ORIGINAL RESEARCH PAPER

Volume-7 | Issue-5 | May-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

TESTICULAR STRAIN ELASTOGRAPHY IN FERTILE AND INFERTILE MEN- A COMPARATIVE PROSPECTIVE STUDY

Urology

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ABSTRACT

OBJECTIVE: The purpose of this study is to prospectively evaluate the diagnostic value of Strain elastography values in fertile and infertile men, and the correlation between SE results with semen parameters and hormone profiles of the patients.

MATERIALS AND METHODS: A total of 82 patients and 164 testes were evaluated. Patients evaluated in our andrology outpatient clinic with the diagnosis of infertility and referred to radiology department for investigation of reproductive organs between January 2017 and December 2017 were included. Patients were divided into two groups according to semen analyses results as normal (Group 1) and abnormal (Group 2). Hormone profiles, semen analyses, B-mode, coloured Doppler ultrasonography and sonoelastography examinations were performed for each patient. Measurements of testicular volumes, strain values and strain ratio (SR) were recorded.

RESULTS: Mean testicular volumes (Group 1, 20.38+5.6 mL, and Group 2, 16.34±2.86 mL) were significantly different between groups ($p < 0.001$).Mean Strain values in group 1 and 2 were 5.32±2.02 and 5.61±2.24 respectively and the mean strain ratio in Group 1 & 2 were0.13±0.16 and 0.24±0.08 respectively, both of which showed a statistically significant difference with $P < 0.001$. Strain values were shown to have an inverse relationship with total sperm count and total motile sperm counts. However, the inverse relationship between strain values and total motile sperm count was alone shown to be statistically significant. Our data also revealed that SR values were significantly higher in patients with abnormal semen parameters allowing it to be a valuable tool in evaluating infertile men.

CONCLUSION: Strain elastography results were found to be significantly different in patients with abnormal sperm counts. This technique may provide promising results, however, further large scale studies may help to clarify the value of this imaging modality in the assessment of male infertility.

KEYWORDS

Male infertility, semen analysis, sperm, strain elastography

INTRODUCTION:

The World Health Organization(WHO) defines infertility as "a disease of the reproductive system defined by failure to achieve a clinical pregnancy after 12 months or more of unprotected sexual intercourse". It is found that one in six couples seek treatement for infertility and a male factor is responsible in half of the cases. In addition to physical examination and semen analysis, a scrotal ultrasonography (USG) may aid in detecting either obstruction or testicular dysgenesis. Since it is non-invasive, USG became the first line imaging modality in evaluating male genital tract. In addition it is safe and there is absence of exposure to radiation.

However, conventional Ultrasound imaging is limited in its ability to assess the functional status of testicular tissue. This is overcome by elastography, which is a promising technique in this field. Elastography which was first described by Ophir et al. is a relatively new imaging technique that displays the images of tissue stiffness. Strain Elastography (SE) measures the strain response of tissues in real time from sonography signals during externally applied compression–decompression cycles. As a semiquantita tiveelasto graphic technique, SE compares the elasticity and stiffness of target tissues with nearby normal ones. In our study we tried to evaluate the diagnostic efficacy of SE in infertile men.

AIM OF THE STUDY

The aim of our study was to evaluate the diagnostic value of SE of testicular tissues in infertile men with normal and abnormal semen parameters. It is also aimed to correlate SE results of testicular tissues with semen analysis parameters such as concentration, motility and morphology and hormone profiles of infertile patients.

MATERIALS AND METHODS:

Ours is a prospective comparative study performed between January 2017 and December 2017 in GovenmentRoyapettah hospital and Kilpauk Medical College Hospital, Kilpauk, Chennai. A total of 82 men were included in this study and were divided into two groups according to the results of semen analyses. Group 1 included 41 men with normal semen parameters whereas 41 men in group 2 had abnormal sperm features.

Men who were between 20–45 years of age, clinically diagnosed with primary infertility and did not receive any previous fertility treatment constituted the study population.Participants who did not undergo semen analysis, varicocoele of any degree, history of undescended testis, orchidectomy or testicular biopsy, testicular atrophy, trauma, acute or chronic orchitis and prior surgical interventions to testis, testicular mass, testicular microlithiasis, hydrocele and infarct were excluded from the study. Local ethics committee approved the study design and an informed consent was obtained from each patient.

All patients were evaluated by a detailed history taking, physical examination, a semen analysis and endocrine profiles. Participants were also evaluated according to the presence of varicoceles. A colour Doppler scrotal US was performed on all patients and the largest diameter of veins of plexus pampiniformis was measured. A diameter of more than 2 mm was accepted as varicocele.

Participants underwent both B-mode sonography and free hand real-time SE examination in the supine position with a digital sonography scanner (using GE-Logic S7 machine) supplied with SE software and using a linear 12 MHz multifrequency transducer. All imaging modalities were performed by an experienced radiologist. First, locations, contours, echo patterns and volumes of both testes were evaluated with grayscale sonograms. Afterwards, real time elastograhy was performed for both testes of the patients. During probe movement, grayscale sonograms of the testicular tissues were visualized adjacent to elastographic images on the screen. Images were obtained from middle portion of testis and scrotal skin layers. Due to the ovoid shape of the testis, upper and lower poles could not be included into images. After 10–12 compression–decompression cycles, acquisition of elastographic images was finalized, and images were produced automatically on the ultrasound machine by comparing two adjacent frames during tissue compression and decompression.

Measurements were performed during the decompression phase since there was no pressure from the outside, therefore, only the internal dynamics were measured in this phase. SR values of tissues were measured by putting multiple equally sized regions of interest (ROIs) on the testicular tissue (A) and scrotal subcutaneous fatty tissue (B).

SR value (B/A) reflecting the feature of stiffness was automatically calculated on the sonography machine by comparing normal testicular tissue (A) to the adjacent scrotal subcutaneous fatty tissue (B) for each patient and mean values were obtained. SR value increases when the tissue is harder (stiffer) (B). To prevent the variability of the technique, three measurements were performed for each patient.

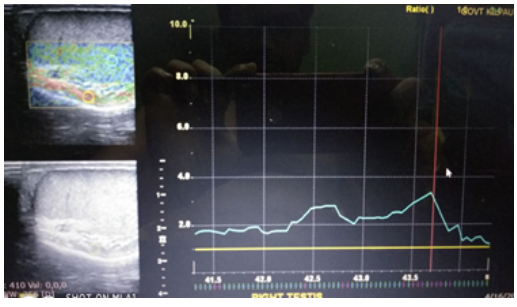
Data were presented as mean±SD. Continuous variables were evaluated by mean and SD, and compared by Studen's T test. Correlation of serum hormone measures (T, FSH and estradiol) and semen parameters with SE results were tested by Spearman's correlation and Mann-Whitney U test. A P value of less than 0.05 was accepted as statistically significant.

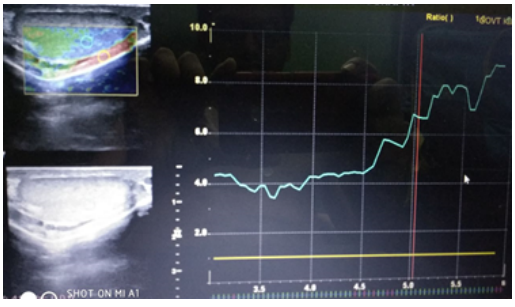
RESULTS AND ANALYSIS:

In this study, 164 testes of 82 patients (41 with normal and 41 with abnormal parameters) were investigated in terms of grayscale sonograms and strain elastography. Of the 41 patients in Group 2, 17 had oligozoospermia, 15 had asthenozoospermia and 9 had teratozoospermia.Mean age of participants in our study was 31.5+5.2 years. Mean testicular volumes (Group 1, 20.38+5.6 mL, and Group 2, 16.34±2.86 mL) were significantly different between groups (p <0.001)).

Mean Strain values in group 1 and 2 were 5.32±2.02 and 5.61±2.24 respectively and the difference was statistically insignificant. Mean strain ratio in Group 1 was 0.13±0.16 and in Group 2, it was 0.24±0.08 which showed a statistically significant difference with $P < 0.001$. The total number of spermatozoa were 73.4±24.6and10.8±18.4 x 10^6 ml in group 1 and 2 respectively and the percentage of total number of motile sperm were38.37+3.66and9.2+10.68respectively. The percentage of spermatozoa with normal morphology in Group 1 was 5.5+1.63 and in group 2 it was 0.32+0.58. The mean FSH (mU/mL) and mean total testosterone (ng/dL) in Group 1 and 2 were 4.81+1. 68&392. 18+148.76 and 13.5+17.98&398.65+177.98 respectively.

Clinical Characteristics	GROUP 1	GROUP 2	P value
Number of patients(n)	41	41	
Mean testicular volume (mL)	20.38±5.6	16.34±2.86	<0.001
Mean strain values	5.32±2.02	5.61±2.24	0.657
Mean strain ratios	0.13±0.16	0.24±0.08	<0.001
Number of spermatozoa (nx106/mL)	73.4±24.6	10.8±18.4	<0.001
Normal Morphology (%)	5.5±1.63	0.32+0.58	<0.001
Mean number of total motile sperm (%)	38.37±3.66	9.2±10.68	<0.001
Mean FSH (mU/mL)	4.81±1.68	13.5±17.98	<0.001
Mean total testosterone (ng/dL)	392.18±148.76	398.65±177.98	0.754





Strain values had inverse relationship with total sperm count and total motile sperm counts. However, the inverse relationship between strain values and total motile sperm count alone was shown to be statistically significant. The mean strain ratios between the groups showed significant difference, whereas the mean strain values were not significantly altered between two groups.Our data revealed that SR values were significantly higher in patients with abnormal semen parameters. This allows strain ratios obtained by elastography to be a promising tool in evaluating infertile men. Although FSH values showed significant difference among groups, any correlation between FSH and elastographic parameters could not be displayed. Similarly correlation between testosterone and SR did not show any significant difference among both the groups.

DISCUSSION:

Infertility is a common public health issue since more than 15% of couples may be affected and subsequent psychosocial problems may impair partner relationships. Imaging modalities are becoming more commonly used to define the reasons of infertility. Among them, with recent technological advancements, US is the first option for male genital tract evaluation. In addition to B-mode and color Doppler US, elastography with strain and shear wave developments were reported to be used in the investigation of testicular tissues and spermatogenesis.

Strain elastography is based on the principle that compression produces strain within the tissue and the amount of strain is lower in stiffer tissue than in softer. Recently, shear wave elastography (SWE) which combines B-mode image with color-coded US generating a quantitative image SWE (kPa) of the tissue stiffness started to be used to exhibit different hardness among different tissue regions in real-time conditions. With the use of SWE, different elasticity values dependent on testicular volume and functional properties have been demonstrated. SWE produces more reproducible results than other forms of sonoelastography. Transformation and change in tissue hardness should be therefore confidently documented by SWE. However, we do not have this modality in our radiology department and, for this reason, the study was performed with SE.

Elastography creates images of tissue stiffness which can be thought as an extension to the ancient palpation techniques; however, it gives better spatial localisation information and is less subjective. Two main types of elastography are currently in use. One is real-time elastography and the other is strain elastography (SE). In this modality, tissue displacement in response to gentle pressure is used to compute and image tissue strain. Basic assumption of SE is that soft tissues can be more deformable than hard ones which can be displayed on US as a colour map overlaid to the grey scale image. The resultant strain ratio (SR) represents the ratio of stiffness of the target and normal tissues. Studies reported that objectively measured tissue stiffness by SE may be used as a diagnostic marker in clinical practice for the differentiation between benign and malignant tissues in various organs.

The use of SE for the evaluation of testicular tissues is a new concept. Aigner et al. reported that elastography can be used with high sensitivity rate to differentiate benign and malignant testicular lesions. However, data about the results of SE on testicular tissues are still limited. In this study, it has been hypothesized that abnormal semen parameters might be related to testicular parenchymal abnormalities those not depicted by conventional US.

A few recent studies investigating the use of elastography in order to clarify the reason of infertility have been published in the literature. Tissue elasticity generally correlates with pathological conditions of the testicular parenchyma. In most of the cases, a normal testicular biopsy excludes the diagnosis of testicular pathologies. Some focal testicular lesions such as testicular microlithiasis, azoospermia and lesions with a diameter of <10 mm, particularly if they are not palpable, were investigated with the use of sonoelastography technique. The results of testicular biopsies of azoospermic male patients showed that along with the increasing grade of histological criteria, diameter of seminiferous tubules and height of spermatogenic epithelium are gradually reduced, while the thickness of the lamina propria is gradually increased. Tissue stiffness was increased in azoospermic patients and SR may be useful for diagnosing azoospermia. Similarly, the present study demonstrated that the elasticity of testicular tissue had a negative correlation with sperm

concentration and total motile sperm count.

Some studies reported that SR may provide more objective data with a higher diagnostic accuracy than elastography. Further studies evaluating the relationship between strain elastography results and testicular sperm retrieval rates are needed to increase the diagnostic accuracy of this imaging modality. Our data revealed that SR values were significantly higher in patients with abnormal semen parameters.

Many studies stated that testicular volume may be a predictor of spermatogenetic function. Tijani et al. reported that testis volume was significantly different in fertile and infertile groups. Besides, they showed that testis volume measured by US was correlated with the severity of oligozoospermia. Other studies also revealed that testicular volume had a significant association with semen volume, sperm count and motility. In their preliminary study Condorelli et al., reported that testis volume was associated with some biofunctional sperm parameteres and stated that the biofunctional sperm parameters worsen with decreasing testicular volume. Schurich et al. reported that elastography can be used for structural analysis of testicular tissues in order to find out any pathological tissue alterations. They also determined that the elasticity pattern of the testis seemed to be related to testicular function and volume.

Our study also determined a significant relationship between testis volume and sperm counts. Since seminiferous tubules which constitute 80% of testicular volume were responsible from spermatogenesis, it can be hypothesized that testicular volume can be related to sperm count. Also the sperm morphology and total motile sperm count were related to testicular volume in both groups.

Dede et al. investigated the relationship between elastography scores, serum FSH levels and varicocele. They concluded that testicular elasticity was inversely correlated with serum FSH and varicocele grade. However, in our study, we could not find out any correlation between FSH levels and elastography findings among groups.

One major limitation of our study was the low number of study population which prevented us from classifying patients into categories of oligozoospermia, azoospermia and teratozoospermia and to investigate their relationships with sonoelastographic findings. Besides, participants were not evaluated according to tobacco smoking, alcohol intake and any other endocrinological problems which may affect sperm characteristics.

CONCLUSION:

In conclusion, elastographic techniques are becoming more popular in the evaluation of male infertility. With the aid of SE, we have demonstrated that testicular elasticity was inversely related to sperm parameters. In addition, SR may correlate with sperm morphology and testicular volume. Further studies with large patient populations which investigate the relationship between SE values and sperm features may provide new insights into the noninvasive investigation of testicular tissues in infertile men.

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