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Original Article

Diagnostic evaluation of Transvaginal Sonographic Elastography to identify Endometrial Carcinoma

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ABSTRACT

Background: Transvaginal sonographic elastography is a useful technique for the differentiation of benign and malignant lesions in different part of body. In recent researches on strain elastography it has been concluded that different endometrial parts showed different stiffness features. Our goal in this study is to assess the diagnostic utility of transvaginal sonographic elastography in differentiating benign masses from endometrial cancer.

Method: Patients undergoing routine pelvic ultrasonography examinations and suspected intracavitary uterine focal lesions with abnormal uterine bleeding were the subjects of this prospective study. Two types of sonography were performed on the 200 patients: elastography and traditional B-mode sonography. For qualitative analysis, endometrial lesions were divided into three categories, and for quantitative analysis, the strain ratio (SR) was calculated. Additional pathological exams were carried out in order to get a final diagnosis.

Result: There were 103 patients diagnosed with benign lesions and 103 patients with endometrial cancer. While 94.6% of type 3 endometrial lesions were found to be malignant, all type 1 lesions were found to be benign. The AUC for SR was 0.903 with 95% CI between 0.867 and 0.943 for quantitative elastography results. The optimal cut-off SR value, as determined by ROC curve analysis, was 3.03, achieving 82.5% sensitivity, 84.6% specificity, 82.8% positive predictive value, 84.3% negative predictive value and accuracy 83.6%. These findings suggested that SR has good diagnostic performance and that transvaginal sonographic elastography is a useful diagnostic tool for separating benign masses from endometrial cancer.

Conclusion: We have concluded that transvaginal sonographic elastography is a potentially useful method for identifying benign and malignant endometrial lesions in addition to standard sonography.

Keywords: Elastography, endometrial carcinoma, gynecology.

INTRODUCTION

Endometrial cancer is one of the most frequent gynecologic malignancies and is becoming more and more dangerous for postmenopausal women in developed nations and the primary symptom is bleeding. [1] The patient's age, the type of histology, the degree of invasion, and the existence of metastases all have a significant role in prognosis of the disease. [2]

If a patient is diagnosed with endometrial cancer at stage I, the overall 5-year survival rate ranges from 85% to 90%, which is a favorable result. Patients who have cervical stroma invasion or myometrial invasion typically have a worse prognosis. [3] This means that lowering the locoregional recurrence rate for endometrial cancer requires precise diagnosis, staging of the illness, and appropriate adjuvant therapy selection.[4].

Noninvasive preoperative diagnostic procedures are preferable to other intra-operative exams among all the methods used in clinical practice for the diagnosis of endometrial diseases because they allow healthcare resources to be optimized and operation to be customized to prevent unwanted morbidity. [5] Tumor staging, therapy planning, evaluating treatment response, and identifying recurring illness have all always benefited greatly from radio-imaging.The most popular imaging technique for screening women for endometrial cancer is transvaginal ultrasonography because of its accessibility, affordability, and lack of radiation. [6]

The abilities and clinical background of the examiner, however, play a major role in the lesions' detection. Accordingly, interobserver variance is most likely to occur with traditional transvaginal ultrasonography. [7] Therefore, the use of a unique technique that could assess the tissue properties both qualitatively and quantitatively could improve the disease's diagnosis accuracy. Since its introduction in the 1990s, elastography—an ultrasonic technology—has been used to accurately and non-invasively measure the mechanical characteristics and stiffness of tissues. [8]

Two techniques are available to assess the stiffness of the tissue: imaging the shear and mechanical waves, or measuring the strain in the tissue under stress. [9] A compression is delivered to the tissue using the quasi-static method of elastography in order to visualize the stiffness of the areas under examination and to produce a color-coded strain map. Differentiating solid tumors from normal tissues is made possible by elastography, which uses the altered elasticity of soft tissues to identify specific disease processes. The guidelines released by the European Federation for Ultrasound in Medicine and Biology suggest potential therapeutic applications, such as determining the degree of liver fibrosis and distinguishing between breast lesions, thyroid nodules, and prostate abnormalities. [10,11] In clinical practices of obstetrics and gynecology, possible application of elastography includes successful labor induction and prediction of preterm delivery. [12, 13] A real-time study on elastographical revealed high degree of agreement with diagnosis compared to magnetic resonance imaging (MRI) for adenomyosis and fibroids. [14]

The purpose of this study is to assess the diagnostic performance of elastography in differentiating between endometrial malignancies and benign tumors, taking into account the possibility that endometrial cancer may cause changes in tissue elasticity. The gold standard in this analysis will be the pathological results, when they are available.

MATERIALS AND METHODS

This analytical cross-sectional investigation was carried out in the Department of Obstetrics and Gynecology in collaboration with Radiology Department, from January 2021 to December 2022 at Rama Medical College, Hospital & Research Centre, Kanpur, U.P.

The research protocol was approved by the institutional ethical committee. The written consent was received from the participant for this prospective research. Women with atypical uterine

hemorrhage, suspected intracavitary uterine focal lesions, and/or patients receiving routine pelvic ultrasound examinations were among the participants. The respondents underwent a comprehensive evaluation that comprised a review of their medical history, a comprehensive general check-up that included a gynecological examination, and a preliminary transvaginal ultrasound before being referred to the present research.

Including criteria: We included those patients who had intrauterine lesions that were verified by B-mode sonography.

Excluding criteria: Patients with adenomyosis, uterine fibroids, uterine abnormalities, or who had recently undergone hormone therapy were not included in our sample.

Study design: Total 200 female participants were observed and to measure the stiffness of the intrauterine lesion, all participants had transvaginal sonographic elastography performed on the day of hospital admission. The next day, hysteroscopy or dilation and curettage (D&C) was performed, and the lesions were sent for histo-pathologic analysis to verify the ultimate diagnosis. The elastographic and sonographic results were not shared with the pathologists (single blind test).

All elastographic and sonographic examinations were analyzed by the same radiologists (Dr. Dushyant K. Varshney and Dr. Aditya P. Mishra) who have three years of experience in gynecology.

Both B-mode ultrasonography and elastography were performed using a digital sonography scanner to measure the endometrial thickness and endometrial volume in real-time. The patients were instructed to breathe normally during the radio-diagnostic procedure, and the uterus's elastographic images were produced by the patient's breathing patterns and arterial pulsation. Color-coded maps were used to evaluate the elasticity of the areas of interest (ROIs), designating red as soft, yellow as medium soft, blue as medium hard, and dark blue as hard.

Lesions were qualitatively categorized based on the predominant elastographic color pattern, with type 1, predominantly non-blue, type 2, partly blue and partly non-blue, and type 3, predominantly blue, representing the percentages of the various colors in the overall area. In order to prevent ROI bias, ROIs were modified to incorporate the maximum amount of thick and homogeneous tissue. For every participant, an average of 3 (range 2-5) clips and 4 (range 3-6) static photos were acquired. To provide a quantitative assessment of the endometrium's stiffness, the strain ratio (SR) was calculated. Two separate observers conducted at least three independent

SR measurements using various static pictures. The ultimate outcome was noted as the average SR.

Statistical analysis: Kolmogorov-Smirnov Test was carried out for continuous variables. Student's T-test was performed for comparisons between different types of benign lesions and endometrial cancer. Additionally, a receiver operating characteristics (ROC) curve was built, and the cut-off SR value to distinguish between benign masses and endometrial cancer was found by calculating the area under the ROC curve (AUC) with a 95% confidence interval. Calculations were made for sensitivity, specificity, positive predictive value, and negative predictive value, in that order. Level of significance was set at $P < 0.05$ for all statistical analysis.

RESULTS

Total 200 female participants with confirmed histo-pathological diagnosis were included in the present study. The average age of participants was 46.3 years (SD± 4.7 years). The detailed demographics profile of participants is summarized in Table No 1.

Out of 200 patients, 97 patients were confirmed to have endometrial cancer based on pathological findings. Out of 97 confirmed endometrial cancer cases, 29 cases were pre-menopausal and 68 cases were post-menopausal.

Endometrial hyperplasia (n=59) and endometrial polyps (n=44) were the two forms of benign endometrial lesions identified in the remaining 103 patients. The mean age of 59 patients diagnosed with endometrial hyperplasia was 36.4 year (SD ±4.6 years) and the mean age of 44 patients diagnosed with endometrial polyps 45.9 years (SD ± 6.4 years). Following D&C in 34 patients and hysterectomy in 25 cases, endometrial hyperplasia was verified. All cases were followed up on over time, and patients were asked to undergo routine ultrasounds every six months, given that surgical removal is not advised for benign lesions such as endometrial polyps.

Table No.1: Demographic and Histopathological diagnosis of participants (n=200)

Features	**Malignant (n=97)**	**Benign (n=103)**	***p* value**
Age (years)	42.8 ± 5.9	54.6 ± 5.6	0.0008
Body weight (Kg)	69.5 ± 8.6	74.2± 9.4	0.0061
Height (cm)	146.4 ± 6.8	148.3± 8.4	0.0483
BMI (Kg/m^2)	34.6 ± 1.8	36.4 ± 1.6	0.0141
Final diagnosis: n (%)			
Endometrial cancer	97 (48.5%)	103 (51.5%)	--
Endometrial hyperplasia		59 (57.3%)	--
Endometrial polyps		44 (42.7%)	--
Endometrial thickness (mm)	17.4 ± 9.2	6.9 ± 4.6	0.0008
Endometrial volume (cm^2)	8.2 ± 4.1	3.6 ± 2.4	0.0006
Strain ratio	5.1 ± 2.6	2.6 ± 1.6	0.0009

p value <0.001 is significant

The individuals with benign endometrial lesions were substantially younger than those with endometrial cancer, and their body mass index (BMI) was significantly higher (P = 0.005). Furthermore, patients with endometrial cancer had noticeably greater values for both endometrial thickness and endometrial volume, as determined by conventional B-mode sonography.

Table 2 displays the distribution of endometrial lesions based on qualitative elastography and the final diagnosis once the results have been interpreted. While 95.8% of type 3 endometrial lesions were determined to be malignant, all type 1 lesions were identified as benign. The SR values of benign and malignant lesions are displayed in Table No. 2 and are the outcome of a quantitative evaluation of elastography.

Table No.2: Qualitative and quantitative elastographic analysis of endometrial lesions

Elastographic features	**Malignant lesion (n=97)**	**Benign lesion (n=103)**	***P* value**
Type 1	**0**	**69 (66.9%)**	**0.0009**
Type 2	**12 (12.4%)**	**33 (32.1%)**	**0.0007**
Type3	**85 (97.6%)**	**1 (0.9%)**	**0.0008**
Strain ratio	**2.1 (SD±0.9)**	**4.3 (SD±1.4)**	**0.0009**
P<0.001 is significant			

The SR values were substantially greater ($p < 0.005$) in patients with endometrial cancer than in those with benign endometrial lesions. The AUC for SR is 0.903, with a 95% confidence interval spanning 0.867 to 0.943. There were 103 patients diagnosed with benign lesions and 103 patients with endometrial cancer. While 94.6% of type 3 endometrial lesions were found to be malignant, all type 1 lesions were found to be benign. The AUC for SR was 0.903 with 95% CI between 0.867 and 0.943 for quantitative elastography results. The optimal cut-off SR value, as determined by ROC curve analysis, was 3.03, achieving 82.5% sensitivity, 84.6% specificity, 82.8% positive predictive value, 84.3% negative predictive value and accuracy 83.6%. These findings suggested that SR has good diagnostic performance and that transvaginal sonographic elastography is a useful diagnostic tool for separating benign masses from endometrial cancer.

DISCUSSION

This is a small scale study to assess the effectiveness of strain elastography in distinguishing between endometrial cancer and other benign endometrial masses including participants of Indian population. Our research showed that elastography is a sensitive method that can be used in addition to conventional B-mode sonography to detect endometrial cancers. Its resultant SR value performed exceptionally well in separating endometrial cancer from benign lesions using strain elastography. Elastography can therefore be used in clinical settings and offer increased diagnostic precision in day-to-day tasks. Clinicians typically perform D&C and pathological diagnosis to confirm a definitive diagnosis when endometrial abnormalities are suspected. [15, 16] Although biopsy, cytology, and D&C results are the gold standards methods for establishing an absolute diagnosis worldwide, individuals with vaginal or cervical stenosis may experience substantial consequences from these invasive procedures. [17, 18]

Most of patients do not like to go through any type of invasive pathological testing. As a result, after the medical evaluation, no treatment plans are recommended or received, which wastes medical resources. Sonography has significantly established itself as the primary diagnostic technique for determining the underlying cause of clinical gynecological issues and preventing needless treatments. It is a safe, easily accessible, and reasonably priced imaging modality.

Some studies in the past have shown that triaging individuals with abnormal uterine bleeding was frequently done using ultrasonography measurement of endometrial thickness. [20,21] Even though endometrial cancer diagnosis has a high level of sensitivity, endometrial thickness

measurement has a well established false negative rate. Naftalin *et al.* [21] has described two different cases of endometrial cancer in which a conventional B-mode ultrasonography revealed a thin, normal endometrium. This implied that adenomyosis foci within the myometrium, which have a normal endometrial appearance, could potentially be the source of cancer. Therefore, assessing endometrial thickness alone is insufficient and might miss certain cases of endometrial cancer.

Fortunately, conventional scanning combined with elastography, as an extension of conventional sonography, is more potent than either one of them separately. Different forms of elastography showed great potential in clinical settings such as screening for abnormalities in the prostate, classifying benign and malignant lymph nodes, assessing gastrointestinal tract contractility, detecting thyroid nodules, and assessing fibrosis in chronic liver diseases [11]. Additionally, elastography's diagnostic utility for uterine problems was examined in some earlier gynecological studies.For example, Lu R et al [22] noted that elastography performed well in detecting cervical lesions that are probably malignant, and that among the many elastic scores, SR produced the best results in differentiating between malignant and benign cervical lesions.

Preis K *et al* [25] studied different endometrial pathologies and found that normal endometrial and atrophic tissues were the softest tissues among all pathological conditions, followed by hypertrophy and endometrial polyps. According to present study, endometrial cancer showed the highest SR compared to other benign diseases, similar to other tumorous tissues that are typically harder than the healthy tissue. Elastography was found to be sensitive in the early detection of endometrial pathologies with thicker endometrium, but it was not able to differentiate between different benign endometrial lesions, such as endometrial hyperplasia and endometrial polyps, according to a recent research. [24] According to a study conducted by Stoelinga B *et al* [14] while distinguishing adenomyosis and fibroids, elastographical observations were in full agreement with those of MRI results [16].

We did not stage the endometrial cancer patients any further in this investigation in order to look into potential relationships between malignancy and SR staging. Future research on this subject would be really intriguing. We did not examine how well elastography performed as a diagnostic tool in comparison to traditional B-mode sonography. It would still be worthwhile to investigate this topic, even if we think the combination of the two approaches provides greater diagnostic

value than either one alone. Finally, selection bias may arise because all of the patients included in this study were chosen based on B-mode findings.

CONCLUSION

Our research led us to the conclusion that transvaginal sonographic elastography is a potentially useful diagnostic technique for identifying benign and malignant endometrial lesions in addition to standard sonography. The diagnostic performance of elastography might be enhanced by the application of both qualitative and quantitative techniques, and SR has shown strong diagnostic performance.

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Conflict of interest: None.

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