ONCOLOGÍA
roe-solca.ec
ORIGINAL ARTICLE

Relationship between ultrasound-measured endometrial thickness and risk of endometrial cancer in postmenopausal women. A single-center observational study

Crhistian Raúl Morales Velasco*[1], Josefina Ramírez Amaya[1].

1. Postgraduate Coordination, Faculty of Medical Sciences, University of Guayaquil, Ecuador.

***Correspondence:**

drcristian_morales@hotmail.com

Address:
Av Kennedy Y Av Delta, Guayaquil, Guayaquil, Ecuador, Guayaquil. Telephone: (593) 04 228 1148.

Conflict of interest: The authors declare that they have no conflicts of interest.

Received: September 8, 2022
Accepted: October 4, 2022
Published: December 2, 2022
Editor: Dra. Evelyn Valencia Espinoza.

Cite:
Morales C, Ramírez J. Relationship between ultrasound-measured endometrial thickness and risk of endometrial cancer in postmenopausal women. A single-center observational study. Rev. Oncol. Ecu 2022;31(3):282-290.

ISSN: 2661-6653

DOI: https://doi.org/10.33821/660

Abstract

Introduction: Endometrial cancer is the most frequent oncological pathology in postmenopause and is associated with abnormal uterine bleeding. Different studies have found a significant relationship between increased endometrial thickness and the risk of endometrial cancer. This study aimed to measure the association between these variables and perform diagnostic tests in a regional reference center in Guayaquil, Ecuador.

Methodology: This analytical study was carried out at the University Pediatric-Obstetric-Gynecological Hospital of the city of Guayaquil-Ecuador from January to December 2018, with a nonprobabilistic sample, including postmenopausal women with uterine bleeding and endometrial thickening equal to or greater than 3 millimeters to the transvaginal ultrasound study who were subjected to curettage with a histopathological report. The dependent variable was the histological presence of endometrial neoplasia; the independent variable was the ultrasound endometrial thickness.

Results: The analysis included 148 patients, with a mean age of 57.9 ± 5.4 years. Obesity was observed in 22 cases (10.9%), type 2 diabetes in 20 cases (9.95%), and hypertension in 11 cases (5.47%). There were 19 cases of endometrial cancer and 129 cases of endometrial hyperplasia. The mean endometrial thickness was 3.560 ± 0.49969 mm. Thickness >3.5 mm OR 54.03 (95% CI 3.19-914.34) P=0.0057. The sensitivity was 100%, the specificity was 58.1%, the positive predictive value was 26.0%, and the accuracy was 63.5%.

Conclusion: The sensitivity of measuring endometrial thickness >3.5 mm as a predictor of endometrial cancer in symptomatic postmenopausal women is high; however, it does not have reasonable specificity or positive predictive value, which limits its clinical use.

Keywords:
MESH: Endometrium, Endometrial neoplasms, Ultrasonography, Uterine hemorrhage, Relative odds.

Introduction

Endometrial thickness varies with the menstrual cycle and with age, being almost linear in the postmenopausal stage [1]. The cutoff points for considering a pathological thickness of the endometrium on ultrasound are 16 mm in reproductive age, 5 mm for postmenopause, and 8 mm in postmenopause with hormone replacement therapy (HRT). Some argue that the cutoff point should be the same for women on or without HRT.

There are several published studies on the relationship between endometrial cancer and ultrasound endometrial thickness with high sensitivity (greater than 90%) and specificity of 75.47% [2]. When analyzing the risk coefficient for endometrial cancer based on endometrial thickness measured in postmenopausal women, the application of endometrial ultrasound for the diagnosis of endometrial cancer may help developing countries.

For postmenopausal women with abnormal uterine bleeding (AUB), the sensitivity and specificity for the diagnosis of endometrial cancer with an endometrial thickness ≥ 4-5 mm are 96% and 61%, respectively [3], similar to what was presented in this study with high sensitivity and low specificity.

The ultrasound size of the endometrium has been classically used to decide whether to perform an endometrial biopsy in postmenopausal women with abnormal uterine bleeding.

Another group recently reported that with an endometrial thickness of 3 mm, the sensitivity and specificity for the diagnosis of endometrial cancer in postmenopausal women with AUB were 98% and 35%, respectively, recommending the use of 3 mm endometrial thickness as a cutoff value to decide which women require endometrial biopsy [4]. Since type II endometrial cancer can present in an atrophic endometrium that is very thin on ultrasound, some authors propose that all postmenopausal women presenting with AUB should undergo a histological study of the endometrium [5].

Despite the different reports observed, few studies have evaluated the cutoff level of endometrial thickness in asymptomatic postmenopausal women. It has been proposed that an endometrial thickness ≥ 11 mm would be equivalent to having an endometrial thickness of 5 mm in symptomatic women, concerning the risk of endometrial cancer [5]. However, ultrasound screening for the diagnosis of endometrial cancer in asymptomatic women is not recommended since the prevalence of endometrial cancer in this group is low (0.62%) [6]. Given the options shown (3 or 5 mm in symptomatic postmenopausal women and 11 mm in asymptomatic postmenopausal women), we believe that it is necessary to determine the endometrial thickness that allows selecting the women who will benefit from an endometrial biopsy, explicitly having a level of a cut above which biopsy is necessary and below which expectant management is reasonable.

In clinical practice, estimating endometrial thickness is an adequate predictor of endometrial cancer, considering that values greater than 3 mm are statistically significant and figures above 5 mm have a positive predictive value close to 90% in postmenopausal women with symptoms such as uterine bleeding [7].

This study aimed to determine the relationship between endometrial thickness measured by ultrasound and the risk of endometrial cancer in postmenopausal women.

Materials and methods

Study design

The present study is observational-analytic. The source is retrospective.

Study area

The study was carried out in the Gynecology-Obstetrics service of the Gynecological-Obstetric-Pediatric University Hospital of Guayaquil, in Guayaquil-Ecuador. The study period was from Jan 1, 2018, to Dec 31, 2018.

Universe and sample

The universe was made up of all the patients registered in the institution. The sample size calculation was nonprobabilistic, census type, where all incident cases in the study period were included.

Participants

Cases of postmenopausal women with abnormal uterine bleeding who presented endometrial thickening equal to or greater than 3 millimeters in the transvaginal ultrasound study and who underwent uterine curettage with a histopathological report were included.

Variables

The descriptive variables were age, obesity, arterial hypertension, diabetes mellitus, early menarche, late menopause, nulliparity, use of hormone replacement therapy, and a family history of endometrial cancer.

The dependent variable was the histological presence of endometrial neoplasia; the independent variable was the ultrasound endometrial thickness.

Procedures, techniques, and instruments.

The data were collected from the clinical history in a form designed exclusively for this purpose. Endometrial cancer diagnoses were made by histopathological analysis, and different pathologists read the plates. For the collection of cases, the search for "Abnormal uterine bleeding" was used under the ICD/10 coding: N938.

Avoidance of bias

To guarantee the reliability of the information, the researchers were trained in data collection. A double checklist was used to include the cases. The data were validated and cured by the principal investigator.

Statistical analysis

Once the information was compiled in an Excel spreadsheet, it was entered into a data matrix of SPSS™ 22.0 software (IBM, Chicago, USA). Descriptive statistics were used based on frequencies and percentages for the qualitative variables and the quantitative measures of central tendency. The odds ratio was used to measure the association with a 95% confidence interval and *P value*.

Results

The analysis included 148 patients.

Clinical characterization

The mean age was 57.9 ± 5.4 years. The minimum age was 45 years, and the maximum was 65 years. The group under 60 years old corresponded to 46 cases (22.89%), and the group over 60 years old corresponded to 102 cases (77.11%). The general description of the sample is presented in Table 1.

Table 1. Descriptive variables of the sample

Variable	No.=148
<60 years	46 (22.89%)
Obesity	22 (10.95)
Chronic hypertension	11 (5.47%)
Tipe 2 diabetes Mellitus	20 (9.95%)
Early menarche	17 (8.46%)
Late menopause	12 (5.97%)
Hormone therapy	18 (8.96%)
Family pathological history: endometrial cancer	2 (1.0%)

There were 19 cases of endometrial cancer and 129 cases of endometrial hyperplasia (Table 2).

Table 2. Histopathology of the study group

Histopathological finding	No. of cases	Percentage
Simple hyperplasia without atypia	52	35.14%
Simple hyperplasia with atypia	36	24.32%
Complex hyperplasia	25	16.89%
Complex hyperplasia with atypia	16	10.81%
Endometrial adenocarcinoma	8	5.41%
Mucinous carcinoma	5	3.38%
Clear Cell Carcinoma	3	2.03%
Squamous cell carcinoma	1	0.68%
Serous carcinoma	1	0.68%
Undifferentiated carcinoma	1	0.68%

Endometrial thickness

The mean endometrial thickness was 3.560 ± 0.49969 mm. Table 3 presents the analysis that compares the endometrial thickness in the group with neoplasia and the group with endometrial hyperplasia.

Table 3. Association between endometrial cancer and ultrasound endometrial thickness.

	Endometrial cancer No.=19	Endometrial hyperplasia No.=129	OR		
			OR	95% CI	*P*
Endometrial thickness >3.5 mm	19 (100%)	54 (41.86%)	54,028	3.1924-914.34	0.0057

PPH: personal pathological history. FPH: Family pathological history. Ca: Cancer. OR: Odds ratio. CI: confidence interval.

Diagnostic tests

Table 4 shows the group of diagnostic tests using ultrasound endometrial thickness as a predictor of endometrial cancer.

Table 4. Diagnostic tests of ultrasound endometrial thickness as a predictor of endometrial cancer.

		95% CI for a proportion	
	Proportion	Lower limit	Upper limit
Prevalence:	12.84%	12.39%	13.28%
Sensitivity:	100%	100%	100%
Specificity:	58.14%	57.49%	58.79%
False Negative Rate:	0%	0%	0%
False Positive Rate:	41.86%	41.21%	42.51%
Positive Predictive Value:	26.03%	25.45%	26.61%
Negative Predictive Value:	100%	100%	100%
Youden index: _	58.14%	57.49%	58.79%
Accuracy:	63.51%	62.88%	64.15%
Likelihood ratio:	0	-	-
Likelihood ratio:	2.39	-	-

Discussion

The main finding of the present investigation is that endometrial thickness >3.5 mm measured by ultrasound in postmenopausal women admitted to the hospital with transvaginal bleeding has a very high association with endometrial cancer (OR 54.03 (95% CI 3.19-914.34), *P* =0.0057). The sensitivity of endometrial thickness >3.5 mm to predict the presence of endometrial cancer was 100%, with a specificity of 58.14% and a positive predictive value of 26.03%.

The average endometrial thickness observed in the population was 3.5 mm, which contrasts with those previously published with reports >5 mm for symptomatic postmenopausal women [5].

Regarding the average age for endometrial cancer, the data obtained in this investigation suggest that the incidence is marked from 57 years of age, data that correlate with previous studies with a maximum incidence peak between 50 and 54 years of age and a mortality peak from the age of 60 [8]. It has been reported that the risk of endometrial cancer has a rising curve from 55 in countries such as the United States, Canada, and France. This variance in the age ranges is probably because, in these countries, there are screenings so that cases are detected at a younger age [9].

Regarding the observed risk factors, it was determined that metabolic disorders carry a relative risk for oncological diseases confined to the endometrium. According to the data obtained, the observed percentage was 9.95% for diabetes and 10.95% for obesity, which indicates that the peripheral conversion of sex hormones from fatty deposits leads to structural alterations of endometrial cells.

The previously presented data are similar to those obtained by Raglan et al. [10], who, in a meta-analysis of 12,657 patients, observed that 12.01% of the women presented high an-

thropometric indices, and 8.03% indicated a dietary intake rich in carbohydrates and a sedentary lifestyle. In any case, it seems that body mass index and waist-hip ratio were associated with a higher risk of cancer in premenopausal women; as reported, a body mass index equal to or greater than 28 confers a relative risk of 3 to 1 to develop endometrial cancer [11].

Concerning the histopathological findings, women with abnormal uterine bleeding and thick endometrium had a high incidence of simple hyperplasia without atypia at 35.14%, simple hyperplasia with atypia at 24.32%, complex hyperplasia without atypia at 16.89% and complex hyperplasia with atypia. 10.81%. Currently, simple hyperplasia is also the main histopathological finding observed in women with abnormal uterine bleeding, with a cancer incidence of 4.75%, given by specific endometrial cell mutations [12].

Another relevant piece of information was the use of hormonal therapy in menopause and postmenopause; according to the data obtained herein, it had an incidence of 8.96%, data that correlate with that provided by Santen [13], who in his results obtained an incidence of 9.71%, which suggests similarity in the observed risk patterns.

The present study has the weaknesses of a retrospective source; new prospective studies should evaluate the prognostic value and the cutoff point of 3.5 mm of endometrial thickness in symptomatic postmenopausal women.

Conclusions

The high sensitivity of measuring endometrial thickness >3.5 mm as a predictor of endometrial cancer in symptomatic postmenopausal women is high; however, it does not have reasonable specificity and positive predictive value, limiting its clinical use.

Editor's note

The Revista Oncología Ecu remains neutral regarding jurisdictional claims on published maps and institutional affiliations.

Acknowledgments

The authors thank the employees and patients of the Gynecological-Obstetric-Pediatric University Hospital of Guayaquil, who collaborated in developing this research.

Administrative information

Abbreviations

AUB: abnormal uterine bleeding.
Ca: Cancer.
CI: confidence interval.
FPH: Family pathological history.
HRT: hormone replacement therapy.
OR: Odds ratio.

Additional Files

None declared by the authors.

Financing

The authors did not receive any financial recognition for this research work.

Availability of data and materials

Data are available upon request to the corresponding author. No other materials are reported.

Author contributions

Crhistian Raúl Morales Velasco: conceptualization, validation, visualization, methodology, project management, writing: review and editing.

Josefina Ramírez Amaya: conceptualization, data curation, formal analysis, fundraising, research, resources, software, writing - original draft.

All authors read and approved the final version of the manuscript.

Ethics committee approval

It does not apply to studies of databases or medical records.

Consent for publication

The present study is a database analysis; it does not apply to this type of study.

References

1. Giri SK, Nayak BL, Mohapatra J. Thickened Endometrium: When to Intervene? A Clinical Conundrum. J Obstet Gynecol India. 2021 Jun;71(3):216-225. DOI: 10.1007/s13224-020-01415-4. Epub 2021 Feb 2. PMID: 34408340; PMCID: PMC8310815.

2. Bagnoli VR, Fonseca AMD, Massabki JOP, Arie WMY, Azevedo RS, Veiga ECA, Soares Junior JM, Baracat EC. Gynecological cancer and metabolic screening of 1001 elderly Brazilian women. Rev Assoc Med Bras (1992). 2019 Nov 7;65(10):1275-1282. DOI: 10.1590/1806-9282.65.10.1275. PMID: 31721959.

3. Gharibvand MM, Ahmadzadeh A, Asadi F, Fazelinejad Z. The diagnostic precision of apparent diffusion coefficient (ADC) in the grading of malignant endometrial lesions compared with histopathological findings. J Family Med Prim Care. 2019 Oct 31;8(10):3372-3378. DOI: 10.4103/jfmpc.jfmpc_142_19. PMID: 31742171; PMCID: PMC6857380.

4. Santoro A, Piermattei A, Inzani F, Angelico G, Valente M, Arciuolo D, Spadola S, Martini M, Fanfani F, Fagotti A, Gallotta V, Scambia G, Zannoni GF. Frozen section accurately allows pathological characterization of endometrial cancer in patients with a preoperative ambiguous or inconclusive diagnoses: our experience. BMC Cancer. 2019 Nov 12;19(1):1096. DOI: 10.1186/s12885-019-6318-5. PMID: 31718623; PMCID: PMC6852930.

5. Raby B T, Sierra P, Tsunekawa H, Craig J, Carvajal J, Cuello M. Capacidad diagnóstica de la ecografía para detectar cáncer de endometrio en mujeres posmenopaúsicas sintomáticas y asintomáticas: experiencia de la Universidad Católica de Chile. Rev. chil. obstet. ginecol. 2014 Jun;79(3):166-172. DOI:10.4067/S0717-75262014000300004.

6. Verrier Y, Serrano N, Campos M. Características clínico-epidemiológicas y manejo del cáncer endometrial (2010-2013). Rev Cubana Obstet Ginecol 2016;42(1):1-6. Disponible en: scielo.cu/S0138.

7. Kazandi M, Akşehirli S, Cirpan T, Akercan F. Transvaginal sonography combined with saline contrast sonohysterography to evaluate the uterine cavity in patients with abnormal uterine bleeding and postmenopausal endometrium more than 5 mm. Eur J Gynecol Oncol. 2003;24(2):185-90. PMID: 12701976.

8. Makker V, MacKay H, Ray-Coquard I, Levine DA, Westin SN, Aoki D, Oaknin A. Endometrial cancer. Nat Rev Dis Primers. 2021 Dec 9;7(1):88. DOI: 10.1038/s41572-021-00324-8. PMID: 34887451; PMCID: PMC9421940.

9. Jou J, Charo L, Hom-Tedla M, Coakley K, Binder P, Saenz C, Eskander RN, McHale M, Plaxe S. Practice patterns and survival in FIGO 2009 stage 3B endometrial cancer. Gynecol Oncol. 2021 Nov;163(2):299-304. DOI: 10.1016/j.ygyno.2021.09.005. Epub 2021 Sep 22. PMID: 34561099.

10. Raglan O, Kalliala I, Markozannes G, Cividini S, Gunter MJ, Nautiyal J, Gabra H, Paraskevaidis E, Martin-Hirsch P, Tsilidis KK, Kyrgiou M. Risk factors for endometrial cancer: An umbrella review of the literature. Int J Cancer. 2019 Oct 1;145(7):1719-1730. DOI: 10.1002/ijc.31961. Epub 2019 Feb 20. PMID: 30387875.

11. Lee YY, Choi MC, Park JY, Suh DH, Kim JW. Major clinical research advances in gynecologic cancer in 2020. J Gynecol Oncol. 2021 Jul;32(4):e53. DOI: 10.3802/jgo.2021.32.e53. PMID: 34085794; PMCID: PMC8192228.

12. Cancer Genome Atlas Research Network, Kandoth C, Schultz N, Cherniack AD, Akbani R, Liu Y, Shen H, Robertson AG, Pashtan I, Shen R, Benz CC, Yau C, Laird PW, Ding L, Zhang W, Mills GB, Kucherlapati R, Mardis ER, Levine DA. Integrated genomic characterization of endometrial carcinoma. Nature. 2013 May 2;497(7447):67-73. DOI: 10.1038/nature12113. Erratum in: Nature. 2013 Aug 8;500(7461):242. PMID: 23636398; PMCID: PMC3704730.

13. Santen RJ. Vaginal administration of estradiol: effects of dose, preparation and timing on plasma estradiol levels. Climacteric. 2015 Apr;18(2):121-34. DOI: 10.3109/13697137.2014.947254. Epub 2014 Oct 18. PMID: 25327484.