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Testicular volume and fertility potential in men operated due to varicocele and testicular hypotrophy in adolescence

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Introduction. Failure to perform surgical repair of varicocele before puberty is among the common causes of male infertility. The purpose of this study was to evaluate the testicular volume and fertility potential in men after laparoscopic varicocelectomy conducted in adolescence due to varicocele and concomitant testicular hypotrophy.

Material and methods. From 1996 through 2011, eighty–two adolescents were operated on for unilateral primary varicocele with testicular hypotrophy. Sixty–eight patients were subject to the current analysis. The age of the patients was 13 to 17 years (mean 15.3 years). Clinical diagnosis was established on the basis of andrologic examination and ultrasonography with an assessment of testicular size and varicocele severity. Laparoscopic surgical repair was performed by a transperitoneal approach with division of testicular vein only.

Results. An increase in left testicular volume when compared with the contralateral testis was found in 25 (78.1%) young men with clinical grade 2 varicocele (p = 0.02) and in 32 (88.8%) subjects with grade 3 abnormality (p = 0.04). An increase in left testicular volume was found in 46 (85.1%) of 54 patients with unilateral varicocele and in 12 (85.7%) of 14 subjects operated on for bilateral disease. A left testicular volume increase was comparable independent of the use of uni– or bilateral repair. Fifty–eight (85.2%) of our 68 patients had normozoospermia.

Conclusions. Laparoscopic varicocele repair resulted in a significant increase of hypotrophic testicular volume in 83.8% of our subjects.

Key Words: varicocele ‹› testicular hypotrophy ‹› laparoscopy

INTRODUCTION

For several years, a male factor has been recognized in the diagnosis and treatment of all infertility; approximately 40% of marital infertility is due to a male factor. A varicocele is among the common causes of male infertility. It is a condition characterized by persistent enlargement and elongation of the pampiniform plexus, venous convolution, and sinus formation with transient or permanent backflow. The etiopathogenesis of varicocele remains unclear and, at present, there is still no unequivocal explanation of their formation and effect on the excretory and secretory functions of the testis. Anatomical conditions promote the development of varicocele on the left side. The left testicular vein runs vertically and joins the left renal vein opposite the origin of the lower adrenal vein. Thus, blood turbulence occurs in the vicinity of the opening of the testicular vein and, in consequence, retrograde flow of renal metabolites and adrenal hormones to the testis is observed. The elevated hydrostatic pressure within the testicular vein leads to venous stasis within the testis resulting in testicular hyperemia and compromised testicular oxygen concentration [1, 2].

One of the hypotheses of spermatogenesis impairment is the concept of atrophic changes within convoluted tubules due to increased scrotal temperature or tissue hypoxia; in consequence, testicular growth is arrested in children and adolescents on the affected side [3, 4].

All examiners emphasize diagnostic pitfalls. A high–grade varicocele may be detected during a meticulous andrologic examination involving inspection and palpation of the genital organs while standing

up. Grading the varicocele is usually based on the Dubin–Amelar 1 to 3 scale. We believe that a diagnosis based on inspection and palpation should subsequently be confirmed by accessory ultrasound. Doppler examination allows the assessment of pampiniform plexus diameters, presence and character of backflow, as well as objective and comparative analysis of the size of both testes [1, 5, 6].
A palpable varicocele with testicular hypotrophy on the affected side, confirmed by color Doppler, is an indication for surgical repair. Early intervention improves male fertility potential [7–10].

MATERIAL AND METHODS

From 1996 to 2011, eighty–two adolescents were operated on for idiopathic varicocele with testicular hypotrophy. Sixty–eight patients were subjected to the current analysis (14 men were lost in follow–up). The age of the patients was 13 to 17 years (mean 15.3 years). This is a retrospective study, where data from patients' charts were analyzed. As the study is not an experimental one it did not need approval from the ethics committee. The clinical diagnosis was established on the basis of physical and andrologic examinations with an assessment of testicular size and varicocele severity on the Dubin–Amelar 1 to 3 scale [1]. Color Doppler ultrasound was performed in all patients; testicular size was measured according to Costabile with an orchidometer [11]. In subjects with varicocele disease, a difference in testicular volume of $\geq$2 mL was used as the criterion of testis hypotrophy.
Laparoscopic repair was performed via a transperitoneal approach with division of the testicular vein only. The age of the subjects at follow–up was 18 to 25 years (mean 22.5 years). The evaluation of surgical outcome was carried out at 1 to 9 years following laparoscopic varicocele repair, and was based on ultrasound evidence of varicocele subsidence and increase of testicular volume on the affected side. According to WHO directions, all subjects had their semen parameters checked twice after they had turned eighteen. The abnormal values of semen parameters were consistent with WHO 2010 guidelines also adopted in Poland [12, 13]. Blood tests to determine levels of testosterone (T), follicle stimulating hormone (FSH), and lutenizing hormone (LH) were also performed and presented as qualitative variables (normal/abnormal). Abnormal adopted levels of the abovementioned hormones were: less than 300 ng/dl for testosterone and less than 1.5 IU/l for both LH and FSH. Statistical analysis was carried out using the t–Student test (Statistica version 7.0). For dependent variables, the paired test was applied and for independent variables, the unpaired t–test was used. All tests were two–tailed. The threshold of significance was set at $p < 0.05$.

Table 1. *Patients divided according to preoperative varicocele severity and postoperative improvement in testicular diameter and semen parameters*

	Severity	Number of pts. (%*)	Testicular improvement (left/right in both sides)		
			Size, n (%*)		Semen, n (%*)
Operated on left side	2	26 (38.2)	21 (30.8)		24 (35.2)
	3	28 (41.1)	25 (36.7)		26 (28.2)
Operated on both sides	2	6 (8.8)	4 (5.8)	5 (7.3)	4 (5.8)
	3	8 (11.7)	7 (10.2)	7 (10.2)	4 (5.8)

*Number in brackets reflects % of the whole group

RESULTS

A grade 2 varicocele was found in 32 (47.1%) subjects and a grade 3 was found in 36 (52.9%) (Table 1). Before laparoscopic repair, mean left and right testicular volumes were 16.2 (SD = 4.3) cm^3 and 19.7 (SD = 6.4) cm^3, respectively. Thus, left testicular volume was significantly lower compared to that of the right testis ($p = 0.03$). An increase in left testicular volume when compared to the contralateral testis was found in 25 (78.1%) subjects with clinical grade 2 varicocele, and in 32 (88.8%) subjects with grade 3 abnormality.
In patients with unilateral grade 2 varicocele mean baseline left and right testicular volumes were 16.7 (SD = 4.2) cm^3 and 19.8 (SD = 2.4) cm^3, respectively. After surgery the respective volumes were 20.9 (SD = 3.7) cm^3 and 21.4 (SD = 1.6) cm^3; the increase was statistically significant ($p = 0.01$).
In patients with unilateral grade 3 varicocele, mean initial left and right testicular volumes were 16.2 (SD = 2.3) cm^3 and 18.7 (SD = 3.9) cm^3, respectively. After surgery the respective volumes were 19.9 (SD = 2.5) cm^3 and 20.2 (SD = 3.3) cm^3; the increase was statistically significant ($p = 0.03$).
An increase in left testicular volume was found in 46 (85.1%) of 54 patients with unilateral varicocele and in 12 (85.7%) of 14 subjects operated on for bilateral disease.
In patients with bilateral varicocele mean baseline left and right testicular volumes were 15.5 (SD = 6.6) cm^3 and 17.9 (SD = 3.2) cm^3, respectively. After surgery the respective volumes were 19 (SD = 6.9) cm^3 and 20.2 (SD = 5.6) cm^3.
The left testicular volume increases were comparable irrespective of whether unilateral or bilateral repair

was performed. Bilateral hypotrophy was seen in two (14.2%) of fourteen subjects with bilateral disease; they had no testicular volume increase at follow–up.
Semen analysis was performed in all subjects who had undergone laparoscopic varicocele repair in adolescence. The check revealed normozoospermia in 58 (85.2%) of our 68 patients while the remaining 10 (14.7%) had oligozoospermia (<15 million sperm/ml) or low percentage of motile spermatozoa, ie., asthenozoospermia (<40%) or low percentage of normally shaped sperm, ie., teratozoospermia (<4%) with persistent testicular hypotrophy.
Normozoospermic men also had normal FSH, LH, and T levels as opposed to 10 subjects with different variants of spermatogenesis abnormalities, who showed FSH and LH elevation with low T levels.
Varicocele recurrence was only observed in two (2.9%) patients; they underwent repeat repair. Complications developed in six (8.8%) of patients, and included a hydrocele testis – five patients (7.3%), and epididymitis – one patient (1.4%). The operating time was 18 to 40 minutes (mean 25.4 minutes). Hospital stay was 1 to 3 days (mean 2.1 days) and overall convalescence was 7 to 12 days (mean 8.2 days).

DISCUSSION

The varicocele was described in antiquity; since the end of the XIX century it has been considered one of the causes of male factor infertility. Although several convincing hypotheses exist to explain the etiology and pathomechanisms of varicoceles, there is no consensus about the advisability of early surgical repair and harmful effect of the vascular lesion on male fertility potential.
We agree with Greenfield, Cayan, and other authors that in the case of suspicion or preliminary diagnosis of genital abnormality, the patient should be referred to a urologist or andrologist [2, 6, 14, 15, 16]. Testicular hypotrophy has been observed in both pediatric and adult patients with varicocele. An increase in testicular volume on the affected side indicates the efficiency of surgical repair. We also agree that varicocele with testis hypotrophy on the affected side, confirmed by color Doppler ultrasound, is an indication for surgical repair [2, 9, 15, 19, 20, 21]. Laparoscopic varicocele repair resulted in significant increase in hypotrophic testicular volume in 58 (83.8%) of our subjects.
Numerous surgical techniques have been developed for treatment of varicocele, which are aimed at closing incompetent veins of the spermatic cord, thus preventing retrograde blood flow towards the testis and venous stasis in dilated vessels of the pampiniform plexus.
Surgical repair of varicocele can be achieved by conventional open varicocelectomy, laparoscopic, microsurgical intervention, or transdermal sclerotherapy and embolization of the testicular vein. Technological progress of the last twenty years has allowed the introduction of a new minimally invasive surgical modality, ie., laparoscopic surgery. We believe that laparoscopic varicocele repair as described by Palomo (ligation and division of both testicular vein and artery) or Bernardi (testicular artery sparing) should be recommended as the treatment of choice for the vascular lesion. However, opinions of experts on the efficacy of the above–mentioned modalities are divided [2, 9, 17, 18]. While recognizing the value of both procedures for varicocele correction, it is assumed that the laparoscopic Bernardi technique should be given priority in boys and adolescents.
Nonetheless, functional and histologic changes in the testis can develop in boys. Spermatogenesis abnormalities associated with disturbances on the hypothalamic–pituitary–testis–axis occur earlier than their physical manifestation, ie., decreased testicular volume and consistence especially on the varicocele–affected side. Concomitant damage to the right testis results when a immunological factor is present as it is in the case of unilateral cryptorchidism or unilateral testicular torsion.
Hormonal regulation of the reproductive system in adolescent boys and men of procreative age depends on Sertoli and Leydig cells stimulation in the testis by pituitary–produced gonadotropic hormones, ie. lutenizing hormone (LH) and follicle stimulating hormone (FSH). LH causes Leydig cells to synthesize and, subsequently, secrete testosterone, which controls meiosis and spermatid transformation into a spermatozoon. FSH acts with testosterone to induce the secretory activity of Sertoli cells; they synthesize proteins indispensable for normal spermatogenesis. Clinical observations and results of experimental research also suggest important roles of estradiol (E_2) and prolactin (PRL) in the process [1, 2, 15, 20, 23, 24].
Postoperative follow–up of young men after they turn 18 facilitates objective evaluation of the efficacy of surgical varicocele repair. Our results, based on sperm examination at 1 to 9 years after laparoscopic intervention, mostly revealed normal sperm count, motility, and morphology. Other authors also report a significant improvement of sperm parameters following surgical varicocele repair, thus confirming the advisability of surgical correction for the vascular lesion. Normal FSH, LH, and T levels found in young men operated on in adolescence are also significant; late diagnosis and treatment frequently result in spermatogenesis disturbances and abnormal concentrations of sex hormones [2, 23, 25, 26].

CONCLUSIONS

Laparoscopic varicocele repair resulted in significant increase of hypotrophic testicular volume in 83.8% of our subjects.

Assessment of the efficacy of surgical varicocele repair should include hormonal tests and semen analysis in procreative age group.

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