Diagnostic Accuracy of Transvaginal Ultrasound Versus Hysteroscopy in Evaluation of Endometrial Pathology in Breast Cancer Women Receiving Tamoxifen: Correlation with Histopathological Examination

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ABSTRACT

Background: Multiple endometrial lesions have been reported in tamoxifen -treated breast cancer patients. As a consequence, a thorough uterine cavity examination is often necessary.

Aim of the study: To compare the efficacies of transvaginal ultrasound versus hysteroscopy in detecting the endometrial changes in tamoxifen-treated breast cancer patients, and to correlate the findings of both methods with histopathological examination of endometrial biopsies.

Patients and Methods: Twenty seven patients who had mastectomies for breast cancer and receiving tamoxifen (TAM) were enrolled in this prospective study. They underwent transvaginal ultrasonography (TVUS) and hysteroscopy for endometrial assessment. Endometrial biopsy was taken from all participants for histopathological examination. The ultrasonographic and hysteroscopic findings were compared and correlated with the histopathological results.

Results: The diagnostic accuracy of TVUS versus hysteroscopy in detecting endometrial changes in breast cancer TAM treated women was as follows; TVUS had a sensitivity (82.4%), specificity (30.0%), PPV (66.7%), NPV (50.0%) and accuracy (63%) ;while, the hysteroscope had sensitivity (94.1%), specificity (60.0%), PPV (80.0%), NPV (85.7%) and accuracy (81.5%).

Conclusion: Because of certain discrepancies between TVUS and histopathological results in TAM treated women, TVUS is not the best tool for evaluating the endometrium in those patients. The utility of the hysteroscopic image processing helps in the triage of women who require endometrial surveillance, so it will reduce the pathologist’s workload and the patient’s apprehension while waiting for histopathology results. Nevertheless hysteroscope cannot establish a conclusive diagnosis of premalignant or malignant lesions, but it provides a direct view for targeted biopsies to create a definitive diagnosis.

Keywords: Transvaginal ultrasound; Hysteroscopy; Endometrial Changes; Breast cancer; Tamoxifen.

INTRODUCTION

Breast cancer accounts for around a quarter of all cancers diagnosed in women worldwide. Breast cancer is estimated to be the most prevalent cancer among Egyptian women, accounting for 37.7% of all cancers in women and 29.1% of cancer-related deaths 1.

It has recently been demonstrated that Tamoxifen (TAM) can prevent breast cancer in high-risk women. Also the use of adjuvant TAM has significantly improved the survival rates 2,3. Despite the fact of TAM has an antiestrogen in the breast tissue but it has an estrogenic effect on endometrium and myometrium.TAM treatment for a long time has been linked to an increase in risk of endometrial polyps, leiomyomas, endometrial hyperplasia, adenomyosis and even endometrial cancer 1. However, the beneficial effects of tamoxifen in women with breast cancer outweigh the potential endometrial adverse effects of the drug 1.

Nevertheless, the widespread of TAM use in breast cancer, an appropriate endometrial surveillance technique remains a source of debate, especially in asymptomatic women 3.
TVUS is the most widely used gynaecological surveillance method, endometrial thickness is an important surveillance indicator 6,7.

Hysteroscopy allows for direct visualisation of the endometrium and accurate biopsy tissue sampling, hysteroscopy when used in conjunction with TVUS, enables the detection of intracavitary lesions, as well as determining if a lesion is endometrial or subendometrial 1.

This study aimed to compare the efficacy of transvaginal ultrasound versus hysteroscopy in detecting endometrial changes in tamoxifen-treated breast cancer patients, and to correlate the findings of both methods with histopathological results of endometrial biopsies.

PATIENTS AND METHODS

From March 2018-April 2021, a prospective study was performed at Alazhar University Hospital on 27 women, aged ranging from 32 to 65, they had undergone to mastectomy for breast cancer and were receiving tamoxifen as an adjuvant therapy. They selected from obstetrics and gynaecology outpatient clinics, as well as surgery and radiology departments. The research was done in light of the 2013 Helsinki Declaration on Human Experimentation and approved by the faculty of medicine's ethical committee for girls (Cairo), Al Azhaer University, Egypt. Before enrolling in this study, all participants gave their written consent to have their endometrium tested using TVUS and hysteroscopy with D&C biopsy. Women with mastectomy who were pre- or postmenopausal, symptomatic (vaginal bleeding) or receiving TAM as part of their care plan were included. While patients with breast cancer who were not receiving TAM, as well as virgins, were excluded. The patients were subjected to complete history and examination to fulfill inclusion and exclusion criteria. Regarding the history we focused on, date of mastectomy,type of mastectomy, type of surgery (modified radical mastectomy or lumpectomy), report of breast histopathology, family history of malignancy, adjuvant treatment of breast cancer (chemotherapy, radiotherapy, hormonal treatment), duration of TAM therapy, abnormal vaginal bleeding (menorrhagia, metrorrhagia, postmenopausal bleeding), history of endometrial biopsy & its result.

All participants were referred to radiology department for radiological assessment for a uterus and adnexa. Real-time ultrasound was performed using Toshiba Aplio 400 (Toshiba Medical Systems, Japan) and GE Logiq P5 (GE Healthcare, Milwaukee, WI) ultrasound machines with the vaginal transducer (5–10 MHz). Transvaginal probe was used, for measuring the uterus, in longitudinal and transverse views. We checked the myometrium for echo pattern & its regularity and for any focal lesion.

The endometrium should be measured in a sagittal plane. Endometrial thickness (ET) was measured from the echogenic interface of the anterior basal layer to the echogenic interface of the posterior basal layer, thus representing a double layer. Also it was measured in follicular phase in perimenopausal women because it may reaches to a 16 mm in secretory phase in normal women 8 so it may denote misinterpretation.

We considered as per the majority of researchers 8,9,10 the average or the cut off value of ET was 5-7 mm & <8 mm in asymptomatic post-and premenopausal women respectively. Malignancy is suspected if there was an ill defined endometrial/myometrial junction with loss of subendometrial halo, or hetrogenus endometrial echotexture. Ovaries were evaluated for; antral follicles and ovarian volume (especially in cases of young age); ovarian cyst and mass. Douglas pouches evaluated for the presence of abnormalities.

Each participant was then scheduled for a hysteroscopic examination and D&C biopsy. Hysteroscopy was performed at any time in postmenopausal women. But the Premenopausal women subjected to hysteroscopy during the follicular phase of thier cycle, because the secretory endometrium may be overdiagnosed with endometrial polyps due to the endometrium may appear polypoid during this time 11. The participant underwent to regional or general anesthesia regarding to anesthesiologists opionion. Hysteroscopy was performed with a diagnostic MGB 4 mm rigid hystroscope having a 30-degree oblique aperture view with a 5 mm sheath. The entire uterine cavity was observed in an orderly manner up to the cornu. Ultimately we commented on the cervix, uterus, endometrium (colour, thickness, and any focal lesion or polyp). Samples were taken from all aspects of endometrial cavity and fixed in 10% formalin and sent for histopathological examination in histopathology department of Alzharra University Hospital. The results of TVUS and hysteroscopy were compared and correlated with the gold standard histopathological reference and statistical analysis was performed.

Statistical analysis

Astatistical package for social sciences, version 23.0 was used to analyse the results. Qualitative data were expressed as frequency and percentage. Quantitative data were expressed as mean± standard deviation (SD) data. The sensitivity, specificity, PPV and NPV were calculated for 2D gray scale ultrasound and hysteroscopic evaluation. P-value < 0.05 was considered as statistically significant.
RESULTS

The demographic data was summarized in (Table 1). The prevalence of normal and abnormal endometrium in the sample population, as determined by TVUS, hysteroscopy, and histopathological examination, was demonstrated in (Table 2).

| Participants Characteristic items | N =27 |
|-----------------------------------|-------|
| Maternal age (years):             |       |
| Mean ± SD Range                   | 52.14 ± 1.4 | 32-65 |
| BMI (kg/m2):                      |       |
| Mean ± SD                         | 27.46 ± 1.97 | Range |
| Parity                            |       |
| Mean± SD                          | 1.01±1.15 | Range |
| Duration of therapy               |       |
| Mean± SD                          | 2.72±1.34 | Range |
| Premenopause                      |       |
| NO.                               | 11    | %    |
| Postmenopause                     |       |
| NO.                               | 16    | 59.3 |
| Family history                    |       |
| +ve                               | 10    | 37.1 |
| -ve                               | 17    | 62.9 |
| Breast surgery                    |       |
| Modified Radical Mastectomy        | 23    | 88.5 |
| Lumbectomy                        | 4     | 21.5 |
| Histopathology of breast cancer types |     |
| Ductal carcinoma advanced         | 17    | 63   |
| Lobar carcinoma                   | 6     | 22.2 |
| Duct carcinoma grade 1.2.         | 4     | 14.8 |
| Vaginal bleeding                  |       |
| yes                               | 5     | 18.5 |
| no                                | 22    | 81.5 |
| Endometrial thickness measures    |       |
| Average thickness                 | 6     | 22.2 |
| - Increase endometrial thickness without cystic change | 11 | 40.7 |
| - Increase endometrial thickness with cystic change | 7 | 25.9 |
| - Polyp                            | 3     | 11.1 |
| - Endometrial atrophy susceptible lesion | 2 | 7.4 |
| - Endometrial atrophy             | 2     | 7.4 |
| - Suspicious lesion               | 0     | 0%   |
| Associated lesions                |       |
| Adenomyosis                       | 2     | 7.4 |
| Histopathological Examination     |       |
| Normal findings                   | 10    | 37.9 |
| Abnormal findings                 |       |
| Typical simple endometrial hyperplasia | 17 | 62.1 |
| - Typical Complex hyperplasia     | 5     | 15.8 |
| - Atypical hyperplasia            | 4     | 14.8 |
| - Polyp                            | 3     | 11.1 |
| - Atrophy                         | 2     | 7.4 |
| - Endometrial cancer              | 0     | 0%   |

Table 1: Demographic data of the study group.

There was a statistical insignificant difference between symptomatic and asymptomatic women, regarding, the frequency of endometrial changes which identified by TVUS and hysteroscopy and verified by histopathological results (Table 3). No cases of insufficient tissue sample was reported. When TVUS results were compared to the final histopathology results, (82.3%) were true positives, (70%) were false positives, (17.7%) were false negatives, and (30%) were true negatives (Table4, Figure 1.2.3). However when the hysteroscopic results were compared to the final histopathological result, (94.1%) were true positives, while, (5.9%) were false negative, (60%) were true negatives and 40% were false positive (Table 4, Figure 4).

The diagnostic efficacy of TVUS and hysteroscopy in the evaluation of endometrial changes in relation to histopathology findings was revealed that; TVUS had sensitivity (82.4%), specificity (30.0%), PPV (66.7%), NPV (50.0%) and accuracy (63%), while, the hysteroscope had sensitivity (94.1%), specificity (60.0%), PPV (80.0%), NPV (85.7%) and accuracy (81.5%), (Table 4).

There was no significant difference in the frequency of endometrial changes based on the length of TAM usage, i.e., between patients who had used TAM for< 2 or >2 years, p>0.05 (Table 5).

Table 2: TVUS, hysteroscopy and histopathological findings in study group (Descriptive data).
### Parameters

|                    | Symptomatic (n=5) | Asymptomatic (n=22) | p-value |
|--------------------|-------------------|---------------------|---------|
| **US findings**    | No. | %   | No. | %   |         |
| Irregular endometrium | 2   | 40.0% | 10  | 45.5% | 0.641  |
| Regular endometrium   | 3   | 60.0% | 12  | 54.5% |         |
| Average thickness    | 0   | 0.0%  | 6   | 27.3% | 0.153  |
| Diffuse thick endometrium without cystic changes | 2 | 40.0% | 9 | 40.9% |         |
| Diffuse thick endometrium with cystic changes | 2 | 40.0% | 5 | 22.7% |         |
| Polyp               | 1   | 20.0% | 0   | 0.0%  |         |
| Endometrial atrophy  | 0   | 0.0%  | 2   | 9.1%  |         |
| **Hysteroscopic Finding** | No. | %   | No. | %   |
| Normal finding      | 0   | 0.0%  | 7   | 31.8% | 0.370  |
| Endometrial hyperplasia | 4 | 80.0% | 11  | 50.0% |         |
| Polyp               | 1   | 20.0% | 2   | 9.1%  |         |
| Endometrial atrophy  | 0   | 0.0%  | 2   | 9.1%  |         |
| Suspicious lesion    | 0   | 0.0%  | 0   | 0.0%  |         |
| **Histopathologocal Findings** | No. | %   | No. | %   |
| Normal findings  | 0   | 0.0%  | 10  | 45.4% | 0.284  |
| Typical simple hyperplasia | 1 | 20.0% | 2   | 9.1%  |         |
| Typical complex hyperplasia | 1 | 20.0% | 4   | 18.2% |         |
| Atypical hyperplasia | 2 | 40.0% | 2   | 9.1%  |         |
| Polyp               | 1   | 20.0% | 2   | 9.1%  |         |
| Atrophy             | 0   | 0.0%  | 2   | 9.1%  |         |
| Suspicious lesion    | 0   | 0.0%  | 0   | 0.0%  |         |

Table 3: Comparison between asymptomatic and symptomatic participants regarding the US, hysteroscopic and histopathological findings.

| Histopathology | Abnormal (n=17) (62.9%) | Normal (n=10) (37.1%) | Sensitivity | Specificity | PPV | NPV | Accuracy |
|----------------|-------------------------|-----------------------|-------------|-------------|-----|-----|----------|
| **US**         |                         |                       |             |             |     |     |          |
| Endometrial change |                     |                       | 82.4%       | 30.0%       | 66.7% | 50.0% | 63.0%    |
| Abnormal (n=21)  | TP=14(82.3)             | FP=7(70)              |             |             |     |     |          |
| Normal (n=6)     | FN=3(17.7)              | TN=3(30)              |             |             |     |     |          |
| **Hysteroscopy** |                         |                       |             |             |     |     |          |
| Abnormal (n=20)  | TP=16(94.1)             | FP=4(40)              | 94.1%       | 60.0%       | 80.0% | 85.7% | 81.5%    |
| Normal (n=7)     | FN=1(5.9)               | TN=6(60)              |             |             |     |     |          |

Table 4: Diagnostic performance of U/S versus hysteroscopy in detection of endometrial disease.
Fig 1: Gray scale transvaginal ultrasound image (A) demonstrating diffuse endometrial thickening with multiple variable sized cystic changes. Gray scale transverse ultrasound image (B) of the same endometrium showing the cystic changes in thickened endometrium. Color Doppler image of the endometrium (C) demonstrating color flow in the central portion of the complex cystic endometrial lesion. Ultrasound diagnosis: endometrial hyperplasia with cystic changes. Histopathological diagnosis: complex cystic hyperplasia without atypia: true positive result.

Fig 2: Grayscale (A) and color Doppler (B) sagittal view by transvaginal ultrasound showing a thickened homogenous echogenic endometrium, measuring about (12.3 mm) in maximal anteroposterior diameter (A), with irregular borders, preserving subendometrial halo. Ultrasound diagnosis, simple endometrial hyperplasia while histopathological result revealed endometrial hyperplasia with polyp: true negative result.

Fig 3: Gray scale transverse (A) and sagittal (B) TVUS images showing well defined echogenic lesion in the endometrial cavity. A thin fluid rim is noted separating the lesion from the endometrial lining at a few places. Cystic changes are noted within this echogenic lesion. Uterine myometrium shows normal echopattern. The sonographic findings suggest endometrial polyp. Ultrasound diagnosis: endometrial polyp which matched with histopathology result, endometrial polyp with no malignant cells: true positive result.

Fig 4: (A) Hysteroscopic picture of endometrial hyperplasia which was matched with histopathology: true positive result. (B) Hysteroscopic picture of endometrial hyperplasia with polyp which matched with histopathology: true positive result. (C) Thin smooth atrophic endometrium, with petechial and subendometrial hemorrhage which matched with histopathological result: true positive result.
Abnormal vaginal bleeding was experienced by 5 patients (18%) who were symptomatic VS 22 patients (82%) who were asymptomatic with TAM use ranging 1-4 years in both groups. The incidence of symptomatic patients in our study was close to that found in Hetta et al. 12 Also Jindal et al. 13 conducted study in line with our study, in which 88% of the participants were asymptomatic and only 12% were symptomatic.

Endometrial thickening on TVUS is a strong signal that is also suggestive of endometrial pathology. 14 There is no precise definition of an abnormal ET for pre- or postmenopausal women receiving TAM due to its estrogenic effect on subendometrial gland which leading to increase ET 15. Various cutoff values for detection of the endometrial disease in asymptomatic postmenopausal women under TAM were reported, 5, 9, 10mm 14,15,16; however the findings of the previous studies are hampered by verifying bias and a small sample size. There is consensus about if postmenopausal and premenopausal women experience bleeding and their ET is >5 mm, >8mm respectively, further investigation is needed. 9,10,17

The mean ET in our patients was 9.52±4.32 with range 3-30mm. Six participants (22.2%) had average thickness and 21 women (77.8%) had endometrial changes, which manifested as, diffuse thickened endometrium without cystic changes in 7 patients (40.7%), diffuse thickened endometrium with cystic changes in 11 patients (25.9%), polyp in one patient (3.7%) and atrophic endometrium in 2 patients (4.0%). No suspicious endometrial lesion was found. TVUS also revealed 2 patients had adenomyosis as associated lesion and that was expected with TAM. TVUS sometimes detects the polyp as a nonspecific thickening of the central endometrial complex, with or without cystic changes, but it may also skip the diagnosis 8.

Our results were matched with Amer et al. 1 and Le Donne et al. 17 who reported the same results regarding increased ET in patients receiving TAM after mastectomy. In term of endometrial regularity, we found, 12 patients (44.5%) had irregular endometrial line. Although, Irregular or poorly defined ET is usually indicative of malignancy. However, in women receiving TAM, because of underlying benign diseases as adenomyosis, or polyp, poor definition of ET is not a helpful for the diagnosis of endometrial carcinoma. Also our results were in accordance with the results of Le Donne et al. 17 who found that cystic endometrial appearance was frequent in patients under TAM.

Regarding the hysteroscopic findings, we found that, 7 patients (25.9%) had normal endometrium but 20 patients (74.1%) had abnormal endometrium as follow, I- 15 participants (55.6%) had endometrial hyperplasia (EH), (Figure 4). Really inspite of some studies were demonstrated the hysteroscopic morphology for each type of EH as Butureanu et al. 18 but this was not practically established, we only suspected, EH when the endometrium appears thicker on hysteroscopy than standard proliferative endometrium, which has a glistening, mucoid, pink-gray look. It's also likely that it's polypoid in nature. Small cysts and dilated, clogged sinusoids can be visible underneath the surface, 9, but it was difficult to distinguish between its types le typical and atypical forms. De Francis et al. 19 reported that up till now, the EH morphological criteria that detected by hysteroscopy are based on the operator’s subjective assessment and, therefore, are not reliable. 2-Three patients (11.1%) had polyps, 2 of which were missed by TVUS. It was found that women under TAM, either they experienced vaginal bleeding or not, the endometrial polyps usually are expected but they are common in asymptomatic women. 2 At hysteroscopy, the majority of polyps have smooth, glistening surfaces and are pink-gray to white in colour (Figure. 4). The polyps may be connected to a long or narrow stalk. Unlike endometrial carcinoma, they usually do not bleed readily when touched. Sometimes, the whole polyp or only the tip of the polyp may be hemorrhagic or infarcted 5.

3-Our study revealed 2 participants (7.4%) had atrophic endometrium. A hysteroscopic diagnosis of atrophic endometrium is established when uterine cavity was regular and the uterine lining was smooth, thin, and pale white with clearly visible network vessels . (Figure 4) Regarding the adenomyosis, the hysteroscope plays little role in its detection especially the diffused form, so TVUS is superior in detecting of adenomyosis over US.

Regarding the histopathological findings there was 10 patients (37.1%), revealed normal reports while 17 patients (62.9%) revealed pathology. as follow, 3 patients (11.1%) had simple EH, 5 (18.5%) had mixed cystic hyperplasia, 4 (14.8%) had atypical hyperplasia that noticed in patients used TAM > 2 years, 3 patients (11.1%) had polyp. All polyps were detected by hysteroscopy versus only one polyp detected by

| Duration of Treatment | Endometrial Change | P value |
|-----------------------|-------------------|---------|
|                       | Yes              | No      |         |
| 6 months -2 Years     | 7 (41.2%)        | 5 (50%) | 0.965   |
| ≥2 -4 Years           | 10 (58.8%)       | 5 (50%) |         |
| Total                 | 17 (100%)        | 10 (100%) |        |

Table 5: Effect of the duration of tamoxifen therapy on endometrial changes in a study group.
TVUS. Two participants (7.4%) had endometrial atrophy which was easily detected by both US and hysteroscopy. Our result was in agreement with Amer et al, who found that the most common histopathological finding was EH (31.3%).

In term of atypical EH, Hetta et al. reported higher incidence with atypia in patients with TAM treatment. However Saccardi et al. reported less incidence of EH with atypia. This may be attributable to different sample size.

No cases of endometrial cancer was found in our study, several studies were reported a significant correlation between TAM therapy and benign uterine pathologies and the majority of TAM's proliferative influences on endometrium are unlikely to progress to cancer. On other hand some researchers found in their studies cases of endometrial cancer among TAM treated women. But we can attributed that to our small sample size and or short duration of drug treatment, most of our participants didn’t take TAM more than 4 years and most of researchers as Le Donne et al. and Jones et al. inferred the increase the frequency of endometrial cancer to the long term use of TAM.

Our study revealed that no difference was found between the symptomatic and asymptomatic participants in the incidence of endometrial changes, p>0.05 (Table 3). Jindal et al., in agreement with our result, they found that increased endometrial changes On TVUS in asymptomatic postmenopausal women with breast cancer and receiving TAM. But, Cohen et al. found that the frequency of endometrial pathology was significantly higher in symptomatic patients receiving TAM, which contradicted our findings. In reality, the need for screening and surveillance in asymptomatic TAM patients is a subject of debate among researchers, as it has been demonstrated that asymptomatic patients are more likely to have a disease that can be easily detected when they visit care facility. If asymptomatic TAM patients were not recommended to keep track of for endometrial assessment, they may be lost.

Upon correlating the ultrasound and hysteroscopic findings and their efficiency in detection of endometrial changes with histopathology results, we only checked the correlation and diagnosis from the hand, identification of the presence or absence of endometrial changes, but not the condition of lesion, i.e, benign, orpremalignant (atypical EH) or malignant. Our study revealed that regarding TVUS, 14 (82.3%) were true positives, 7 patients (70%) were false positive i.e, inspite of increased the ET in those patients more than the cut off values, but, they revealed normal proliferative endometrium on histopathological reports.3 patients (17.7%) had false negativ results, this resulting from missed diagnosis of 2 cases of polyp and one case with normal ET revealed simple EH on histopathology, three cases (30%) were true negative (Table 4, Figure 1, 2, 3).

Regarding the hysteroscopic findings when they correlated with histopathology, 16 (94.1%) cases were true positives, 4 (40%) were false positive (i.e, revealed normal with histopathology), 1 (5.9) was false negative and 6 (60%) were true negatives (Table 4, Figure 4).

The diagnostic performance of ultrasonography and hysteroscopy in detection of endometrial changes regarding the histopathological reference, we found that hysteroscopy was more sensitive than ultrasound in the diagnosis of endometrial lesions, table 4, and this was consistent with the result of Le Donne et al. who showed a significant association between hysteroscopy and histological findings regarding the diagnosis of endometrial atrophy, polyps, hyperplasia and cancer (P<0.001). Similarly, Mukhopadhay et al. found a high sensitivity (71.4%) and specificity (100.0%) for hysteroscopy for diagnosing polyps. Amer et al. found that TVUS was not accurate in identifying hyperplasia and polyps. Moreover, Dijkhuize et al. reported that, due to the echogenic, irregular, cystic effect induced by TAM on endometrial stroma and gland and on the myometrium, without essentially inducing epithelial changes, therefore endometrial thickness cannot be used in those patients to define abnormalities. Similarly Jeon et al. reported that TAM causes subendometrial glandular hypertrophy, so ET can increase even in absence of pathologies. Some researchers suggested that TVUS endometrial testing has limited predictive value in asymptomatic patients with false positive result. Additionally, TVUS has been confirmed to provide false-negative diagnoses of small polyps, localised atypical hyperplasia and endometrial cancer.

On Contrary, Hetta et al. and Cohen et al. disagree with our result, they revealed that TVUS was more diagnostic than hysteroscopy.

In the paractice, inspite the value of hysteroscopy in detecting the endometrial pathology, however it doesn’t distinguish between typical and atypical hyperplasia, unless the latter is associated with focal lesion, additionally, in this situation hysteroscopy is only suspecting but not confirming the pathology. Similarly Barati et al. reported that, EH can develop visible space-occupying lesions that are simple to diagnose by hysteroscopy, but it may not noticeable, particularly in the early stages of the disease, so, histopathology tests are essential for the definitive diagnosis of exact pathology.

We couldn't find a correlation between the duration of TAM therapy and the occurrence of endometrial changes, similarly Donnez et al. didn't observe any relation between duration of TAM use and endometrial changes, nevertheless the previous authors found that increased the incidence of endometrial cancer in patients used TAM for more than four years. In the present study we also found, inspite there no relation was found between the incidence of endometrial changes and duration of TAM therapy, but, there was association between the
latter and the severity of endometrial changes, i.e., our study revealed all patients who had atypical hyperplasia were used TAM > 2 years duration. This means that incidence of premalignant lesion is increased with lengthing the duration of treatment.

Despite the fact that our research found a higher rate of endometrial changes in asymptomatic patients than previous studies, we assume that this is a strength point of this study, because it prompts gynecologists to carefully screen asymptomatic women receiving TAM. The study's limitations include the small sample size and absence of patient that used TAM for more than 4 years.

CONCLUSION

TVUS is a suitable for endometrial screening for intrauterine pathology. However, because of certain discrepancies between TVUS and histopathological results in TAM treated women, TVUS is not the ideal tool for evaluating the endometrium in those patients. The utility of the hysteroscopic image processing helps in the triage of women who require endometrial surveillance, so it will reduce the pathologist's needless workload and the patient's apprehension while waiting histopathology result. Nevertheless hysteroscope cannot establish a conclusive diagnosis of premalignant or malignant lesion, but it provides a direct view of the endometrium for detection of focal lesion and chance of conducting targeted biopsies to create a definitive diagnosis.

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