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ORIGINAL ARTICLE

# Evaluation of Transvaginal Sonographic Elastography in Differentiating Endometrial Hyperplasia From Endometrial Carcinoma in Perimenopausal Women

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**Abstract**

*Background*: **It is noticed that 70 % of gynecological complaints in the peri- and postmenopausal women is abnormal uterine bleeding, so it is a considerable issue. This study aimed to assess the value of transvaginal sonographic elastography in differentiating endometrial hyperplasia from endometrial carcinoma.**

*Patients and methods*: **It is a prospective study, applied on patients with perimenopausal bleeding over 2 years duration between April 2020 and April 2022. We applied this study on 72 women; the mean age of the endometrial carcinoma group was 50.11 ± 1.27, 46.77 ± 2.75 for typical endometrial hyperplasia group, 48.36 ± 2.42 for atypical endometrial hyperplasia group, and the control group was 47.76 ± 2.57. The comparison between strain index values by transvaginal sonographic elastography in each group was done by a one-way analysis of variance (ANOVA) and Post Hoc test: Tukey's test.**

*Results*: **The mean value of the strain index was 10.9 ± 3.72 in the endometrial carcinoma group, 2.73 ± 1.70 in the endometrial hyperplasia group, and 1.01 ± 0.19 in the control group with a statistically significant higher mean value of the strain index in the endometrial carcinoma group followed by the endometrial hyperplasia group and the control group is the lowest one, with a *P*-value ($P < 0.001$). The strain index value greater than 5.4 is considered as a cutoff value characterizing endometrium carcinoma from endometrial hyperplasia, with sensitivity 88.9 % and specificity 85.7 %.**

*Conclusion*: **Transvaginal sonographic elastography is a beneficial tool in differentiating between endometrial hyperplasia and endometrial cancer.**

*Keywords:* Carcinoma, Elastography, Endometrium, Sonography

## 1. Introduction

It is noticed that 70 % of gynecological complaints in the peri- and postmenopausal women is abnormal uterine bleeding (AUB), so it is a considerable issue. Endometrial carcinoma accounts for about 10 % of cases with postmenopausal bleeding, And nearly 12 % are diagnosed in the perimenopausal period.[1] Increasing the endometrial thickness by ultrasound is not a diagnostic feature and must be confirmed by biopsy and histopathological examination.[2] The dilatation and curettage with biopsy was the procedure of choice for diagnosing abnormal endometrium in women with AUB. But, the dilatation and curettage needs a general anesthesia and not accurate in cases of focal lesions.[3]

Sonographic elastography technique is theoretically based on tissue elasticity.[4] The application of compressions owing to elasticity degrees, quantitative assessment of elasticity, and stiffness of compressible tissues in various places are employed in sonographic elastography to characterize tissue.[5] Although the elastography had been used in diagnosing malignant lesions in the breast, prostate,

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thyroid, and kidneys, only a few studies were focused on the value of sonographic elastography for assessment of endometrial pathologies.[6] Transvaginal ultrasonography is easy to be applied at the clinic in a short time and is inexpensive also, which remains the primary investigating tool for gynecological evaluation. When adding the elastography mode, it provides mapping information and acts as a complementary diagnostic tool.[7]

This work aimed to assess the value of transvaginal sonographic elastography in differentiating endometrial hyperplasia from endometrial carcinoma.

## 2. Patients and methods

It is a prospective study, applied on patients with perimenopausal bleeding in Sayed Galal Maternity Hospital – Alazhar University and International Medical Center (for availability of digital ultrasonographic machine equipped with real-time tissue elastography software), and was carried out over 2 years duration between April 2020 and April 2022.

Selection of patients: The study was discussed with the patient and consent was taken by the investigator. The eligibility criteria for the trial: patients with perimenopausal bleeding, and the exclusion criterion includes patients using hormonal therapy and tamoxifen or with history of radiotherapy, submucosal leiomyoma and adenomyosis, patients with myometrial invasion or previously diagnosed as endometrial hyperplasia or endometrial carcinoma, patients with a sonographic finding of a retroverted uterus because it is more difficult to compress a retroverted uterus than an anteverted uterus, and history of previous uterine surgery including myomectomy and endometrial interventions.

Population: Eligible patients in the study formed the groups according to histopathological examination and elastographic values: the group with endometrial hyperplasia (typical and atypical), the group with endometrial cancer, and normal endometrium as a control group.

Study procedure: All patients were examined by transabdominal and transvaginal ultrasound for selection according to the inclusion and the exclusion criterion. Eligible patients in the study performed transvaginal sonographic elastography and then pathological examination for the endometrial biopsies taken by endometrial sampling. Transvaginal sonographic elastography was done using the designed protocol and operated by a single sonographer to avoid any bias. All patients were laid in lithotomy position after empting the bladder, then transvaginal B-mode ultrasound, color Doppler study, and then transvaginal sonographic elastography mode were used to assess the stiffness of the endometrium. The normal myometrium nearby the thickened endometrium was presented in the elastographic box. The regions of interest (ROI) were then applied on normal myometrium and the thickened endometrium inside the box to measure the strain index.

Monitoring and operation: A digital ultrasonographic machine (Logiq E9, GE Healthcare) equipped with real-time tissue elastography software, by using 5–7.5 MHz multifrequency transvaginal transducer, was used in the study by the same sonographer to assess the patients by using transvaginal B-mode, color Doppler, and then transvaginal sonographic elastography.

### 2.1. Measurement

Strain index (SI) was automatically acquired by measuring the strain ratio of the thickened endometrium and nearby normal myometrium and recorded for each patient. All patients were assessed three times, and then the mean value was recorded. Then, the elastographic results were compared with the pathological results. Doppler evaluation of the endometrium by color Doppler score, the vascularity is assessed subjectively by the use of color score from 1 to 4, as (1) for no color/flow, (2) minimal, (3) moderate, and (4) abundant color/flow.

### 2.2. Statistical analysis

The Statistical Software for Social Sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA), was used to analyze the recorded data. The mean and standard deviation (SD) were used to convey quantitative data. Frequency and percentage were used to convey qualitative data. Further tests were conducted: when comparing more than two means, use a one-way analysis of variance (ANOVA). And Post hoc test was used for numerous comparisons between various variables, Tukey's test was employed. To determine the overall predictability of the parameter and the appropriate cutoff value with detection of sensitivity and specificity at this cutoff value, receiver-operating characteristic (ROC curve) analysis was employed. The allowable margin of error was set at 5 %, while the confidence interval was set at 95 %. Hence, the *P*-value was considered significant when *P*-value less than 0.05.

## 3. Results

We applied this study on 84 women, while there were 12 cases excluded as they were diagnosed as

hyperplastic endometrial polyp after histopathological examination, so the total was 72 women. The mean age of the endometrial carcinoma group was 50.11 ± 1.27, 46.77 ± 2.75 for typical endometrial hyperplasia group, 48.36 ± 2.42 for atypical endometrial hyperplasia group, and 47.76 ± 2.57 for the control group, with no statistically significant difference between histopathological types according to age in 'years', with *P*-value ($P > 0.05$).

Measurement variables monitored in the study were endometrial thickness, color Doppler, and strain index between the histopathological types. The mean endometrial thickness was 24.89 ± 5.13 in the endometrial carcinoma group, 16.52 ± 3.13 in the endometrial hyperplasia group, while it was 11.10 ± 2.26 in the control group, with a statistically significantly higher mean value of endometrial thickness in the endometrial carcinoma group, followed by the endometrial hyperplasia group and then the normal endometrium group was the lowest value, with *P*-value ($P < 0.001$). But, the mean value of endometrial thickness was 16.71 ± 3.08 in typical endometrial hyperplasia and 17.82 ± 1.99 in atypical endometrial hyperplasia with no statistical significance between them (Table 1).

As regards color Doppler values, there was a statistically significantly higher mean value of color Doppler score in the endometrial carcinoma group, followed by the endometrial hyperplasia group and then the normal endometrium group was the lowest value, with *P*-value ($P < 0.001$).

The strain index (SI) ranged from 0.6 to 15.5 with mean value 3.25 ± 2.51 among study groups. The mean value of the strain index was 10.9 ± 3.72 in the endometrial carcinoma group (Fig. 1), 2.73 ± 1.70 in the endometrial hyperplasia group (Figs. 2 and 3), and 1.01 ± 0.19 in the control group with a statistically significantly higher mean value of strain index in the endometrial carcinoma group followed by the endometrial hyperplasia group and then the control group was the lowest value, with *P*-value ($P < 0.001$). Also, the mean value of strain index was 1.87 ± 0.74 in typical endometrial hyperplasia and 5.15 ± 1.21 in atypical endometrial hyperplasia with a statistically significant difference with *P*-value ($P < 0.001$) (Table 2).

The ROC curve in Fig. 4 was applied to define the cutoff SI value greater than 5.4 to differentiate endometrial cancer from endometrial hyperplasia, with sensitivity 88.9 %, specificity 85.7 %, positive predictive value 57.1 %, and negative predictive value 97.3 %. The area under the curve (AUC) was 0.889. Another ROC curve in Fig. 5 was applied to define the cutoff SI value greater than 2.7 to differentiate atypical endometrial hyperplasia from typical endometrial hyperplasia, with sensitivity 90.9 %, specificity 87.1 %, positive predictive value 71.4 %, and negative predictive value 96.4 %. The area under the curve was 0.892.

## 4. Discussion

The study depends on the fact that malignant lesions were characterized by rigidity and stiffness than the soft benign lesions. The value of elastography on the uterine pathologies was assessed in some studies. Lu and colleagues found positive values of elastography in determining the malignant lesions of the cervix, and the SI provided the optimal results in differentiating benign and malignant cervical lesions.[8] When using elastography in the assessment of abnormal endometrium, the atrophic and normal endometrium were the softest tissues followed by endometrial polyps and then hyperplasia was more rigid.[9]

As regards endometrial thickness (ET), in the study by Metin et al., the median ET was 15.00 mm (interquartile range [IR]: 13, range: 8.30–64.00 mm).[2] Also, by using B-mode ultrasonography, there were higher significant values on endometrial thickness in patients with endometrial cancer.[10] In another study by Abdel Latif et al., there was a significant

*Table 1. Comparison between histopathological types according to endometrial thickness (ET), color Doppler, and strain index (SI).*

| | Normal endometrium | Endometrial hyperplasia | Endometrial carcinoma | Test value | *P*-value |
|---|---|---|---|---|---|
| Endometrial thickness | | | | | |
| Mean ± SD | 11.10 ± 2.26C | 16.52 ± 3.13B | 24.89 ± 5.13A | 59.230 | <0.001[a] |
| Range | 8–16 | 10–25 | 17–31 | | |
| Color Doppler score | | | | | |
| Mean ± SD | 1.00 ± 0.00C | 1.79 ± 0.90B | 3.22 ± 0.44A | 31.244 | <0.001[a] |
| Range | 1–1 | 1–4 | 3–4 | | |
| Strain index (SI) | | | | | |
| Mean ± SD | 1.01 ± 0.19C | 2.73 ± 1.70B | 10.90 ± 3.72A | 96.476 | <0.001[a] |
| Range | 0.6–1.4 | 0.9–6.8 | 5.4–15.5 | | |

[a] *P*-value less than 0.001 is highly significant.

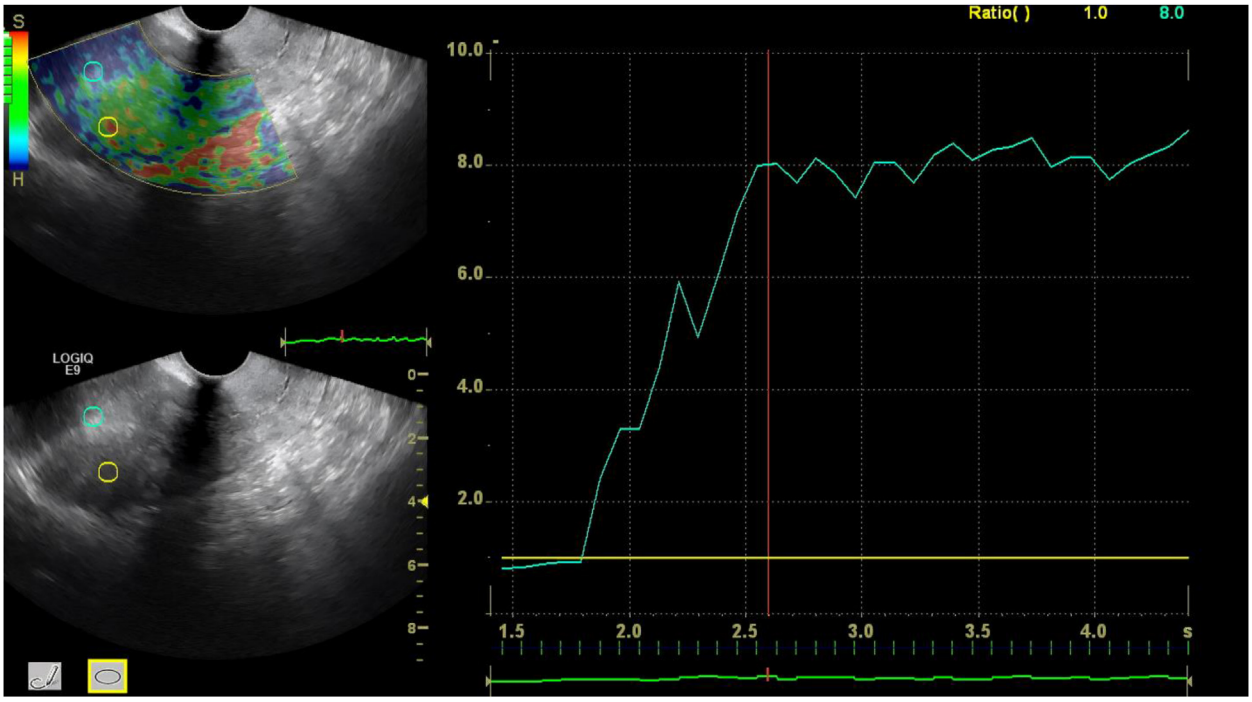


*Fig. 1. Sonographic elastography image with strain index for endometrial cancer by a digital ultrasonographic machine (Logiq E9, GE Healthcare). A 50-year-old woman with endometrial thickness of 22 mm and diagnosed as endometrial cancer by histopathological examination, with strain ratio = 8.*

difference between endometrial cancer group (mean ET was 21.9 mm) and the hyperplasia group (mean ET was 14.8 mm). But, there was no statistically significant difference between groups of typical and atypical endometrial hyperplasia.[11] In this study, the mean endometrial thickness was

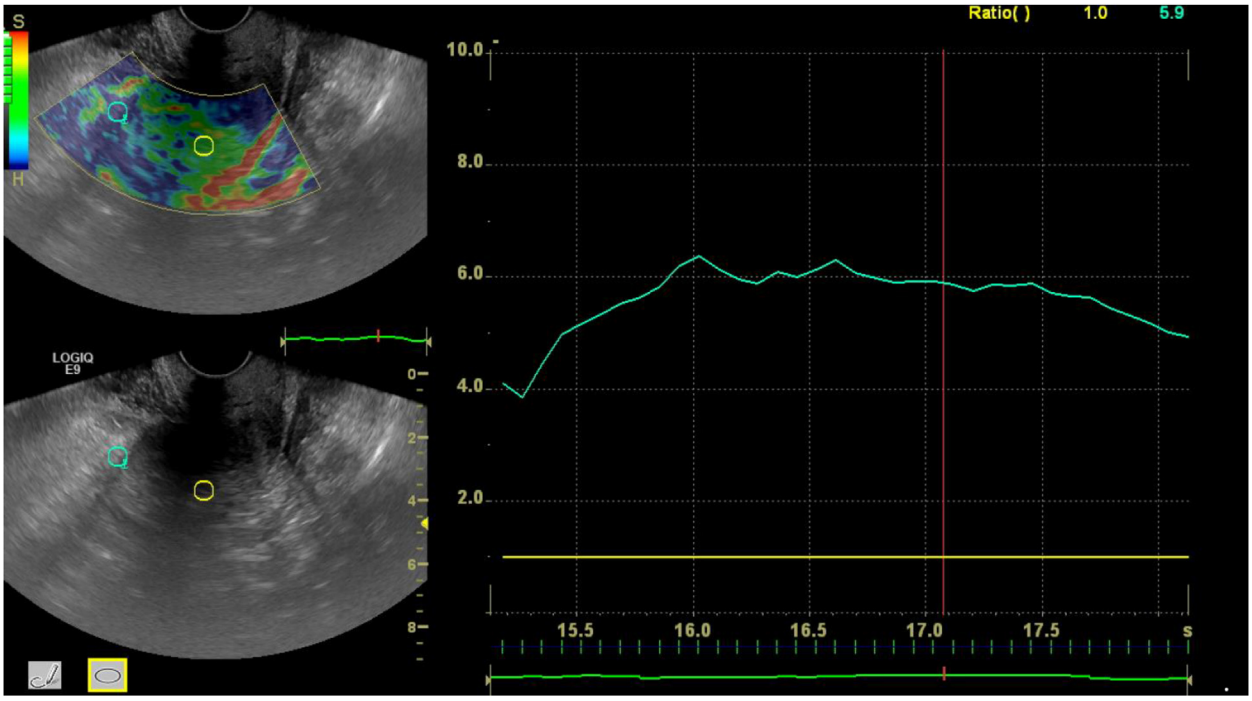


*Fig. 2. Sonographic elastography image with strain index for atypical endometrial hyperplasia by a digital ultrasonographic machine (Logiq E9, GE Healthcare). A 50-year-old woman with endometrial thickness of 21 mm and diagnosed as atypical endometrial hyperplasia by histopathological examination, with strain ratio = 5.9.*

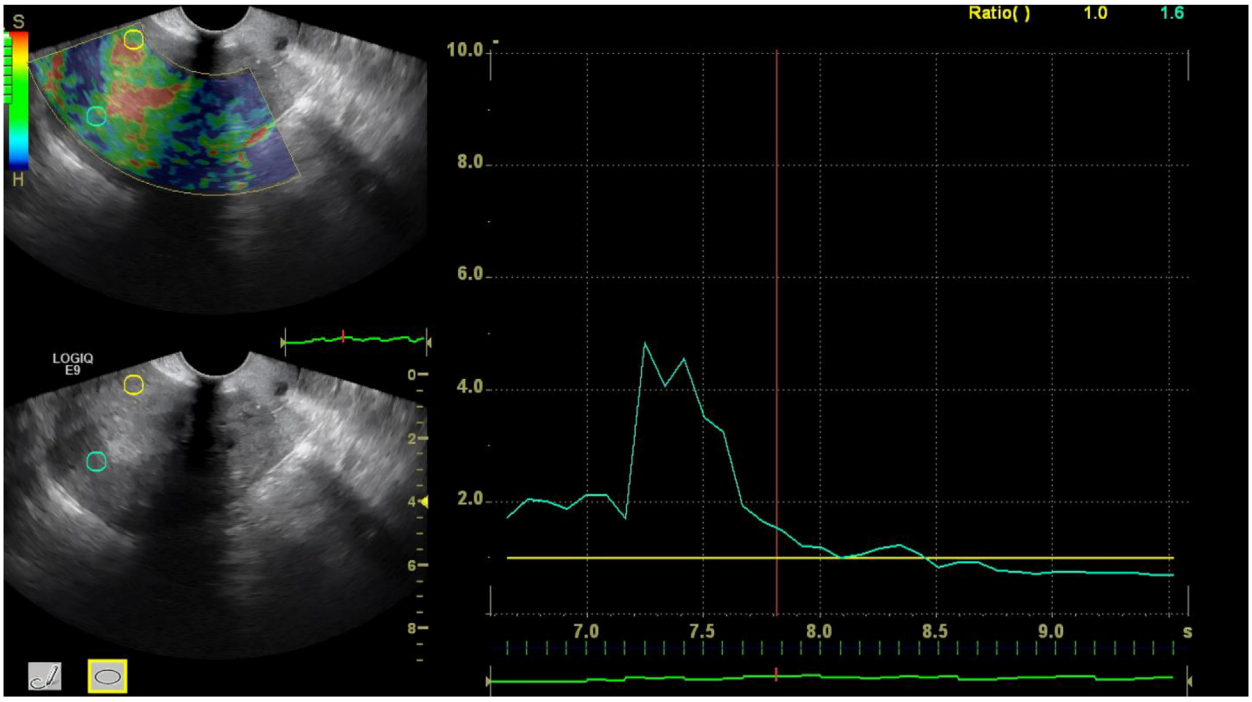


*Fig. 3. Sonographic elastography image with strain index for typical endometrial hyperplasia by a digital ultrasonographic machine (Logiq E9, GE Healthcare). A 44-year-old woman with endometrial thickness of 17 mm and diagnosed as typical endometrial hyperplasia by histopathological examination, with strain ratio = 1.6.*

*Table 2. Comparison between histopathological types according to age and strain index 'SI'.*

| | Normal endometrium | Typical endometrial hyperplasia | Atypical endometrial hyperplasia | Endometrial carcinoma | Test value | *P*-value |
|---|---|---|---|---|---|---|
| Age (y) | | | | | | |
| Mean ± SD | 47.76 ± 2.57 | 46.77 ± 2.75 | 48.36 ± 2.42 | 50.11 ± 1.27 | 1.543 | 0.460 |
| Range | 40–51 | 42–52 | 44–52 | 48–52 | | |
| Strain index (SI) | | | | | | |
| Mean ± SD | 1.01 ± 0.19D | 1.87 ± 0.74C | 5.15 ± 1.21B | 10.90 ± 3.72A | 115.955 | <0.001[a] |
| Range | 0.6–1.4 | 0.9–3.8 | 2.7–6.8 | 5.4–15.5 | | |

[a] *P*-value less than 0.001 is highly significant.

24.89 ± 5.13 in the endometrial carcinoma group, 16.52 ± 3.13 in the endometrial hyperplasia group, while it was 11.10 ± 2.26 in the control group, with a statistically significant higher mean value of endometrial thickness in the endometrial carcinoma group, followed by endometrial hyperplasia group and then the normal endometrial group was the lowest value, with *P*-value ($P < 0.001$). But, the mean value of endometrial thickness was 16.71 ± 3.08 in typical endometrial hyperplasia and 17.82 ± 1.99 in atypical endometrial hyperplasia with no statistical significance between them.

As regards color Doppler study, Goncharenko and colleagues proved that transvaginal sonoelastography is a valuable diagnostic tool for abnormal endometrium. And there was abundant vascularity on Doppler imaging, and the rigidity of tissues was more specific for atypical endometrial hyperplasia than glandular cystic hyperplasia ($P < 0.01$).[12] In another study by Abdel Latif and colleagues when using power Doppler, a significant difference between the endometrial cancer group and endometrial hyperplasia group was found ($P < 0.001$).[11] In this study, there was a statistically significant higher mean value of color Doppler in the endometrial carcinoma group, followed by endometrial hyperplasia group and then the normal endometrium group was the lowest value, with *P*-value ($P < 0.001$).

As regards the strain index, Metin and colleagues showed a significant difference between the endometrial cancer group (median SI 1.8) and endometrial hyperplasia (median SI 0.8) and control group (median SI 1) ($P < 0.0001$).[2] But, in the study by Dehong Che and colleagues the endometrial cancer

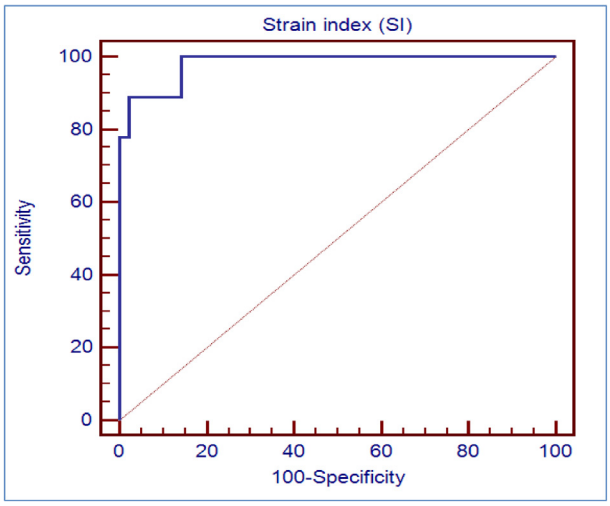


*Fig. 4. Receiver operating characteristic analysis to define the cutoff Strain index value to differentiate endometrial cancer from endometrial hyperplasia.*

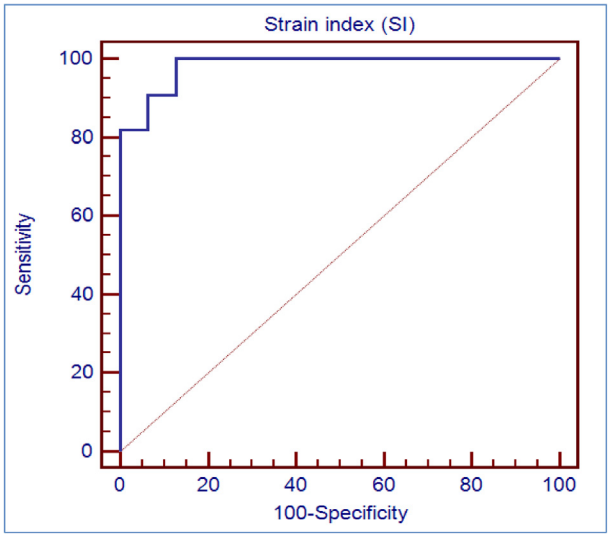


*Fig. 5. Receiver operating characteristic analysis to define the cutoff Strain index value to differentiate atypical endometrial hyperplasia from typical endometrial hyperplasia.*

group had a significantly higher SI value that was 4.5 ± 2.3 than the endometrial benign group, the SI value was 2.8 ± 1.3 ($P < 0.001$).[10] In a previous study by Abdel Latif et al., there was a higher significant difference between the endometrial cancer group (mean SI was 11.4) and endometrial hyperplasia group (mean SI was 2.7), with $P < 0.001$. Also, when comparing typical (mean SI was 1.9) and atypical endometrial hyperplasia group (mean SI was 5.6), there was a significant statistical difference between both groups ($P < 0.001$).[11] In this study, the mean value of the strain index was 10.9 ± 3.72 in the endometrial carcinoma group, 2.73 ± 1.70 in the endometrial hyperplasia group, and 1.01 ± 0.19 in the control group. Also, the mean value of the strain index was 1.87 ± 0.74 in typical endometrial hyperplasia and 5.15 ± 1.21 in atypical endometrial hyperplasia with a statistically significant difference with *P*-value ($P < 0.001$).

As regards sensitivity and specificity of sonoelastography, Abdel Latif and colleagues used SI of 7.2 as a cutoff value to differentiate between endometrial cancer and endometrial hyperplasia, sensitivity was 92.3 % and specificity was 100 %.[11] In another study by Metin and colleagues the sensitivity was 81.3 % and specificity was 100 % between the endometrial cancer group and endometrial hyperplasia group.[2] In the study by Dehong Che and colleagues they compared the endometrial cancer group with benign endometrial group that included endometrial polyps and hyperplasia with different tissue elasticity and characters, by using the cutoff SI of 3.02, to differentiate the endometrial cancer group from benign endometrial group, sensitivity was 81.7 % and specificity was 85 %.[10] In this study, we used the cutoff SI value greater than 5.4 to differentiate endometrial cancer from endometrial hyperplasia, with sensitivity 88.9 %, specificity 85.7 %, positive predictive value 57.1 %, and negative predictive value 97.3 %.

As regards the differentiation between typical and atypical endometrial hyperplasia, Abdel Latif and colleagues used a cutoff SI value less than or equal to 4 to differentiate between typical and atypical endometrial hyperplasia, with sensitivity 100 % and specificity 85.7 %.[11] In this study, we used the cutoff SI value greater than 2.7 to differentiate between atypical endometrial hyperplasia and typical endometrial hyperplasia, with sensitivity 90.9 %, specificity 87.1 %, positive predictive value 71.4 %, and negative predictive value 96.4 %.

One of the limitations to this study is the limited patients' numbers who need further assessment by sonographic elastography on a large number of patients. In addition, we did not investigate the relation between SI values and endometrial cancer stages, so it would be a leading study for the future researches.

### 4.1. Conclusion

Transvaginal sonoelastography is a beneficial tool, complementary to traditional B-mode ultrasonography in detecting endometrial malignancies. It is a practical tool in diagnosing endometrial abnormalities, and can differentiate between typical endometrial hyperplasia, atypical endometrial hyperplasia, and endometrial cancer.

## Conflicts of interest

The authors declared no conflict of interest.

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