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Varicocele – literature review

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Abstract

Introduction and objective

Varicocele is the most common reversible cause of male infertility. This article describes the entire disease entity, in particular the pathophysiology and potential methods of treating this condition.

Review methods

A literature review was conducted using the PubMed database to gather knowledge about varicocele. The main search terms were „varicocele”, „varicocele pathophysiology” and „varicocele treatment”.

Description of the state of knowledge

Varicocele is usually asymptomatic, and in other cases may cause nonspecific symptoms, such as discomfort or pain in the scrotum. Diagnosis is based on physical examination, and in doubtful cases, ultrasound can be used. There are several theories about the development of varicocele. These include the anatomical, nutcracker, embryological, or valve-related theories. Impaired blood flow from the testicles leads to oxidative stress and hyperthermia, which affects the deterioration of sperm quality. The most common indication for treating varicocele is difficulty getting pregnant. In such cases, non-pharmacological treatment is used.

Conclusions

The surgical techniques used differ in the frequency of complications, their type, and the percentage of improvement in semen parameters. Despite numerous successes in the treatment of varicocele, there remains a large group of patients who still have problems having children.

Keywords: Varicocele, varicocele pathophysiology, varicocele treatment

Introduction:

Varicocele affects up to 15% of the male population, and its incidence reaches up to 35% in men with abnormal semen parameters. [1] In as many as 85% of cases, they affect only the left side, and in the remaining cases, they are bilateral. They are usually asymptomatic, but in other cases they may cause a feeling of heaviness or pain in the scrotum. This is the most common reversible cause of male infertility. [2], [3]

Definition:

Varicocele is an abnormal dilatation of the lumen of the venous vessels of the spermatic cord. Increased blood flow causes temperature to rise what can lead to some problems with fertility. We can distinguish three grades of varicocele. 1) perceptible varicocele during Valsalva maneuver in a standing position 2) perceptible varicocele without Valsalva maneuver in a standing position 3) Varicocele visible through the skin of the scrotum [4]

Grade	Description
1	Palpable only with the patient standing and performing a concurrent Valsalva maneuver
2	Palpable with the patient standing, without a Valsalva maneuver
3	Visible through the scrotal skin and palpable with the patient standing

Table 1: Clinical grading system defined by Dubin and Amelar

Epidemiology

Varicocele are present among 15% of general adult and adolescent male population. Frequency of occurrence increases among males with primary infertility to 25-35% and secondary infertility to 80%. There are rarely detected varicocele among children under age of 10 and they begin to occur during puberty. The correlation between age and prevalence remains strong and increases by 10% every decade. [5]

Diagnosis:

The main method for diagnosing varicocele remains a physical examination of the scrotum. The examination should be performed in a warm place and a friendly environment, as cold and stress may cause scrotal contraction and may falsify the examination. The examination is performed in a standing position and physician tries to feel dilation of the veins. Patient may be asked to exhale air forcefully what is called Valsalva maneuver. Based on the examination, the presence of varicocele and its grade can be determined. Ultrasound is also a useful diagnostic tool, which allows for better visualization of varicocele and differentiation with other pathologies. Due to its ease of use and high sensitivity, it is widely used among urologists. Ultrasonography seems to be superior to Prader orchidometers and venography but physical examination remains gold standard for diagnosing varicocele and USG should be used only in uncertain cases. [6] [7]

Pathogenesis:

The pathogenesis of varicocele remains not fully understood, but there are several theories that may explain the way they develop. [8]

Anatomical theory

In most cases, varicocele occurs only on the left side. The main cause may be the anatomy of the spermatic veins. The left spermatic vein is longer than the right one by about 8-10 cm, which makes it easier to dilate. Additionally, it enters the renal vein at a right angle, which also impedes blood flow from this vessel. [8] [9]

Nutcracker syndrome theory

There is a theory that connects the development of varicocele with the so-called nutcracker syndrome. Compression of the left renal vein by the aorta and superior mesenteric artery leads to an increase in hydrostatic pressure in the internal spermatic vein. This results in reflux and dilatation of the pampiniform plexus. [8] [10]

Valve theory

In the course of the spermatic vein, there is often a reduced number or even absence of valves preventing reverse blood flow. However, the existing ones often have disturbed structure and functionality. This may be the main cause of reflux in these vessels. [8] [11]

Embryological theory

During embryonic development, the spermatic vein, adrenal veins and renal vein join into one renal vein. This may cause overload of the venous system, resulting in the formation of varicocele during puberty. [8]

Pathophysiology:

Despite some evidence of a negative impact of varicocele on spermatogenesis and semen parameters, the pathophysiology is not fully understood. Possible mechanisms involved in the development of varicocele are presented below. [12]

Testicular hyperthermia

Spermatogenesis is a process very sensitive to temperature fluctuations and is most effective at 35-36 degrees. [12] The pampiniform plexus is responsible for maintaining the appropriate temperature in the scrotum, which is able to lower the temperature by about 1-2 degrees. [8] It is not fully known how hyperthermia affects the process of spermatogenesis, but it is suspected to damage DNA and the structure of seminiferous tubule cells and Leydig cells. Men with varicocele have a higher temperature inside the scrotum compared to healthy men, which results from impaired blood outflow through the spermatic vein. Despite this, the temperature in the scrotum is on average 0.3 degrees higher on the varicocele side. Interestingly, there was no significant difference in scrotal temperature between men with varicocele and those with post varicocelectomy in the supine position. A higher temperature appeared only in the group with varicocele after assuming a standing position. Although varicocele occurs in the vast majority of cases on the left side, histopathological examinations often did not show significant differences between the left and right testicle. [13]

Oxidative stress:

Patients with varicocele usually have higher levels of ROS than healthy people. It has been proven that ROS adversely affects the structure and function of sperm by denaturing proteins, fatty acids and DNA. Oxidation of the fatty acid-rich cell membrane causes a decrease in membrane fluidity and depletion of axonal proteins, which results in a decrease in sperm motility. Apoptosis is also more intense, which translates into a decrease in the number of sperm and an increase in abnormal forms. Apoptosis can be intensified not only by ROS, but also by genetic factors and excess cadmium. This element induces apoptosis and its increased level is found in both testicles in patients with varicocele. [12] [14]

ROS also have deleterious effects on nuclear and mitochondrial DNA. It has been proven that removal of varicocele improves DNA integrity and the process of spermatogenesis itself. [12]

Symptoms:

Varicocele is usually asymptomatic, but some patients report certain symptoms. Most often it is pain, swelling or discomfort in the scrotum or groin. The symptoms worsen with age, physical activity or at the end of the day. [8] Some patients report the bag of worms symptom, which results from the dilatation of the veins. [6]

Treatment:

The most effective way of treating varicocele remains non-pharmacological methods using surgery and interventional radiology. Subinguinal varicocelectomy, retroperitoneal varicocelectomy or inguinal varicocelectomy remain surgical procedures while radiological interventions include embolization, sclerotherapy, the selective closure of dilated vessels using a balloon or coil. [15] The most common indication for surgery is reduced semen parameters causing problems with getting pregnant. The varicocele removal procedure aims to improve male fertility. The second most common indication is testicular atrophy. [16] Each surgical method statistically leads to an increase in pregnancy rates in patients with abnormal sperm parameters and clinical varicocele. However, depending on the method, this ratio may vary as well as the frequency of complications, including recurrence of varicocele or testicular hydrocele.

Sclerotherapy:

This method is relatively new and involves closing the lumen of the pathological vessel. This is achieved by injecting a sclerotizing agent, which leads to the destruction of the intima of the vessel and, consequently, its narrowing. [15]

Embolization

It is a minimally invasive method that involves injecting a sclerosant or using tissue adhesives or detachable metal coils. For left-sided varicocele, this method achieves similar results to surgical methods and even provides additional benefits of shorter recovery time and avoidance of complications caused by general anesthesia. However, this technique should not be suggested in patients with bilateral varicocele, as the failure rate reaches 13-19% compared to 5% using techniques microsurgical. This is most often due to failure to close the right gonadal vein. [17]

Laparoscopy

Laparoscopy is the most invasive method of treating varicocele and requires a great deal of experience and skill on the part of the operator. Although it is less likely to lead to complications such as hydrocele, the need for general anesthesia and the seriousness of other possible complications mean that it is not always a preferred method of treatment. The most serious complications include damage to the intestines, large abdominal vessels, and peritonitis. Another disadvantage of this technique is the inability to operate on the external spermatic veins, which often leads to recurrence of varicocele. [18]

Retroperitoneal varicocelectomy

Retroperitoneal varicocelectomy, also known as the suprainguinal method, is an open procedure that involves the dissection of the testicular artery and vein and their ligation. In no other technique are the vessels ligated so high. As most authors claim, this method is less likely to lead to varicocele recurrence and is preferred in patients who have previously undergone surgery for varicocele. The disadvantage of this procedure is the inability to spare the lymphatic vessels. [19]

Inguinal and subinguinal microsurgical varicocelectomy (SMV)

SMV is a recognized gold standard in surgical treatment of varicocele. For this reason, it is the most commonly used technique. It is less frequently associated with varicocele recurrence or other complications. In addition, the improvement in semen parameters and pregnancy rates after SMV is higher than with other techniques. [20] [21]

In some cases, the inguinal approach may be a better choice than the subinguinal approach. In thin, young patients, or those who have previously undergone SMV, the inguinal approach may be more beneficial. In addition, the inguinal approach is associated with fewer small-diameter vessels, which is somewhat easier for the operator. [20]

There is some uncertainty whether there is a difference in the quality of SMV with or without TD. Liao et al. conducted a meta-analysis in which they showed that both surgical techniques have similar effectiveness in terms of pregnancy rate, operation time, sperm concentration and sperm motility. However, MSV with TD had a lower rate of varicocele recurrence and lower postoperative testosterone levels at the cost of a higher rate of complications compared with MSV without TD. [22]

Conclusions:

Varicocele remains the most common reversible cause of male infertility. Despite the existence of many treatment techniques, mainly surgical, many patients still fail to conceive. For this reason, further research will be needed to improve the quality of treatment. A better understanding of the pathogens of varicocele will be helpful in this, as there are many theories about their formation.

Disclosure:

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