Shear wave elastography: Can it be a new radiologic approach for the diagnosis of erectile dysfunction?

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Abstract

Introduction: Erectile dysfunction (ED) is a common health problem among males, and radiology has limited use in its diagnosis and treatment. Shear wave elastography (SWE) is a new sonographic technique. In this study, we examined the significance of SWE in the diagnosis of ED.

Methods: The study included a total number of 70 participants. The mean age of the participants was 54.14 ± 8.03 years (range: 39 and 71 years old). We composed two groups. Group 1 had 35 patients who presented to the urology clinic in our hospital complaining of ED, and had a score of 17 or lower from the International Index of Erectile Function (IIEF) questionnaire. Group 2 consisted of 35 healthy volunteers who did not have ED. SWE measurements were performed from corpus cavernosum penis in both groups, and the results were noted. Differences between the groups were evaluated statistically.

Results: The difference between the mean SWE measurements of two groups (Group 1: 20.94 ± 6.23 kPa and group 2: 24.63 ± 7.58 kPa) was found to be statistically significant ($p = 0.027$; $p < 0.05$). For a cut-off value of 17.1 kPa, the SWE method has specificity, sensitivity, positive predictive value, and negative predictive value regarding diagnosis of ED as 94.29%, 34.29%, 85.71%, and 58.93%, respectively. The mean age of the groups did not show a statistically significant difference ($p = 0.287$; $p > 0.05$).

Conclusions: Due to its high specificity and positive predictive value, SWE can offer useful data in the radiologic evaluation of ED cases.

Keywords

Sonoelastography, shear wave, penile dysfunction

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Introduction

Erectile dysfunction (ED) can be defined as the difficulty of initiating and maintaining erection. It is a common problem among males, and its prevalence among men above the age of 20 has been reported as 20%.¹ This rate is estimated to increase by 2025.² ED has been categorized into two groups depending on whether it is caused by organic or psychological reasons.³ Execution of erection involves neuronal, hormonal, vascular, and penile factors. Psychological factors also have a significant role in erection.¹ Diagnosis of ED is made upon detailed clinical and laboratory investigations.⁴ The International Index of Erectile Function

(IIEF) questionnaire is a clinical test commonly used for making the diagnosis.⁵ This questionnaire is filled-in by the physician in a face-to-face interview with the patient. Patients are classified according to the score that they obtain from this questionnaire.

In the management of ED, other male sexual dysfunctions (such as premature ejaculation, hypogonadism, disorders of orgasm) should be ruled out.⁶

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Although organic causes are most commonly encountered reasons for ED, situational factors may play significant role in the setting of ED. Before treatment, reversible causes (blood pressure, blood glucose level, lipid profile, smoking) should be managed and then appropriate treatment options can be selected for the patient. First line treatment is with oral medication and if this fails then more invasive second line treatment option consists of intracavernosal medications. If second line treatment fails then surgery becomes the last option for treatment.⁶

Radiology has limited place in ED, and has been used only in selected patients for diagnosis and guidance of treatment.⁴ Doppler sonography is a frequently used imaging method for evaluation of vascular pathologies. During this procedure, intracavernosal administration of a vasodilator agent is undertaken, and measurements are performed from the cavernosal arteries. Based on the results of this examination, vascular pathology is categorized as arterial, veno-occlusive, or combined type insufficiency.^{7,8} Besides this method, cavernosonography (for diagnosis of veno-occlusive insufficiency) and angiography (for diagnosis of arterial insufficiency) are gold standard methods, although they are quite invasive techniques.^{7,8} Magnetic resonance imaging has limited use in the diagnosis of ED, and has only been used as a noninvasive modality for demonstration of vascular penile pathologies.⁹

Elastography is a new and noninvasive imaging modality used for assessing the stiffness of tissues.¹⁰ It has two main types: strain elastography and shear wave elastography (SWE). Strain elastography is a semi-quantitative method, and accuracy of results is highly dependent on user ability. In strain elastography, a manually applied external force is used and the displacement of tissue is analyzed and finally the stiffness of the area of interest is depicted within a color box.^{10,11}

In SWE, ultrasonographic waves generated by the transducer is sent to the region of interest (ROI) and they create shear waves in the tissue. These waves are detected by the transducer and their speed is used to calculate Young modulus of the tissue which is directly related to the stiffness of the tissue.¹² SWE measures tissue stiffness quantitatively. It has been tested for the evaluation of many organs and pathologies, which has yielded effective results such as breast, thyroid, prostate and liver diseases, and tumors.¹³ To our knowledge, no previous study has evaluated the effectiveness of SWE in the diagnosis of ED. In this study, we aimed to determine the effectiveness of SWE in the diagnosis of ED, and discuss its potential contributions to the management of ED.

Materials and methods

The ethics committee of our hospital approved this prospective study, and all patients provided informed consent. Patients that scored 17 or less according to the IIEF questionnaire and presented to our urology clinic with complaint of ED were included in the study. The duration of all patient complaints was not longer than 1 year. Patients that were diagnosed with Peyronie's disease, or had history of penile trauma or penile operation for any reason were excluded. Smokers were also excluded from the study. A total of 35 patients that met these criteria made up the ED group (Group 1). In addition, 35 healthy volunteers who did not have any complaints or any of the exclusion criteria comprised the control group (Group 2). In each group, SWE was performed by an experienced sonographer (R.T.) with a linear transducer (12-16 MHz) using Aplio 500 platinum (Toshiba, Tokyo, Japan) ultrasonography device (Figures 1 and 2). Patients were asked to hold the glans penis gently and put the penile shaft on their

Figure 1. Ultrasound image of transverse section of penis from the healthy group (group 2). Using region of interest, SWE measurement was performed on corpus cavernosum.

Figure 2. Ultrasound image of transverse section of penis from the patient group (group 1). SWE measurement from corpus cavernosum in the region of interest.

Table 1. Evaluation of age versus corpus cavernosum (kPa) measurement

	Total (<i>n</i> = 70)	Patient (<i>n</i> = 35)	Control (<i>n</i> = 35)	<i>p</i>
Age (years)				
Min-max (median)	39–71 (53.5)	39–67 (53)	44–71 (54)	0.287 ^a
Mean ± SD	54.14 ± 8.03	53.11 ± 8.52	55.17 ± 7.48	
Corpus cavernosum (kPa)				
Min-max (median)	10.3–44.4 (20.2)	10.3–37.5 (20.0)	16.8–44.4 (23.4)	0.027 ^{b*}
Mean ± SD	22.78 ± 7.13	20.94 ± 6.23	24.63 ± 7.58	

^aStudent *t*-test.

^bMann-Whitney *U* test.

**p* < 0.05.

pubic region. Measurements were performed from the middle portion of penis (while it was flaccid) with the probe held in a transverse plane. The ROI circle was placed 1 cm deep on the corpus cavernosum penis. We performed five measurements per patient and calculated the average for the final SWE value. The measurement results were noted in kilo Pascal (kPa) units. The differences of measurements between the two groups were analyzed statistically.

Results

Statistical analysis

Number Cruncher Statistical System (NCSS) 2007 (Kaysville, UT) software was used for statistical analyses. In addition to descriptive statistical methods (mean, standard deviation, median, frequency, proportion, minimum, maximum), comparison of continuous variables between the two groups was made with a Student's *t*-test for normally distributed data and a

Mann-Whitney *U*-test for non-normally distributed data. The comparison of categorical variables was made with Yates' continuity correction test. The cut-off value for corpus cavernosum sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated and ROC curve analysis was employed. Statistical significance was evaluated at *p* < 0.01 and *p* < 0.05 levels.

The study was conducted on 70 males in our radiology clinic between November 2015 and August 2016. Their age varied between 39 and 71 years, with a mean age of 54.14 ± 8.03 years. The mean age was 53.11 ± 8.52 years for the patient group (group 1) and 55.17 ± 7.48 years for the control group (group 2). There was no statistically significant difference between the groups in terms of age (Table 1), (*p* = 0.287; *p* > 0.05). The duration of complaint by patients in group 1 was no longer than 1 year.

The mean corpus cavernosum SWE measurement value was 20.94 ± 6.23 kPa in the patient group and 24.63 ± 7.58 kPa in the control group. The corpus

Figure 3. ROC curve of corpus cavernosum measurement for the determination of the presence of erectile dysfunction (ED).

cavernosum measurement values in the patient group compared to the control group were statistically significant (Table 1) ($p = 0.027$; $p < 0.05$).

On the basis of this statistically significant difference, we considered calculating a cut-off value for corpus cavernosum measurement. In order to establish a cut-off value, ROC analysis was employed along with calculation of sensitivity, specificity, PPV, and NPV. The cut-off value of corpus cavernosum measurement for determination of the presence of ED was calculated as 17.1 kPa. For a cut-off value of 17.1 kPa, sensitivity, specificity, PPV, and NPV of corpus cavernosum SWE measurement were 94.29%, 34.29%, 85.71%, and 58.93%, respectively.

In the calculated ROC curve, the area under the curve was 65.4% with a standard error of 6.6% (Figure 3). For a cut-off value of 17.1 kPa, the corpus cavernosum SWE measurement showed statistically significant association with ED (Table 2) ($p = 0.001$; $p < 0.01$). The odds ratio for corpus cavernosum measurement was calculated as 8.609 (95% CI: 1.758–42.164).

Discussion

ED is a serious health issue affecting the lives of both men and their partners. Its prevalence among men increases with age. Several factors including vascular, neuronal, hormonal, and psychological factors are implicated in its etiology.¹⁴ The corpus cavernosum in penis is made up of highly specialized vascular structure which functions to promote erection. Approximately 50% of the cross-sectional anatomy of the penis is made up of smooth muscle cells (SMC).¹⁵ Another

Table 2. Association between erectile dysfunction (ED) and corpus cavernosum measurement (kPa)

Group	Corpus cavernosum (kPa)				<i>p</i>
	≤17.1		>17.1		
	<i>n</i>	%	<i>n</i>	%	
Erectile dysfunction	12	34.3	23	65.7	0.007 ^{a,**}
Control	2	5.7	33	94.3	

Note: Cut-off value: 17.1.

^aYates' continuity correction test.

^{**} $p < 0.01$.

important structural unit of the penis is the collagen. SMC and collagen not only constitute the structure but are also responsible for penis function.¹⁶ The number of SMCs has been shown to decrease in cases of ED.^{17,18} Furthermore, studies have also shown that the collagen content of the penis is altered in cases of ED.^{18,19}

Radiology has limited use in the diagnosis and management of ED. Often, Doppler ultrasonography is the imaging modality of choice in cases that require thorough investigation and determination of treatment methods. As a new and noninvasive sonographic method, SWE is a rapid and practical radiological method used to assess the tissue stiffness quantitatively. Camoglio et al.²⁰ used the penile strain elastography method in children that had hypospadias. In that study, preoperative sonoelastography showed areas where the tissue had greater stiffness. This allowed decisions to be made on the most appropriate surgical technique for the particular patient. In a case report, a patient with severe penile curvature did not have a palpable plaque, and the plaque could neither be visualized sonographically. SWE demonstrated greater stiffness within a particular area, and the patient saw benefit from the local injections made to that region.²¹

Zhang et al.²² reported that SWE can quantitatively demonstrate SMC in rat penis. A reduced amount of SMCs resulted in higher measurements in the SWE. The association between SWE measurement values and histopathological examination findings in the rat penis led to the conclusion that SWE can be used in quantitative assessment of penile SMCs.²² In another study, SWE measurement values were significantly lower in rats that were sexually in a declining period compared to the sexually active rats.²³ Alterations in collagen composition were held responsible for this difference. Nonetheless, the amount of SMCs in the penile

tissue is known to diminish with aging.^{17,19} Therefore, it is not clear how they attributed the changes in SWE measurements only to the alterations in collagen tissue, while overlooking the contribution of the change in the quantity of SMCs. In our study, we found lower SWE in patients with ED compared to the control group (group 1: 20.94 ± 6.23 kPa, group 2: 24.63 ± 7.58 kPa). When a SWE Cut off value of 17.1 kPa is used, it may contribute to diagnosis of ED, which may be due to the high specificity (95%) and positive predictive value (85%). The amount of SMCs is diminished in cases of ED. One study involving rat penises showed that the reduced amount of SMCs was associated with higher penile SWE values.²² This finding seems to be contradictory to our results. Possible reasons may be explained as follows. Qiao et al.²³ reported that collagen alterations occurring in ED results in decreased SWE values. This finding is consistent with our results. To our knowledge, there are no studies that explain how ED may alter SWE measurement values in humans. ED is a complex pathology that can develop due to several factors. Tissue response may vary depending on the nature of the cause of the disease.¹⁴ On the other hand, it is also important for how long cases of ED live with this problem. We believe the duration of disease may affect the proportion of the amounts of SMCs and collagen in the tissue.^{14,23–25} In our study, some patients had a history of diabetes mellitus ($n=20$), hypertension ($n=10$), and psychological reasons ($n=5$), which could predispose to ED. None of our cases complained of ED lasting longer than 1 year. This patient group showed decreased SWE measurement values compared to the controls. This difference may be caused by the change in the amount of collagen despite the reduction in the number of SMCs.

Our study has some limitations. First, we do not have histopathologic confirmations of our results. Second, our patient group is not homogenous and in that it may affect the SWE values in some degree. But we show that there is statistically significant difference between ED group and control group ($p=0.027$; $p<0.05$). We excluded from our study patients with Peyronie's disease, or patients who had history of penile trauma or penile operation because it is known that these pathologies create some degree of fibrosis in the tissue that can increase the SWE values significantly. On the other hand, it is not known as to what sort of changes can be observed with SWE in other etiologies of ED. We believe that above mentioned pathologies should be investigated separately.

In the clinical setting, there can be cases where clinicians may face difficulties in differentiation of ED and other male sexual dysfunctions. SWE can provide valuable data in the radiologic assessment of ED patients

due to its high specificity and positive predictive value. SWE evaluations may also provide additional data in the selection of treatment options. We believe further studies with SWE may contribute to more frequent use of radiological imaging in these patients.

Declaration of Conflicting Interests

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Ethical approval

Institutional Review Board approval was obtained for this study. All participants provided a written consent for the study.

Guarantor

RT.

Contributors

RT researched literature for this review article. RT wrote the first draft of the manuscript. RT and EI authors sourced images for the article. All authors wrote and approved the final version of the manuscript.

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