

## ADOLESCENT VARICOCELE AND ITS TREATMENT

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### ABSTRACT

Varicocele, which has an important role in the etiology of infertility, causes testicular atrophy, abnormalities in sperm morphology and function. There is no uniformly accepted etiologic theory. It is usually diagnosed by physical examination. However, there is no available practical diagnostic method with high sensitivity and specificity. In this study, the issue of varicocele in an adolescent age group, a speciality in itself, is reviewed in addition to contemporary approach to varicocele pathology, diagnosis and treatment methods.

**Key Words:** Varicocele, Infertility, Treatment.

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Varicocele is a pathologic condition characterized by elongated, dilated and tortous spermatic veins within the pampiniform plexus. The mean incidence of left-sided varicoceles is 13.4% (1). Varicocele is on the left side in 90% of the cases. Left varicoceles have been detected in 30% of primary infertile male patients and 75-81% of secondary infertile male patients. Isolated right varicoceles are seen in only 2% of normal or infertile men. Bilateral varicoceles are uncommon in normal men, but are found in up to 20% of infertile men (2).

### Etiology:

There is no universally accepted etiologic theory. However, several anatomically-based theories have been proposed to explain the genesis of varicoceles. The left internal spermatic vein is 10 cm longer than the right and tends to join the left renal vein at right-angle with frequent incompetent or absent vein valves. In contrast, the right internal spermatic vein is shorter and inserts obliquely into the inferior vena cava with rare absence of vein valves. As a result, higher venous pressure is transmitted to the left than the right scrotal venous plexuses (3).

Another mechanism is the "nutcracker" phenomenon: compression of the left renal vein as it passes between the aorta and superior mesenteric artery (classic form) or more distal compression of the left common iliac vein as it crosses the common iliac artery at the pelvic brim and increases venous pressure in the external spermatic veins (distal form) (4).

Furthermore, another theory is the reflux theory. It depends on the presence of either incompetent or absent gonadal vein valves, and anomalous collateral veins that allow blood to shunt around otherwise competent gonadal veins causing retrograde reflux into the pampiniform plexuses. This may explain how left-sided venous reflux can cause certain cases of right varicoceles or the bilateral testicular effect associated with a solitary left varicocele. In the presence of isolated right varicocele vena cava thrombosis or

occlusion, or situs inversus should be considered.

### **Pathologies Induced by Varicocele:**

#### **1) Effects on Testis:**

The presence of varicocele is associated with testicular atrophy, which is characterized by hypospermatogenesis, decreased tubular diameter, peritubular fibrosis, incomplete spermatogenic arrest at the spermatid and spermatocyte levels with disorganized spermatogenesis. It was shown that apoptosis may have a significant role in spermatogenic dysfunction associated with varicocele (5). It has been demonstrated that varicocele correction can reverse this atrophy by promoting Sertoli and Leydig cell function in adolescents (6-10).

#### **2) Effect on Semen Parameters:**

The pathologies caused by varicocele on sperm parameters are: decrease in sperm motility (asthenospermia; 90% of cases) and in sperm count (oligospermia; <20 million/ml; 65% of cases), MacLeod "stress pattern" of sperm morphology, namely increase in the number of amorphous cells (teratospermia), increase in the number of immature cells (spermatid), and decrease in the fertility function of sperm (75% of cases). These pathologies are independent of the size or grade of varicocele. However, the "stress pattern" of sperm morphology is not specific for varicocele. It is identified in viral illnesses, acute allergic reactions and other environmental insults. It is debatable, whether varicoceles with high grade are more harmful than those with lower grade, but they show more improvement following varicocele treatment. The earlier varicocele is diagnosed and treated, the better results are obtained and progressive deterioration in sperm parameters relieve (11).

Several generalizations have been reported from controlled studies: improvements in sperm morphology (44%) tend to be accompanied by improvements in both sperm concentration (51%) and motility (70%) after varix repair (8-10, 12). No particular pattern of pre-ligation semen parameters reliably predicts postoperative improvement. There is no particular semen pattern change absolutely characteristic of post-varix ligation patients. Conception can be achieved after varix ligation without measurable improvements in conventional sperm parameters (13).

#### **3) Effects on Fertility:**

The effect of varicoceles on fertility is more debatable than their effect on semen parameters. There are two means to investigate fertility: pregnancy rate (mean 43%) (12) and the fertilizing ability of sperm in vitro. It was reported that egg fertilization rates improved from 9% before varicocele ligation to 36% after repair (14).

#### **4) Effects on Endocrine Profile:**

It was revealed that in patients with varicocele serum concentrations of testosterone, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), spermatic vein levels of testosterone and estradiol, and LH, FSH and testosterone responses to gonadotropin-releasing hormone (GnRH) assays were normal. However, in cases with settled testicular atrophy due to an uncorrected varix, severe spermatogenic failure with pituitary-gonadal hormonal dysfunction in response to GnRH assays is observed. Thus, the endocrinopathy is not a cause, but a result secondary to varicocele (15).

#### **5) Metabolite Reflux:**

Toxic renal or adrenal metabolites can damage the testicle, if blood from the renal vein can flow in a retrograde fashion through the internal spermatic vein either because of incompetent valves or collateral veins which bypass competent valves (16). It has been realized that in patients with varicocele, internal spermatic vein levels of catecholamines, prostaglandin E and F (having antispermatogenic effect), renal-derived serotonin, renin-angiotensin-1 and phospholipase A2 are higher than those in peripheral veins (15, 17).

After demonstration of normal levels of testicular venous oxygen tension, pH and CO<sub>2</sub> pressure, the theory suggesting retrograde reflux in the spermatic veins of varix-associated testes, which causes deterioration in spermatogenesis by increase in hydrostatic pressure, in turn congestion and hypoxia, has been abandoned as explanation for the varicocele effect (15).

#### **6) Scrotal Hyperthermia:**

Retrograde reflux or stasis of warm venous blood in the pampiniform plexus, with disruption of the usual countercurrent heat exchange balance that normally exists, has been proposed as a possible cause of spermatogenic failure. However, it was

shown that all infertile men, regardless of varicocele status, exhibit increased scrotal temperature (18). Ambulatory monitoring of scrotal temperatures in normal and varicocele patients has exposed both marked diurnal variation and no temperature decrease after varicocele ligation (19). Furthermore, the hyperthermia theory has failed to explain the fact that unilateral varicoceles put forth bilateral effects or that scrotal temperatures do not accurately reflect testicular temperatures. In conclusion, scrotal hyperthermia theory has not been reliably confirmed.

#### **Varicocele Diagnosis:**

- Physical examination: The diagnosis of a varicocele is commonly made on examination in otherwise healthy patients, mostly adolescents, with scrotal discomfort or testicular atrophy. Although accurate for larger varicocele, it is inadequate to diagnose smaller lesions. Frequently, varicocele has no symptoms.

Classification of varicoceles according to size is performed by physical examination while the patient is standing:

— Grade 1 varicocele: Small varicocele, can be palpated only with difficulty under Valsalva maneuver,

— Grade 2 varicocele: Intermediate grade varicocele, can be palpated, becomes more evident with the help of Valsalva maneuver,

— Grade 3 varicocele: Large in size and easily visible at a distance.

Today, no available single diagnostic tool that provides both exceptional sensitivity and specificity in varicocele detection:

- Venography: It is accepted as the “gold standard” of varicocele diagnosis. It is not routinely used because of its invasiveness. However, it can be used for testing alternative diagnostic techniques. On the other hand, selective internal spermatic venography (SISV) was found to be insufficient in detecting recurrent venous reflux after conventional varicocelectomy (20).

- Doppler ultrasonography: It is used for diagnostic confirmation of clinically suspicious

but not overtly palpable varicoceles. It yields significantly false positive results.

- Radionuclide angiography: It depends on blood pooling within the scrotum, smaller varicoceles can be missed and cause a high false negative result. Therefore, it has no role in early diagnosis of varicocele.

- Scrotal thermography: It gives in a false positive rate of 16-20% and a false negative rate of 20-32%. Thus, it has no advantage over other methods for varicocele screening.

- Scrotal ultrasonography: It has no standard diagnostic criteria. However, non-invasive and subclinical non-palpable or suspicious lesions on physical examination can be diagnosed by scrotal ultrasonography. Its sensitivity and specificity are 92% and 100% (21).

#### **Subclinical Varicocele:**

Subclinical varicocele is the presence of reflux in the internal spermatic vein without palpable distension of the pampiniform plexus. There is still no consensus on the need to diagnose or treat subclinical varicoceles. Venographic studies showed that the incidence of coexisting subclinical right varicocele in the presence of palpable left varicocele was 21-60%. Pregnancy rate has not correlated with varicocele grade. It was reported that the majority of patients with subclinical varicocele experience improvements in sperm parameters and pregnancy rates in the 30-40% following varicocele ligation (22). Today, the most approved approach is the treatment of subclinical varicoceles in infertile patients.

#### **Adolescent Varicocele:**

Adolescent varicocele is defined as the onset of a varicocele during or after puberty. Its incidence is 16%. It is diagnosed almost exclusively by physical examination in patients with complaint of scrotal pain. Infertility is not a presenting symptom. However, adolescent varicocele causes arrest of testicular development and inhibition of spermatogenesis.

#### **Measures of Testicular Damage:**

To define the pathophysiologic potential of the adolescent varicocele, the following factors are used:



- **Testis biopsy:** It is useful in patients with azospermia or oligospermia to evaluate spermatogenesis, testicular structure and to exclude ductal obstruction. However, not all patients exhibit altered histology. Therefore, other factors should also be considered.

- **Testis volume:** Atrophy of the testis ipsilateral to the varicocele is commonly found in adults, but if it occurs in children or early adolescents, it is known as growth retardation. While adolescent testis volume is mostly unaffected by grade 1 varicocele, a loss of testis volume is seen in almost one third of patients with grade 2 varicocele and two third of patients with grade 3 varicocele. The catch up growth in testis volume after varicocele ligation in adolescents was well shown. On the other hand, as the relationship between testis volume and semen quality has not been precisely defined, it is not certain that varicocele ligation has a preventive effect on later fertility problems. Based on the reversibility of testis atrophy, it is suggested that a discrepancy of more than 2 cc volume between testes in a patient with varicocele should be regarded as an indication for immediate correction (23).

- **Sperm analysis:** This test may also show the pathologic potential of varicocele.

- **Endocrine status:** In 31% of adolescents with a varicocele, an excessive release of FSH and LH levels in response to GnRH stimulation test is seen due to measurable abnormalities of the hypothalamic-pituitary-gonadal axis. In one study it was shown that 75% of patients who exhibited an excessive, abnormal GnRH stimulation test had significant volume loss in the testis ipsilateral to the varicocele, whereas only 50% of patients with a normal GnRH response exhibited atrophy (24). GnRH test response is more testis volume-specific than varicocele-specific. Therefore, this test can define an abnormality of the pituitary-gonadal axis in a subset of patients with varicocele and may be used as a predictor of subsequent testis damage. However, the relationship between an abnormal GnRH test and future problems with fertility has not yet been clarified.

**Treatment:**

The main indications of varicocele ligation are presence of grade 2 or grade 3 varicocele,

concomitant ipsilateral testicular maldevelopment or scrotal pain. The varicocele treatment is based on ligation or occlusion of varicous veins. The best method for treatment of adolescent varicocele remains unclarified. In general, all methods available for adults are available for adolescents. The available treatment methods are percutaneous ablation, laparoscopic ligation or open surgical ligation. There have been no randomized, controlled, prospective clinical studies comparing all of these methods. However, through published series, one can conclude that the best results have been obtained by inguinal or subinguinal open microsurgery .

1) **Percutaneous or transvenous ablation:** Sclerosing agents or coils are used to ablate varicous veins. Recurrence rate has been reported as 6-15%. It takes 1-3 hours even by experienced radiologists and usually needs sedation in addition to local anesthesia. The mean dose of radiation exposure to testicles is 26 mRads. Today, it is accepted that this treatment method should be reserved for cases of failed surgical ligation.

2) **Laparoscopic ligation:** It has been performed mainly in adults. Therefore, experience in adolescents is limited. Elimination of an abdominal incision, better identification of testicular artery and veins, shorter postoperative convalescence, decreased requirements for pain medication are advantages of this method. However, because of requirement for general anesthesia, possible major complications and high recurrence rate due to collateral veins, laparoscopy is not presently considered equivalent to open surgery as a first-line therapy, except in the presence of bilateral varicocele in experienced laparoscopists. It was recently reported that laparoscopic Palomo varicolectomy for varicocele is safe in boys who have undergone previous inguinal surgery (25).

3) **Open or incisional surgical ligation:** Although this may require general anesthesia in boys, as it takes a short time and is a minimally morbid procedure, it remains the mainstay of varicocele treatment in adolescents. This technique can be performed at one of three levels: in the retroperitoneum, above the level of the vas

deferens (Palomo); in the region of inguinal canal (Ivanissevich); in the subinguinal region. In adult varicocele patients, it was shown that 78% of patients have either internal spermatic vein reflux or a bypass of a competent internal spermatic vein at the renal vein level, both of which are amenable to ligation either at the suprainguinal or inguinal level (4). However, in 22% of patients, pelvic collaterals are the main cause of varicocele pathology: mainly external spermatic, ductus deferens and scrotal venous collaterals. Then, theoretically Ivanissevich or subinguinal varicocelectomy seems to be feasible. Therefore, in adolescents, usually Ivanissevich technique or subinguinal repair is preferred.

- Palomo varicocelectomy: Ligation is performed over vas deferens in retroperitoneal region. Two types of Palomo techniques may be used: A high ligation of the internal spermatic vein and the internal spermatic artery are undertaken in classic Palomo repair. In artery-sparing Palomo technique, only the vein is ligated.

The advantage of Palomo technique is providing good exposure for easy differentiation of spermatic vein and artery. Its disadvantage is a high recurrence rate seen in artery-sparing technique. Comparative studies revealed that lesser recurrence rate was seen in classic technique (26). However, arterial ligation may not be a completely benign procedure, poorer sperm quality postoperatively may be observed when compared to artery-spared cohort (27). But, there is no available study demonstrating testis atrophy following classic technique.

- Inguinal varicocelectomy: This technique is performed at the level of the inguinal canal with incision of the external inguinal fascia. Its advantage is providing good exposure of the testicular artery, vein, lymphatic and periarterial veins and also external spermatic veins by getting the spermatic cord outside the incision. However, it is difficult to perform in patients who are obese or those who have experienced inguinal surgery previously.

- Subinguinal varicocelectomy: The varicose veins are ligated just below the external inguinal ring. It provides good exposure for testicular artery, vein, lymphatic, periarterial veins and external spermatic veins by getting spermatic

cord outside the incision. It causes less pain and rapid recovery because of not requiring incision of the external oblique fascia. However, at this level, significantly more veins are encountered, the artery is more often surrounded by a network of tiny veins and is often divided into branches, making arterial identification and preservation more difficult. Also, compression of the artery on the edge of the external ring makes its identification somewhat more difficult.

Since all adults with varicocele may not have a fertility problem, the main goals in the treatment of adult varicocele should be to treat patients with affected sperm analysis, infertile men or those with grade 2 or 3 varicocele due to the risk of testicular failure. Improvement in sperm parameters is relatively higher in patients with high-grade varicocele than in those with lower grade varicocele.

The problem of how best to compare the various treatment options for efficacy will be handled by four commonly applied outcome measures: success rates, semen improvement and pregnancy rates, complication rate and relative cost.

Success is measured by the rate of varicocele recurrence or persistence after treatment. Subinguinal ligation results in similar recurrence rates with inguinal method (0-0.6%). Artery sparing Palomo technique is associated with 11-15% recurrence rates. This higher recurrence rate is thought to be secondary to the presence of more distal inguinal and collateral veins or venous collaterals closely associated with the gonadal artery, which are not ligated with this approach (28). However, in classic Palomo technique, the rates are equal to those with inguinal method. The recurrence rate ranges between 4-24% in percutaneous ablation of the internal spermatic veins. Varix recurrence or persistence rates in laparoscopic approach have been reported as 0-11% (29). Microsurgical technique provides a very low risk of recurrence. No appreciable differences can be seen in semen improvement and pregnancy rates after surgery in comparison of inguinal, retroperitoneal and subinguinal approaches (66% improvement in semen parameters, achievement of pregnancy in 43% of couples). These values are 60% and 10-50% in percutaneous varix ablation and 50-



70% and 12-32% in laparoscopic varix repair (12).

Operative complications of open surgery include incidental testicular artery ligation with subinguinal approaches which may cause testicular atrophy and azospermia in some degree in adults, occasional damage to the ilioinguinal nerve within the inguinal canal, occurrence of hematoma, scrotal edema (frequent in inguinal technique) and hydrocele (due to ligation of lymphatics; frequent in retroperitoneal approaches, 7%). The risk of hydrocele development has been lowered by sparing lymphatics with the help of microsurgical ligation techniques. Percutaneous ablation of varicoceles is dependent on the skill of the radiologist. Complications seen in this technique are a 2% risk of contrast allergy, thrombotic or bleeding injuries to the vascular tree, postoperative coil migration, embolization or venous thrombosis, exposure of testicles to radiation.

Laparoscopic ligation is associated with the complications of unexplained bleeding, usually from injured epigastric vessels, and ileus, nausea, and vomiting from unrecognized bowel injury, other organ injuries, air embolization and peritonitis.

Varicocele treatments are performed in an outpatient setting. Percutaneous ablation of varix costs are generally equal to open surgery. However, laparoscopy costs are double inguinal varicocelectomy costs.

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