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Original Article

The role of acoustic radiation force impulse imaging in the diagnosis of cervical carcinoma

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Abstract

Aim: To investigate the diagnostic value of acoustic radiation force impulse imaging in the detection of cervical cancer, and to assess the contribution of this imaging method in distinguishing histological subtypes of cervical carcinoma.

Materials and Methods: Twenty four patients with malignant cervical mass and 25 healthy volunteers were included in this prospective study. Ultrasonographic evaluation were performed using a 3.5–6-MHz convex abdominal transducer and adequate software for performing elastographic examinations in quantitative acoustic radiation force impulse mode (Virtual Touch Quantification®). Every examination consisted of at least three independent shear wave velocity measurements. The mean shear wave velocity values were calculated, and used for statistical analysis. Postoperative pathology results of the lesions were used as the reference standard.

Results: The mean shear wave velocity values were calculated as 2.79±1.03 m/s in cervical carcinomas, and as 1.86±0.62 m/s in control group. The mean shear wave velocity value of cervical carcinomas was significantly higher than the control group (p=0.003). The mean shear wave velocity values in squamous carcinoma, adenocarcinoma, and adenosquamous carcinoma subtypes were calculated as 2.78±0.93 m/s, 3.16±1.46 m/s, and 1.90±0.21 m/s, respectively. There were no significant differences between cervical carcinoma subtypes in terms of their shear wave velocity values (p=0.247).

Conclusion: Acoustic radiation force impulse imaging is a non-invasive and cost-effective, promising adjunct modality that enables objective quantitative measurement, which may contribute to the diagnosis of malignant cervical masses.

Keywords: Acoustic radiation force impulse; ARFI; cervical carcinoma; ultrasonography

INTRODUCTION

Cervical cancer is one of the three most common female malignancies worldwide. Also it is the genital tract cancer with the highest mortality rate among women, with a particularly high incidence in countries with low socioeconomic status (1). Histological subtype and grade of differentiation of cervical cancer may determine the course of the disease, the therapeutic outcome and patient survival (2). Cervical mass may be diagnosed by clinical examination, computed tomography (CT), magnetic resonance imaging (MRI) or ultrasonography (US). MRI with high contrast resolution of soft tissue is the ideal modality of visualization of the cervix (3). Moreover, in diffusion weighted imaging (DWI), which is an advanced version of MRI technique, the apparent diffusion coefficient (ADC) map shows potential for assessing pathological subtypes and for tumor grade differentiation (4-6). Although MRI plays a key role in the evaluation of cervical cancer, it is a long-term examination that is not easily tolerable for patients. In addition, contrast medium is used in the dynamic evaluation and therefore side effects may occur. Therefore, to put forth a reliable, noninvasive easily tolerated method for the diagnosis of malignant cervical masses could be useful.

US is gaining clinical interest due to its rapid, cost-effective, non-invasive and safe nature, particularly for patients repeatedly undergoing examination (7). US elastography is a novel, non-invasive imaging method used to evaluate tissue stiffness. There are several types of elastographic techniques. Acoustic radiation force impulse (ARFI) imaging is an elastography technique that provides an objective numerical evaluation of tissue stiffness differently from the other elastography techniques (8). It provides an estimate of tissue elasticity by measuring

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the propagation of shear waves emitted during induced tissue displacements (9). The speed of the shear waves can be measured as shear wave velocity (SWV) and it is expressed quantitatively in meters per second (m/s). Stiffer tissues are associated with a higher SWV (10). The benefits and usefulness of ARFI imaging have been shown in many clinical conditions, such as lesion detection and classification (e.g., in the breast, thyroid and prostate) and liver fibrosis staging (8,11-14). However, there are few studies regarding the contribution and reliability of ARFI imaging to the diagnosis of cervical cancer (7, 15). Moreover, to our knowledge, there are no studies evaluating the role of ARFI imaging in distinguishing histological subtypes of cervical carcinoma. The aim of this prospective study is to investigate the diagnostic value of ARFI imaging in the detection of cervical cancer, and to assess the contribution of this imaging method in distinguishing histological subtypes of cervical carcinoma.

MATERIALS and METHODS

Study Population

A total of 24 patients who were admitted to the gynecology outpatient clinic with various complaints, who underwent biopsy due to a cervical mass as a result of physical examination, and whose pathology was malignant were included in this prospective study. All of the patients were evaluated with CT or MRI for staging. Most of the patients were evaluated with MRI. However, some patients were evaluated with CT due to the reasons of MRI incompatibility, such as being obesity, having claustrofobia, or having MRI incompatible devices like pacemaker. And then the patients were assessed with ARFI, before the surgery. The patients who had large cystic areas compatible with necrosis in the lesions, in the CT or MRI, were excluded. Also, the patients whose cervix lesion diameter <10 mm and skin to cervix lesion depth >80 mm, who has recurrent mass, history of gynecological surgery, and history of chemotherapy or pelvic radiotherapy were exluded. For control group, postmenauposal or postmenstruel non-pregnant 25 volunteers, who admitted to the US unit of our department for the other organ system complaints or diseases, were enrolled. Volunteers with known history of pelvic diseases such as pelvic inflammatory disease, myoma uteri, polyp, adenomatosis, endometriosis, or abscess were excluded from the study. This study was approved by Baskent University Institutional Review Board and Ethics Committee (Project no: KA20/284). Informed consent was obtained from all subjects, according to the World Medical Association Declaration of Helsinki, revised in 2000, Edinburgh.

Imaging Technique

Ultrasonographic studies were performed using a 3.5–6-MHz convex abdominal transducer (Acuson S2000, Siemens Healthcare, Erlangen, Germany) and adequate software for performing elastographic examinations in quantitative ARFI mode (Virtual Touch Quantification®, VTQ). All patients were examined by the same radiologist who had more than 10 years of experience in ultrasonography, and more than 5 years of experience in ARFI imaging. The patients were asked to lie in supine position with a half-full bladder and not to move. First, B-mode US was performed for all patients in order to assess the shape, size, boundary and echoes of the masses. The dimensions of masses were measured. Then, ARFI (VTQ) mode was performed. The region of interest (ROI), which was 6x10 mm in diameter, was placed inside the lesion. The depth of ROI was <80 mm. Every examination consisted of at least three independent ARFI measurements (SWV). The mean SWV value of all SWV measurements was calculated for each lesion, and used for further analysis. Postoperative pathology results of the lesions were used as the reference standard.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, Version 23.0 (SPSS, Chicago, IL, USA). Mean and standard deviation were calculated for numerical variables with a normal distribution, whereas for variables with a non-normal distribution, median and range were calculated. However, both the mean and median values were presented together. Kolmogorov-Smirnov test was used to test the distribution of numerical variables. SWV did not have a normal distribution according to Kolmogorov Smirnov test. Thus, for statistical analysis, the non-parametric Mann-Whitney U test was used to compare the SWV values in control group and patient group, and Kruskall Wallis variance analysis test was used to compare the SWV values of cervical carcinoma subtypes. A p value of <0.05 was considered statistically significant.

RESULTS

The mean age of patients with cervical carcinoma was 47±11.4 years (31-70 years), and the mean age in healthy control group was 34.5±8.3 years (22-46 years). The mean depth was 63.2±15 mm (36-80 mm) in the patient group, and 61.5 ±15 mm (36-80 mm) in the control group. The mean lesion size was 32.2 mm (with a range of 24-89 mm) in cervical carcinomas.

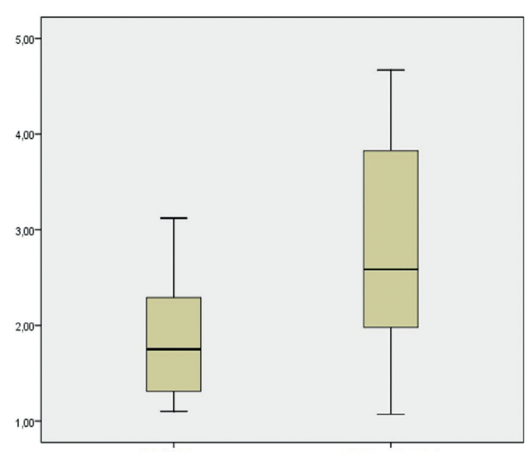

Figure 1. Box plots of mean shear wave velocity (SWV) values of control group and cervical carcinomas. The thick line passing through each box represents the median SWV values in m/s

The mean SWV values were calculated as 2.79±1.03 m/s in cervical carcinomas, and as 1.86±0.62 m/s in control group. The mean SWV value of cervical carcinomas was significantly higher than the control group (p=0.003) (Figure 1).

Table 1. The mean shear wave velocity (SWV) values of squamous carcinoma, adenocarcinoma, and adenosquamous carcinoma subtypes

Subtype of cervix carcinoma (n)	SWV values (m/s)*
Squamous carcinoma (17)	2.78 ± 0.93
Adenocarcinoma (5)	3.16 ± 1.46
Adenosquamous carcinoma (2)	1.90 ± 0.21

*SWV: Shear wave velocity; m/s: Meter/second

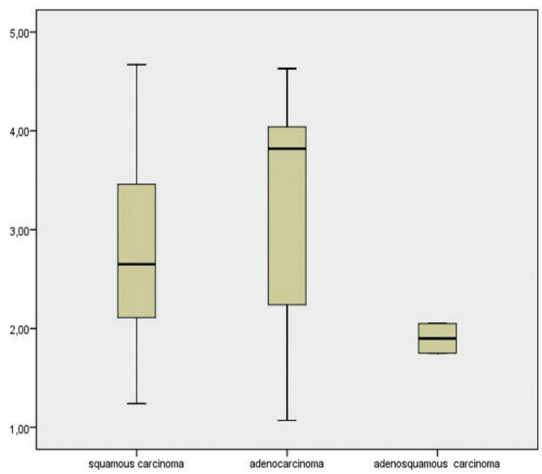

Figure 2. Box plots of mean shear wave velocity (SWV) values of subtypes of cervical carcinoma. The thick line passing through each box represents the median SWV values in m/s

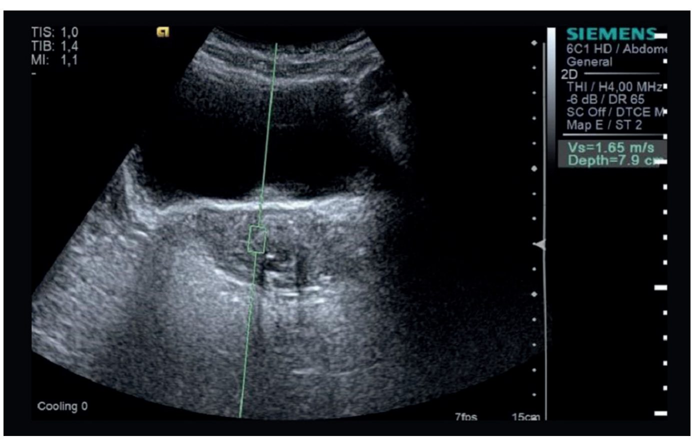

Figure 3. Shear wave velocity (SWV) measurement of a 35-year-old female in control group admitted to our department due to angiomyolipoma control. SWV of the cervix was measured with a fixed-area sample measurement of 6x10 mm. In this patient, the mean SWV of the cervix was calculated as 1.69 m/s

Of the 24 malignant cervical lesions, 17 (70.83%) were squamous carcinoma, 5 (20.83%) were adenocarcinoma, and 2 (8.33%) were adenosquamous carcinoma. The mean SWV values of squamous carcinoma, adenocarcinoma, and adenosquamous carcinoma subtypes were demostrated in Table 1. There were no significant differences between cervical carcinoma subtypes in terms of their SWV values (p=0.247) (Figure 2,3,4).

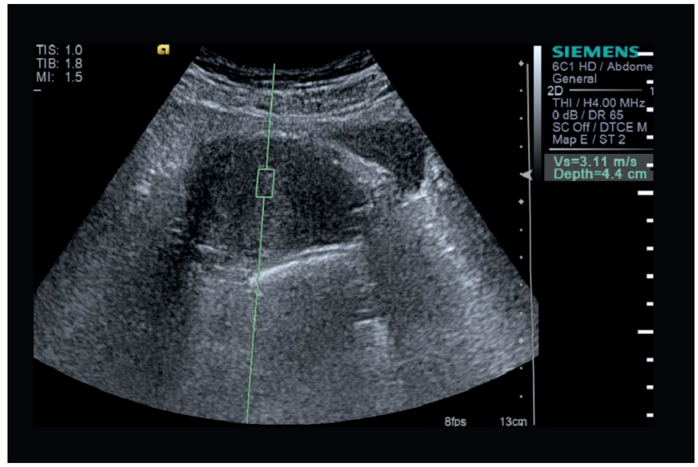

Figure 4. Shear wave velocity (SWV) measurements of a 46-year-old patient, with a cervical mass of 8.1x5.3 cm with findings of parametrial invasion detected by computed tomography and histopathologically diagnosed as adenocarcinoma. SWV of the lesion was measured with a fixed-area sample measurement of 6x10 mm. In this patient, the mean SWV of the lesion was calculated as 3.68 m/s

DISCUSSION

Our data demonstrate that ARFI imaging is a modality that may be used in the detection of cervical cancer. In the literature, there are various studies on the diagnosis of cervical cancer with different elastography methods. In these studies, it has been shown that the elasticity of malignant and normal cervical tissue is different (16-19). In their study, Bakay et al. demonstrated the elasticity differences between non-malignant and malignant pathologies of the cervix using color maps and stated that the cervix remained elastic in all non-malignant pathologies. Moreover, in this study performed using transvaginal US, they also showed the benefits of elastography in the evaluation of tumor invasion, a very important factor in the staging of cervical cancer (17).

Similarly, in studies performed using ARFI imaging, a shear wave elastography method, it was shown that SWV values obtained quantitatively using VTQ method was different in normal cervical tissue and malignant mass. Using transabdominal probe, Su et al. reported that ARFI imaging has high sensitivity and specificity for the evaluation of cervical cancer and therefore has diagnostic value in clinical practice. In this study, the mean SWV value of the surrounding normal tissue was 2.11±1.19 m/s while it was 3.41±1.59 m/s in malignant lesions (7). In our study, the mean SWV value of the normal cervical tissue was 1.86±0.62 m/s while the mean SWV value of the malignant lesions was 2.79±1.0 3m/s. And we also found statistically significant difference between the SWV values of the malignant lesions and normal cervical tissue. In the study by Liu et al. using Aixplorer® diagnostic US equipment and transvaginal probe, the mean SWV value was 4.91±1.12 m/s in malignant cervical pathologies, 3.53±0.52 m/s in benign cervical pathologies and 2.86±0.23 m/s in the normal cervix. They found a statistically significant difference between malignant cervical pathologies, benign cervical pathologies and control group in terms of maximum and mean SWV values. They stated that shear wave elastography is an effective method that can help the diagnosis of cervical diseases and accurate detection of tumor invasion by quantitatively analyzing the elasticity characteristics of cervical cancers (15). The US device we used in our study does not have ARFI mode in transvaginal probe. Thus, the study was performed via transabdominal probe. Examination performed via transabdominal route has certain limiting factors such as subcutaneous and abdominal adipose tissue thickness of the patient and intestinal gas. Depending on these factors, the compression used during examination can also change. It is possible to obtain different SWV values from examinations performed through transvaginal and transabdominal probes. With transvaginal US, it is possible to have a more detailed imaging of mass boundaries and evaluation of the lesions without being affected by the depth and intestinal gas, and obtain information that will contribute to staging such as bladder or rectal invasion.

An important point to consider when obtaining SWV values is that necrotic areas must not be included in the measurement. However, in clinical practice, when performing multiple measurements, this is not always possible. To eliminate this limitation, some researchers suggest the maximum SWV value at the non-necrotic areas to be evaluated. They argued that by this way, the actual elasticity of malignant tumors that are non-homogenous and especially can undergo liquefaction and necrosis more easily, may be demonstrated more effectively (20).

Histological subtype and grade of differentiation of cervical cancer may determine the course of the disease, the therapeutic outcome and patient survival (2). Squamous cell carcinomas constitute approximately 69% and adenocarcinomas constitute approximately 25% of cervical cancers (21). It is still a matter of debate whether squamous cell carcinomas and adenocarcinomas differ in terms of their clinical outcome. However, rare tumor subtypes such as neuroendocrine tumors are known to have a poor prognosis (22). In our study, there was no significant difference between the SWV values of squamous carcinoma, adenocarcinoma, and adenosquamous carcinoma subtypes of cervical carcinoma.

The major limitation of this study is the small sample size. Moreover, since all lesions included in this study were malignant, the difference between malignant and benign lesions could not be evaluated. Another limitation can be the use of transabdominal route for examination. Studies are required with larger sample size, where the same patients will be examined both via transabdominal and transvaginal probe and the cut-off values for both examinations will be determined.

CONCLUSION

In conclusion, ARFI imaging is a non-invasive and cost-effective, promising adjunct modality that enables objective quantitative measurement, which may contribute to the diagnosis of malignant cervical masses.

Competing interests: The authors declare that they have no competing interest.
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Ethical approval: This study was approved by the medical ethics committee of Baskent University Ankara hospital (Project no: KA20/284).

REFERENCES

1. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 2019;144:1941-53.
2. Katanyoo K, Sanguanrungsirikul S, Manusirivithaya S. Comparison of treatment outcomes between squamous cell carcinoma and adenocarcinoma in locally advanced cervical cancer. Gynecol Oncol 2012;125:292-6.
3. Fischerova D, Cibula D, Stenhova H, et al. Transrectal ultrasound and magnetic resonance imaging in staging of early cervical cancer. Int J Gynecol Cancer 2008;18:766-72.
4. Mainenti PP, Pizzuti LM, Segreto S, et al. Diffusion volume (DV) measurement in endometrial and cervical cancer: a new MRI parameter in the evaluation of the tumor grading and the risk classification. Eur J Radiol 2016;85:113-24.
5. Kuang F, Ren J, Zhong Q, et al. The value of apparent diffusion coefficient in the assessment of cervical cancer. Eur Radiol 2013;23:1050-8.
6. Liu Y, Ye Z, Sun H, et al. Grading of uterine cervical cancer by using the ADC difference value and its correlation with microvascular density and vascular endothelial growth factor. Eur Radiol 2013;23:757-65.
7. Su Y, Du L, Wu Y, al. Evaluation of cervical cancer detection with acoustic radiation force impulse ultrasound imaging. Exp Ther Med 2013;5:1715-9.
8. Sporea I, Sirli R, Popescu A, et al. Acoustic Radiation Force Impulse (ARFI)-a new modality for the evaluation of liver fibrosis. Med Ultrason 2010;12:26-31.
9. Samier-Guérin A, Saraux A, Gestin S, et al. Can ARFI elastometry of the salivary glands contribute to the diagnosis of Sjögren's syndrome? Joint Bone Spine 2016;83:301-6.
10. Matsuzuka T, Suzuki M, Saijo S, et al. Stiffness of salivary gland and tumor measured by new ultrasonic techniques: Virtual touch quantification and IQ. Auris Nasus Larynx 2015;42:128-33.
11. Barr RG. Elastography in clinical practice. Radiol Clin North Am 2014;52:1145-1162.
12. D'Onofrio M, Crosara S, De Robertis R, et al. Acoustic radiation force impulse of the liver. World J Gastroenterol 2013;19:4841-9.

13. Sporea I, Sirli R, Bota S, et al. ARFI elastography for the evaluation of diffuse thyroid gland pathology: Preliminary results. World J Radiol 2012;4:174-8.
14. Tozaki M, Isobe S, Sakamoto M. Combination of elastography and tissue quantification using the acoustic radiation force impulse (ARFI) technology for differential diagnosis of breast masses. Jpn J Radiol 2012;30:659-70.
15. Liu C, Li TT, Hu Z, et al. Transvaginal Real-time Shear Wave Elastography in the Diagnosis of Cervical Disease. J Ultrasound Med 2019;38:3173-81.
16. Thomas A, Kummel S, Gemeinhardt O, et al. Real-time sonoelastography of the cervix: tissue elasticity of the normal and abnormal cervix. Acad Radiol 2007;14:193-200.
17. Bakay OA, Golovko TS. Use of elastography for cervical cancer diagnostics. Exp Oncol 2015;37:139-45.
18. Lu R, Xiao Y, Liu M, et al. Ultrasound elastography in the differential diagnosis of benign and malignant cervical lesions. J Ultrasound Med 2014;33:667-71.
19. Sun LT, Ning CP, Liu YJ, et al. Is transvaginal elastography useful in pre-operative diagnosis of cervical cancer? Eur J Radiol 2012;81:888-92.
20. Houelleu Demay ML, Monghal C, Bertrand P, et al. An assessment of the performance of elastography for the investigation of BI-RADS 4 and BI-RADS 5 breast lesions: correlations with pathological anatomy findings. Diagn Interv Imaging 2012;93:757-66.
21. Downey K, Riches SF, Morgan VA, et al. Relationship between imaging biomarkers of stage I cervical cancer and poor-prognosis histologic features: quantitative histogram analysis of diffusion-weighted MR images. AJR Am J Roentgenol 2013;200:314-20.
22. Cohen JG, Kapp DS, Shin JY, et al. Small cell carcinoma of the cervix: treatment and survival outcomes of 188 patients. Am J Obstet Gynecol 2010;203:341-6