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ORIGINAL ARTICLE

Evaluation of the Effect of Varicoceles and Infertility Status on Volumetry and Shear-Wave Elastography

Varikosel ve İnfertilitenin Volumetri ve Shear-Wave Elastografi Üzerindeki Etkilerinin Değerlendirilmesi

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ABSTRACT

Aim: This study aims to compare the volumetry and shear-wave elastography findings in infertile and fertile patients and evaluate the effect of presence of varicoceles on the parameters.
Materials-Methods: 40 infertile and 20 fertile patients (120 testes) (mean age 29,3±6,7) between January 2018-November 2018 were included in this prospective study. All patients underwent testicular B-mode and doppler ultrasonography (US) and shear-wave elastography (SWE). Patients were sub-grouped according to fertility status and presence or absence of varicoceles.
Results: Testis stiffness was significantly higher in testes without varicoceles than those with varicoceles (p=0.021). It was also higher in fertile patients than infertile patients (p=0.015). Testes volumes were higher in fertile patients and patients with varicoceles (p=0.011 and p=0.028, respectively).
Conclusion: SWE is a non-invasive, cheap and reproducible technique with promising results for diagnosis and follow-up in the evaluation of infertility.

Keywords: Infertility; Varicocele, Shear-wave elastography; Testis stiffness; Testis volume

ÖZ

Amaç: Fertil ve infertil hastalarda volumetri ve shear-wave elastografi (SWE) bulgularının; ve varikosel varlığının bu parametreler üzerindeki etkisinin araştırılması
Gereç-Yöntem: Ocak 2018-Kasım 2018 arasında radyolojiye yönlendirilmiş 40 infertil ve 20 fertil hasta (120 testis) (ortalama yaş 29,3±6,7) bu prospektif çalışmaya dahil edildi. Tüm hastalara testise yönelik B-mod, doppler USG ve SWE yapıldı. Hastalar fertilite durumu ve varikosel varlığına göre alt gruplara ayrıldı.
Bulgular: Varikoseli olmayan hastalarda varikoselli hastalara göre testis sertliği anlamlı şekilde artmıştı (p=0.021). Fertil hastalarda infertil hastalara göre testis sertliği anlamlı şekilde artmıştı (p=0.015). Fertil hastalarda ve varikoselli hastalarda testis hacmi daha yüksekti (sırasıyla p=0.011 ve p=0.028).
Sonuç: SWE invaziv olmayan, ucuz ve tekrarlanabilir bir teknik olup infertilite tanı ve takibinde kullanımı umut vaat etmektedir.

Anahtar Kelimeler: infertilite, varikosel, shear-wave elastografi, testis sertliği, testis hacmi

Introduction

Varicoceles result from the venous reflux at the pampiniform plexus and present as abnormally dilated and tortuous veins with retrograde flow. Palpable varicocele incidence is 15% in the population, and this number may rise up to 30-40% in patients who are evaluated for infertility. Although the underlying pathogenesis is still not fully understood, varicoceles remain as the leading treatable cause of infertility. Varicoceles may or may not affect the sperm analysis findings, and even when it does it may affect all parameters or a few, even just one (1, 2).

B-mode and doppler ultrasonography (US) are cheap, non-invasive, practical and reliable methods in the diagnosis of varicoceles (3, 4). Most of the varicoceles are asymptomatic and could only be detected by US (5), in which 2 mm threshold is reported to have 95% sensitivity. Increase in diameter with Valsalva maneuver as well as venous reflux lasting more than one second are also important criteria for diagnosis (6, 7).

In this study we aimed to evaluate the differences in testis volumes and SWE findings in infertile and fertile patients as well as the effect of varicoceles on the parameters.

Materials-Methods

Patient selection

This prospective study was approved by the institutional board. Infertile patients (with known semen analysis results) who were referred to radiology clinic for scrotal doppler US between January to November 2018 were recorded. All patients underwent testicular B-mode and doppler ultrasonography (US) and shear-wave elastography (SWE). Patients who had previous history of genitourinary trauma or surgery, patients with masses, significant parenchyma heterogeneity and/ or atrophy, ipsilateral hydrocele, extensive microlithiasis and bilateral varicocele were excluded from the study. In

the end, 40 infertile patients (80 testes) were included in the study. For the fertile group, consecutive patients with known fertility (had children or known semen analysis) with similar ages were recorded. Exclusion criteria was also performed on these patients. At the end, results of 20 fertile patients were included in the study. All patients gave oral informed consent before being included in the study. After that, patients were sub-grouped according to fertility status and presence or absence of varicoceles as: group 1 (infertile with varicoceles); group 2 (infertile without varicoceles); group 3 (fertile with varicoceles); and group 4 (fertile without varicoceles).

Doppler US and Shear-wave elastography

The radiologists were blind to the semen analysis results during the US examinations. Sonographic evaluation was performed using a Toshiba Aplio 500 ultrasound scanner (Toshiba Medical Systems Corporation, Otawara, Japan) and a 7.5 MHz linear array transducer while the patient is lying supine while the torso is mildly elevated. The maximum diameters of the testis were measured in three planes (length x height x width) and the volume was calculated automatically. For varicoceles, the level of inguinal canal and the upper lateral edge of testis was evaluated. Maximum diameters of veins were measured during rest and Valsalva's maneuver. Presence of veins larger than 2 mm diameter at rest was considered as a varicocele. If reflux was noted, the duration, mean and maximum velocity, and flow volume of reflux during Valsalva were recorded. Reflux longer than one second was also considered as a varicocele. Varicoceles were then graded according to the simplified Sartechi classification based on doppler US findings (8).

After doppler US, at the same session testicular stiffness was evaluated with ARFI technique. For SWE mode, an ultrasonic radiation pressure is created in the tissues by focused US for some hundreds of microseconds. This pressure acts as a shear-wave source. Starting from this point a shear-wave spreads and using ultrafast US imaging this propagation and shear-wave velocity (SWV) is calculated. Thus, with the formula below, SWV is displayed in real time 2D-map (9).

$E = 3\rho\ (SWV)^2$

E: Young's modulus in kPa

ρ: density of the medium (~1000 kg/m3)

SWV: shear-wave velocity (m/s)

Measurements were made from the upper 1/3, middle 1/3 and lower 1/3 of the testis and mean values were calculated (Figs 1 and 2).

Statistical Analysis

Statistical analysis was done using SPSS 22 program. Descriptive statistics for the variables were presented as the mean, standard deviation (SD), minimum, and maximum values. Testis volumes and stiffness were compared using Mann-Whitney U test and Kruskal Wallis test. The relationship between volume and the stiffness was studied using Spearman's correlation test. For all analyses, a p-value of less than 0.05 was considered statistically significant.

Results

The mean age of 60 patients was 29,3±6,7. The mean age, median testis volume and SWVs of the four groups are listed in Table 1. The differences between mean ages were not statistically significant (p>0.05).

Median testis volume was 20.3 cm^3 (10.5-36.3) in total, and 17.80 cm3 (10.5-29.8) in infertile patients and 23.30 cm3 (16.6-36.3) in fertile patients. Median testis volumes were significantly lower in infertile patients (group 1 and 2) compared to fertile patients (group 3 and 4) (p=0.011). Patients with varicoceles (groups 1 and 3) had significantly larger testicular volumes compared to those without varicoceles (groups 2 and 4) (p=0.028). Median testicular volume was the highest in group 3 (fertile with varicoceles).

Testicular stiffness showed a strong negative correlation with testis volume (r2= -0.8, p<0.001) (Fig. 3). The testicular stiffness was highest in group 4 (infertile patients without varicoceles) and the difference was statistically significant (p=0.035). When patients were grouped according to the presence of varicoceles, the mean testicular stiffness was significantly higher in patients without varicoceles (1.22 m/s vs 1.12 m/s, p=0.021). There was no significant difference in mean testicular stiffness between varicocele grades (p>0.05) (Table 2). Testicular stiffness was also statistically higher in infertile patients compared to fertile patients (1.20 m/s vs 1.14 m/s, p=0.015).

Patient age showed no statistically significant correlation with mean testicular stiffness or median testicular volume (p>0.05). In the infertile group, presence of varicoceles was also not affected by the age (p>0.05).

Table 1. Mean age, testis volume and shearwave velocities of the subgroups.

Subgroup	N	Mean age	MTV (cm^3)	MSWV (m/s)
Group 1	25	23.67±3.93	23.8	1.15±0.06
Group 2	55	24.5±4.37	15.7	1.25±0.04
Group 3	3	30.8±9.52	26.2	1.09±0.07
Group 4	37	38.5±9.35	19.8	1.20±0.08

MTV: Median testis volume; MSWV: Mean shearwave velocity

Table 2. Mean age and shearwave velocities of patients according to varicocele grades.

Varicocele grade	N	Mean age	MSWV (m/s)
Grade 1	2	20.67±0.5	1.120.01
Grade 2	7	25.73	1.120.07
Grade 3	12	29.08.65	1.130.08
Grade 4	7	277,5	1.110.09

MSWV: Mean shearwave velocity

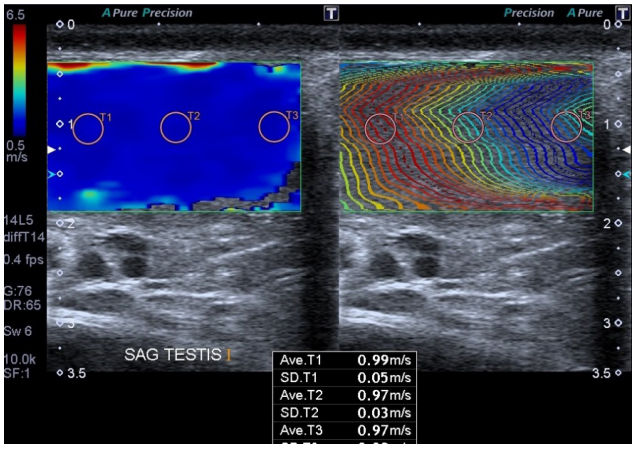

Fig 1. Shear wave elastography findings of right testis in 24 year-old fertile male without varicoceles.

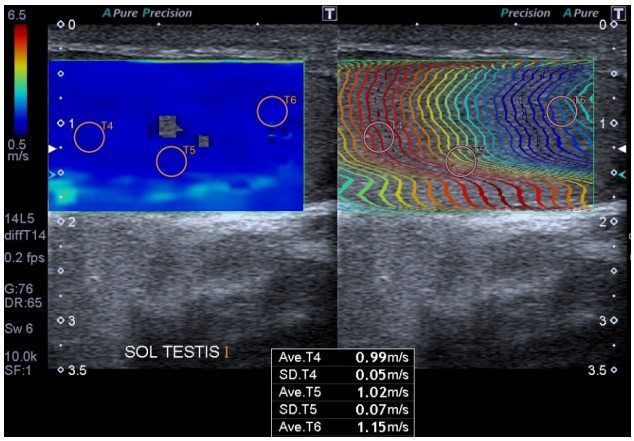

Fig 2. Shear wave elastography findings of left testis in 32 year-old fertile male with varicoceles.

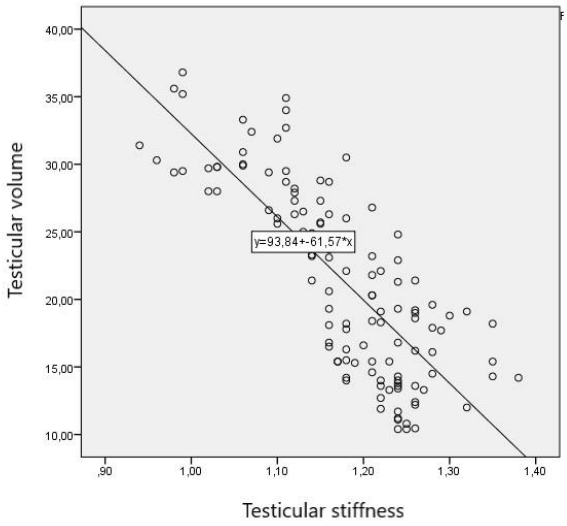

Fig 3. Correlation of testicular stiffness and median testicular volume.

Discussion

Varicoceles are defined as the abnormal dilatation of pampiniform plexus veins due to venous reflux. On US examination, there are dilated and tortuous veins, associated with retrograde flow in testicular veins and pampiniform plexus (6). Varicoceles are the most common treatable cause of infertility (10). Semen quality has been shown to improve 60-80% after varicocelectomy in the literature (11). Physical examination is still the standard method for varicocele diagnosis; yet only 40% of the small varicoceles can be diagnosed solely by palpation (12, 13). Subclinical varicoceles, which indicate varicoceles that can be diagnosed on radiological evaluations but not on physical examination, plays an important role in infertility (14). Postoperative paternity rates were lower in patients with unilateral subclinical varicoceles with decreased testis volumes (15). Thus, accurate diagnosis of subclinical varicoceles is just as important as that of varicoceles (14).

Ultrasonography and doppler US are non-invasive and non-ionizing effective radiological methods that are also easily applicable and reproducible (16, 17). A diameter more than 2 mm is the most common criteria for varicocele diagnosis. Gonda et al. reported 95% sensitivity for 2 mm threshold in their study (18); however, vein diameter is not enough for varicocele diagnosis alone. Chiou et al. reported 93% sensitivity and 85% specificity for new criteria (vein diameter, reflux duration and velocity during Valsalva maneuver) compared to physical examination alone (8). Color change on doppler US is a subjective and unassured parameter and should be supported with spectral analyses.

There are a number of studies in literature comparing age, testicular volumes and stiffness. A positive correlation between testicular mean shear-wave velocity and advanced age has also been reported.

The authors attributed this to the increased stiffness with aging (19). On the other hand, in our study shear-wave velocity values did not differ with age. This might be due to the close range of ages and the testicular volumes in the infertile group.

An animal study on the effect of torsion on spermatogenesis and testicular stiffness, the authors revealed that stiffness values increased while spermatogenesis decreased after torsion. They also underlined that SWE could be used for the evaluation of spermatogenesis disorders (20). A negative correlation between sperm count and testicular stiffness has been shown in some studies (20, 21). Although infertile group was not subdivided according to sperm counts, the significantly increased shear-wave velocities in our study may also corroborate with this finding.

The testicular volumes and stiffness showed a strong negative correlation, similar to results of Yavuz et al. (21). Testis volumes have been shown to be higher in patients with higher sperm counts (21, 22). As with SWE values, although patients were not divided based on sperm counts, still, fertile patients had significantly larger testes compared to infertile patients in our study.

How the varicocele causes infertility is still not clear. The main mechanism is thought to be via increased temperature and flow disorders, resulting in spermatozoal death (23, 24). The relationship of SWE values and presence or grade of varicoceles is debatable. Our study showed a significant decrease in SWE velocities in patients with varicoceles, yet there was no significant difference among varicocele grades. Dede et al. also supported our findings in their study (10). However, some studies suggest no significant correlation between testicular parenchyma stiffness and presence of varicoceles (21, 25).

Testicular volumes were significantly higher in patients with varicoceles in our study, but the difference was not significant among different grades. On the other hand, Podesta et al. found no significant correlation in their study (26).

Our study has many limitations. Small sample size, as well as the unbalanced distribution of the grades of the varicoceles sharply limited the statistical analysis. Secondly, due to small sample size, patients could not be subdivided based on the sperm counts. Lastly, most of the infertile patients were within 20-30 years of age and younger than the fertile group, therefore age-related analysis was also limited.

In conclusion, US and doppler US are practical, feasible and cost-effective diagnostic tools that are widely used in varicocele diagnosis. Evaluation of testicular stiffness by SWE reveals promising results for both predicting infertility and the effect of varicocele on the testicular parenchyma. Further studies with subgroup analyses are needed for both technical standardization and evaluation of the effect of varicoceles.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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