



Is Semen Analysis Necessary for Varicocele Patients in Their Early 20s?

Choon Sig Kwon¹, Jun Ho Lee²

¹Department of Economics and Finance, College of Business Administration, Kwandong University, Gangneung, ²Department of Urology, National Police Hospital, Seoul, Korea

Purpose: To determine whether it is necessary to analyze the semen of varicocele patients in their early 20s who are not complaining of infertility.

Materials and Methods: Data was collected retrospectively from 128 men with varicocele with no complaint of infertility, but with complaints of pain/discomfort or a mass/swelling during a 4-year period beginning in January 2009. The varicocele cases were matched 4 : 1 by age to 32 hemospermia controls.

Results: The median patient age was 22.0 years in the case group and 24.0 years in the control group. The median values of the percentage of normal motility, normal morphology, and density in the case group were 42.5%, 40.0%, and $51.0 \times 10^6/\text{mL}$, respectively. The median serum testosterone level was 4.2 ng/mL and 7.0% of the total patients had low serum testosterone levels in the case group. The number of patients with asthenospermia (17.2%), oligospermia (10.9%), and teratospermia (5.5%), and those with at least one abnormal semen parameter (19.5%) was significantly higher in the case group than the control group. The median values of the motility, morphology, and density of the case group were significantly lower than those of the control group. The multivariate analysis showed that patient characteristics (age, presence of pain, duration of symptoms, and grade of varicocele) cannot help to predict abnormal semen parameters (asthenospermia, oligospermia, teratospermia, or cases of at least 1 abnormal semen parameter) or serum testosterone levels < 3.0 ng/mL.

Conclusions: Semen analysis is required as a screening test for semen abnormalities regardless of the chief complaint in varicocele patients in their early 20s.

Key Words: Infertility, male; Pain; Varicocele

INTRODUCTION

Varicoceles are abnormal dilatations of the pampiniform venous plexus in the spermatic cord. Varicocele is found in 12% of the general population and 25% to 40% of infertile men [1,2]. A varicocelectomy, by itself or in

conjunction with *in vitro* fertilization, is cost-effective as compared to intracytoplasmic sperm injection and intra-uterine insemination [3,4]. A recent article also revealed that varicocele is associated with hypogonadism in some infertile patients, and varicocelectomy significantly improves serum testosterone levels [5].

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Correspondence to: Jun Ho Lee

Department of Urology, National Police Hospital, 123 Songi-ro, Songpa-gu, Seoul 138-708, Korea.
Tel: +82-2-3410-1266, Fax: +82-2-431-3192, E-mail: sinbanpolee@gmail.com

However, whether semen analysis should be performed at the time of the first visit for young varicocele patients who do not complain of infertility is unclear from the existing research.

Thus, this retrospective chart review study sought clarification by evaluating the ratio of abnormal semen parameters and serum testosterone levels in young varicocele patients (≤ 25 years of age) who did not have complaints of infertility and compared these parameters with a hemospermia control group. Additionally, we identified predicting factors for abnormal semen parameters and serum testosterone levels in the varicocele group.

MATERIALS AND METHODS

1. Materials

The institutional review board of the National Police Hospital approved this study in January 2013. Data was collected retrospectively on 158 men (≤ 25 years of age) with varicocele who did not have complaints of infertility, but did complain of pain/discomfort or a mass/swelling during a 4-year period beginning in January 2009. Among the 158 patients, semen analysis was performed and the serum testosterone level was checked simultaneously in 137 patients. Patients who had other possible causes of abnormal semen parameters and testosterone levels such as chronic hepatitis ($n = 1$), tuberculosis ($n = 1$), pituitary adenoma ($n = 1$), use of antipsychotic medication ($n = 1$), and previous scrotal surgery ($n = 5$) were excluded. In the end, the data of 128 patients was included in the study.

The evaluation of the patients included a complete history, physical examination, semen analysis, and measurement of the serum testosterone concentration. The varicocele was graded as grade I (palpable only with the Valsalva maneuver), grade II (palpable without Valsalva), and grade III (visible from a distance) [6]. The serum level of testosterone was checked in the morning (between 8:00 and 11:00 a.m.). The semen analysis was performed after a 3-day abstinence from ejaculation. All of the semen specimens were collected and analyzed according to World Health Organization (WHO) criteria in a single testing laboratory [7]. Asthenospermia was defined as WHO grade a+b sperm motility $< 50\%$ and $< 25\%$, respectively. Additionally, oligospermia and teratospermia were de-

defined as sperm concentrations of $< 20 \times 10^6$ sperm/mL and $< 15\%$ normal morphology (by strict criteria), respectively.

The control group included men visiting the clinic for hemospermia during a period of 4 years beginning in January 2009. Among these patients, those with other possible causes of abnormal semen parameters and testosterone levels were excluded. We excluded men with the aforementioned conditions because the serum testosterone level could have affected the analysis of semen, though we did not check the serum testosterone levels in the control group. Using age (less than 5 years' difference), 32 hemospermia controls were matched 1 to 4 with 128 varicocele cases.

2. Statistical analyses

The median values of the sperm parameters and ratios of asthenospermia, oligospermia, and teratospermia, patients with at least one abnormal semen parameter, and the serum testosterone levels of < 3.0 ng/mL were calculated [8]. We compared the median values of the semen parameters and ratios of asthenospermic, oligospermic, and teratospermic cases, and the patients with at least 1 abnormal semen parameter between the varicocele group and the hemospermia control group.

The associations of asthenospermia, oligospermia, teratospermia, and the patients with at least one abnormal semen parameter or a serum testosterone level of < 3.0 ng/mL with patient characteristics (age, presence of pain, duration of symptoms, or grade of varicocele) were evaluated to determine predicting factors for the abnormal semen parameters and the serum testosterone levels.

A Mann-Whitney test, Fisher's exact test, and multiple logistic regression analysis were conducted using SPSS version 15.0 for Window (SPSS, Chicago, IL, USA). $p < 0.05$ was considered statistically significant.

RESULTS

The median patient age was 22.0 years in the varicocele group. Eighty-six patients complained of scrotal pain or discomfort. The median percentages of normal motility and morphology, and the median density were 42.5%, 40.0%, and 51.0×10^6 /mL, respectively. The median serum testosterone level was 4.2 ng/mL (Table 1). The sperm

Table 1. Patient characteristics

Characteristic	Varicocele group (n=128)	Hemospermia group (n=32)
Age (yr) ^a	22.0 (22.0~23.0)	24.0 (23.0~28.0)
Grade		
I	15 (11.7)	-
II	26 (20.3)	-
III	87 (68.0)	-
Symptom duration (mo)	9.0 (3.0~24.0)	-
Reason for visit		
Pain or discomfort	86 (67.2)	-
Swelling or mass	42 (32.8)	-
Semen analysis		
pH	8.0 (8.0~8.0)	8.0 (8.0~8.0)
Volume (mL)	3.0 (2.0~4.0)	3.5 (3.0~4.0)
Motility (%) ^a	42.5 (30.0~60.0)	75.0 (65.0~80.0)
Morphology (%) ^a	40.0 (35.0~60.0)	65.0 (55.0~80.0)
Density ($\times 10^6$ /mL) ^a	51.0 (42.0~81.0)	80.0 (68.0~126.0)
Testosterone (ng/mL)	4.2 (3.3~5.6)	-

Values are presented as median (interquartile range) or number (%).

^a $p < 0.05$.

Table 2. Comparisons of semen parameters and serum testosterone levels between the varicocele group and hemospermia (control) group

Variable	Varicocele group (n=128)	Hemospermia group (n=32)
Semen parameter		
Asthenospermia ^a	22 (17.2)	2 (6.3)
Oligospermia ^a	14 (10.9)	1 (3.1)
Teratospermia ^a	7 (5.5)	0 (0.0)
Patients with at least one abnormal semen parameter ^a	25 (19.5)	2 (6.3)
Hormonal assay		
Testosterone < 3.0 ng/mL	9 (7.0)	-

Values are presented as number (%).

Asthenospermia: World Health Organization grade a+b sperm motility $< 50\%$ and a $< 25\%$, Oligospermia: sperm concentration $< 20 \times 10^6$ sperm/mL, Teratospermia: $< 30\%$ normal morphology.

^a $p < 0.05$.

motility, morphology, and density differed significantly between the two groups ($p < 0.05$).

The leading semen abnormality in the varicocele patients was asthenospermia (17.2%), followed by oligospermia (10.9%) and teratospermia (5.5%). A total of 19.5% of the varicocele patients had at least one abnormal semen parameter. The ratios of asthenospermia, oligo-

spermia, teratospermia, and the patients with at least one abnormal semen parameter were significantly higher than those of the hemospermia control group. In terms of the serum testosterone level, 7.0% of the total patients had a low serum testosterone level (Table 2).

Based on the multivariate analysis, the patient characteristics (age, presence of pain, duration of symptoms, and grade of varicocele) did not correlate with the abnormal semen parameters (asthenospermia, oligospermia, teratospermia, or cases with at least 1 abnormal semen parameter) or a serum testosterone level < 3.0 ng/mL (Table 3).

DISCUSSION

We evaluated the ratio of the abnormal semen parameters in the varicocele patients who did not have a complaint of infertility and compared them with a hemospermia control group. Furthermore, we searched for predicting factors for abnormal semen parameters. The data showed that 19.5% of the patients had at least one abnormal semen parameter. The sperm motility, morphology, and density of the two groups were significantly different. Additionally, age, grade of varicocele, duration of symptoms, and symptoms of pain/discomfort or a swelling/mass did not independently predict the presence of abnormal semen parameters.

Table 3. Multivariate analysis of prediction factors for abnormal semen parameters and serum testosterone levels

Variable	OR	95% CI	p value
Oligospermia			
Age	1.098	0.987~1.222	0.086
Reason for visit			
Swelling or mass	1.000	Reference	
Pain or discomfort	1.372	0.295~6.386	0.687
Symptom duration	1.004	0.979~1.029	0.763
Grade			
I~II	1.000	Reference	
III	0.513	0.085~3.093	0.467
Asthenospermia			
Age	1.068	0.966~1.182	0.2
Reason for visit			
Swelling or mass	1.000	Reference	
Pain or discomfort	1.032	0.281~3.793	0.962
Symptom duration	0.993	0.967~1.020	0.63
Grade			
I~II	1.000	Reference	
III	0.588	0.138~2.501	0.473
Teratospermia			
Age	0.753	0.360~1.575	0.451
Reason for visit			
Swelling or mass	1.000	Reference	
Pain or discomfort	5.274	0.360~77.203	0.225
Symptom duration	1.018	0.974~1.063	0.429
Grade			
I~II	1.000	Reference	
III	1.201	0.094~15.297	0.888
Cases with at least one abnormal semen parameter			
Age	1.004	0.884~1.141	0.945
Reason for visit			
Swelling or mass	1.000	Reference	
Pain or discomfort	0.210	0.023~1.906	0.165
Symptom duration	0.983	0.944~1.023	0.402
Grade			
I~II	1.000	Reference	
III	0.757	0.154~3.720	0.732
Testosterone<3.0 ng/mL			
Age	0.922	0.718~1.184	0.525
Reason for visit			
Swelling or mass	1.000	Reference	
Pain or discomfort	0.576	0.117~2.834	0.498
Symptom duration	1.013	0.983~1.045	0.386
Grade			
I~II	1.000	Reference	
III	5.059	0.859~29.791	0.073

Asthenospermia: World Health Organization grade a+b sperm motility <50% and a <25%, Oligospermia: sperm concentrations <20×10⁶ sperm/mL, Teratospermia: <30% normal morphology. Statistical analysis performed using multiple logistic regression analysis; differences between groups considered statistically significant at p<0.05.

OR: odds ratio, CI: confidence interval.

The literature is scant concerning semen analysis in varicocele patients who complain of scrotal pain/discomfort or a swelling/mass. A retrospective study recruiting 202 varicocelectomy patients with no history of infertility (mean age 23.5 years; range 15.0 to 35.0 years) demonstrated that 90.6% of the patients had oligospermia ($<20 \times 10^6$ sperm/mL) [9]. Another similar study enrolled 268 varicocelectomy patients (mean age 24.5 ± 6.0 years) with no complaints of infertility but complaints of pain or swelling; 63.1% of the patients had at least one abnormal semen parameter on initial semen analysis. The authors concluded that semen analysis should be performed in men with clinical varicocele regardless of the chief complaint [10]. However, the data from the aforementioned studies concerned varicocelectomy patients, which could have introduced a potential selection bias. Data from a study conducted in Austria, which analyzed 716 infertile varicocele patients, reported that about 66.7% had at least one abnormal semen parameter. The fact that the ratio of sperm abnormality was similar to or higher than the data from the patients with infertility and varicocele supports our claim of bias. In the present study, approximately 20% of the patients had at least one abnormal semen parameter. To our knowledge, the data concerning the ratio of abnormal semen parameters in a young, healthy population is scant. Therefore, we compared the semen parameters with a hemospermia control group. The data suggest that the number of cases of asthenospermia, oligospermia, teratospermia, and patients with at least one abnormal semen parameter was significantly higher in the varicocele group as compared to the hemospermia control group. Additionally, the median value of the percentage of normal motility, normal morphology, and density was 42.5%, 40.0%, and 51.0×10^6 /mL, respectively, which are all lower than the corresponding values in the hemospermia control group. We believe that these data could be evidence that semen analysis is necessary in varicocele patients who do not complain of infertility in order to identify potentially infertile young men and counsel and treat them.

The median serum testosterone level was 4.2 ng/mL, and 7.0% of the total patients had low serum testosterone levels. There is scant androgen data available from healthy young individuals with which to compare our results.

Further clinical data are needed to define the usefulness of serum testosterone as a screening test for semen abnormalities in varicocele patients in their early 20s who are not complaining of infertility.

In the present study, age, grade of varicocele, duration of symptoms, and symptoms of pain/discomfort or a swelling/mass did not significantly and independently predict the abnormal semen parameters and the serum testosterone levels. Recent studies that enrolled infertile varicocele patients have highlighted the controversy concerning the relationship between varicocele grade and the degree of spermatogenic dysfunction [11-14]. The other factors (e.g., age, duration of symptoms, and symptoms of pain/discomfort or a swelling/mass) have been poorly investigated as prognostic factors. It seems that there are no definite predicting factors for abnormal semen parameters (asthenospermia, oligospermia, teratospermia, or cases with at least 1 abnormal semen parameter) or serum testosterone levels. These results indirectly support the view that semen analysis is needed as a screening test for semen abnormalities because there are no specific patient characteristics or physical findings that predict such abnormalities.

A meta-analysis that included 17 studies indicated that surgical varicocelectomy significantly improves the semen parameters in infertile men with palpable varicocele [15]. Varicocele patients without any evidence of infertility as well as infertile men with palpable varicocele and abnormal semen parameters showed significant improvement after microsurgical varicocelectomy [9,10]. It seems clear that varicocelectomy improves semen parameters regardless of the chief complaint. We think that this is additional evidence that semen analysis is needed as a screening test for semen abnormalities regardless of the chief complaint.

Several limitations of the present study warrant mention. First, the cross-sectional nature of the dataset makes causal inferences problematic. Second, the control group in this study was not healthy men, but rather those with hemospermia. Third, the age was significantly different between the case and control group, although the difference between the two groups was minimal (less than 2 years). Well-designed follow-up studies are needed. In addition, as this study consisted of data from a single institution, there may be a potential for selection bias.

Finally, the data of our study were limited to those in their early 20s. Further research including other age groups would be more informative for generalizing our results.

CONCLUSIONS

In the present study, 19.5% of patients had at least one abnormal semen parameter. The leading abnormality was asthenospermia, followed by oligospermia and teratospermia. Additionally, 7.0% of the total patients had a low serum testosterone level. We could not find a predicting factor for the abnormal semen parameters. Therefore, semen analysis would be warranted as a screening test for semen abnormalities regardless of the chief complaint in young varicocele patients. Future investigations should explore the role of semen analysis and testosterone evaluation in young men with varicocele. The confirmation of the aforementioned results in a multi-center prospective longitudinal data set would be informative.

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