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ORIGINAL RESEARCH

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Can elastographic evaluation be a new approach in prediction of endometrial cancer prognostic markers?

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Abstract

Background: Pathological parameters are the main factors that determine surgical radicality and disease prognosis. Strain sonoelastography is a novel non-invasive method that can be predicted pathological prognostic factors preoperatively. This prospective cohort study study aimed to evaluate the power of strain sonoelastography in prediction of endometrial cancer pathological prognostic factors. **Methods**: From December 2022 to July 2023, 63 patients with pathologically confirmed endometrial carcinoma were included, prospectively. Cases were evaluated with B-mode ultrasound and strain sonoelastographic together. Strain ratios (SR) of tumors and pathological prognostic factors (tumor diameter, grade, myoinvasion, lymphovascular space invasion, lymph node metastasis and surgical stage) in final pathology reports were compared. Pearson and Spearman's rank correlation analyzes were used for continuous variables. Student-*t* Test and Kruskal Wallis analysis was used to compare the continuous variables in independent groups. The diagnostic performance of strain ratio was determined with receiver operating characteristic (ROC) curve analysis. Cut-off values of strain ratios in different prognostic parameters were determined. **Results**: Median SR-corpus and cervix were detected as 1.55 and 0.99, respectively. SR-corpus values were correlated with all prognostic factors except lymph node metastasis and menopausal status, while SR-cervix values correlated with all of them except menopausal status. There was a correlation between low and high risk groups in SR-cervix grup, there was a correlation between all risk factors in SR-corpus group. Cut-off values of SR-corpus and cervix were determined. **Conclusions**: This preliminary study showed that sonoelastographic strain ratios were significantly correlated with pathologic prognostic factors. So, this method may be good option during the decision of treatment alternatives and radicality of surgery in endometrial cancer. **Clinical Trial Registration**: This study was recorded in the Clinicaltrial registry (NCT06623916).

Keywords

Strain-elastography; Endometrial cancer; Prognostic factors; Tumor stiffness; Strain-ratio

1. Introduction

Endometrial cancer is the most common gynaecologic cancer, particularly in developed countries. Today, it ranks as the sixth most prevalent cancer among women [1]. Although 4% of endometrial cancer patients are premenopausal, the most common symptom of the disease is postmenopausal bleeding. Endometrial Pipelle biopsy, dilatation and curettage and hysteroscopic excision are the main methods of obtaining a pathological sample to be used in endometrial cancer diagnosis. The prognosis of the disease depends on age, grade, myometrial invasion-histologic type of tumour, lymph node metastasis and distant metastasis [2].

In addition to pathologic reports, transvaginal ultrasound is the most commonly used preoperative, non-invasive, non-radiation-related and low-cost imaging method to assess the endometrial cavity, endo-myometrial invasion, tumour diameter and cervical and adnexal involvement. Some of these risk factors can be easily detected with transvaginal ultrasound as well as intraoperative frozen-section examination.

Sonoelastography is a novel technique, which evaluates tissue stiffness, both qualitatively and quantitatively, and can distinguish among different lesions in various organs, such as liver, breast and thyroid [3, 4]. Strain imaging and shear-wave imaging are two elastographic techniques that are typically used with ultrasound technology. In the first method, the operator exerts manual compression on the tissue with an ultrasound transducer [5]. Strain elastography evaluates tissue elasticity by measuring the degree of distortion caused by compression and decompression of soft tissues. Strain ratio (SR) is calculated by proportioning the tissue elasticity of the

suspicious pathologic area with a reference point. Manual compression works fairly well for superficial organs, such as breast, superficial lymph nodes and thyroid, but is challenging for assessing elasticity in more deeply located organs, such as liver [6]. Strain elastography is a semi-quantitative method because of the variations in compression and decompression pressures and selected regions of interest (ROIs) by practitioners. Using the SR makes this relative and subjective technique more objective.

In shear-wave elastography, the ultrasound transducer is held steadily, and tissue displacement is generated by an internal physiologic motion (*e.g.*, cardiovascular, respiratory). Since this method does not depend on superficially applied compression, variations among practitioners are negligible, and it may be used to assess more deeply located organs [7].

In the clinical practice of gynaecology, sonoelastography has recently been used in different conditions, such as ovarian and endometrial benign lesions [8]. In the endometrial cancer diagnostic process, elastography is not well established yet.

In this study, we aimed to determine whether sonoelastography could be a new prognostic predictor of endometrial cancer. Accordingly, we examined the relations between the elastographic features of the lesions and known pathologic prognostic factors in endometrial cancer cases.

2. Materials and methods

This prospective cohort study was conducted in a single institution, Adnan Menderes University, Gynaecologic Oncology Surgery Department, from December 2022 to July 2023. This study was approved by the Clinical Research Ethics Committee of Adnan Menderes University (protocol number 2022/179) and was recorded in the Clinicaltrial registry (NCT06623916). The research was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. Informed consent was obtained from all patients before evaluation. In total, 90 patients with biopsy-confirmed (by Pipelle sampling or dilatation and curettage) endometrial cancer were evaluated. Diagnoses of different types of tumours over the last five years, presence of synchronous malignancy, presence of non-epithelial uterine tumour, lack of patient data, presence of full-thickness uterine and cervical involvement (due to the lack of safe boundaries between pathologic and normal tissue for elastographic evaluation), lack of patient compliance for transvaginal ultrasound, and inoperable cases (lack of definitive pathologic report) were the exclusion criteria used in the study. Demographic and clinical data, including age, gravida, parity, weight (kg) and height (cm), were collected through a questionnaire. Body mass index (BMI) was calculated (kg/cm^2). Cancer antigen-125 (CA-125) values (IU/mL) were recorded. Positron emission tomography/computed tomography (PET/CT) imaging was performed to evaluate distant metastasis and exclude inoperable patients before surgery. The maximum standardised uptake value (SUVmax) of the tumour in the uterus was recorded. In total, 63 patients who met the criteria were evaluated with transvaginal ultrasound and the strain elastography mode of ultrasound. Before the measurements, the strain elastography technique was defined and figures were added to ensure reproducibility. The strain measurements are displayed on a semi-transparent coloured map called an elastogram, which is overlaid on the B-mode image (Fig. 1). Typically, low strain (stiff tissue) is displayed in blue, and high strain (soft tissue) is shown in red, although the colour scale can vary, depending on the ultrasound vendor. SR (a pseudo-quantitative measurement) can be used, which is the ratio of the strain measured in the adjacent (usually normal) reference tissue ROI to the strain measured in a target lesion ROI. SR >1 means that the target lesion compresses less than the normal reference tissue, indicating lower strain and greater stiffness [9]. With this general information, each patient's cervix and uterus were examined in the sagittal plane using the transvaginal B-mode ultrasonography and elastography mode on the day before the surgery during examination. The size of the lesion in the cavity, the degree of myometrial invasion, and the possible presence of cervical and adnexal involvement were evaluated. The uterine cervix and intact myometrium were chosen as reference points because they are adjacent to the target lesion and can be evaluated in the same window in the elastography mode. After the elastography window was opened, the reference (intact myometrial area and cervical area) and target (endometrial lesion) ROI were determined, and compression and decompression cycles were applied with the transvaginal probe manually in one-second periods to create pressure tracing. The patients who could not tolerate the procedure were excluded from study. SR was calculated at the peak of the pressure in the area where the trace was regular. SR-corpus is defined as the comparison between the intact myometrium and the target tissue. SR-cervix denotes the comparison between the cervix and the target tissue. SRs were calculated at least three times, and the mean SR was saved. All ultrasound examinations were performed by a single gynaecologist oncologist with Voluson S8 (GE Healthcare, Chicago, IL, USA, equipped with a 4.0–9.0 MHz multifrequency transvaginal probe). When the definitive pathology results of the cases were reported in the postoperative period, tumour diameter, grade, myoinvasion, cervical involvement, lymph node metastasis and distant metastasis data were recorded. According to the prognostic factors specified in the pathology report, endometrial cancer risk groups defined by European Society of Gynaecological Oncology-European Society of Medical Oncology-European Society of Radiotherapy and Oncology (ESGO-ESMO-ESTRO) guidelines were determined as low, intermediate or high risk [10].

The data were analysed using SPSS 21.0 (SPSS, Chicago, IL, USA) statistical program. The distribution of continuous variables was analysed with visual and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Mean and standard deviations were used in the normal distribution, while median and minimum-maximum values were applied in the non-normal distribution. Chi-square test was performed to show the difference between the categorical variables. Pearson's and Spearman's rank correlation analyses were conducted for the continuous variables. Student's-*t* test and Kruskal-Wallis analysis were employed to compare the continuous variables in independent groups. The receiver operating characteristic (ROC) analysis was used to determine whether the mean SR values had a statistically significant effect on the differentiation in prognostic factors. A p-value < 0.05 was considered to

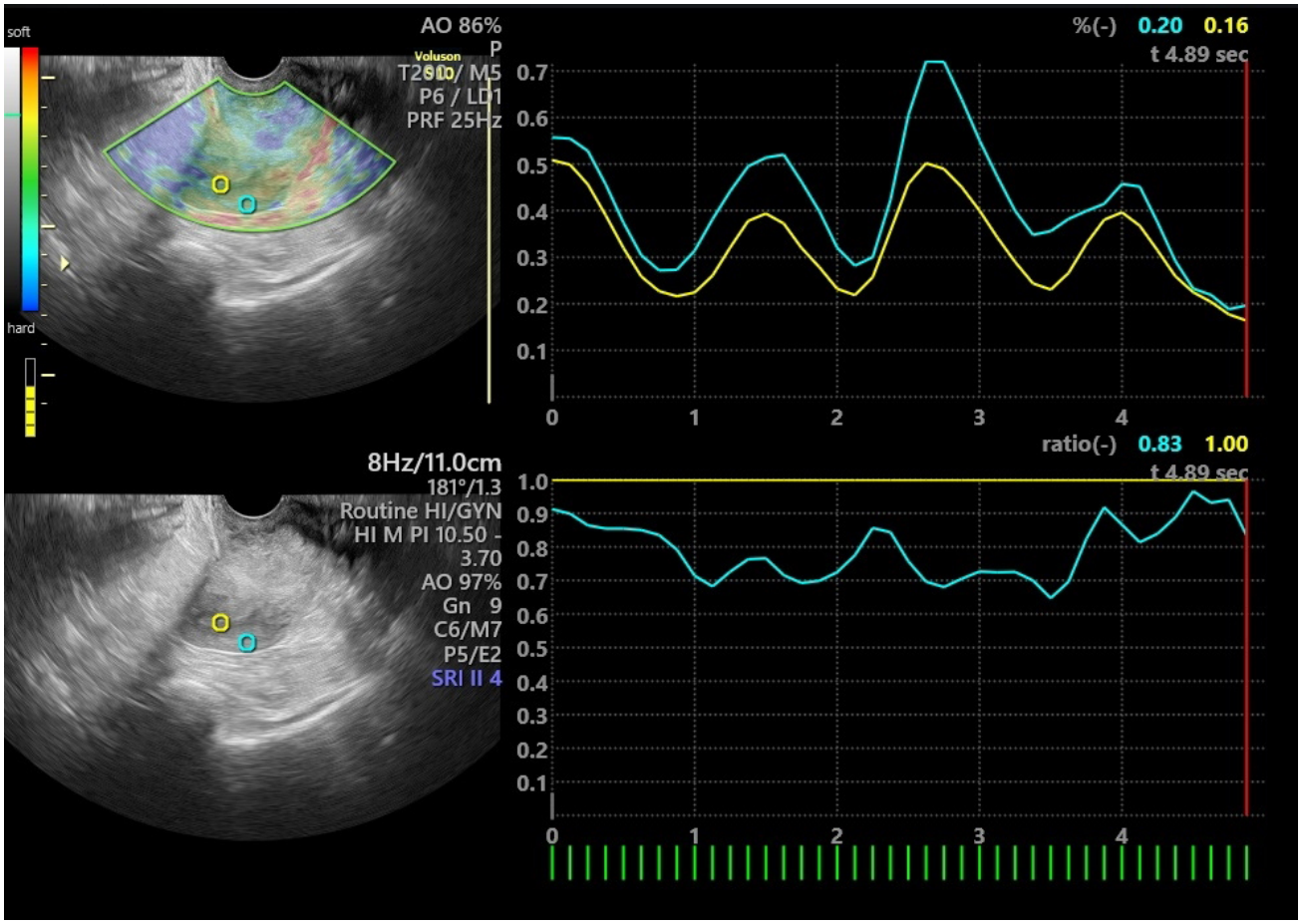

FIGURE 1. Transvaginal strain sonoelastography image of a 58-year-old woman with endometrial carcinoma. The right side shows the two images obtained by transvaginal sonographic transducer. The upper shows the elastography mode while the lower shows the routine B-mode sonography. The two circles represent the target lesion and the reference Region of Interest (ROI) which were used for the calculation of Strain Ratio (SR). Green circle (reference Region of Interest) is placed on the endometrium and the yellow circle on the intact myometrium. The right lower side shows the lines obtained from the Region of Interests (ROIs) and indicates the Strain Ratio (SR) of endometrial lesion versus intact myometrium.

indicate statistical significance.

3. Results

The patients' demographic characteristics and menopausal status are summarised in Table 1. Their median age was 63. The majority of the patients were postmenopausal; only 19 (16%) were premenopausal. Tumour characteristics and pathologic prognostic factors are summarised in Table 2. In the study population, 48 cases (76.1%) had grade-1 or grade-2 histology, and 54 (85%) cases were reported as surgical stage-I. Lymph node metastasis was observed in 4 (6.35%) cases. No distant metastasis was detected. The low-, intermediate- and high-risk groups comprised 28 (44.4%), 22 (34.9%) and 13 (20.6%) patients, respectively. The mean tumour diameter and SUVmax of uterine lesion, as shown in PET-CT, were 3.72 cm and 20.53, respectively. The mean CA-125 value was 13.8. The median SR-corpus and SR-cervix were detected as 1.55 and 0.99, respectively. The SR-corpus and SUVmax, as shown in PET-CT, had a weak positive correlation, while no significant correlation was found in the SR-cervix group (Table 3). The correlations between the prognostic factors and SR-corpus and SR-cervix values are presented in Table 4. The SR-corpus values were correlated with all prognostic factors except lymph node metastasis (1.51 versus 2.7, $p = 0.086$) and menopausal status (1.59 versus 1.55, $p = 0.54$), while the SR-cervix values were correlated with all of them except menopausal status (1.04 versus 0.98, $p = 0.89$). In detail, while there was a correlation between low- and high-risk groups in the SR-cervix group, all risk factors in the SR-corpus group showed correlations. The cutoff values in the SR-corpus and SR-cervix groups are detailed in Table 5. Although all cut-off SR-cervix values had lower sensitivity and specificity than those of the SR-corpus, histologic grade and high-risk patients that were defined in ESGO/ESTRO/European Society of Pathology (ESP) guidelines [10] had the highest sensitivity and specificity in both groups.

4. Discussion

With this study, we primarily evaluated the effectiveness of strain sonoelastography in predicting endometrial cancer prognostic factors and determined the cutoff values of the SRs in preoperative endometrial cancer cases. Second, we compared

TABLE 1. Demographic and clinical characteristics of the cases.

Patient demographics (n = 63)	Mean ± SD/ Median (min–max)/n (%)
Age (yr)	63 (40–81)
Height (cm)	158 (150–167)
Weight (kg)	78.6 ± 14.6
BMI (kg/m^2)	31.81 ± 5.96
Gravida	3 (0–7)
Parity	2 (0–5)
Menopausal status	
Pre	10 (15.9)
Post	53 (84.1)

BMI: Body Mass Index; SD: Standard Deviation; min: minimum; max: maximum.

the sensitivity and specificity of the cutoff values of SR-corpus and SR-cervix to determine the optimal reference ROI.

Comprehensive staging surgery in endometrial cancer increased morbidity and mortality when it was routinely performed in all cases. Thus, risk groups were defined in endometrial cancer using pathological parameters [11]. However, there is no consensus on selecting patients who need comprehensive staging surgery using imaging techniques or tumour biology tests. Therefore, prediction of known risk factors remains crucial in decision-making. In recent years, sentinel node mapping has been defined as a promising procedure in endometrial cancer management. More recently, assessment of tissue stiffness using sonoelastography has been found to be efficacious in a number of applications in various organ tissues [3]. It is an established application for assessing more superficial organ lesions, such as thyroid and breast lesions. The use of sonoelastography in gynaecologic cancer is less established in comparison to other gynaecologic and obstetric situations.

To our current knowledge, this can be considered a preliminary study, that compares the endometrial cancer pathological prognostic factors with sonoelastographic features. Similarly, Zhang *et al.* [12] evaluated the power of tri-dimension magnetic resonance imaging (3D MRI) elastography in predicting tumour aggressiveness in endometrial cancer. Che *et al.* [13] compared the elastographic features between the cases of endometrial cancer and benign lesions and reported that endometrial cancer tissues had a significantly higher SR value ($p < 0.001$) than the others. They set the SR cutoff value at 3.02 for the prediction of malignancy rather than benign lesions, with sensitivity, specificity, positive predictive value and negative predictive value set at 82–85% [13]. In the present study, the relations between the sonoelastographic SR and parameters such as tumour diameter, grade, myoinvasion, lymph node metastasis and stage in endometrial cancer cases were compared. The positive correlation between SR values and known pathological risk factors revealed the necessity of comprehensive surgical staging procedures for patients whose endometrial cancer tissues were above the cutoff value, while

TABLE 2. Pathological and clinical characteristics of cases.

Tumor characteristics (n = 63)	n (%)
Grade	
I	15 (23.81)
II	33 (52.38)
III	9 (14.29)
Serous	5 (7.94)
Clear	1 (1.59)
LVSI	
−	49 (77.78)
+	14 (22.22)
Myoinvasion	
<50%	35 (55.56)
≥50%	28 (44.44)
Lymph node metastasis	
−	59 (93.65)
+	4 (6.35)
Surgical stage	
IA	32 (50.79)
IB	22 (34.92)
II	3 (4.76)
IIIA	2 (3.17)
IIIC1	2 (3.17)
IIIC2	1 (1.59)
IVA	1 (1.59)
Risk groups[1]	
Low	28 (44.44)
Intermediate	22 (34.92)
High	13 (20.63)
	Mean ± SD/Median (min–max)
Tumor diameter (cm)	3.72 ± 1.98
Strain ratio—Cervix	0.99 (0.07–4.62)
Strain ratio—Corpus	1.55 (0.45–5.86)
SUVmax value	20.53 ± 7.53
CA-125 (U/mL)	13.80 (5.00–345.00)

[1]*Risk groups were defined in ESGO-ESMO-ESTRO Guidelines. SUVmax: maximum standardised uptake value; CA-125: Cancer antigen-125; LVSI: lymphovascular space invasion; SD: Standard Deviation; min: minimum; max: maximum.*

TABLE 3. Correlation analysis between SUVmax value and strain ratios.

	Strain ratio—Corpus	Strain ratio—Cervix
SUVmax value		
R[1]	0.281	0.209
p	0.026	0.100

[1]*Correlation coefficient. SUVmax: maximum standardised uptake value.*

TABLE 4. Changes in strain ratio values according to pathological prognostic factors.

	Strain ratio—Corpus	*p*	Strain ratio—Cervix	*p*
	Mean ± SD/Median (min–max)		Median (min–max)	
Grade				
I–II (n = 48)	1.27 (0.45–3.73)	0.0001	0.91 (0.07–4.62)	0.001
III (n = 15)	3.12 (0.65–5.86)		1.76 (0.50–3.56)	
Tumor diameter				
<2 cm (n = 12)	0.98 (0.45–4.52)	0.022	0.71 (0.11–1.66)	0.005
≥2 cm (n = 51)	1.91 (0.46–5.86)		1.02 (0.07–4.62)	
LVSI[1]				
− (n = 49)	1.30 (0.45–4.32)	0.001	0.94 (0.07–4.62)	0.001
+ (n = 14)	3.21 (0.65–5.86)		1.90 (0.30–3.56)	
Myoinvasion				
<50% (n = 35)	1.06 (0.45–2.61)	0.0001	0.86 (0.07–4.62)	0.005
≥50% (n = 28)	2.71 (0.46–5.86)		1.56 (0.30–3.56)	
Lymph node metastasis				
− (n = 59)	1.51 (0.45–5.86)	0.086	0.98 (0.07–4.62)	0.028
+ (n = 4)	2.70 (1.91–3.54)		1.95 (1.22–3.00)	
Surgical stage				
I–II (n = 57)	1.49 (0.45–5.86)	0.011	0.98 (0.07–4.62)	0.009
III–IV (n = 6)	2.98 (1.91–4.87)		1.95 (1.02–3.00)	
Risk groups				
Low (n = 28)	1.20 ± 0.49		0.86 (0.07–2.10)	
Intermediate (n = 22)	2.10 ± 1.21	0.0001[2.3.4]	0.99 (0.30–4.62)	0.002[3]
High (n = 13)	3.34 ± 1.34		1.68 (0.50–3.56)	
Menopausal status				
Pre (n = 10)	1.59 (0.45–3.42)	0.541	1.04 (0.46–4.62)	0.895
Post (n = 53)	1.55 (0.46–5.86)		0.98 (0.07–3.56)	

[1]*lymphovascular space invasion.*
[2]*Statistically significant difference between the low risk group and the intermediate risk group.*
[3]*Statistically significant difference between the low risk group and the high risk group.*
[4]*Statistically significant difference between the intermediate risk group and the high risk group.*
LVSI: lymphovascular space invasion; SD: Standard Deviation; min: minimum; max: maximum.

TABLE 5. Cut-off values of strain ratio-corpus and cervix according to the pathologic prognostic factors and risk groups.

	Cut-off value	Sensitivity	Specificity	AUC (95% CI)	*R*
Corpus					
Grade (State variable = Grade 3)	2.47	0.800	0.875	0.835 (0.695–0.976)	0.001
Tumor diameter (State variable = ≥2 cm)	1.21	0.667	0.667	0.713 (0.553–0.873)	0.022
LVSI (State variable = +)	2.00	0.714	0.714	0.783 (0.616–0.950)	0.001
Myoinvasion (State variable = High)	1.51	0.857	0.743	0.851 (0.745–0.957)	0.001
Risk groups (State variable = High)	2.19	0.846	0.820	0.865 (0.755–0.976)	0.001
Cervix					
Grade (State variable = Grade 3)	1.21	0.733	0.729	0.799 (0.666–0.931)	0.001
Tumor diameter (State variable = ≥2 cm)	8.70	0.706	0.750	0.761 (0.626–0.896)	0.005
LVSI (State variable = +)	1.21	0.714	0.714	0.781 (0.629–0.933)	0.001
Myoinvasion (State variable = High)	1.01	0.643	0.743	0.708 (0.574–0.841)	0.005
Risk groups (State variable = High)	1.21	0.769	0.720	0.782 (0.638–0.925)	0.002

LVSI: lymphovascular space invasion; AUC: Area Under Curve; CI: Confidence Interval.

unnecessary surgeries and related complications would be reduced for patients with endometrial cancer tissues below the cutoff values.

In this study, SR was higher in grade-3 and non-endometrioid histologies than in low-grade tumours (3.12 versus 1.27, $p < 0.001$). Similarly, preliminary findings showed that SRs of endometrial cancers were higher in high-grade histologies using MRI elastography [12]. Moreover, MRI elastography established that SR in poorly differentiated hepatocellular carcinoma was higher than in well-differentiated or mildly differentiated histological types [14]. There are two possible explanations for these results. First, in the International Federation of Gynecology and Obstetrics (FIGO) grading system, the tumour grade becomes worse as endometrial cancer cells transform from the glandular to the solid pattern. Second, poorly differentiated tumours have high proliferation rates and high cellularity. A solid pattern and high cellularity are associated with high density and higher SR status. Similar results were found in a study on prostate cancer. Although the Glison scores were correlated with elastographic parameters, the correlation with share-wave elastography was found to be higher than with strain elastography [15].

In the present study, SR increased with tumour size. When the cutoff value of the tumour size was set at 2 cm, SRs were found to be statistically significantly higher in the >2-cm tumour size group (0.98 versus 1.91, $p = 0.02$). In their study, Zhang *et al.* [12] compared tumour size with other pathological parameters (FIGO stage, tumour grade, histological subtypes and myometrial invasiveness). Only the FIGO stage was significantly correlated with tumour size ($p = 0.03$). Our findings provide preliminary data that evaluate the correlation between tumour size in transvaginal ultrasound and tumour stiffness, as reported in the literature.

Myoinvasion whose depth is greater than that of the inner half of the myometrium had a significant correlation with higher tumour stiffness and SRs (1.06 versus 2.71, $p < 0.0001$). Similar results were reported in another study that used MR elastography [12]. We observed some difficulties in measurement during elastography when the tumour extended into the uterine serosa and covered all the uterine tissue or when the patient had a huge tumour diameter. The reference ROI (a marked point on intact myometrium) could not be distinguished. In this condition, the cervix can be used as a reference ROI for SR calculation. However, generally, as discussed later, measuring the SR-cervix is not as useful as measuring the SR-corpus.

In the literature related to elastography, we found no data that compared elastographic parameters with lymph node status. In this study, lymph node metastasis was detected in four (6.3%) cases. The SR-cervix values in the node-positive group were statistically significantly higher than those in the node-negative group (0.98 versus 1.95, $p = 0.02$). Although SR-corpus values were higher in the node-positive group, these did not reach statistical significance (1.51 versus 2.70, $p = 0.86$). All cases with lymph node metastasis had deep myoinvasion, LVSI+ and grade-2 or poorly differentiated histology in this study. This may cause bias since subgroup analysis cannot be performed in the node-positive group due to the limited sample size.

All SR-corpus values were higher than SR-cervix values. A possible explanation for this outcome was that uterine corpus tissue with a more elastic property due to muscle and elastic fibres can be stretched more than cervical tissue. In the SR-corpus group, there was a statistically significant difference in all risk factors, while a significant difference was found between low-risk and high-risk factors in the SR-cervix group. Therefore, using the cervix as a reference point in strain ratio calculation is not reliable.

After correlations were found between both SR-corpus and SR-cervix values and pathologic prognostic factors, cutoff values were set for each group (Table 5). Sensitivity and specificity ratios were higher in the SR-corpus group than in the SR-cervix group. SR-corpus cutoff values reached up to 80–86% sensitivity and 74–88% specificity in the grade, myometrial invasion and high-risk groups, while LVSI (sensitivity and specificity, 0.71 and 0.66, respectively) and tumour diameter (sensitivity and specificity, 0.66 and 0.71, respectively) groups had lower values. These data were defined first in the literature.

The SUVmax of tumour tissue, as shown in the PET-CT scan, is a metabolic activity indicator. In general, poorly differentiated and more aggressive tumours have higher metabolic activity and glucose consumption. In the study conducted by Groheux *et al.* [16], grade-3 tumours showed higher uptake than lower-grade tumours ($p = 0.006$). Based on this fact, we compared the SUVmax of tumours in the uterine cavity, as revealed in PET-CT, with SR-corpus and SR-cervix values, which were correlated with other pathological parameters. A significant correlation was found in the SR-corpus group ($r = 0.281$, $p = 0.02$).

In recent years, based on the outcomes reported in the Cancer Genome Atlas and the Proactive Molecular Risk Classifier for Endometrial Carcinoma (EC) (ProMisE), tumours are divided into molecular subgroups as a Polymerase Epsilon mutant (POLEmut), p53 wild type (copy number loss (CNL) or non-specific molecular profile (NSMP)) p53 null/missense mutations (high copy number) and mismatch repair deficient (MMRd), according to the presence of polymerase epsilon (POLE) exonuclease domain mutations (EDMs), and protein 53 (p53) immunohistochemistry and mismatch repair (MMR) proteins [17]. Due to the lack of molecular profile data, we could not compare elastography results with molecular parameters.

Our study was prospectively designed, and we present our preliminary findings about sonoelastography used in endometrial cancer diagnosis. Our study has some limitations as well. The small number of patients, the technical inadequacy of strain elastography in certain conditions, such as those of patients with obesity, ascites and retroverted uterus, and difficulties in standardisation of strain elastography among practitioners (producing manual compression cycles and measurements) are weaknesses of this study. Measurements in strain elastography can be subjective since the magnitude of the applied stress (manual compression or physiologic motion when used as a stimulus) is also operator dependent. The ROI is also selected by the operator and can thus introduce variability [18]. The measurements by a single specialist

presented both a strength and a limitation of our study. We believe that reproducibility bias was negligible since we used a well-described standardised protocol (Fig. 1). Additionally, operator-related variability problems can be minimised or solved with shear-wave sonoelastography and MRI elastography that can measure tissue stiffness automatically. The shear-wave system generates quantitative elastograms and can partially exclude operator-dependent false measurements [19].

Other limitations are caused by the nature of the tumour tissue. In contrast to other tissues, it is difficult to determine optimal tissue stiffness (SR) due to the heterogeneous characteristic of tumour tissue, which contains stiff elastic regions (*e.g.*, fibrosis, calcifications) as well as soft viscous regions (*e.g.*, blood pools, cystic degeneration areas) with variations on scales with different lengths [20]. In our study, menstrual cycle dates were not detailed in premenopausal patients. Uterine corpus and cervix stiffness may vary with the menstrual cycle. A previous study showed that stiffness changed in the uterine corpus during the menstrual cycle, which was related to the anatomic and functional alteration of both the myometrium and the endometrium [21].

5. Conclusions

In our study, the data showed that elastographic SRs were significantly correlated with pathologic prognostic factors. Thus, elastographic assessment of tumour tissue can be a valuable method when making decisions about treatment alternatives and radical surgery in endometrial cancer cases. With the analyses of our data and further studies involving a large number of patients and using long-term follow-up data, elastographic measurements may be clinical prognostic markers of endometrial cancer in the future. Widespread clinical use of this method will be important in reducing unnecessary radical surgeries (related to postoperative complications and delayed treatment processes) and improving endometrial cancer patients' outcomes. Although this is a non-invasive and easily applicable method in clinical practice, factors such as interpractitioner incompatibilities and technical difficulties due to patients' conditions (obesity, ascites, retroverted uterus, large tumour size, *etc.*) limit its use. These problems may be partially solved with shear-wave or 3D MRI elastography.

AVAILABILITY OF DATA AND MATERIALS

Data available on request due to privacy/ethical restrictions.

AUTHOR CONTRIBUTIONS

AS—Study conception and design; Writing–original draft preparation. AS, EK—Acquisition of data; Formal analysis and investigation; Writing–review and editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by Clinical Research Ethics Committee of Adnan Menderes University with a protocol number 2022/179. Written informed consent was obtained for participation in this study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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