

## Evaluation of the Effect of Varicoceles on Testicular Stiffness by Shear Wave Elastography

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### **ABSTRACT:**

#### **BACKGROUND:**

Varicocele is a disease characterized by abnormally engorged veins of the pampiniform plexus. The prevalence of varicocele is approximately 15% in adult males. Multiple classification systems are available for grading varicoceles, all of them are non-ideal. Ultrasound elastography (USE) is a new imaging technology that examines tissue stiffness. Elasticity imaging by USE provides stiffness measurement as additional information to conventional US.

#### **AIM OF THE STUDY:**

Is to examine changes in testicular stiffness in varicocele in an attempt to assess the role of Shear wave elastography in testicular varicoceles and to provide additional diagnostic data to further improve and unify a grading system for varicoceles.

#### **PATIENTS AND METHODS:**

A cross sectional descriptive study undertaken on sixty-three patients which took place at Al-Yarmouk Teaching Hospital, Baghdad, Iraq, in the period between Jan. 10<sup>th</sup> to Nov. 11<sup>th</sup>, 2020. Standard scrotal ultrasonography followed by two-dimensional shear wave elastography were done for all patients. Sixty-three patients (126 testes) were divided to three groups; group (A): testes with a maximum venous diameter of less than 1.9mm representing non-varicose testes, group (B): those with a venous diameter between 2 and 3.4mm, and group (C): with venous diameter of equal or more than 3.5mm. Three stiffness measurements were taken by elastography in supine position with another three measurements in erect posture.

#### **RESULTS:**

Twenty-seven percent of subjects had normal testes, while 73% had varicoceles. 50% of varicoceles were bilateral, while 48% were left sided. Only one case (2%) had a right sided varicocele. There were no statistically significant differences between the mean volumes of the aforementioned groups. A weak negative correlation observed between the pampiniform venous plexus diameter and testicular stiffness, the mean testicular stiffness of group A was  $2.85 \pm 0.47$  while groups B and C showed a mean stiffness of  $2.80 \pm 0.51$  and  $2.73 \pm 0.44$  kilo Pascals respectively. The differences were statistically insignificant between these groups. There was a highly significant difference between supine and erect testicular stiffnesses. Normal testes showed 19% increase in their mean stiffness in upright posture, as compared to varicose testes which demonstrated 13% increase.

#### **CONCLUSION:**

Shear wave elastography is a modern technology, however; its role in discriminating between grades of varicoceles is limited.

**KEYWORDS:** Varicoceles, Shear wave elastography, Pampiniform venous plexus, Testicular stiffness.

### **INTRODUCTION:**

Varicocele is an abnormality caused by excessively dilated venules of the pampiniform plexus, and primarily results from incompetent or absent valves

in the spermatic vein<sup>(1)</sup>. In adult males varicoceles achieve a prevalence of approximately 15%<sup>(1-3)</sup>. The incidence of varicoceles increase with age; however, it's uncommon below 10 years<sup>(4)</sup>. Varicoceles represent the most common correctable cause of male infertility<sup>(5,6)</sup>. The link between varicoceles and male infertility is documented<sup>(7,8)</sup>.

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The diagnosis is based on history and physical examination, and sonography. Most patients are either asymptomatic or may complain of mild pain in the scrotum, increasing during standing<sup>(4)</sup>. Ultrasound is the preferred imaging technique in patients with varicocele<sup>(4,9)</sup>. Generally, veins larger than 2 mm in diameter, that show increased size during the Valsalva maneuver are the typical ultrasound findings of varicoceles<sup>(1)</sup>.

Ultrasound elastography (USE) is an imaging technology used to assess tissue stiffness. It provides additional information to conventional ultrasound that can be used to differentiate affected from normal tissue for diagnostic applications<sup>(10,11)</sup>.

### **PATIENTS AND METHODS:**

A cross sectional descriptive study performed on 63 patients having an age range from 20 to 60 years complaining of either testicular pain or history of infertility referred by specialist urologists for scrotal Doppler ultrasound were included in this study, which took place at Al-Yarmouk Teaching Hospital, Baghdad, Iraq, in the period between Jan. 10<sup>th</sup> to Nov. 11<sup>th</sup>, 2020.

#### **Exclusion criteria:**

Patients discovered to have the following findings were excluded from the study:

- Patients with testicular parenchymal pathology like tumors.
- Patients with orchitis/epididymo-orchitis. This is to avoid the effect of testicular parenchymal edema on stiffness.
- Patients with hydroceles, as hydroceles caused distortion of the shear waves resulting in artifacts.
- Patients with ectasia of the rete testes.
- Patients with unilateral orchidectomy due to trauma.
- Patients taking anabolic steroids or any other body-building preparations, as these patients tend to have an above-normal sized testes and stiffness readings higher than others. This aided in avoiding biased stiffness measurements.

Sixty-three patients (126 testes) were divided to three groups; group (A): testes with a maximum

diameter of less than 1.9mm representing non-varicose testes, group (B): those with a maximum venous diameter between 2 and 3.4mm, and lastly group (C): with venous diameter of equal or more than 3.5mm.

#### **Examination procedure:**

Ultrasound examination took place in an isolated room, after maintaining adequate patient privacy utilizing GE® LOGIQ® P7 color Doppler ultrasound machine, with L3-12MHz linear array probe and Shear wave elastography. The machine's default scrotal examination preset settings were used. The patient was asked to lie supine after performing sufficient exposure of the scrotum down to the level of mid-thigh, holding the penis onto the lower abdominal wall to maintain good working space for the assessment of the testes. Formal examination is started with assessment for the testicular echotexture, comparing both testes together in split-screen frozen images, then single view of both testes in the same frozen screen image. Color Doppler imaging is then started to assess testicular and epididymal vascularity with comparison between both sides using split-screen viewing. Assessment for the presence of pampiniform plexus varicosity is then performed in the supine position, before and after Valsalva maneuver, to check for blood flow reversal during Valsalva.

Testicular volume estimation was performed using split-screen images with sagittal and axial views of one testis; images were saved in the ultrasound machine memory, and then repeated for the other testis. The default ellipse volume formula ( $\text{Length} \times \text{Width} \times \text{Height} \times 0.52$ ) that is embedded in the device's default scrotal examination preset was applied

With the patient still in supine position, and gentle probe pressure (just sufficient to produce a reliable image), Shear wave elastography is activated, sampling box is placed on the right testis viewed longitudinally (but away from the rete testis) in split screen mode, then the trigger button is pressed.

## VARICOCELES BY SHEAR WAVE ELASTOGRAPHY

A homogeneously blue testicular stiffness sampling window is observed. The same procedure is performed for the left testis.

After having a split view of testicular stiffness for both testes in one split-screen, proper labelling of the testes was done, then three measurement circles were drawn covering the upper pole, mid testes, and lower testicular pole for each side. This yielded three testicular stiffness records for each

testis in supine position. Testicular stiffness numbers were displayed in Kilo Pascals (kPa). At this stage, the image is saved into the ultrasound machine's memory (Figure 1). After that, the patient is asked to stand upright, then, assessment of the maximum venous diameter of pampiniform plexus on both sides is done and recorded (Figure 2), followed by a second reading of testicular stiffness in the same aforementioned procedure.

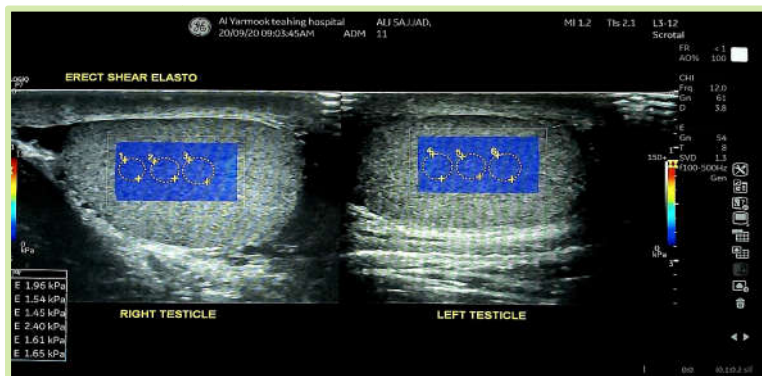


Figure 1: Acquiring testicular stiffness for both testes.



Figure 2: Measuring pampiniform venous plexus maximum diameter.

Statistical analysis was performed using Microsoft® Office Excel® 2016. Data were expressed in the form of mean, standard deviation, and percentages. Pearson's coefficient ( $r$ ) was used to assess the correlation between maximum pampiniform plexus diameter and testicular stiffness.

Student's t-test was used to look for the statistical significance of the relationship between the age of patients with normal testes and those with varicoceles.

Paired t-test was utilized to examine the difference between the mean stiffness of right versus left testes, then used to see the significance of patients' postural change (from supine to erect) on the mean testicular stiffnesses.

Single factor ANOVA test was implemented to look for the differences between the mean testicular volumes and mean testicular stiffnesses of all studied groups. A P-value of  $<0.05$  is considered to be significant.

## VARICOCELES BY SHEAR WAVE ELASTOGRAPHY

Assessment of the percentage of change in stiffness with posture for each testis was calculated using the formula:

$$\text{Percentage of change in stiffness} = \frac{\text{Erect stiffness} - \text{supine stiffness}}{\text{Supine stiffness}} \times 100\%$$

**Table 1: Clinical and some demographic data of all studied patients.**

	No.	Percentage	Mean age $\pm$ SD*
Normal	17	27%	32.5 $\pm$ 8.73
Varicocele	46	73%	32.1 $\pm$ 7.87
All patients	63	100%	32.2 $\pm$ 8.04

SD: standard deviation  
\* Student's t-test: not significant ( $P=0.87$ )

### RESULTS:

Sixty-three patients examined having mean age of 32.2 $\pm$ 8.04 years. Student's t-test revealed no significant difference between the ages of patients with normal testes and those with varicoceles ( $P=0.87$ , Table 1). Of all examined cases, 17 (27%) had normal testes, while the majority 46 (73%) had varicoceles.

Half of cases of varicoceles were bilateral 23 (50%), while 22 cases (48%) were left sided. Only one case (2%) showed isolated right sided varicocele with no intraabdominal pathology (Table 2).

**Table 2: Distribution of varicoceles according to location.**

Side of varicoceles	No.	Percentage
Right	1	2%
Left	22	48%
Bilateral	23	50%
Total	46	100%

### Testicular volume:

The mean testicular volume of group A was 14.9 $\pm$ 3.4 mL, and that of group B was 14.8 $\pm$ 4 mL, while group C showed a mean volume of 14.1 $\pm$ 3.9

mL (Table 3). ANOVA test for single factor revealed no statistically significant differences between the mean testicular volumes of the above groups ( $P=0.68$ ).

**Table 3: Mean testicular volume in different groups.**

Groups	No.	Mean testicular Volume (mL) $\pm$ SD*
A: $\leq$ 1.9 mm	58	14.9 $\pm$ 3.39
B: 2-3.4 mm	51	14.8 $\pm$ 3.98
C: $\geq$ 3.5 mm	17	14.1 $\pm$ 3.87

mL: Milliliters

SD: standard deviation

\* Single factor ANOVA test between groups: not significant,  $P=0.68$

## VARICOCELES BY SHEAR WAVE ELASTOGRAPHY

### Testicular stiffness:

The mean testicular stiffness is noted to be subtly reduced as the venous diameter increases as seen in Table 4, a weak negative correlation is observed

between the venous plexus diameter and the testicular stiffness (*Pearson's r = - 0.1*); however, ANOVA test showed insignificant difference between groups ( $P = 0.67$ ).

**Table 4: Mean testicular stiffness in different groups according to pampiniform venous plexus diameter.**

Groups	No.	Mean Stiffness (kPa) ± SD*
A: ≤1.9 mm	58	2.85 ± 0.47
B: 2-3.4 mm	51	2.80 ± 0.51
C: ≥3.5 mm	17	2.73 ± 0.44

SD: Standard deviation.

kPa: kilo Pascals.

\* ANOVA test for single factor: not significant ( $P=0.67$ )

### Postural testicular stiffness:

Changing patients' posture from supine to erect produced noticeable increase in the testicular stiffness in all patients that was statistically

significant ( $P<0.01$ ) (Table 5). Normal testes showed 19% increase in their mean stiffness in upright posture, while varicose testes showed 13% increase (Table 6)

**Table 5: Postural mean testicular stiffness of right and left testes of all patients.**

	Mean stiffness (kPa)		Percentage of change with posture	P value*
	Supine position	Erect position		
Normal testes (n=58)	2.63	3.06	19%	0.21
Varicocele testes (n=68)	2.63	2.93	13%	

kPa: Kilo Pascals

\*Student's t-test of mean postural change of stiffness between normal and varicocele testes is not significant

**Table 6: Postural differences in mean testicular stiffness between normal and varicose testes**

Side	Mean stiffness (kPa)		p-value*
	Supine position	Erect position	
Right (n=63)	2.66±0.5	3.06±0.7	0.000012
Left (n=63)	2.61±0.4	2.92±0.5	0.000002

kPa: Kilo Pascals

\*Paired t-test: statistically significant

## DISCUSSION:

Varicocele is the commonest cause of male infertility<sup>(12)</sup>. Multiple classification systems exist for grading varicoceles<sup>(5)</sup>. The majority of these classification systems are based on the presence or absence of reflux for categorizing varicoceles. Other studies assess the reflux time for the same purpose, while the remaining studies use variable venous diameter cut-off values. None of which is ideal. Reflux timing is largely dependent on performing Valsalva manoeuvre, which by itself is

highly variable, some patients may perform it well, others may perform it sub-optimally. Certain number of patients may not understand how to perform Valsalva at all. This fact renders the assessment of reflux or reflux time inaccurate. Measurement of maximum venous diameter during Valsalva is also affected, as inadequate Valsalva may demonstrate a shorter reflux time, no reflux, or smaller than actual venous diameter.

This may at the end result in false under grading of varicoceles. The minimum value for pampiniform plexus diameter to diagnose varicocele is two millimeters<sup>(3)</sup>; however, this study did identify patients with a diameter of less than that presenting with history of infertility. This study is aimed to see if there are any discernible changes in testicular stiffness in varicocele patients that may aid in redefining or adjusting a better grading system for varicoceles.

Patients were distributed into three groups; (A): those having a pampiniform plexus diameter of equal or less than 1.9mm; (B): between 2 and 3.4mm; and (C): those in whom the plexus diameter equals or exceeds 3.5mm representing moderate to advanced varicocele.

The mean testicular volume in the above groups was noticed to be reduced as the grade of varicocele advances, however; this was statistically insignificant in the studied patients. This result is compatible with a study presented by Erdogan et al. 2020 (3). Turna and Aybar (2020) also identified a smaller testicular volume at the side of varicocele, with negative correlation between the testicular volume and grade of varicocele ( $r = -0.321$ ,  $P = 0.014$ ). They reported that changes in testicular volume were more noticeable with the chronicity of varicocele (1).

The testicular stiffness values are noted to be insignificantly lower in varicocele testes as compared with normal ones. Dede et al. (2016) (13) also identified a lower testicular stiffness in varicocele testes, but showed statistically significant difference (13). They also demonstrated a significant negative correlation between the grade of varicocele and testicular elasticity ( $r = -0.7$ ,  $P < 0.01$ ); however, this study revealed that such correlation is very weak and statistically insignificant ( $r = -0.1$ ,  $P = 0.3$ ). Dede et al. (2016) used strain elastography compared to the more modern 2D-SWE used in this study.

Turna & Aybar (2020) and Erdogan et al. (2020) have found that testicular stiffness is higher in varicocele testes (1,3). Turna & Aybar (2020) have shown no correlation between the grade of varicocele and testicular elasticity (1). The statistically insignificant elasticity difference observed in this study is probably due to the fact that Iraqi patients seek prompt medical care far before profound testicular parenchymal changes or fibrosis occurs.

This study disclosed a highly significant change in testicular stiffness with patients' posture. All patients demonstrated statistically significant increase in testicular stiffness in erect position ( $P < 0.001$ ). This phenomenon is probably attributed to the effect of gravity causing parenchymal engorgement. Normal testes showed an average of 19% increase in stiffness, while varicocele testes displayed only 13%. This observation is possibly due to either the normal testes are more resilient than their varicose counterparts, or that the pampiniform plexus of veins and testicular parenchyma are already engorged in varicocele testes and accept no major changes in hydrostatic pressure exerted by the gravity. The difference in the effect of postural change between normal and varicocele testes recorded in this study is yet to be significant ( $P = 0.21$ ). Review of literature revealed no studies analyzed the effect of posture on testicular stiffness till now.

### Limitations of the study:

This study is limited by the lack of correlation with seminal fluid data. Actually, very limited seminal fluid analysis results were collected in the beginning of this study, but the COVID-19 crisis and subsequent lock-down lasting for several months caused a dramatic time loss and caused an urge to halt collecting such valuable information.

### CONCLUSION:

SWE is still a naïve technology, it is very sensitive to small changes in testicular elasticity; however, the differences of testicular stiffness in different grades of varicocele were trivial. Thus, limiting the role of SWE in discriminating between grades of varicoceles.

### Recommendations:

Elastography may not be suitable for grading of varicoceles; however, correlation with seminal fluid profile may reveal a stiffness cut off value that may anticipate testicular damage.

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## VARICOCELES BY SHEAR WAVE ELASTOGRAPHY

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