



Journal Homepage: - [www.journalijar.com](http://www.journalijar.com)  
**INTERNATIONAL JOURNAL OF  
ADVANCED RESEARCH (IJAR)**

Article DOI: 10.21474/IJAR01/21632  
DOI URL: <http://dx.doi.org/10.21474/IJAR01/21632>



## RESEARCH ARTICLE

# ENDOMETRIAL THICKENING IN PATIENTS ON TAMOXIFEN: CURRENT INSIGHTS AND MANAGEMENT STRATEGIES

Douha Ziane, Chadia Khalloufi, Houda Moustaide and Saad Benkirane

Department of Gynecology and Obstetrics, University Hospital Center Mohamed VI of Tangier, Faculty of Medicine and Pharmacy of Tangier, Abdelmalek Essaadi University, Morocco.

---

### Manuscript Info

---

#### Manuscript History

Received: 18 June 2025  
Final Accepted: 20 July 2025  
Published: August 2025

---

### Abstract

---

Tamoxifen, a selective estrogen receptor modulator (SERM), remains a cornerstone adjuvant treatment for hormone receptor-positive breast cancer because of its anti-estrogenic effects on breast tissue. However, its partial estrogen-like activity on the endometrium raises concerns about endometrial thickening and related pathologies. Recent data indicate that up to 66% of women receiving tamoxifen show an endometrial thickness of  $\geq 8$  mm on ultrasound. According to several studies, about 50–60% of women on tamoxifen have an endometrium measuring  $\geq 8$  mm on imaging, yet more than half of these cases reveal a benign or atrophic endometrium on biopsy, highlighting that routine invasive investigations may be unnecessary in asymptomatic patients. This mismatch between imaging findings and histology calls into question the value of systematic invasive evaluation in women without symptoms. A review of recent clinical and imaging studies, predictive models incorporating machine learning, and updated clinical guidelines suggests that risk stratification could be improved through nomograms that integrate both clinical and radiologic data. Furthermore, experimental research indicates that certain agents, such as rapamycin, may help limit tamoxifen-induced endometrial proliferation. Ultimately, while endometrial thickening is common in this population, it is not always a sign of malignancy. Current evidence supports a more selective, symptom-driven approach to further evaluation, with personalized follow-up strategies aimed at avoiding unnecessary procedures while ensuring early detection of clinically relevant lesions.

"© 2025 by the Author(s). Published by IJAR under CC BY 4.0. Unrestricted use allowed with credit to the author."

---

## Introduction:

Tamoxifen is a well-established adjuvant therapy for hormone receptor-positive breast cancer due to its anti-estrogenic effects on breast tissue [1]. However, its partial agonist activity on the endometrium exposes patients to an increased risk of endometrial changes, ranging from benign thickening to hyperplastic or neoplastic lesions [2]. Recent studies have shown that up to 66% of women receiving tamoxifen have an endometrial thickness  $\geq 8$  mm on ultrasound, yet nearly half of these cases reveal atrophic endometrium on biopsy [2]. This discrepancy between sonographic findings and histological results raises a key clinical question: which cases of thickened endometrium warrant further investigation? This article aims to provide an updated overview of the current knowledge regarding tamoxifen-associated endometrial thickening and to discuss evidence-based management strategies guided by recent clinical recommendations and emerging diagnostic tools.

### Tamoxifen and Endometrial Thickening:

Tamoxifen, a selective estrogen receptor modulator (SERM), is widely recognized as a cornerstone in the adjuvant treatment of hormone receptor-positive breast cancer, where it has been shown to reduce both recurrence and mortality rates [2]. Despite these clear benefits, its partial estrogen-like activity on the endometrium has long raised concerns, particularly regarding the risks of hyperplasia and, in some cases, malignancy [3].

Endometrial thickening is a frequent finding in women receiving tamoxifen, but its clinical significance is often limited. In one study, Love and colleagues reported that around 41% of asymptomatic women on tamoxifen showed a thickened endometrium on ultrasound, yet nearly half of these cases were atrophic when examined histologically [4]. More recent investigations have confirmed this discrepancy, showing that close to 50% of women with an endometrial thickness of  $\geq 8$  mm ultimately present benign or atrophic findings on biopsy, underscoring the weak correlation between sonographic appearances and true pathology [5].

### Pathophysiology and Imaging Limitations :

The alterations in the endometrial lining noted in women undergoing tamoxifen therapy are associated with its intricate interaction with estrogen receptors present in the uterine tissue. This phenomenon may lead to the occurrence of stromal edema, cystic dilation of the glands, and, in certain instances, the formation of polyps [6]. Although these modifications may appear alarming during ultrasound examinations, histological evaluations frequently uncover non-neoplastic characteristics. Clinical guidelines underscore this uncertainty: the 2024 Canadian recommendations (JOGC No. 451) discourage routine investigations in asymptomatic postmenopausal females exhibiting an endometrial thickness of less than 11 mm, notwithstanding their tamoxifen usage [7]. In a similar vein, the American College of Obstetricians and Gynecologists (ACOG) asserts that the assessment should be predominantly motivated by clinical manifestations, such as postmenopausal hemorrhaging, rather than relying solely on imaging outcomes [8]. An additional complication arises from tamoxifen's ability to induce what is termed "pseudothickening" due to subendometrial cyst formation and stromal modifications, which may resemble pathological conditions during ultrasound evaluations. In the absence of correlation with clinical symptoms or the application of supplementary diagnostic techniques such as Doppler imaging, these observations pose a risk of leading to overdiagnosis and unwarranted medical interventions [9].

### Diagnostic and Management Strategies:

In cases of uncertainty, hysteroscopy remains the gold standard, particularly when the endometrial pattern appears heterogeneous, focal, or when bleeding is present. Several studies have confirmed that hysteroscopy provides superior diagnostic accuracy compared to blind curettage in tamoxifen-treated women with endometrial thickening. For instance, Jung et al. (2018) and Korkmazer et al. (2014) demonstrated that hysteroscopic biopsy consistently yields more reliable detection of intrauterine pathology in this population [10,11].

To avoid unnecessary invasive procedures, predictive scoring systems have been proposed. Bottura et al. (2024) developed a nomogram to prioritize hysteroscopy based on a combination of clinical and imaging factors [12]. More recently, Shaoshan et al. (2025) introduced a machine learning-based nomogram with excellent discriminative performance (C-index  $\sim 0.87$ – $0.89$ ), offering individualized risk prediction for endometrial lesions in breast cancer patients undergoing tamoxifen therapy [13].

Together, these approaches highlight the value of combining clinical context, imaging findings, and predictive tools to ensure that hysteroscopy is reserved for women at highest risk, thereby reducing unnecessary interventions while safeguarding against missed pathology.

### Future Directions and Preventive Approaches:

One of the main challenges in monitoring women receiving tamoxifen is determining which patients are truly at risk of developing clinically significant endometrial disease. Recent advances in predictive modeling, particularly machine learning–based nomograms, have shown promise in refining patient selection by integrating clinical variables such as age, duration of therapy, symptom profile, and ultrasound findings [13]. These tools may help clinicians move beyond a “one-size-fits-all” strategy toward a more individualized surveillance approach.

At the same time, pharmacologic prevention is emerging as a potential avenue for protecting the endometrium. In an experimental study, Nakamura et al. (2025) demonstrated that rapamycin, an mTOR pathway inhibitor, was able to suppress tamoxifen-induced proliferation of endometrial stromal cells at doses lower than those typically required in clinical settings [14]. Their findings suggest that targeted modulation of proliferative pathways could represent a novel strategy for reducing tamoxifen-associated endometrial changes, particularly when discontinuation of therapy is not feasible.

Additional predictive models are also being explored in different populations. For instance, Li (2025) proposed a nomogram designed to estimate the risk of endometrial hyperplasia or carcinoma in premenopausal women, further illustrating how individualized prediction tools might guide earlier and more tailored interventions [15].

Although still preliminary, these approaches highlight the potential of a proactive preventive strategy; one that not only responds to symptoms as they appear, but also intervenes directly on the underlying biological mechanisms. Combined with careful ultrasound interpretation, symptom correlation, and selective hysteroscopy, such strategies may enhance vigilance while minimizing unnecessary invasive procedures.

### Conclusion:

Endometrial thickening in women treated with tamoxifen is a frequent and often benign finding. While its estrogenic effects on the endometrium can lead to structural changes, recent studies show that these are not always indicative of pathology. In asymptomatic patients, especially postmenopausal women, routine investigation based solely on endometrial thickness is no longer recommended. A symptom-guided and risk-based approach, supported by current guidelines and predictive tools, offers a balanced strategy to avoid unnecessary procedures while ensuring timely detection of clinically relevant lesions.

### References:

1. Kantarcı A, Gürsoy T, Batur Ş, Akdoğan B, Gökmen S, Şimşek T, et al. Endometrial pathology in tamoxifen-treated breast cancer patients: correlation of endometrial thickness on ultrasound, preoperative sampling, and final pathology. *Anatolian Journal of Medicine*. 2025;27(1):1-9. doi:10.5505/anatoljmed.2025.42385
2. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Tamoxifen for early breast cancer: an overview of the randomised trials. *Lancet*. 1998;351(9114):1451-67. PMID: 9605801. [PubMed](#)
3. American College of Obstetricians and Gynecologists. Committee Opinion No. 601: Tamoxifen and uterine cancer. *Obstet Gynecol*. 2014;123:1394-7. [ACOGPubMed](#)
4. Hann LE, Giess CS, Bach AM, Tao Y, Baum HJ, Barakat RR. Endometrial thickness in tamoxifen-treated patients: correlation with clinical and pathologic findings. *AJR Am J Roentgenol*. 1997;168(3):657-61. doi:10.2214/ajr.168.3.9057510. (Montre qu'~48% avaient un endomètre ≥ 8 mm et détaille la faible corrélation clinique.) [PubMed](#)
5. Love CD, Muir BB, Scrimgeour JB, Leonard RC, Dillon P, Dixon JM, et al. Investigation of endometrial abnormalities in asymptomatic women treated with tamoxifen and an evaluation of the role of endometrial screening. *J Clin Oncol*. 1999;17(7):2050-4. doi:10.1200/JCO.1999.17.7.2050. (Rapporte 41% d'épaississement à l'écho et 46% d'atrophie à l'histologie.)
6. Polin SA, Ascher SM. The effect of tamoxifen on the genital tract. *Radiographics*. 2008;28(2):437-52. doi:10.1148/rg.282075068.
7. Allen VM, Bryson GL, Cheung A, Fleming N, Gysler M, Lemyre M, et al. Guideline No. 451: Asymptomatic endometrial thickening. *J Obstet Gynaecol Can*. 2024;46(3):e301-14. doi:10.1016/j.jogc.2023.11.007.
8. American College of Obstetricians and Gynecologists. Committee Opinion No. 601: Tamoxifen and uterine cancer. *Obstet Gynecol*. 2014;123:1394-7. doi:10.1097/01.AOG.0000450414.37574.a0.
9. Hann LE, Giess CS, Bach AM, Tao Y, Baum HJ, Barakat RR. Endometrial thickness in tamoxifen-treated patients: correlation with clinical and pathologic findings. *AJR Am J Roentgenol*. 1997;168(3):657-61. doi:10.2214/ajr.168.3.9057510.
10. Jung H, Kim HY, Park CT, Shin JH, Kim MJ, Kim JJ. Comparative study on hysteroscopic and histologic findings in tamoxifen-treated patients. *Obstet Gynecol Sci*. 2018;61(5):589-96. doi:10.5468/ogs.2018.61.5.589.
11. Korkmaz E, Solmaz U, Özdemir Ö, Gülseren V, Akbayir O, Aydin S, et al. Assessment of thickened endometrium in tamoxifen therapy: hysteroscopic versus blind curettage findings. *Turk J Obstet Gynecol*. 2014;11(3):140-5. doi:10.4274/tjod.06714.
12. Bottura B, Rocha ALL, Ferreira CN, Candido Dos Reis FJ, Candido EB, Peixoto-Filho FM, et al. Developing a nomogram to prioritize hysteroscopy in women with endometrial abnormalities. *J Clin Med*. 2024;13(4):1145. doi:10.3390/jcm13041145.
13. Shaoshan C, Fang W, Xiaoqing L, Yuxi L, Yuan Y, Meng L, et al. Machine learning nomogram for predicting endometrial lesions after tamoxifen therapy in breast cancer patients. *Sci Rep*. 2025;15:10234. doi:10.1038/s41598-024-82373-z.
14. Nakamura A, Tanaka Y, Amano T, et al. Rapamycin inhibits tamoxifen-induced endometrial proliferation in vitro: a pilot study on endometrial protection in breast cancer patients. *Sci Rep*. 2025;15:2112. doi:10.1038/s41598-025-86586-8.
15. Li Z, Yin J, Liu Y, Zeng F. A risk prediction nomogram for endometrial hyperplasia and endometrial carcinoma in premenopausal women. *Sci R*2025;15:XXXX.