https://doi.org/10.48047/AFJBS.6.Si4.2024.2854-2863

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Relation between Grade of Varicocele and Sperm Motility Improvement after Subinguinal Varicocelectomy

Ahmed Zakaria Ahmed Mohammed[1*]

1. Lecturer of Urology, Faculty of Medicine, Suez Canal University Egypt.

Article History

Volume 6, Issue Si4, 2024
Received : 04 June 2024
Accepted : 25 June 2024
doi:
10.48047/AFJBS.6.Si4.2024.2854-2863

Abstract

Background: The testicular varicocele is the dilatation, elongation, and tortuosity of pampiniform plexus of the testis, due to venous stasis. It is more common on the left side. We aimed to assess the relation between grade of varicocele and sperm motility improvement after subinguinal varicocelectomy.

Methods: This observational cohort study was conducted on 80 male patients aged from 20 -60 years, with subclinical varicoceles having normal sized testis and normal FSH level and suffering from clinical varicocele with >1 year of primary infertility and impairment of at least one semen parameter. All patients were subjected to complete history taking including personal, past, drug and family history of similar conditions, general examination including general appearance of the patient, conscious level, decubitus and vital signs, examination of the head, chest, abdomen and extremities, local examination including assessment of characteristics of varicocele, grading, size of testis and any associated swelling, routine full laboratory investigations and special investigations including semen analysis.

Results: Regarding the sperm concentration, postoperative sperm concentration was significantly increased compared to preoperative concentration in patients with grade I varicocele (39.85 ± 2.95 vs. 33.04 ± 5.34, P<0.001), in patients with grade II varicocele (47.48 ± 9.62 vs. 29.74 ± 4.87, P<0.001), and in patients with grade III varicocele (53.58 ± 4.26 vs. 30.16 ± 5.61, P<0.001).

Conclusions: We included significant improvement in semen parameters after varicocelectomy, where postoperative sperm concentration and overall motility were significantly increased compared to preoperative concentration and motility in patients with grade I, II and III varicocele.

Keywords: Grades; Varicocele; Sperm; Motility; Improvement; Subinguinal Varicocelectomy

Introduction

The testicular varicocele is the dilatation, elongation and tortuosity of pampiniform plexus of the testis, due to venous stasis. It is more common on the leftside[1].Varicocele means pooling of blood in scrotum andrise of testicular temperature and reflux of blood thathas adverse effect on sperm production andtestosterone function[2].Varicocele is the most common cause of infertility in men, which can be treated by operation. It isestimated that 15%of men suffer

from varicocele.It has been reported in 17% of fertile men and about39% of infertile men[3].Testicular varicoceles interfere with testiculartemperature regulation which is usually maintainedat 2-3c. less than core body temperature[4]

Dubin and Amelar introduced the varicocele grading system in 1970 when they evaluated whether preoperative varicocele size was related tosemen parameter changes. The grading system classifies grade 1 varicocele as varicocele palpableonly by the Valsalva manoeuvre, grade 2 as palpable at rest but not visible and grade 3 as easily visible[5].The AUA and ASRM guidelines group all clinical varicoceles together and do not distinguish by grade. However, it is intuitive that the degree of testicular impairment resulting from a varicocele might be influenced by the grade of the varicocele[6].

Varicocele surgery is intended to eliminate retrograde backflowfrom the abdomen to the pampiniform plexus, while preserving the internal spermatic arteries, vas deferens, spermatic cord, andthe lymphatics[7].Varicocelectomy is by far the most common procedure to treat male subfertility in patients with clinical varicocele. It reduces intratesticular temperature to the normal range.Hence, semen parameters not uncommonly show significant improvement following varicocele ligation[8].

There are many approaches for varicocelectomy.4-6 Initially open surgical approach was the standard, but now there are alternative approaches, such as embolization and laparoscopy.The effect of varicocelectomy on semen analysis is controversial[9-11].

Several studies documented improvements in semen parameters, hormonal profiles, and pregnancy rates after varicocele repair[12, 13].Many studies have reported that varicocelectomy promotes Leydig cell function based on testosterone levels. In addition, research indicates that ageing in men can induce a reduction in serum testosterone levels[14, 15].

We aimed to assess the relation between grade of varicocele and sperm motilityimprovement after subinguinal varicocelectomy.

Materials and Methods

This observational cohort study was conducted on 80 male patients aged from 20 -60years, with subclinical varicoceles having normal sized testis and normal FSH level. The patients provided informed written consent before participating in the study. The research was conducted within the approved guidelines of the institutional ethical committee of Suez Canal University.

We included varicocele men suffering from clinical varicocele with >1 year of primaryinfertilityand impairment of at least one semen parameter.

Exclusion criteria were fertile men with varicoceles presented withscrotal pain and/or swelling, recurrent varicoceles, azoospermia, receiving exogenous androgens, with history of testicular torsion,tumors,and undescendedtestis,with abnormalhormone levels.

All patients were subjected to complete history taking including; personal history as (name, age,occupation, residence, marital status, testicular trauma mumps orchitis and special habits), past historyincludinghistory of previous surgery, history of other comorbidities (as diabetesmellitus,hypertension, cardiac, renal and hepatic diseases),drug history including history of receiving medications known to elicitimbalance androgen levels and the duration oftaking it, historyof drug allergy, family history of similar conditions, general examination including general appearance of the patient, conscious level, decubitus and vital signs(pulse, blood pressure and temperature) and examination of the head, chest, abdomen and extremities and local examination including assessment of characteristics of varicocele (right, left or both), grading, size of testis and any associated swelling. Length, weight and body mass index (BMI) of all patients were also recorded.

Varicoceles were graded from I to III according to Dubin and Amelar varicocele grading system; grade I, palpable only during Valsalva's manoeuvre, grade II, palpable at rest but notvisible and grade III, palpable and visible at rest[16].The presence of varicocele was

diagnosedby physical examination in a temperature-controlled room atover 23◦C under adequate illumination.

Under spinal or general anesthesia, the institutional standard technique wasperformed in all patients. The spermatic cord was approached through a 2-cmtransverse skin incision centred over the external inguinal ring. The incisionwas deepened, and the spermatic cord was then grasped with a Babcock clamp,delivered, and placed over an artery forceps. Gentle pressure was applied ontothe ipsilateral hemi-scrotum to engorge the spermatic veins. All identifiable external spermatic veins were ligated and divided. After opening the spermaticfascia, the internal spermatic veins were separated, ligated, and divided. Theonly identified artery (or arteries) and lymphatics were preserved. In microsurgical subinguinal varicocelectomy, theoperative microscope was brought intothe operating field and all steps done under 8–15-power magnification. Allpatients were discharged on the day of operation[17].

Investigations:

Routine full laboratory investigations including randomblood sugar, serum creatinine, liverfunction tests, complete blood count, INR, andblood grouping.

Special lab investigations including semen analysis that were obtained from infertile menby masturbation after 3-5 days of sexualabstinence. Semen analysis was done beforesurgery and repeated (3-6 months) aftervaricocelectomy to evaluate the effects ofvaricocele repair upon the quality of the semenparameters. Semen parameters (concentration,motility, andmorphology) were assessedaccording to WHO guidelines[18]. All varicocele menhad semen analyses before surgery that showed atleast one abnormal parameter (count < 15million/ml, motility < 40% and morphology < 4%normal forms)[19].

Duplex scrotal ultrasound:

Clinical findings were confirmed by duplex scrotalUS. Duplex examination for all patientswas done atSuez Canal UniversityRadiology Unit. Every patientwas examined preoperatively to confirm the clinicaldiagnosis of varicocele and to diagnose a possiblecontralateral subclinical varicocele. Before Duplexexamination, the patient was asked to shave well the scrotum and lower abdomen on both sides. A pencilprobe Duplex (9MHz) stethoscope was used. Thepatient was examined in the upright position and theconducting gel was applied to the upper aspect of thescrotum. There was complete acoustical silence. In varicocele patient, therewas a characteristic audible venous rush (reflux)indicative of retrograde filling of the varicocele. Invaricocele patient during quiet respiration there wascontinuous venous regurge (grade III), intermittentvenous regurge (grade II) or no spontaneous venousregurge (grade I).

We used 2 cmsubinguinal incision over superficial inguinal ring[20].Spermatic cord was delivered, and external spermaticveins and gubernacular veins were ligated anddivided (running parallel to spermatic cord & with thehelp of vascular doppler (8 MHz) and microscope 8-15 power, testicular artery /arteries identified alongwith vas deference and its vessels and lymphaticchannels.

Postoperative testicular venous drainage wasvia vasal veins which drain in internal pudendalsystem. Parameters of study were age, degree ofvaricocele (GI, GII, GIII), sperm count, sperm motility(excellent, good, poor), complications (hematoma,infection, pain, testicular atrophy), hospital stay,grade of motility and sperm count and pregnancy outcome

Statistical analysis:

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%). Paired sample t-test is a statistical technique that is used to compare two population means in the case of two samples that are correlated.A two tailed P value < 0.05 was considered statistically significant.

Results

Our study included 80 males; their mean age was 36.33 ± 9.19 years. Regarding the associated comorbidities, 63 (78.8%) patients had hypertension, 69 (86.3%) patients had diabetes mellitus and 73 (8.8%) patients had hyperlipidemia. **Table 1**

Table 1: Baseline characteristics of the studied patients

		N= 80
Age (years)		36.33±9.19
Comorbidities	**HTN**	63 (78.8%)
	DM	69 (86.3%)
	Hyperlipidemia	73 (8.8%)

Data presented as mean ± SD or frequency (%), HTN: hypertension, DM: diabetes mellitus

Table 2shows that the mean hospital stay of the studied patients was 18.11 ± 3.78 days and the mean duration of infertility of the studied patients was16.3 ± 4.38months.

Table 2: Clinical data of the studied patients

	N= 80
Hospital stay (days)	18.11±3.78
Duration of infertility (months)	16.3±4.38

Data presented as mean ± SD.

Among the studied patients, 68 (85%) patients had the varicocele on the right side where 12 (15%) patients had the varicocele on the left side. Regarding the grade of varicocele, grade I was detected in 26 (32.5%) patients, grade II was detected in 23 (28.8%) patients and grade III was detected in 31 (38.8%) patients.**Table 3; Figure 1**

Table 3: Varicocele data of the studied patients

		N= 80
Side of varicocele	**Right**	68 (85%)
	Left	12 (15%)
Grade of varicocele	**Grade I**	26 (32.5%)
	Grade II	23 (28.8%)
	Grade III	31 (38.8%)

Data presented as frequency (%).

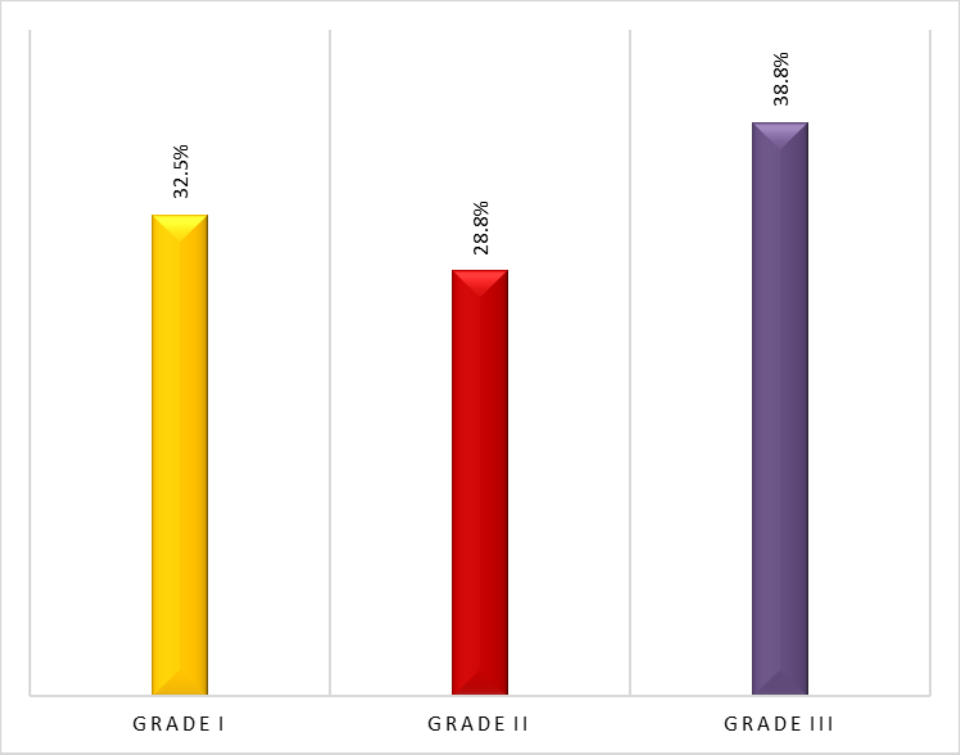

Figure 1: Grade of varicocele of the studied patients

Regarding the sperm concentration,postoperative sperm concentration was significantly increased compared to preoperative concentration in patients with grade I varicocele (39.85 ± 2.95 vs. 33.04 ± 5.34, P<0.001), in patients with grade II varicocele (47.48 ± 9.62vs. 29.74 ± 4.87, P<0.001), and in patients with grade III varicocele (53.58 ± 4.26 vs. 30.16 ± 5.61, P<0.001). **Table 4**

Table 4: Pre-and postoperative sperm concentrationof the studied patients

		Spermconcentration(million sperm / ml)	**P value**
Grade I (n=26)	**Preoperative**	33.04±5.34	**<0.001***
	Postoperative	39.85±2.95	
Grade II (n=23)	**Preoperative**	29.74±4.87	**<0.001***
	Postoperative	47.48±9.62	
Grade III (n=31)	**Preoperative**	30.16±5.61	**<0.001***
	Postoperative	53.58±4.26	

Data presented as mean ± SD, *: statistically significant as P value <0.05.

Concerning the sperm motility, postoperative sperm motility was significantly increased compared to preoperative concentration in patients with grade I varicocele (51.19 ± 7.77 vs. 46.27 ± 7.99, P=0.029), in patients with grade II varicocele (59.48 ± 8.94 vs. 45.65 ± 8.09, P<0.001), and in patients with grade III varicocele (66.48 ± 13.79 vs. 42.16 ± 4.8, P<0.001). **Table 5**

Table 5: Pre-and postoperative spermmotility of the studied patients

		Spermmotility (%)	**P value**
Grade I (n=26)	**Preoperative**	46.27±7.99	**0.029***
	Postoperative	51.19±7.77	
Grade II (n=23)	**Preoperative**	45.65±8.09	**<0.001***
	Postoperative	59.48±8.94	
Grade III (n=31)	**Preoperative**	42.16±4.8	**<0.001***

	Postoperative	66.48±13.79	

Data presented as mean ± SD, *: statistically significant as P value <0.05.

Table 6 shows that effect of varicocelectomy of the studied patients, where 12 (46.2%) patients with grade I varicocele, 16 (69.6%) patients with grade II and 25 (80.6%) patients with grade III varicocele showed improvement after varicocelectomy.

Table 6: Effect of varicocelectomy of the studied patients

		Postoperative improvement
Grade I (n=26)	**Yes**	12 (46.2%)
	No	14 (53.8%)
Grade II (n=23)	**Yes**	16 (69.6%)
	No	7 (30.4%)
Grade III (n=31)	**Yes**	25 (80.6%)
	No	6 (19.4%)

Data presented as frequency (%).

Discussion

Although varicocele is an important and commoncause of men infertility, fortunately, it is well treatable, and the best treatment of it, is agreed by mostresearchers to be surgery. Thevaricocele has beenconsidered the most effective treatable cause of maleinfertility[21, 22].

The current analysis was done to determinewhether varicocele grade could be incorporated intoimprovement of sperm motility and count after varicocelectomy.The key findings of this study show improvement insemen concentration and motility after varicocelectomy with greater improvement in patients withhigher grade varicocele. This has major implicationsforthe management of infertility.Despite some persistent controversy, the efficacyofvaricocelectomy as a treatment of varicoceleassociated infertility is wellestablished and supported by high quality clinical studies[23].

Adjei et al.[24]performed a systematic review and found that baseline sperm concentration was directly relatedto varicocele grade. They reported that some studies in a total of 294men with grade 3 varicoceles showed a mean baseline concentration of 32.79 million sperm per ml[25-27]. In other studies, in a total of 381 men with grade 2-3 varicocele showed a mean baseline of 20.3 million spermper ml[28-30]. In other studies, in a total of 213 men with grade 2varicocele showed a mean baseline concentrationof 27.6 million sperm per ml[25, 27]. Studies found that in a total of 211men with grade 1 varicocele showed a mean baselineof 30.1 million sperm per ml[31, 32]. Regarding motility the mean baseline total motility was also directlyrelated to varicocele grade. Previous studies found that in a total of156 men with grade 3 varicocele reported a meanbaseline motility of 30.8%[27, 33]. It was reported that a total of 445men with grade 2/3 varicocele showed a mean baseline motility of 29.4%. andin a total of 131 men withgrade 2 varicocele had a mean baseline of 33.5%[27]Previousstudies showed that in a total of 101 men with grade 1 varicoceleshowed a mean of 35.3%[32, 34].Adjei et al. [24]concluded that mean improvements in the sperm concentration and the percent of overall motility after treatment of grade 1 varicocele were statistically significant but small in magnitude. In contrast, mean improvements in the sperm concentration and the percent of overall motility after treatment of grade 2-3 varicoceles were greater and highly likely to be clinically significant.

A previoussystematic review also revealed statistically significant improvement in the overallpercent ofsperm motility after varicocelectomy in men with allvaricocele grades). The magnitude ofimprovement was also directly related to varicocelegrade. Mean improvement in the percent of totalmotility in men with grade 1, 2, and 3 varicocelewas 9.6%, 10.6%, and 17.7%, respectively.High heterogeneity was observed among studiesincluded in

spermconcentration analysis in menwith grade 1, 2and 3 varicocele (I2[76.2%, 92.4%and 96.0%, respectively)[35].

Epidemiological data suggest that grade 1 varicocele accounts for 34.6% to 76.6% of varicoceles insubfertile men[36, 37].In Adjei et al. [24]study patients withgrade 1 varicocele accounted for 33.9% of men whounderwent varicocele treatment.They reported that men with grade 1 varicocele may be at lower riskfor varicocele related testicular dysfunction thanmen with larger varicoceles due to the less severephysiological alterations which would be expected toresult from milder venous dilatation and congestion.

Recent data on a large, multinational,population-based study of semen quality in healthy European men supports the notion that the testicular injury resulting from varicocele does indeeddepend on varicocele grade[15]. In their study theproportion of men with low semen quality amongthose with grade 1 varicocele did not differ from thatof men without varicocele (35.1% vs 31.4%). However, the proportion of men with grade 2 and 3varicocele who had low semen quality was significantly higher than in men without varicocele(40.4% and 54.9%, respectively vs 31.4%).Adjei et al. [24]study is consistent with recently published,population-based data from Europe. It suggests thatmen with larger varicoceles have a lower baselinesperm concentration and a lower percent of overallmotility than men with smaller varicoceles. Additionally, their data demonstrate that the magnitude ofthe treatment response to varicocelectomy is higheramong men with grade 2-3 than grade 1 varicocele.

In another study Najari et al. [38]studied a total of thirtypatients. One group had 17 infertile patients and othergroup had 13 patients with palpable varicoceles as wellas low sex hormones levels. as the sperm count rose significantly witha mean change of 5 ± 9.954 million.

Basureeh et al.[39]in their study included 106 male, presented with infertility and clinicalvaricocele. They showed a significant improvement of sperm count andmotility in patientswith clinical varicocele and infertility after varicocelectomy (P=0.000). This resultwas in agreement with other studies thatassessed the effect of varicocelectomy in men withvaricocele and infertility[40, 41].Basureeh et al. [39]showed that the improvement of sperms parameters among patients withvaricocele grade II was in 63% of cases, while theimprovement in patients with varicocele grade IIIwas in 89% of cases, and the improvement amongall included patients with varicocele grade II and IIIwas in 81% of cases. They found that varicocele grade III is more prevalentand accounts for 70% of included patients, whilegrade II varicocele accounts for 30% of cases. Thisperhaps may be due to the lack of awareness amongthose who had varicocele and present themselves late.However, they reported that the sperm count, and motility improvedsignificantly after varicocelectomy among patientswith varicocele grade II and III, but the improvementwas higher among patients with grade III. This resultindicates that the improvement of sperms parametersdirectly related to the grade of varicocele.Similar studies have been showed that the improvement of sperm count and motility is directly related tothe grade of varicocele[42, 43].

Additionally, Nasrullah et al.[44]found that number of patients according to grades of varicocele were 19 (G1), 29 (G2) and 35 G3. Preoperative mean sperm count was 7.2±1.6 while preoperative sperm motility was less than 20% in excellent and good category. Postoperatively at three months the sperm count improved as 47.3% (GI), 55.1% (G2) and 74% (GIII). Motility improved after operation as 1.7, 1.9 and 2-fold in GI, G2 G3 respectively.

Our study was limited with Semen characteristics like pH, volume, sperm morphology, and percentage of dead and alive sperms have not been considered which affect the results and fertility. Also, our small sample size

Conclusions:

We included significant improvement in semen parameters after varicocelectomy, where postoperative sperm concentration and overall motility were significantly increased compared to preoperative concentration and motility in patients with grade I, II and III varicocele.Incorporating varicocele grade into shared decision-making discussions with affected couples may improve the ability to select patients who are the best candidates for treatment.

Financial support and sponsorship: Nil

References

1. Paick S, Choi WS. Varicocele and testicular pain: A review. World J Mens Health. 2019;37:4-11.
2. Joensen UN, Jensen CFS, Wiborg MH, Fojecki G, Fode M. [Varicocele testis]. Ugeskr Laeger. 2020;182:78-81.
3. Jensen CFS, Østergren P, Dupree JM, Ohl DA, Sønksen J, Fode M. Varicocele and male infertility. Nat Rev Urol. 2017;14:523-33.
4. Fang Y, Su Y, Xu J, Hu Z, Zhao K, Liu C, et al. Varicocele-mediated male infertility: From the perspective of testicular immunity and inflammation. Front Immunol. 2021;12:729-35.
5. Bertolotto M, Cantisani V, Drudi FM, Lotti F. Varicocoele. Classification and pitfalls. Andrology. 2021;9:1322-30.
6. Franco A, Proietti F, Palombi V, Savarese G, Guidotti M, Leonardo C, et al. Varicocele: To treat or not to treat? J Clin Med. 2023;12:34-8.
7. Cho CL, Esteves SC, Agarwal A. Indications and outcomes of varicocele repair. Panminerva Med. 2019;61:152-63.
8. Su JS, Farber NJ, Vij SC. Pathophysiology and treatment options of varicocele: An overview. Andrologia. 2021;53:135-76.
9. Parrilli A, Roberti A, Escolino M, Esposito C. Surgical approaches for varicocele in pediatric patient. Transl Pediatr. 2016;5:227-32.
10. Yuan R, Zhuo H, Cao D, Wei Q. Efficacy and safety of varicocelectomies: A meta-analysis. Syst Biol Reprod Med. 2017;63:120-9.
11. Napolitano L, Pandolfo SD, Aveta A, Cirigliano L, Martino R, Mattiello G, et al. The management of clinical varicocele: Robotic surgery approach. Front Reprod Health. 2022;4:791-7.
12. Jangkhah M, Farrahi F, Sadighi Gilani MA, Hosseini SJ, Dadkhah F, Salmanyazdi R, et al. Effects of varicocelectomy on serum testosterone levels among infertile men with varicocele. Int J Fertil Steril. 2018;12:169-72.
13. Madhusoodanan V, Patel P, Blachman-Braun R, Ramasamy R. Semen parameter improvements after microsurgical subinguinal varicocele repair are durable for more than 12 months. Can Urol Assoc J. 2020;14:80-3.
14. Christe N, Meier CA. Hypotestosteronaemia in the aging male: should we treat it? Swiss Med Wkly. 2015;145:142-6.
15. Damsgaard J, Joensen UN, Carlsen E, Erenpreiss J, Blomberg Jensen M, Matulevicius V, et al. Varicocele is associated with impaired semen quality and reproductive hormone levels: A study of 7035 healthy young men from six european countries. Eur Urol. 2016;70:1019-29.
16. Dubin L, Amelar RD. Varicocele size and results of varicocelectomy in selected subfertile men with varicocele. Fertil Steril. 1970;21:606-9.
17. Abdel-Maguid AF, Othman I. Microsurgical and nonmagnified subinguinal varicocelectomy for infertile men: a comparative study. Fertil Steril. 2010;94:2600-3.
18. Boitrelle F, Shah R, Saleh R, Henkel R, Kandil H, Chung E, et al. The sixth edition of the WHO manual for human semen analysis: A critical review and swot analysis. Life (Basel). 2021;11:350-9.

19. Kamar MA, Mohamed TY, Latif AMA, AbdElmodaber AM. Effects of Varicocele on Serum Testosterone Levels and Changes of Testosterone Levels after Varicocelectomy among Infertile Men: A Prospective Controlled Study. Egypt J Hosp Med. 2021;84:1731-8.
20. Tian RH, Zhao LY, Chen HX, Yang C, Li P, Huang YH, et al. Microsurgical subinguinal varicocelectomy with spermatic cord double traction and vein stripping. Asian J Androl. 2020;22:208-12.
21. Arya D, Balasinor N, Singh D. Varicocoele-associated male infertility: Cellular and molecular perspectives of pathophysiology. Andrology. 2022;10:1463-83.
22. Almekaty KM, Elsharkawy AM, Zahran MH, Ragab MM, Rashed AS, Soliman MM, et al. Bilaterality of varicocele: The overlooked culprit in male infertility. Case series study. Arch Ital Urol Androl. 2023;95:115-34.
23. Lamy SH, Mohammedkhalil AK, Bafaqeeh HM, Alsuwaida SA, Alhindi ASK, Maqboli SA, et al. Efficacy of varicocelectomy on semen parameters and conception rates. Urol Ann. 2023;15:256-60.
24. Asafu-Adjei D, Judge C, Deibert CM, Li G, Stember D, Stahl PJ. Systematic review of the impact of varicocele grade on response to surgical management. J Urol. 2020;203:48-56.
25. Mohamid MA. The effect of magnified bilateral varicocele ligation on semen quality and the natural paternity rate in subfertile men, based on the sum of varicocele grading. Arab J Urol. 2012;10:434-9.
26. Hosseinifar H, Sabbaghian M, Nasrabadi D, Modarresi T, Dizaj AV, Gourabi H, et al. Study of the effect of varicocelectomy on sperm proteins expression in patients with varicocele and poor sperm quality by using two-dimensional gel electrophoresis. J Assist Reprod Genet. 2014;31:725-9.
27. Ni K, Steger K, Yang H, Wang H, Hu K, Zhang T, et al. A comprehensive investigation of sperm DNA damage and oxidative stress injury in infertile patients with subclinical, normozoospermic, and astheno/oligozoospermic clinical varicocoele. Andrology. 2016;4:816-24.
28. Leung L, Ho KL, Tam PC, Yiu MK. Subinguinal microsurgical varicocelectomy for male factor subfertility: ten-year experience. Hong Kong Med J. 2013;19:334-40.
29. Tavalaee M, Bahreinian M, Barekat F, Abbasi H, Nasr-Esfahani MH. Effect of varicocelectomy on sperm functional characteristics and DNA methylation. Andrologia. 2015;47:904-9.
30. Guo L, Sun W, Shao G, Song H, Ge N, Zhao S, et al. Outcomes of microscopic subinguinal varicocelectomy with and without the assistance of doppler ultrasound: A randomized clinical trial. Urology. 2015;86:922-8.
31. Grasso M, Lania C, Castelli M, Galli L, Franzoso F, Rigatti P. Low-grade left varicocele in patients over 30 years old:the effect of spermatic vein ligation on fertility. BJU Int. 2000;85:305-7.
32. Minayoshi K, Okada H, Fujisawa M, Yamasaki K, Kamidono S. Hemodynamic evaluation of left testicular varicocele by scrotal scintigraphy. Eur Urol. 2001;39:30-5.
33. Lehtihet M, Arver S, Kalin B, Kvist U, Pousette A. Left-sided grade 3 varicocele may affect the biological function of the epididymis. Scand J Urol. 2014;48:284-9.
34. Ishikawa T, Fujisawa M. Effect of age and grade on surgery for patients with varicocele. Urology. 2005;65:768-72.
35. Tinga DJ, Jager S, Bruijnen CL, Kremer J, Mensink HJ. Factors related to semen improvement and fertility after varicocele operation. Fertil Steril. 1984;41:404-10.
36. Soylemez H, Atar M, Ali Sancaktutar A, Bozkurt Y, Penbegul N. Varicocele among healthy young men in Turkey; prevalence and relationship with body mass index. Int Braz J Urol. 2012;38:116-21.

37. Bozhedomov VA, Lipatova NA, Rokhlikov IM, Alexeev RA, Ushakova IV, Sukhikh GT. Male fertility and varicocoele: role of immune factors. Andrology. 2014;2:51-8.
38. Najari BB, Introna L, Paduch DA. Improvements in patient-reported sexual function after microsurgical varicocelectomy. Urology. 2017;110:104-9.
39. Basureeh OA, Alyamani AS. Efficacy of varicocelectomy on sperms count and motility in patients with clinical varicocele and infertility. HJMS. 2014;3:247-52.
40. Poulakis V, Ferakis N, de Vries R, Witzsch U, Becht E. Induction of spermatogenesis in men with azoospermia or severe oligoteratoasthenospermia after antegrade internal spermatic vein sclerotherapy for the treatment of varicocele. Asian J Androl. 2006;8:613-9.
41. Okeke L, Ikuerowo O, Chiekwe I, Etukakpan B, Shittu O, Olapade-Olaopa O. Is varicocelectomy indicated in subfertile men with clinical varicoceles who have asthenospermia or teratospermia and normal sperm density? Int J Urol. 2007;14:729-32.
42. Ku JH, Son H, Kwak C, Lee SE, Lee NK, Park YH. Impact of varicocele on testicular volume in young men: significance of compensatory hypertrophy of contralateral testis. J Urol. 2002;168:1541-4.
43. Cakan M, Altuğ U. Induction of spermatogenesis by inguinal varicocele repair in azoospermic men. Arch Androl. 2004;50:145-50.
44. Nasrullah F, Khan MS, Mughal MA. Relation between grade of varicocele and improvement in semen parameter after microvaricocelectomy. Pak J Med Health Sci. 2015;9:617-8.