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Should ultrasound assessment of the endometrium be necessary in patients treated with Tamoxifen?

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Abstract
Tamoxifen is a nonsteroidal selective estrogen receptor modulator that is used mainly for adjuvant treatment of estrogen receptor-positive breast cancer. However, tamoxifen, due to its estrogen-mimicking effects, has been linked to various uterine conditions including menstrual irregularities, and endometrial cancer. Considering that in women taking tamoxifen, ultrasonographical endometrial thickness can be increased without an underlying pathology and that the tamoxifen induces only an extra endometrial cancer in 1 per 1000 women per year of use, patients undergoing tamoxifen treatment don't typically undergo regular examinations of the endometrium, including ultrasonography. Routine ultrasonographic screening for endometrial lesions could result in excessive intervention for non-symptomatic endometrial conditions, undue stress, and might even negatively affect patients' adherence to tamoxifen therapy, which is crucial for reducing breast cancer recurrence and mortality. Nevertheless, if any unusual bleeding arises, an endometrial evaluation is necessary.

KEYWORDS
tamoxifen, endometrial thickness, ultrasound, breast cancer

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Tamoxifen is a nonsteroidal selective estrogen receptor modulator that is used mainly for adjuvant treatment of estrogen receptor-positive breast cancers in premenopausal women [1] and as chemoprevention in patients at increased risk for breast cancer [2].

In premenopausal patients, the effect of tamoxifen on the hypothalamic-pituitary-ovarian axis is similar to clomiphene, increasing follicle-stimulating hormone (FSH) and estradiol levels, and in those women having abnormal uterine bleeding, up to 23 percent will be found to have underlying (benign) endometrial pathology. In postmenopausal women, tamoxifen exerts a strong estrogenic effect that can stimulate endometrial proliferation and DNA damage [2].

Unlike raloxifene, tamoxifen has been linked to various uterine conditions such as menstrual irregularities, blood clots, uterine sarcoma, uterine carcinosarcoma [2], and endometrial thickening, fibroids, polyps, and endometrial cancer due to its estrogen-mimicking effects [3]. However, tamoxifen induces only an extra endometrial cancer in 1 per 1000 women per year of use, with endometrial cancer being extremely rare in asymptomatic premenopausal patients [4]. Thus, patients undergoing tamoxifen treatment don't typically undergo regular examinations of the endometrium, including ultrasonography [5] and the American College of Obstetricians and Gynecologists (ACOG) endorses against screening asymptomatic patients on tamoxifen for endometrial cancer [6]. On the contrary, some authors recommend the assessment of thickened endometrium in tamoxifen therapy [7].

Tamoxifen typically induces sub-endometrial cysts at ultrasonography which correspond to cystically dilated endometrial glands at histology [8], although an atrophic endometrium could be discovered in some cases. Furthermore, tamoxifen is associated with endometrial polyps (ultrasonographically discovered) which are not precursors of malignancy, and a large proportion of tamoxifen users, without endometrial pathology at the start, will develop such subclinical lesions [8]. Nevertheless, if any unusual bleeding arises, an endometrial evaluation is necessary due to the marginally heightened risk of endometrial cancer associated with tamoxifen. More than half of premenopausal patients and up to a quarter of postmenopausal patients on tamoxifen therapy experience abnormal uterine bleeding [9]. This condition necessitates further investigation. Endometrial biopsy or Hysteroscopy with curettage is imperative in most cases [7]. Furthermore, the first procedure has generally replaced the need for diagnostic dilation and curettage.

The point is to be sure that there is no endometrial cancer [10]. Nevertheless, the presence of spotting as a clinical symptom is crucial to propose more investigation. One difficulty of diagnosis that could hide an endometrial cancer occurs in patients with very tight or closed cervix [11].

As a conclusion, conducting routine ultrasonographic screenings for endometrial lesions in asymptomatic patients on tamoxifen could result in excessive intervention for non-symptomatic endometrial conditions, undue stress, and might even negatively affect patients' adherence to tamoxifen therapy, which is crucial for reducing breast cancer recurrence and mortality.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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