

Longitudinal Study of Semen Quality in Adolescents with Varicocele: To Treat or Not?

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OBJECTIVES

To assess the role of varicocelectomy in pediatric patients through a careful semen analysis.

METHODS

A total of 214 patients with grade 2 and 3 left idiopathic varicocele were enrolled. Of these 214 patients, 106 (group 1) were treated surgically for testicular hypotrophy, 54 (group 2) were treated surgically with a normal testis, and 54 with a normal testis (group 3) were observed with follow-up visits every 6 months. The spermogram results for each group were divided into two subgroups: normal, if they met the evaluation criteria and abnormal in the remaining cases.

RESULTS

The spermogram analysis for groups 1 and 2 showed no statistically significant difference in terms of normal and abnormal spermogram findings ($P > 0.01$). Even though the patients included in group 3 had reported no testicular hypotrophy or pain, the qualitative semen analysis showed the same trend observed in patients affected by varicocele, but the difference was not statistically significant in the variables considered for the other groups ($P > 0.01$). Preservation of the testicular artery in patients with hypotrophy was associated with better results in terms of semen quality.

CONCLUSIONS

Testicular hypotrophy remains the most objective indication for surgical treatment of varicocele, and preservation of the testicular artery gives better results in terms of semen quality only in patients affected by testicular hypotrophy. UROLOGY 70: 989–993, 2007. © 2007 Elsevier Inc.

Idiopathic varicocele is one of the most common andrologic diseases in hypofertile males, influencing male reproductive capacity by affecting semen quality and quantity.^{1–3} Many studies have described the relationship between varicocele and hypofertility/infertility in males, with significant improvement of semen quality after varicocelectomy.^{4–7} Some investigators still believe that surgical treatment of varicocele should not be applied to all patients and should, in some cases, be completely avoided.⁸

During childhood, varicocelectomy is performed if the homolateral testis has a smaller volume than the contralateral, but doubts still exist about the surgical treatment of varicocele when it is painful.⁸ Many techniques have been suggested to treat varicocele, although no reference standard has been agreed on for pediatric patients.⁹ During childhood, it is not possible to perform preoperative spermograms. For this reason, no reference or predictive value is available for comparison with the

postoperative semen analysis to determine whether any functional improvement occurred related to the varicocelectomy. Very often, an empirical approach is used to decide how to treat varicocele, because its early treatment prevents hypofertility/infertility. Published trials have shown that this is not always true; that is not all patients will benefit from this treatment.^{7–9}

The purpose of this study was to assess the role of varicocelectomy in pediatric patients with or without testicular hypotrophy through a careful semen analysis.

MATERIAL AND METHODS

From January 1999 to January 2000, 214 patients with left idiopathic varicocele were enrolled in the study. All patients were 11 to 14 years old (mean 12 ± 3). None of the patients affected by grade 1 left varicocele observed at our department had testicular hypotrophy at diagnosis. Patients with grade 1 varicocele were therefore excluded from the study. Informed consent was provided by the patients' parents.

The inclusion criteria were as follows: no history of previous orchitis, genital trauma, testicular torsion, inguinal surgery, or previous hormonal therapy; continuous spermatic vein reflux assessed by Doppler velocimetry (type IV–V Hirsh classification)¹⁰; and grade 2 or 3 varicocele.

Testicular ultrasonography allowed the measurement of the three diameters of the gonad to assess its overall volume. Ultra-

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sound scans were performed by a specialist radiologist before surgery. The testes were scanned using the Siemens SONOLINE Elegra Ultrasound Imaging System, with a 7.5-MHz probe. The testicular length, width, and height were measured using electronic calipers. The values obtained were then substituted into the formula of a prolate ellipsoid to evaluate the testicular volume (volume in milliliters = $0.523 \times L \times W \times H$).¹¹⁻¹⁶ A testis homolateral to the varicocele with a volume reduction of 20% with respect to its contralateral was defined as hypotrophic.^{17,18}

Treated Patients

The treated patients included those in group 1 (grade 2 and 3 left varicocele with testicular hypotrophy at diagnosis) and those in group 2 (grade 2 and 3 left varicocele without testicular hypotrophy at diagnosis). The 106 patients in group 1 underwent surgical treatment of their testicular hypotrophy, with the testicular artery preserved in 60 patients and full spermatic vessel ligation in 46. The 54 patients in group 2 underwent "preventive" surgery, with the testicular artery preserved in 30 patients and full spermatic vessel ligation in 24. No patient included in group 2 had had testicular hypotrophy.

The decision of whether to preserve or ligate the testicular artery in the patients in groups 1 and 2 was randomly determined by the patient's month of birth. If an even month, the artery was preserved and if odd, full ligation of the spermatic vessels was done. We used these two techniques to determine whether differences in semen quality resulted.

The complications involved with these procedures (ie, persistence, recurrence, and hydrocele) were evaluated for during clinical and instrumental tests performed 1 day and 3, 6, and 18 months after surgery.

The persistence (presence of vein reflux 1 day after surgery) and recurrence (presence of vein reflux at least 3 months after surgery) of varicocele were evaluated by Doppler velocimetry. Vein reflux in the spermatic cord, with or without the Valsalva maneuver, was considered abnormal. The instrument used for all patients was the same as described previously, with 5 to 10-MHz probes.

Untreated Patients

The untreated patients included those in group 3 who had grade 2 or 3 left varicocele without testicular hypotrophy or pain. The 54 patients in group 3 came to our outpatient department for long-term follow-up visits every 6 months. In the case of the onset of testicular hypotrophy, the patients immediately underwent treatment and were excluded from the study.

Semen Analysis

Semen analysis was performed when the patients had attained 18 years of age. The evaluation criteria for semen quality followed World Health Organization indications.¹⁹

The spermogram results were divided into two subgroups: normal, if they met the evaluation criteria and abnormal if not.

Two semen samples, taken at least 3 weeks apart after 4 days of abstinence, were collected immediately after masturbation in a clean plastic container supplied by the laboratory and analyzed within 1 hour of collection. All spermograms were analyzed by the same laboratory.

The semen specimens were collected at the Department of Laboratory Medicine and transferred immediately to the diagnostic semen laboratory, where they were kept at 37°C until liquefied. The sperm concentration was determined by counting

two sides of a hemacytometer. The semen volume was measured by drawing up the entire sample into a graduated pipette. Motility was defined as the proportion of sperm that was progressively motile at 37°C measured with a Makler chamber. Sperm morphology was evaluated by a single examiner using strict criteria.²⁰

Statistical Analysis

For each study group, we considered the following parameters: semen quality differences between patients with a conserved artery versus full spermatic vein ligation; differences between patients with and without testicular hypotrophy; and differences between patients treated surgically and nonsurgically. Statistical analysis was performed using Student's *t* test, the chi-square test, and Fischer's exact test, with significance set at $P < 0.01$.

RESULTS

All patients treated either surgically or nonsurgically completed follow-up, with a compliance of 100%. No patient in group 3 developed testicular hypotrophy; therefore, no patient was excluded from the study.

At the end of the follow-up period (18 years of age), two spermograms were performed on all patients. The surgically treated patients (groups 1 and 2) had an equal distribution of varicocele grades. The three study groups were homogeneous for age and distribution of varicocele grade. The pubertal development of the patients, as observed during the follow-up visits, was normal and completed fully by the end of the follow-up period. No complications were reported during surgery.

The percentage of postoperative complications was similar to that reported in published studies. An increased incidence of postoperative hydrocele was seen in patients treated with full ligation of the spermatic vessels, and persistence/recurrence of varicocele was seen in patients with artery preservation ($P < 0.01$).

After grouping patients according to the spermogram results (meeting or not meeting the World Health Organization criteria), each parameter was considered individually for each group and treatment to obtain an overall comparison of semen quality.

The following semen parameters were analyzed: volume, sperm count per milliliter, percentage of motile spermatozoa, percentage of normal spermatozoa, and percentage of vitality for each group (Table 1).

Semen Characteristics and Analysis

The results of the semen analyses for all three groups are given in Table 2. Currently, the lower limit of the normal range of human semen variables, as set by the World Health Organization, is 2.0 mL for volume, 20×10^6 sperm/mL for concentration, 50% for progressive motility, 30% for normal morphology, and 70% for vitality (Eosina's test).

The 106 patients in group 1 were treated surgically for testicular hypotrophy, with the testicular artery preserved in 60 and full spermatic vessel ligation in 46. Spermio-

Table 1. Patients with normal spermiogram findings by variable and treatment group

WHO Criteria	Group 1 (Hypotrophy; n = 106)			Group 2 (No Hypotrophy; n = 54)			Group 3 (Control Group; n = 54)	P Value		
	Artery Preserved (n = 60)	Artery Ligated (n = 46)	P Value	Artery Preserved (n = 30)	Artery Ligated (n = 24)	P Value		Group 2 vs. 3	Group 1 vs. 3	Group 1 vs. 2
Volume >2 mL	46	44	0.05	22	24	0.05	48	1	0.89	0.99
Form >30%	48	34	0.59	26	20	0.8	36	0.11	0.68	0.78
Motility >50%	26	12	0.19	16	10	0.57	22	0.58	0.77	0.49
Vitality >70%	34	22	0.52	14	12	0.86	32	0.58	0.76	0.82
Concentration >20 million/mL	46	42	0.15	22	22	0.22	52	0.08	0.66	0.95

WHO = World Health Organization.
All P values were not statistically significant.

Table 2. Semen characteristics per treatment group

WHO Criteria	Group 1						Group 2			Group 3		
	Artery Preserved			Artery Ligated			Mean	SD	Median	Mean	SD	Median
Volume >2 mL	3.02	1.2	3.25	3.22	1	3	2.7	0.8	2.6	2.5	0.7	2.3
Form >30%	45.13	19.8	40.5	37.91	18.91	35	46.44	17.87	48	39.25	19.56	35
Motility >50%	44.73	18.8	47	41.34	15.73	42	45.48	15.6	47	48	15.9	43
Vitality >70%	72.83	13.1	75	71.39	11.44	74	72.85	10.05	75	73.4	10.28	75
Concentration >20 million/mL	58.85	45.03	46	75.06	43.9	48	62.3	23.14	42	69.66	40.72	58

WHO = World Health Organization.
Student's *t* test showed no statistically significant relationship among variables per treatment group.

gram analysis showed no statistically significant difference between the two subgroups (preserved and ligated artery) in terms of normal and abnormal spermiogram findings ($P > 0.01$). However, a statistically significant difference was found for motility and vitality (functional results), with more positive results in the subgroup with a preserved artery ($P < 0.01$).

The 54 patients in group 2 were treated surgically, with the testicular artery preserved in 30 and full spermatic vessel ligation in 24. For group 2, the spermiogram results also showed no statistically significant difference between the two subgroups (preserved and ligated artery) in terms of normal and abnormal spermiogram findings ($P > 0.01$). In contrast to the findings for group 1, the patients in group 2 did not have a statistically significant difference in the functional variables ($P > 0.01$).

The 54 patients in group 3 came to our outpatient department for follow-up visits every 6 months. The long-term observation included examination of the external genitals, Doppler velocimetry, and testicular ultrasonography. Spermiogram analysis showed no statistically significant difference between group 3 and groups 1 and 2 in terms of normal and abnormal spermiogram findings. Even though the patients included in group 3 had had no reports of testicular hypotrophy or pain, the qualitative semen analysis showed, and, therefore, confirmed, the same trend toward the alterations of spermatozoa motility, shape, and vitality normally observed in patients affected by varicocele. No statistically significant difference was

found in the variables considered for the other groups ($P > 0.01$).

COMMENT

Although the efficacy of surgery in the treatment of this condition could undoubtedly be shown only through an accurate prospective, randomized, controlled study to assess the impact of varicoectomy on patients' semen parameters and low pregnancy rates, most cases analyzed in published studies have shown a positive result from this treatment. The different outcomes could have resulted from differing clinical selection criteria and success criteria.

Until pubertal development is fully reached, it is not possible to perform spermiograms. Thus, during childhood, it is difficult to opt for early treatment of varicocele. The need for surgical correction is especially clear considering that the testicular lesions caused by this affliction are irreversible.^{21,22}

Because fertility is usually a difficult parameter to assess (clinically, it is more common to talk in terms of fertility potential), during childhood, varicocele is usually treated to remove a possible cause of future hypofertility. The only objective indication for treatment is testicular hypotrophy. Regarding pain, in our experience, only a few patients reported painful symptoms. Moreover, it is a completely subjective parameter and carries the risk of patients being unnecessarily treated. This clinical "error" could disprove many cases reported in published studies, in

which homolateral testicular pain was one of the indications for treatment.

Our study did not include patients with nonsurgically treated varicocele and testicular hypotrophy undergoing long-term observation (difficult to enroll). However, our data showed some interesting results. That no statistically significant differences were found among the three groups in terms of the number of patients with normal versus abnormal spermiogram findings and semen quality would indicate that patients affected by grade 2 and 3 varicocele without hypotrophy and pain (group 3) could undergo long-term observation by monitoring the testicular volume and performing a spermiogram when they attain 18 years of age. Also, the surgically treated patients with grade 2 and 3 varicocele without hypotrophy (group 2) do not have better semen quality than those who were not treated surgically (group 3). Finally, the patients surgically treated for varicocele because of associated testicular hypotrophy (group 1) might benefit from the treatment in terms of semen quality and the number of normal versus abnormal spermiogram findings. These considerations are mere hypotheses because the spermiograms were taken from patients undergoing varicocelectomy. It is not possible to perform long-term observations until the analysis of semen quality (when the patient attains 18 years of age) is performed on patients with testicular hypotrophy and, therefore, it has been assumed that all these patients will benefit from varicocelectomy. However, even if it is true that only patients with testicular hypotrophy need surgery, we also found that not all patients (whether surgically or nonsurgically treated) had normal spermiogram findings. Therefore, regardless of varicocele grade and testicular volume, other varicoceles would require surgery (abnormal spermiogram findings). Our study data showed that the semen quality of patients with a preserved artery was better than that in patients with full ligation. This was true only for those patients also affected by testicular hypotrophy, because we did not observe the same findings in the surgically treated patients with a normal testicular volume. Artery preservation (subgroups of groups 1 and 2) did not improve semen quality with respect to the nonsurgically treated patients (group 3). Consequently, the rationale for preserving the testicular artery in patients with testicular hypotrophy is not yet clear.

Many doubts still exist about the efficacy of treating pediatric varicocele. Published studies have only reported cases of varicocele, with or without hypotrophy, in adult patient. These studies have compared the preoperative and postoperative spermiogram findings, showing improvement in semen quality, even though some patients were still hypofertile after treatment of the varicocele, because of long-term stable gonadal damage.²³⁻²⁷ It is always difficult to determine the exact time of the onset of hypotrophy and, therefore, of the gonadal damage; however, patients with varicocele and no hypotrophy have also demonstrated alterations in the semen.

The relationship between hypofertility/infertility and varicocele will remain under discussion until it is possible to develop suitable diagnostic techniques for the early identification of those patients, with or without hypotrophy, who require surgical treatment.

CONCLUSIONS

It is necessary to perform additional randomized trials to show the importance of surgical procedures in the treatment of varicocele in pediatric patients. The analysis of data collected in this study showed that testicular hypotrophy remains the most objective indication for surgical treatment of varicocele. In published studies, the functional efficacy of artery preservation during varicocelectomy is still under discussion.²⁸⁻³⁰ We believe that the preservation of the testicular artery results in better semen quality than spermatic vessels ligation only in those patients affected by testicular hypotrophy.

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