REVIEW ARTICLE

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Management of ultrasonographic endometrial thickness in postmenopausal asymptomatic women

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INTRODUCTION

Endometrial cancer is the sixth most diagnosed type of cancer in women worldwide[1]. In 90% of patients, it is associated with transvaginal bleeding. Its occurrence is low in menacme. At menopause, the endometrium should be investigated when transvaginal bleeding occurs[2].

The incidental finding of thickened endometrium in postmenopausal women is common, and the cutoff thresholds for investigating the changes in women with transvaginal bleeding are well established. However, there is no consensus in asymptomatic patients[3]. Patients with postmenopausal transvaginal bleeding and endometrial thickness above 4–5 mm have universally accepted cutoff values for cancer investigation[4].

The present study aims to evaluate the need for endometrial investigation with invasive methods of incidental ultrasonographic findings of endometrial thickening in postmenopausal patients without transvaginal bleeding, avoiding unnecessary patient risks, such as perforations, physical and psychological trauma, as well as expenses for health services.

METHODS

Registration

This study comprised a systematic review of articles and was registered with the PROSPERO registry for systematic reviews (ID CRD42022297524).

Study selection

The selection of articles was performed by three independent evaluators, according to the inclusion and exclusion criteria. Articles were initially evaluated by title. Subsequently, the articles were evaluated by abstract. Differences were resolved by consensus among researchers. This method was used to achieve the appropriate methodological quality of the systematic review.

Information sources and search

This systematic revision was based on a review of the literature in the PubMed databases, between 2010 and 2020. The MeSH (Medical Subject Headings) terms used were postmenopause, ultrasonography, systematic revision, and meta-analysis. Endometrial thickness was also a keyword used. Exclusion criteria were articles published before 2010 and publications that were not in the English language. A total of 95 articles were found. After reading the titles of the articles, it was noticed that some of them did not fulfill the criteria of this study. A total of 14 articles were selected for reading the abstract and those that did not relate to the purpose of this study were excluded (Figure 1). Table 1 shows the analyzed studies.

ENDOMETRIAL CANCER AND ULTRASONOGRAPHIC ENDOMETRIAL THICKNESS

The accuracy of ultrasonography addressing gynecology is evaluated in some studies[5,6]. Transvaginal ultrasound is an important examination for the investigation of endometrial cancer in patients with postmenopausal bleeding. However, in asymptomatic patients, there is no consensus on when to investigate. In patients with postmenopausal bleeding, endometrial thickening is recommended and most studies suggest further investigation with endometrial biopsy when they present values greater than 4 or 5 mm on transvaginal ultrasound imaging. In 10% of cancer cases, patients may be asymptomatic[7,8] and are suspected after an annual routine transvaginal ultrasound[9].

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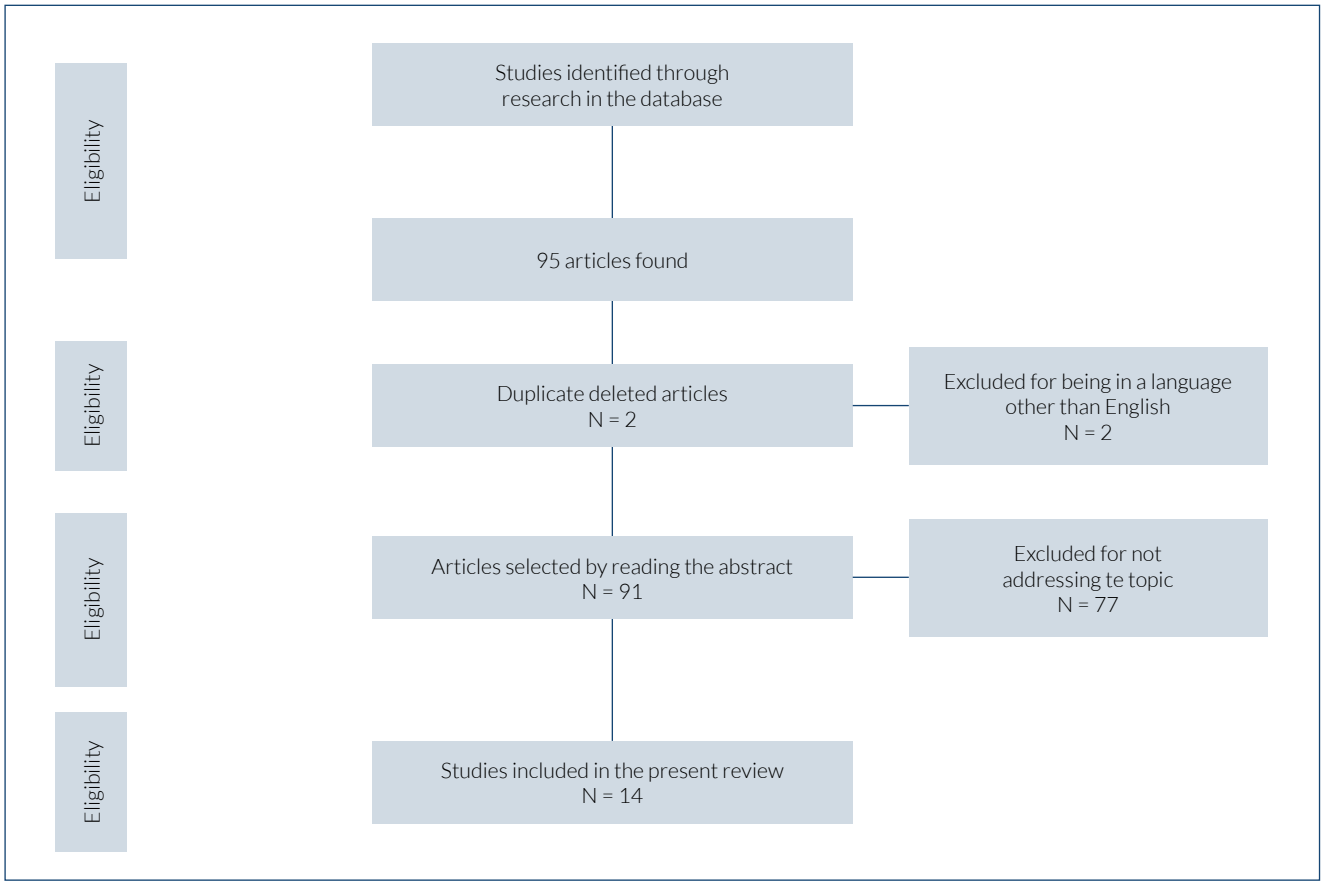

Figure 1. Study flowchart.

Despite increasing relatively the chances of an early diagnosis, ultrasound should not be used as a screening method[10-12], as they may increase the risk of complications[13].

Goldstein et al.[13] demonstrated that the incidence of cancer in asymptomatic patients with polyp images at ultrasound is approximately 0.4%. Therefore, there was no therapeutic advantage in investigating these patients in the absence of transvaginal bleeding, except in patients at high risk for endometrial hyperplasia, polycystic ovary syndrome, metabolic syndrome, diabetes, hypertension, or obesity[13].

A study evaluated 65 patients without transvaginal bleeding in the postmenopausal period. Of these, 11 (16.9%) patients had leiomyomas, 28 (43.0%) had endometrial polyps, 0 had adenocarcinomas, 2 (0.03%) had atypical hyperplasias, and 4 (0.06%) had simple or complex hyperplasia. This study concluded that the value of 5 mm is too small to be investigated in the cases of absence of postmenopausal bleeding, which did not identify any patient with endometrial cancer in asymptomatic patients, with an average endometrial thickening of 9.7 mm[14].

Another study evaluated 259 postmenopausal patients without uterine bleeding. All patients were submitted to transvaginal ultrasound and hysteroscopy. There were 214 (82.6%) patients with atrophic endometrium, 20 (0.07%) with simple hyperplasia, 15 (0.05%) with endometrial polyps, 9 (0.03%) with atypical hyperplasia, and 1 (0.003%) with endometrial cancer. The accuracy of the transvaginal ultrasound was analyzed to detect changes in different cutoff values. It was observed that with 3 mm, there is 84.4% sensitivity and 64.4% specificity and with 9 mm, the sensitivity decreased (26.6%) and specificity increased (99.1%). The study compared the effectiveness of transvaginal ultrasonography in detecting intrauterine lesions compared with hysteroscopy and biopsy. Only one endometrial cancer was found, and the risk of cancer in the endometrium <5 mm is 0.07%, while in the endometrium >5 mm it becomes 7.3%. The value of 11 mm separates patients at low risk of cancer from those at high risk of cancer. According to this study, ultrasonography should be used to screen for intrauterine pathologies in asymptomatic patients and has moderate accuracy[2].

In contrast to the above study, a study concluded that transvaginal ultrasound should not be used routinely in asymptomatic patients. In the study, 1,500 women underwent

Table 1. Results of the studies.

Reference		Author	Year	Main results
1	13	Goldstein et al.	2011	The authors demonstrated that the incidence of cancer in asymptomatic patients with polyp images at ultrasound is approximately 0.4%.
2	14	Worley et al.	2011	The study concluded that the 5 mm value is too thin to be investigated in cases of absence of postmenopausal bleeding.
3	2	Kasraesian et al.	2011	Ultrasonography should be used to screen for intrauterine pathologies in asymptomatic patients and has moderate accuracy.
4	15	Hartman et al.	2013	A transvaginal ultrasound should not be used routinely in asymptomatic patients.
5	16	Gianella	2014	The majority of women had an endometrium between 4 and 7 mm, and none of these had pre-malignant or malignant lesions.
6	11	Aston and Weaver	2014	Investigating asymptomatic women provides relatively rare cancer findings and does not improve the patient's prognosis when compared to investigations initiated within 8 weeks of the first transvaginal bleeding.
7	17	Saatli et al.	2014	The study performed a review of medical records in a service in which routine transvaginal ultrasounds are performed for all patients.
8	18	Korkmazer et al.	2014	Transvaginal ultrasound examination was offered to all patients, and a 5 mm cutoff point was used for the possible presence of intrauterine pathology.
9	4	Layemo et al.	2015	The study concluded that if the cutoff value of 11 mm were adopted, 41 patients would not have undergone unnecessary hysteroscopy.
10	19	Louie et al.	2015	The study concluded that 11 mm would be an optimal cutoff point.
11	20	Yasa et al.	2016	The study indicated low accuracy between transvaginal ultrasounds.
12	10	Ozelci et al.	2019	Considering pre-malignant and malignant lesions, the ideal cutoff was 10.5 mm.
13	21	Ghoubara et al.	2018	Patients with an endometrium greater than 4 mm and without bleeding were included.
14	22	Alcázar et al.	2018	The study concluded that patients with an endometrium ≥11 mm have a risk of 2.59 times greater than patients with an endometrium between 5 and 10 mm.

transvaginal ultrasound; 77.1% had an endometrium <4 mm and 92% had <5 mm. In 101 (6.7%) women, a polyp was suspected using ultrasound imaging. Of these women, 97 of 101 (96%) had an endometrium >4 mm, and 89 of 101 (88%) had an endometrium >5 mm. The study concluded that transvaginal ultrasonography is effective for population screening due to its high negative predictive value in patients with postmenopausal transvaginal bleeding; however, it should not be used routinely for asymptomatic women due to its low positive predictive value. In addition, postmenopausal bleeding is an early predictive symptom consistent with endometrial cancer[15].

Gianella et al.[16] conducted a study on 268 asymptomatic patients with an endometrium ≥4 mm. Endometrial biopsy showed 156 (56.8%) atrophies, 92 (34.4%) polyps, 12 (4.5%) submucosal myomas, 8 (2.9%) endometrial hyperplasia, and 4 (1.4%) adenocarcinomas. The best cutoff value was 8 mm (sensitivity 79.3% and specificity 92.1%). This value would reduce the percentage of unnecessary hysteroscopies by 37.4% while recognizing any premalignant or malignant lesions. The highest cutoff value for not failing to recognize a case of endometrial cancer was 10 mm. This study observed that the majority of women (61.2%) had an endometrium between 4 and 7 mm and none of them had premalignant or malignant lesions, concluding that all hysteroscopies were unnecessary in these cases[16].

Aston and Weaver[11] reviewed medical records of women who underwent hysteroscopy, dilation, and curettage. The sample ranged from 5 to 18.1 mm (average of 9.01 mm), and one case of endometrial cancer was identified. In addition, there were four unwanted outcomes (11.4%), including uterine perforation, severe laryngospasm, and severe post-procedure bleeding. The study found that investigating asymptomatic women provides relatively rare cancer findings and does not improve the patient's prognosis when compared to investigations initiated within 8 weeks of the first transvaginal bleeding[11].

Saatli et al.[17] also performed a review of medical records in a service in which routine transvaginal ultrasounds are performed for all patients. The study found five cases of endometrial adenocarcinoma and concluded that one case of cancer is detected only for every 106 investigations carried out using this method[17].

In the study by Korkmazer et al.[18], 197 patients were evaluated by hysteroscopy and histopathological examination. Transvaginal ultrasound examination was offered to all patients, and a 5 mm cutoff point was used for the possible presence of intrauterine pathology. The hysteroscopic findings revealed that 74 (37.7%) patients had normal uterine cavities, 30 (15.2%) had endometrial hyperplasias, 17 (8.6%) had submucosal fibroids, and 76 (38.5%) had endometrial polyps. No malignant or premalignant lesions were seen below 9 mm[18].

Laiyemo et al.[4] evaluated endometrium between 2.8 and 40 mm (average 10.38 mm). Of the 22 cases who had the value above 11 mm, 2 were malignant (21 and 27 mm), and of those who had the value below 11 mm, no cases of malignancy were detected. The risk above 11 mm was 9.1%. Thus, 61 (92.42%) cases were benign. The study concluded that if the cutoff value of 11 mm were adopted, 41 patients would not have undergone unnecessary hysteroscopy[4].

Louie et al.[19] carried out a retrospective cohort study to obtain an optimum cutoff point for biopsy in ultrasound findings of endometrial thickening above 4 mm. A total of 462 patients were analyzed and 435 had alterations (192 patients had endometrial polyps, 18 had simple hyperplasias, 7 cases had hyperplasia with atypia, and 9 had endometrial carcinoma). In this study, the values above 14 mm were associated with atypical hyperplasia and the value of 15 mm was associated with endometrial carcinoma. The study concluded that the value of 11 mm would be an optimal cutoff point[19].

Yasa et al.[20] evaluated 276 asymptomatic postmenopausal patients undergoing curettage or hysteroscopy. If the cutoff value of endometrium was 4 mm, the results were as follows: 107 (38.8%) patients had polyps, 42 (15.2%) had atrophies, 39 (14.1%) had exposure to estrogen, 19 (6.9%) had normal endometrium, 9 (3.3%) had atypical hyperplasias, 8 were diagnosed of endometrial cancer (2.9%), and 52 had insufficient samples (18.8%). The values between 4 and 7 mm revealed that 83 of 89 cases had benign evaluation; between 8 and 11 mm, 69 of 74 cases were normal; and above 12 mm, 55 of 66 did not present any changes. The study indicated low accuracy between transvaginal ultrasound and carcinoma in these conditions[20].

In the study by Ozelci et al.[10], 266 postmenopausal patients without bleeding with endometrium greater than 6 mm underwent hysteroscopy with biopsy, of which 168 (63.1%) patients had polyps, 24 (9%) had simple hyperplasia, 4 (1%) had atypical hyperplasia, and 8 (3%) had endometrial cancer. Of the total number of patients evaluated, 152 had an endometrium between 6 and 10 mm. The optimal cutoff value was 13.5 mm for malignant lesions and atypical hyperplasia (58% sensitivity and 75% specificity). Considering premalignant and malignant lesions, the ideal cutoff value was 10.5 mm (77% sensitivity and 62% specificity)[10].

In another study, 81 patients with an endometrium greater than 4 mm and without bleeding were included. If the cutoff value was 4 mm, the results obtained were as follows: 77 cases had normal endometrium, 57 cases had benign findings, 20 cases had polyps, and 4 cases had hyperplasia or cancer. If the cutoff value was <10 mm, 42 cases were normal, 4 cases had polyps, and no cases had cancer. When the cutoff value was ≥10 mm, 15 cases were normal, 16 had polyps, and 4 cases had atypical hyperplasia or cancer[21].

Alcázar et al.[22] concluded that patients with an endometrium ≥11 mm have a risk of 2.59 times greater than patients with an endometrium between 5 and 10 mm[22].

The limitations of the systematic review are limited to 10 years and the subject use of English-written manuscripts. The inclusion of articles in the past 10 years can be justified by looking for more up-to-date information. A search for articles in English is limited to the subject of Portuguese literature.

CONCLUSION

There is no consensus on the ideal cutoff value for the investigation of endometrial thickening in asymptomatic postmenopausal patients, but it is clear that the value of 5 mm, used in patients with postmenopausal bleeding, increases the number of unnecessary investigations. Transvaginal ultrasonography is of great value in screening for endometrial pathologies in women with postmenopausal bleeding, but it should not be used in routine asymptomatic women.

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AUTHORS' CONTRIBUTIONS

LRC: Data curation, Methodology, Writing – original draft. **MPJ:** Investigation, Methodology, Writing – original draft. **MKOG:** Data curation, Methodology, Writing – original draft. **EFCM:** Conceptualization, Formal Analysis, Supervision, Validation, Writing – review & editing. **RSN:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Writing – review & editing, Guarantor.

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