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COMPARİSON OF PREOPERATİVE PENİLE ELASTOGRAPHİC ULTRASOUND FİNDİNGS AND PATHOLOGİCAL TİSSUE RESULTS OF PATİENTS İMPLEMENTED WİTH PENİLE PROSTHESİS

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Abstract

Objective Histopathologically to determine the relationship between penile elastography ultrasonography and erectile dysfunction. Material and Method 12 patients who applied to our clinic for erectile dysfunction in the last 1 year and accepted this study were included . Preoperative two-dimensional shear wave elastography imaging was performed in 12 patients and recorded in the Pascal (kPa) unit. Approximately 0.5x0.5x0.5 cm tissue samples were taken from the right and left spongy tissue during penile prosthesis implantation operation. Tissue samples were sent to the pathology department. The percentage of the area covered by muscle fibers and elastic fibers in the corpus cavernosum was noted semi-quantitatively (ratio of muscle fibers and cavernous body elastic fiber score). All data obtained were compared with each other. Results Cavernous body elastic fiber score data(Grouped Score 1, 2 and 3) and percentage of cavernous body muscle fibers data (Grouped %10,%20,%30... %100) were compared with Shear wave elastography data (kPa). The results were not statistically significant according to the Kruskal Wallis Test and Spearman's correlation test. Cavernous body elastic fiber score and the percentage of cavernous body muscle fibers were also compared, it was not statistically significant according to the Kruskal Wallis test and Spearman's correlation test. The data we obtained as a result of our study showed that penile elastographic imaging is not a reliable method in the diagnosis of erectile dysfunction. Conclusions Penile shear wave elastography can be used clinically to quantitatively assess the amount of smooth muscle cells and elastic fibers in the penis, but it deserves to be studied with a larger number of patients and a more specific interpretation of the pathology preparation. Keywords: Penile elastography, erectile dysfunction, penile prosthesis, shear wave

Comparison of Preoperative Penile Elastographic Ultrasound Findings and Pathological Tissue Results of Patients İmplemented with Penile Prosthesis

Running Title: Erectile dysfunction and elastography

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ABSTRACT

Objective

Histopathologically to determine the relationship between penile elastography ultrasonography and erectile dysfunction.

Material and Method

12 patients who applied to our clinic for erectile dysfunction in the last 1 year and accepted this study were included . Preoperative two-dimensional shear wave elastography imaging was performed in 12 patients and recorded in the Pascal (kPa) unit. Approximately 0.5x0.5x0.5 cm tissue samples were taken from the right and left spongy tissue during penile prosthesis implantation operation. Tissue samples were sent to the pathology department. The percentage of the area covered by muscle fibers and elastic fibers in the corpus cavernosum was noted semi-quantitatively (ratio of muscle fibers and cavernous body elastic fiber score). All data obtained were compared with each other.

Results

Cavernous body elastic fiber score data(Grouped Score 1, 2 and 3) and percentage of cavernous body muscle fibers data (Grouped %10,%20,%30... %100) were compared with Shear wave elastography data (kPa). The results were not statistically significant according to the Kruskal Wallis Test and Spearman's correlation test. Cavernous body elastic fiber score and the percentage of cavernous body muscle fibers were also compared, it was not statistically significant according to the Kruskal Wallis test and Spearman's correlation test. The data we obtained as a result of our study showed that penile elastographic imaging is not a reliable method in the diagnosis of erectile dysfunction.

Conclusions

Penile shear wave elastography can be used clinically to quantitatively assess the amount of smooth muscle cells and elastic fibers in the penis, but it deserves to be studied with a larger number of patients and a more specific interpretation of the pathology preparation.

Keywords: Penile elastography, erectile dysfunction, penile prosthesis, shear wave

What is already known about this topic? : Comparison of penile elastography imaging results with cavernous tissue histopathology in the literature was performed by taking cavernous tissue samples from rats.

What does this article add? : There is no study in the literature comparing penile elastography results with human cavernous tissue histopathology. The data we obtained as a result of our study showed that penile elastographic imaging is not a reliable method in the diagnosis of erectile dysfunction.

İntroduction

Penile erection is a complex phenomenon that creates a sensitive and coordinated balance between the vascular, psychological, neurological and smooth muscle compartment. It includes arterial dilatation, activation of the penile corporeal veno-occlusive mechanism and trabecular smooth muscle relaxation in spongiosa tissue.[1] Erectile dysfunction (ED) is defined as the inability to maintain an adequate erection to achieve satisfactory

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sexual performance and maintain an erection.[2] Erectile dysfunction can affect physical and psychosocial health and significantly affect the quality of life of patients and their wifes.[3,4,5] The density of ED in men aged 40-70 study conducted in 69% in Turkey.[6,7] Although it was previously believed that ED is primarily due to psychological factors, today it is known that there is an underlying organic pathology in most of the cases.[8] The penis is primarily composed of sinusoids, smooth muscle cells (SMC), corpora cavernosa, endothelial cells and corpus spongiosum, which contain fibrocytes and elastic fibers that form the anatomical principles of penile erection.The tissue formation of the penis is nearly related to the erectile function of the penis.[9] The change in the tissue structure of the penis (such as the reduction of SMCs, the amount and density of sinusoids, the amount and density of fibrocytes) is directly related to the occurrence and severity of erectile dysfunction (ED).[10] Timely diagnosis of penile tissue abnormalities is very important for the etiological diagnosis of ED. The only way to diagnose a change in the tissue structure of the penis is to biopsy the cavernous tissue.[11] Since biopsy is an invasive method, its clinical application is very limited. Therefore, it is of great clinical importance to investigate a non-invasive and non-contraindicated method for evaluating the tissue structure of the penis. .Real-time two-dimensional ShearWave Elastography (2D-SWE) is a new ultrasound quantitative measurement technology. The basic principle is to use ultrasonic pulses to make the tissue generate transverse shear waves and shear wave velocity (SWV) is to determine the exact.[12,13] Using SWV to calculate tissue stiffness, we obtain the quantitative value of tissue stiffness. Since SWV is determined by the structural properties of the tissue, shear wave stiffness (SWS) is a quantitative parameter that can reflect the tissue structure.[14] At the same time, the 2D-SWE examination is non-invasive and can be performed at any time without contraindications. Thus, we think that 2D-SWE is expected to be a new clinical method for evaluating the tissue structure of the penis.[15] There are two main types: strain elastography and shear wave elastography (SWE). The accuracy of the results largely depends on the ability of the user and strain elastography is a semi-quantitative method.[16,17] Ultrasonographic waves produced by the transducer generate region of interest (ROI) and shear waves in the tissue.[18] These waves are detected by the transducer and the velocities of the waves are used to calculate the tissue young modulus, which is directly related to the stiffness of the tissue.[19] Shear wave propagation velocity is proportional to tissue stiffness, which increases with fibrosis.[20] To our knowledge, a limited number of previous studies have evaluated the efficacy of SWE in the diagnosis of ED. In this study, we aimed to determine the efficacy of SWE in the diagnosis of ED and to discuss its potential contributions to the management of ED

Methods

The study was planned in accordance with the Helsinki Declaration decisions, patient rights regulations and ethical rules. The research was started after the approval of the Medical Research Ethics Committee of Manisa Celal Bayar University Faculty of Medicine. Ethics committee number: 25/12/2019/20.478.486. 12 patients who applied to our clinic for erectile dysfunction in the last 1 year and accepted this study were included . These patients had erectile dysfunction for at least 3 years, did not benefit from phosphodiesterase 5 inhibitor drugs, did not have an erection and tumescent response in the Penile Doppler USG performed in our Hospital Radiology Department, and accepted penile prosthesis implantation. Patients who were diagnosed with Peyronie's disease or had a history of penile trauma or penile operation for any reason were excluded from the study.

Preoperative (2-3 days ago) SWE imaging was performed by an experienced radiologist with a linear transducer (12-16 MHz) using the Aplio 500 platinum (Toshiba, Tokyo, Japan) 2D- SWE device to the patients participating in our study. They were asked to grasp and place the penile shaft in the groin area. Measurements were made from the middle part of the penis (flaccid) with the probe held in a transverse plane. The ROI circle was placed 1 cm deep to the corpus cavernosum penis (Figure 1 and 2). Six measurements were taken per patient, three from the right and left cavernous, and these measurements were recorded as T1, T2 and T3. The median value of these measurements was expressed as Tmed. Measurement results were recorded in kilo Pascal (kPa). Penile prosthesis implantation was performed by penoscrotal technique in all patients. After passing through the penoscrotal skin and subcutaneous layers, the right and left cavernous body tunica albuginea was incised, and tissue samples of approximately 0.5x0.5x0.5 cm were taken from the right and left spongiosis tissue. The samples taken did not cause any deformity in the penis. After the

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sample tissues were taken, a penile prosthesis was inserted into the cavernous body. The samples taken were sent to our hospital pathology department in separate containers. Paraffin embedded blocks were prepared in formalin from tissue samples taken from the right and left corpus cavernosum. The 4µ thick sections obtained from the blocks were stained with Hematoxylin & Eosin (HE), Masson-trichrome(Figure 3A and 3B) and Verhoff's elastic dye(Figure 4A and 4B). By evaluating the HE and Masson-trichrome stained sections together, the ratio of muscle fibers and collagenized areas in the distance between the vascular channels of the corpus cavernosum was examined, and the percentage of the area covered by the muscle fibers was noted semiquantitatively (Grouped %10,%20,%30... %100). The decrease in the ratio of muscle fibers was interpreted as an increase in connective tissue. In the evaluation of the elastic fibers, a semi-quantitative scoring was made by considering the presence and density of the elastic in the distance between the vascular canals. Accordingly, if the elastic fibers are observed more than 50% of the distance, the score is 3; If 50-25% is monitored as decreased, the score is 2; The score was evaluated as 1 if it was observed in less than 25% area and diluted.

Statistical analysis

The data were evaluated using descriptive statistics (number, percentage distribution, mean, median, standard deviation, min-max values, etc.), the Kruskal Wallis test and the Spearman's correlation test. $p < 0.05$ was considered statistically significant. r=–1 is a perfect downhill (negative) linear relationship. r= +1 is a perfect uphill (positive) linear relationship

Results

The study included 12 male individuals who came to Manisa Celal Bayar University Urology outpatient clinic with the complaint of erectile dysfunction for at least 2-3 years. The average age was 57.25 ± 11.71. Six mid-axial penile elastography measurements were performed in all patients pre-op right and left corpus cavernosum . The right T1 median value was 16.95±11.71 kPa, the right T2 median value was 16.40±5.20 kPa , the right T3 median value was 17.90±6.19 kPa and the right Tmed value was 16.90±5.76 kPa. Left T1 median value was recorded as 18.40±5.65 kPa, left T2 median value was 16.25±4.68 kPa, left T3 median value was 15.20±5.22 kPa and left Tmed was 16.4±5.05 kPa (Table 1). Percentage of right cavernous body muscle fibers median value was 85%±8.91 and percentage of left cavernous body muscle fibers median value was 80%±8.90 . Right elastic fiber scores median value was 2±0.83 and left elastic fiber scores median value was 2±0.73 (Table 2). When Masson trichrome was grouped according to their staining percentages, it was observed that right ($p = 0.365$, $r = -0.287$) and left ($p = 0.126$, $r = -0.467$) cavernous body elastographic median values were not correlated with these percentiles according to the Kruskal Wallis test and Spearman's correlation test. Staining on the left cavernous body elastic fibers median value of the patients who underwent score 1 (n: 3) was 15.5±10.02 kPa , the median value of the patients who underwent score 2 (n: 4) staining was 15.16±2.19 kPa and the median value of the patients who underwent score 3 (n: 5) staining was 17.63±1.87 kPa (Table 3) .Staining on the righ cavernous body elastic fibers median value of the patients who underwent score 1 (n: 3) was 15.76±9.59 kPa, the median value of the patients who underwent score 2 (n: 6) staining was 16.71±5.54 kPa and the median value of the patients who underwent score 3 (n: 3) staining was 21.13±3.05 kPa (Table 4). With the increase in the staining scores of elastic fibers in the right cavernosis and left cavernosis, the results of the right Tort and left Tort increased, but the results were not statistically significant according to the Kruskal Wallis Test and Spearman's correlation test. (right side $p = 0.751$ r=0.102) (left side p=0.347 r=0.298). Median masson trichrome staining percentage of pathology specimens with left elastic fiber score 1 (n: 3) was 80%, left elastic fiber score 2 (n: 6) was 82.5% and left elastic fiber score 3 (n: 3) was %75. Median masson trichrome staining percentage of pathology specimens with right elastic fiber score 1 (n: 3) was 75% , percentage of pathology specimens with right elastic fiber score 2 (n: 4) was %85 and percentage of pathology specimens with right elastic fiber score of 3 (n: 5) was 87.5% .When the left cavernous body elastic fiber score was compared with the percentage of left cavernous body masson trichrome staining , it was found that the Kruskal Wallis Test and Spearman's correlation test were not statistically significant. (right side p=0.347 r=0.298) (left side p=0.920 r=-0.033). Pathological data were also incompatible within themselves. The data we obtained as a result of our study showed that penile elastographic imaging is not

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a reliable method in the diagnosis of erectile dysfunction.

Discussion

ED is a serious health problem that affects the lives of both men and their partners. Its prevalence in men increases with age. There are several factors in its etiology, including vascular, neuronal, hormonal and psychological factors.[21] The corpus cavernosum in the penis consists of a highly specialized vascular structure that promotes erection. Approximately 50% of the cross-sectional anatomy of the penis consists of smooth muscle cells (SMC).[22]Another important structural unit of the penis is collagen. SMC and collagen not only build structure but are also responsible for penile erection.[23] It has been shown that the number of SMCs is reduced in ED cases.[24,25] In addition, studies have shown that the collagen content of the penis is altered in cases of ED . Usually, Doppler ultrasonography is the preferred imaging method in cases where a comprehensive examination and treatment methods need to be determined. Radiological imaging has limited use in the diagnosis and treatment of ED. As a new noninvasive sonographic method, SWE is a fast and practical radiological method used to quantitatively evaluate tissue stiffness.[26]

Zhang et al. reported that SWE can quantitatively show SMC in the rat penis. Smaller amounts of SMC resulted in higher measurements in SWE. The relationship between SWE measurement values in the mouse penis and histopathological examination findings concluded that SWE can be used in the quantitative evaluation of penile SMCs.[27] It should also be noted that the amount of SMC in the penile tissue decreases with age.[24,25,26] Therefore, it is unclear how changes in SWE measurements only relate to changes in collagen tissue and neglect the contribution of the change in the amount of SMCs.

Rüştü Türkay et al. found lower SWE in ED patients compared to the control group (group 1: 20.94-1.23 kPa, group 2: 24.63-1.7.58 kPa). According to this study, using a 17.1 kPa SWE Cutoff, higher specificity (95%) and a positive predictive value (85%). The amount of SMCs decreases in ED cases. A study involving rat penises showed that a reduced amount of SMC was associated with higher penile SWE values.[28,29] As far as we know, there are no studies that describe how ED can change SWE measurement values in humans. ED is a complex pathology that can develop due to various factors. Tissue response may vary depending on the nature of the cause of the disease.[21]

On the other hand, how long ED patients have been with this problem is also important. We believe that the duration of the disease can affect the amount of SMC and collagen in the tissue. In our study, a positive correlation was found between the increase in right and left cavernous body elastic fiber score and right and left penile elastographic cavernous body measurements, but it was not statistically significant due to the insufficient number of patients.

There was no correlation or statistical significance between right and left penile elastography cavernous body measurement results and right and left cavernous body masson trichrome staining percentage measurements. There was a positive correlation between the right and left cavernous body elastic fiber scores compared to the percentage of right and left cavernous body masson trichrome staining, but was not statistically significant according to the Kruskal Wallis Test and Spearman's correlation test. The fact that the pathology results were also incompatible for themselves and the insufficient number of patients limited our study. The inability to biopsy the cavernous body tissue of healthy volunteers and the absence of our control group are another factor limiting our study. In the studies in the literature, obtaining pathology samples from rats made our study superior to others.

In addition, studies in the literature have shown that; Due to its high specificity and positive predictive value, SWE can provide valuable data in the radiological evaluation of ED patients. SWE evaluations can also provide additional data in the selection of treatment options. We believe that further studies with SWE may contribute to the more frequent use of radiological imaging in these patients. Due to its high specificity and positive predictive value, SWE can provide valuable data in the radiological evaluation of ED patients. SWE evaluations can also provide additional data in the selection of treatment options. We believe that further studies with SWE may contribute to the more frequent use of radiological imaging in these patients.

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Conclusion:

Perhaps better results could have been obtained if multiple biopsies were performed as the location of biopsies.

Penile SWE can be used clinically to quantitatively assess the amount of SMCs in the penis, but it deserves to be studied with more patients and more specific pathology preparation interpretation.

Conflict of interest: none declared.

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Figure Legends:

Figure 1 : Left Cavern Body Mid Axiel Penile Elastographic Imaging

Figure 2: Right Cavern Body Mid Axiel Penile Elastographic Imaging

Figure 3A: A case with 90% of muscle fibers in the area between the HE and vascular channels. (x100)

Figure 3B: A case with 75% of muscle fibers in the area between the Masson's trichrome and vascular channels.(x100)

Figure 4A : A case where fibers in elastic dye (black color, marked with an arrow) are in all areas (score 3) (x100)

Figure 4B : A case where fibers are very sparse in elastic dye (black color, arrow-marked) (score1) (x100)

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