



Diagnostic Modalities of Varicocele

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Abstract

Background: Varicocele is defined as dilated and tortuous veins of the pampiniform plexus of scrotal veins. Varicocele occurs in approximately 15% of the whole male population and 21-39% of infertile men. Varicocele typically develop during puberty large population-based study showed a prevalence of 0.92% in boys aged between 2 and 10 years and a dramatic rise to 11% in boys aged 11–19 years. Semen is a greyish white bodily fluid that is secreted by the gonads of male. It carries sperm or the spermatozoa and fructose and other enzymes that help the sperm to survive to facilitate successful fertilization. A routine semen analysis is the “gold standard” for the initial investigation of male fertility. The following factors are assessed in the seminal ejaculate: physical characteristics (e.g., color, volume, pH, odor, viscosity, and liquefaction time), sperm concentration, motility, progression, viability, and morphology and leukocyte count. Semen parameters such as sperm concentration, motility, and morphology can act as markers of male fertility and may reflect testicular causes of infertility. The diagnosis of varicocele is mainly clinical. However, a Doppler ultrasound is used to obtain clinical data and to measure testicular size more accurately. Diagnosis of varicocele by ultrasound is superior to clinical diagnosis; however, this method does not detect impairment of testes before testicular softening or atrophy. Shear-wave elastography (SWE) is an imaging modality that estimates tissue stiffness in real time. It was previously used for the assessment of many organs

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Introduction

Varicocele is defined as dilated and tortuous veins of the pampiniform plexus of scrotal veins. Varicocele occurs in approximately 15% of the whole male population and 21-39% of infertile men. **(1)**

Varicocele typically develop during puberty large population-based study showed a prevalence of 0.92% in boys aged between 2 and 10 years and a dramatic rise to 11% in boys aged 11–19 years. **(1)**

Varicocele occurs in approximately 15% of the whole male population and 21-39% of infertile men presenting with primary infertility and 45–81% for those presenting with secondary infertility. **(2)**

The initial description of the varicocele was published nearly 2000 years ago by Celsius who stated that ‘The veins are swollen and twisted over the testicle. The incidence of varicocele in subfertile men is: the left side is 17.6%, the right



side is 1.5% and bilaterally in 80.8%. and associated with progressive decline in fertility with varicocele.(3)

Lt sided varicocele is more common, Varicocele is the result of anatomical differences between the right and left spermatic vein .the right internal spermatic vein inserts directly into the inferior vena cava at an acute angle, while the left internal spermatic vein inserts into the left renal vein at a right angle. which leads to an increase in the hydrostatic pressure of the left spermatic vein causing its dilation. (4)

varicocele has notorious pathophysiologic effect on testicular parenchyma with its seminiferous tubules could be related to hemodynamic insults as gonadal valve incompetence, superior mesenteric obstruction or the nature of drainage angle with renal vein with their effect on increased intra-testicular pressure with its consequences of compensational reduction of the arterial flow and hypoxia. (5,6,7)

in addition to hemodynamic insults, elevated temperature, adrenal hormone reflux, gonad toxic metabolite reflux, anti-sperm antibody formation and oxidative stress also palmed in pathologic and hypotrophy of the bilateral testes. (8, 9)

The pathophysiology of varicocele primarily includes studies on elevated temperature, adrenal hormone reflux, gonad toxic metabolite reflux, altered testicular blood flow, antisperm antibody formation and oxidative stress. It is difficult to explain the mechanisms of action using only one theory because multiple mechanisms may act synergistically. (6)

The increased vein pressure can influence testicular blood flow via compensational reduction of the arterial flow required to

preserve the homeostasis of the intratesticular pressure. (7)

Varicocele could lead to smaller and softer testes, progressive impairment of the ipsilateral testis and hypotrophy of the bilateral testes. (8)

Presence of the testis in the scrotum keeps temperature of testes below 35c, another pathophysiology affect varicocele is hyperthermia. (9)

also we can mention other factor may play important role in pathophysiology of varicocele is hypoxia. hypoxia from a varicocele is a chronic process and results in compensatory changes within the testicle. (10)

Varicocele may lead to a decrease in specific activity enzymatic involved in testosterone synthesis. (11)

Several reports have demonstrated that varicocele are associated with low serum testosterone, which can significantly increase after successful varicocelectomies. (12)

The role of apoptosis in varicocele and the effects of varicocele on testicular tissue and spermatogenesis have not been clearly defined. The changes in testicular tissue seen in varicocele patients have been described as a 'stress pattern'. Stress pattern consists of immature and small cells. These cytomorphologic changes, look like the changes seen in cells that undergo apoptosis. (13)

Unilateral varicocele causes bilateral Leydig cell and Sertoli cell secretory dysfunction resulting in bilateral impairment in spermatogenesis and epididymal sperm maturation. The elevated intrascrotal temperature results in reductions in

testosterone synthesis by Leydig cells and Sertoli cell secretory function. **(8)**

Varicocele are commonly identified in one of three presentations First one young males present for routine examination are noted to have asymptomatic varicocele on physical examination Second, men of reproductive age note difficulty with conception and present to their fertility specialist with a history of primary infertility and a clinically relevant varicocele is noted. Finally, present with history of chronic scrotal pain (orchidalgia.) **(14)**

Evaluation of a patient with a varicocele should be performed with the patient in both the recumbent and upright positions. When a suspected varicocele is not clearly palpable, the scrotum should be examined while the patient performs a Valsalva maneuver in a standing position. Doppler ultrasonography is the gold standard examination for assessing venous reflux. **(14,15)**

Doppler ultrasound is used to obtain clinical data and to more accurately measure testicular size. Diagnosis of varicocele by ultrasound is superior to clinical diagnosis. **(16)**

The most common clinical grading scale was developed by Dubin and Amelar, Radiographic grades via US are most commonly assigned within the Sarteschi classification. **(1)**

A varicocele is the most common surgically correctable abnormality found in infertile men and may be responsible for sperm motility defects as well as defects in sperm count and shape. There is still an ongoing debate among researchers as to if and to what extent varicocele affects semen parameters, which usually vary from normal to mild or moderate asthenospermia, teratospermia or

asthenoteratospermia. Initially, sperm concentration is not seriously affected, though later all three sperm parameters can gradually deteriorate, resulting in azoospermia in very few. **(4)**

There are two approaches to varicocele repair: surgery and percutaneous embolization. Surgical repair of varicocele may be accomplished by various open surgical methods, including retroperitoneal, inguinal and sub inguinal approaches, or by laparoscopy. Percutaneous embolization treatment of a varicocele is accomplished by percutaneous embolization of the refluxing internal spermatic veins. None of these methods has been proven to be superior to the others in its ability to improve fertility. **(17)**

Regardless of the approach, the complication after surgical or percutaneous intervention are relatively similar. Postoperative pain and hematoma can occur to varying degrees but typical improve or resolve over time. Hydrocele formation, typically attributed to the ligation of lymphatic's, can be problematic and occurs with varying frequency depending on the specific surgical approach.**(17)**

For many years varicocele was considered an important cause of male infertility as numerous studies showed improvement (30% to 60%) in semen parameters after varicocelectomy. **(18)**

Semen is a greyish white bodily fluid that is secreted by the gonads of male. It carries sperm or the spermatozoa and fructose and other enzymes that help the sperm to survive to facilitate successful fertilization. **(17)**

Sperm production occurs in the testis, a specialized structure that functions optimally at 2° C to 4° C below body temperature and



generates a mature human sperm in 64 days . Well-integrated cycles and waves of spermatogenesis ensure that human sperm production is constant at about 1200 sperm per second. Spermatogenesis is an androgen-dependent process that occurs with very high intratesticular levels of testosterone. **(19)**

A routine semen analysis is the “gold standard” for the initial investigation of male fertility. The following factors are assessed in the seminal ejaculate: physical characteristics (e.g., color, volume, pH, odor, viscosity, and liquefaction time), sperm concentration, motility, progression, viability, and morphology and leukocyte count. Semen parameters such as sperm concentration, motility, and morphology can act as markers of male fertility and may reflect testicular causes of infertility. **(20)**

Semen volume is 1.5 ml and Concentration greater than 15 million sperm/mL and Total sperm count greater than 39 million sperm and Total motility greater than 40%and morphology greater than 4%. **(21)**

In routine semen analysis, we need to make sure of the correct procedure steps to avoid missing the right results. With an abstinence period of two days minimum and not more than seven days, and it is preferred to have the sample collected by masturbation. **(22)** The main advantages of this collection method is its simplicity, noninvasiveness, and inexpensiveness.**(23)**

The Motility is recognized as the most important predictor of the functional aspect of spermatozoa. Sperm motility is a reflection of the normal development of the axoneme and the maturation that it undergoes within the epididymis. The normal sperm are free from head, midpiece, or tail defects. semen

parameter assessment of morphology is critical in the evaluation of an infertile male because it can be a significant predictor of pregnancy. **(24)**

Several factors can potentially disturb gamete proliferation or differentiation and the intra- or extra testicular mechanisms that regulate spermatogenesis. These include exposure to physical agents such as heat or chemical substances, poor nutrition, obesity, nicotine use, alcohol consumption, ingestion of therapeutic and recreational drugs, bacterial infections, hormonal imbalances, varicocele, testicular cancer and radiation.**(25)**

Testicular hyperthermia can cause the genital heat stress leading to the production of low quality spermatozoa. Heat exposure can lead to many abnormalities in the testis including; dilatation of smooth endoplasmic reticulum, degeneration of mitochondria and wider spaces in spermatid cells. Heat stress leads to damage DNA, autophagy and apoptosis of germ cells due to generation of reactive oxygen species and breakage of strands. **(26)**

Some drugs are also involved in causing male infertility. Sulfasalazine is an anti-rheumatic drug, which is known to reduce male fertility. Methotrexate is an immunosuppressive drug that alters semen quality. **(26)** Combined defects in sperm density, motility, and morphology are known as oligoasthenoteratospermia (OAT) and are most frequently due to a varicocele effect.

Shear Wave Elastography

The diagnosis of varicocele is mainly clinical. However, a Doppler ultrasound is used to obtain clinical data and to measure testicular size more accurately. Diagnosis of varicocele by ultrasound is superior to clinical diagnosis; however, this



method does not detect impairment of testes before testicular softening or atrophy. **(16)**

Ultrasound applications have enabled the assessment of new aspects in the structural and functional analysis of testicular tissue; such advances quantify tissue elasticity. **(21)**

Shear-wave elastography (SWE) is an imaging modality that estimates tissue stiffness in real time It was previously used for the assessment of many organs. **(27)**

The importance of clinical assessment of tissue stiffness has been known since ancient times: In Pharaonic Egypt ,more than 5000 years ago, physicians practiced palpation of body parts to determine tissue nature. They knew that a hard mass within an organ was often a sign of an abnormality. Since then ,palpation has been used for screening and diagnosis, but is also used during interventional procedures to guide the surgeon to the area of pathology. So the One of the key medical methods for detection and characterization of pathologies is the assessment of tissue stiffness by palpation. There are two types of mechanically induced waves : Compression or bulk waves; These propagate very quickly in tissue (1500m/s) by successively compressing tissue layers. Echoes of compressional waves on tissue scatters are used to perform standard ultrasound imaging .And Shear waves; These are much slower than compressional waves (1 to 10 m/s) and propagate by creating a tangential “sliding ” force between tissue layers. **(28)**

Elastography is a relatively new imaging technology that creates images of tissue stiffness. It can be thought of as an extension to the ancient technique of palpation, but one that gives better spatial localization information and is less subjective. **(28)**

Today we have a new diagnostic imaging modality has emerged called elastography, which uses ultrasound to assess tissue differences in stiffness (or elasticity). Tissue stiffness is generally measured by a physical quantity called Young’s modulus and expressed in pressure units - Pascal's, or more commonly kilo Pascal's (kpa).**(1)**

Two main types of elastography are currently in use – strain elastography, where tissue displacement in response to gentle pressure is used to compute and image tissue strain, and Shear wave elastography. The machine applies shear waves that pass through tissue stiffness, thus measuring it acoustic radiation force impulse (ARFI) elastography, where the speed of shear waves traversing the tissue is measured and used to create an image of tissue stiffness. **(29)**

Shear wave Elastography used to estimate the testicular tissue stiffness that reflects underlying pathology secondary to varicocele. It entails the delivery of a high frequency ultrasound pulse into the tissue that creating energy inside followed by a usual ultrasound pulse and measurement of the velocity of the spread of the ultrasound waves across the stimulated tissue within the region of interest. A stiffer tissue will resist the high frequency ultrasound wave and consequently show less resistance to the spread of the ultrasound waves across and shows higher values of stiffness index. A softer tissue will be more stimulated and present more resistance to the spread of ultrasound waves and shows low values of stiffness index. **(27)**

Elastography is a widely used imaging modality gives information of tissue stiffness i.e. breast, thyroid lymph node or prostate, recently, that modality has been applied to scan testicular



torsion to avoid un-indicated orchiectomies, elucidating testicular lesions nature, detection of elasticity loss in testicular damage, varicocele elastisty loss and in the testis of infertile men. . **(30)**

Also the Sonoelastography is a recent radiologic method that can assess the mechanical properties of tissue and can be used in imaging the elasticity of biological tissue Real-time Elastography (RTE) was the first ultrasound technique available for clinical use. This radiologic technique can measure relative elasticity of different tissues in a selected region of interest by depending on fast cross correlation technique and a combined autocorrelation method. The end result is what's known as an elastogram that is superimposed to the B-mode ultrasound image of the tissue and updated in real-time. **(30)**

Although spermogram is the initial and the gold standard method in evaluation of spermatogenic function in varicocele-infertility complex but SWE can be used to assess testicular tissue stiffness both qualitatively and quantitatively, supporting the usefulness of the technique for evaluating that aspect various aspect. **(31)**

Despite the presence of contralateral normal apparent testis in unilateral varicocele patients, but their spermogram profile is not uniform and a considerable percent of these cases need intervention for subfertility. Understanding the exact pathophysiologic insult in varicocele infertility complex in unilateral cases is crucial step in developing a successful treatment strategy and help to determined whom patients need intervention or may highlight its pathology even with euspermogram and that is our research point of interest **(31)**

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