidelines, the indication for further evaluation with histological assessment should be considered in postmenopausal women presenting endometrial thickening of at least 4mm<sup>8</sup>. In our study, following this criterion, we found that approximately 83.3% of postmenopausal women would meet the indication for further evaluation, as recommended by the guideline, while 16.6% did not reach this threshold. These results are highly relevant as they suggest that women with endometrial thickening less than 4mm could have been underdiagnosed.

The results presented by Saccharidi et al. directly corroborate the findings of the present study, in which they found a high prevalence of endometrial cancer in symptomatic postmenopausal patients with endometrial thickness less than 4mm (8.5%) and concluded that the accuracy of endometrial thickening in detecting cancer was very low, precisely with a sensitivity of 75% and specificity of 48.3%<sup>13</sup>.

Similarly, a meta-analysis evaluating sensitivity observed a lower risk of endometrial cancer in studies with partial disease verification (not all women underwent anatomical pathology examination) compared to studies with complete diagnostic verification. This suggests that the disease may have been missed in women with negative first-line test results (e.g., TVUS), but they note that further evaluation may not have been extended in these women due to their low risk<sup>9</sup>.

The results presented raise concerns about the diagnostic approach to EC based on endometrial thickening levels and reinforce the importance of individualized evaluation. We believe it is unsafe to rely solely on the ultrasound findings to determine the need for a biopsy in such situations. It is important to note that TVUS is an operator-sensitive technique, with considerable variation both between and within operators, which can result in significant bias, especially in measurements of small structures.

Given the inherent limitations of the present study, characterized by small sample size and incomplete data in medical records, it was not possible to establish statistically significant associations between endometrial thickening less than 4mm and other clinical, ultrasound, and histological subtype variables. Therefore, it was not feasible to identify a predominant clinical suspicion factor in this group of women. However, it is noteworthy that other sources indicate subgroups of patients in which the accuracy of TVUS for excluding endometrial cancer is limited. Wang et

al. reported that only 65% of their study's patients with type 2 endometrial cancer presented with a thickened endometrial echo complex, 17% had an endometrium measuring less than 5mm, and another 17% had an indistinct endometrial lining<sup>14</sup>.

Other sources suggest that persistent bleeding may be a sign of EC, even in patients with endometrial thickness  $\leq 4$ mm, as a thin or indistinct endometrial stripe does not reliably exclude all cancers, particularly those of non-endometrioid histology. According to Doll et al., the effectiveness of TVUS may be lower in Black patients compared to White patients, due to a higher prevalence of fibroids, which can limit the endometrial assessment in this group<sup>12</sup>.

### Study Limitations

The limitations of the study are essential to contextualize the results obtained. Firstly, the use of a convenience sample, while feasible for this context, may introduce selection bias, compromising the generalizability of the results to the general population. Additionally, the retrospective nature of the medical record analysis can lead to limitations in data accuracy and completeness, depending on the quality and consistency of the information recorded over time. It is pertinent to note that, in some cases, not all patients had all data recorded, which can impact the integrity of the analyses performed. Another important consideration is that, despite the extensive analysis of clinical signs and imaging exams, factors not included in this study could influence the suspicion and diagnosis of endometrial cancer. Thus, it is imperative to interpret the results carefully, recognizing that the conclusions are derived from a small and specific sample and that other unanalyzed variables may contribute to a more comprehensive understanding of the topic.

### CONCLUSION

In summary, this study highlights the complexity and nuances associated with the early detection of endometrial cancer (EC). Despite the inherent limitations of a small sample size and occasionally incomplete data in medical records, our analysis identified patients with subtle endometrial thickening less than 4mm. This finding underscores the potential oversight in diagnosis and treatment if professionals rely exclusively on ultrasound cut-off values described in guidelines. Emphasizing the importance of an individualized approach in diagnostic evaluation is a perspective supported by other authors as discussed in this study. The absence of statistically significant associations between this ultrasound characteristic and other clinical variables suggests the need to consider additional factors in the clinical suspicion of EC. Amid uncertainties, this study highlights the importance of future research to improve diagnostic strategies and the understanding of specific characteristics in patient subgroups, thereby contributing to advances in the prevention and treatment of endometrial cancer.

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THE AUTHORS DECLARE THAT THERE IS NO CONFLICT OF INTERESTS IN RELATION TO THIS ARTICLE.