



Does the type of infertility affect varicocelelectomy efficacy?

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Introduction. Varicocele is recognized as the most prevalent and treatable factor contributing to both primary (PI) and secondary (SI) male infertility. This condition has been widely studied due to its impact on fertility, and varicocelelectomy is a commonly employed surgical intervention aimed at improving reproductive outcomes.

Objectives. The purpose of this study was to evaluate and compare the effectiveness of varicocelelectomy in men with primary and secondary infertility, focusing on changes in semen parameters post-surgery.

Materials and Methods. This prospective single center study included men diagnosed with PI ($n = 22$) and SI ($n = 28$), who underwent varicocelelectomy at the Republican Specialized Scientific-Practical Medical Center of Urology between January 2021 and December 2022. Semen parameters before and after varicocelelectomy were assessed in accordance with the WHO 5th (2010) and 6th (2021) manuals.

Results. Our analysis demonstrated that patients in group I were significantly younger ($p < 0.001$) and experienced a shorter infertility duration ($p < 0.01$) compared to those in group II. Key semen parameters showed notable improvement in group I; for instance, sperm concentration rose by 50 %, from 62.2 ± 8.7 to 93.5 ± 10.0 M/ml, while total motile sperm count increased by 113 %, from 76.7 ± 17.1 to 163.4 ± 27.8 M ($p < 0.05$). In contrast, group II showed a significant increase only in the percentage of progressive motile sperm (up by 107 %, from 13.5 ± 2.6 to 28.0 ± 5.2 %, $p < 0.05$). A notable distinction was observed in the improvement of total motile sperm count between groups I and II (113 % vs. 74 %, respectively, $p < 0.01$). Additionally, a difference was identified between the groups in the correlation coefficient (r) for the initial and post-surgery percentages of progressive motile sperm.

Conclusions. Patients with SI presented with a higher mean age and longer infertility duration than those with PI. Varicocelelectomy led to significant improvements in key semen parameters in patients with PI, whereas for patients with SI, the procedure primarily enhanced only the percentage of progressive motile sperm. These findings indicate that the type of infertility may influence the effectiveness of varicocelelectomy, but only in the context of differences in age and duration of infertility between these groups.

Keywords: varicocele, varicocelelectomy, semen analysis, primary male infertility, secondary male infertility

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Влияет ли тип бесплодия на эффективность варикоцелэктомии?

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Введение. Варикоцеле является наиболее распространенной и поддающейся лечению причиной как первичного (ПБ), так и вторичного (ВБ) мужского бесплодия. Учитывая его влияние на фертильность, варикоцеле до сих пор широко изучается, и варикоцелэктомия часто используется как хирургическое решение для улучшения репродуктивных показателей.



Цель исследования. Цель данного исследования заключалась в оценке и сравнении эффективности варикоцелэктомии у мужчин с ПБ и ВБ с акцентом на изменения параметров спермы после операции.

Материалы и методы. В проспективное одноцентровое исследование были включены мужчины с диагнозом ПБ (группа 1, $n = 22$) и ВБ (группа 2, $n = 28$), прошедшие варикоцелэктомию в Республиканском специализированном научно-практическом медицинском центре урологии с января 2021 г. по декабрь 2022 г. Параметры спермы до и после варикоцелэктомии были проанализированы в соответствии с 5-м (2010 г.) и 6-м (2021 г.) руководствами ВОЗ.

Результаты. Анализ показал, что пациенты в группе 1 были значительно моложе ($p < 0,001$) и имели меньшую продолжительность бесплодия ($p < 0,01$), чем пациенты в группе 2. В группе 1 основные параметры спермы значительно улучшились; например, концентрация сперматозоидов увеличилась на 50 % с $62,2 \pm 8,7$ до $93,5 \pm 10,0$ млн/мл, а общее количество подвижных сперматозоидов возросло на 113 % с $76,7 \pm 17,1$ до $163,4 \pm 27,8$ млн ($p < 0,05$). В то время как в группе 2 значительное улучшение наблюдалось только в проценте прогрессивно подвижных сперматозоидов (на 107 % с $13,5 \pm 2,6$ % до $28,0 \pm 5,2$ %, $p < 0,05$). Заметное различие было выявлено в улучшении общего количества подвижных сперматозоидов между группами 1 и 2 (113 % против 74 % соответственно, $p < 0,01$). Также отмечено различие в коэффициенте корреляции (r) между начальными и послеоперационными процентами прогрессивно подвижных сперматозоидов между группами.

Заключение. У пациентов с ВБ был выше средний возраст и более длительный период бесплодия по сравнению с пациентами с ПБ. Варикоцелэктомия привела к значительным улучшениям основных параметров спермы у пациентов с ПБ, тогда как у пациентов с ВБ процедура в основном улучшила только процент прогрессивно подвижных сперматозоидов. Эти результаты указывают на то, что тип бесплодия может влиять на эффективность варикоцелэктомии, но только в контексте различий в возрасте и длительности бесплодия между этими группами.

Ключевые слова: варикоцеле, варикоцелэктомия, анализ спермы, первичное мужское бесплодие, вторичное мужское бесплодие

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Introduction

In recent years, growing attention has been focused on uncovering the underlying causes of male infertility, with varicocele identified as a major, treatable factor contributing to both primary and secondary infertility. As a result, varicocele repair remains one of the most commonly performed surgical procedures for addressing male reproductive issues [1]. Studies indicate that varicocele is present in 33–40 % of men with primary infertility and can be found in up to 81 % of men with secondary infertility [2].

Recent randomized controlled trials (RCTs) and meta-analyses have shown that varicocele repair, or varicocelectomy, in patients with clinical varicocele and semen abnormalities significantly improves pregnancy rates and semen quality compared to observation-only (control) groups [3–6]. Other RCTs, however, have indicated limited efficacy of varicocelectomy in cases of subclinical varicocele and normal semen parameters [7].

According to a comprehensive review by Ricardo Miyaoka and colleagues, microsurgical ligation of the spermatic cord veins (using inguinal and subinguinal approaches) is considered the most effective surgical option for treating clinical varicocele associated with infertility [8]. Teruo Fukuda and his team studied 71 infertile men who underwent microsurgical varicocelectomy, with semen analysis performed three times: before the procedure, and at 3 and 12 months post-surgery. Findings revealed

significant improvement in semen quality three months after surgery, with no substantial differences between parameters at the 3- and 12-month follow-ups [9].

In a separate study, Walsh et al. concluded that men with primary and secondary infertility who have varicocele may exhibit distinct clinical characteristics, including differences in semen parameters. In particular, men with secondary infertility demonstrated significantly higher sperm concentration [10].

Given these findings, our study aimed to examine initial semen parameters and the effectiveness of varicocelectomy in men with primary and secondary infertility, organizing participants into two separate groups for comparison.

Materials and methods

Ethics Approval and Informed Consent Statements

The Institutional Review Board of the Republican Specialized Scientific-Practical Medical Center of Urology approved the data collection and analysis for this study (Protocol № 8/21, dated January 25, 2021). All procedures followed the ethical principles of the Declaration of Helsinki and adhered to Good Clinical Practice guidelines. A total of 50 patients who provided written informed consent were included in the final analysis.

Study Design

This prospective, single-center study assessed key semen parameters, including semen volume (ml), sperm



concentration (million/ml), total sperm count (million), percentage of progressively motile sperm, total motility (%), and total motile sperm count (TMC), in accordance with the 5th and 6th WHO manuals for semen analysis examination [11, 12]. The presence of varicocele was confirmed through visual inspection, palpation, and Doppler ultrasound of the testis, classified based on the 2000 WHO grading system for varicocele (subclinical, grades I, II, and III) [13].

Patients

The study included participants based on specific inclusion and exclusion criteria.

Inclusion criteria:

- Patients who underwent semen analysis before and 3–6 months after varicocelectomy.
- Presence of at least one abnormal semen parameter.
- Clinical varicocele diagnosis (grades I–III).
- Patients with a history of unsuccessful conception attempts in their partners for 12 months or longer.

Exclusion criteria:

- Patients diagnosed with azoospermia or normozoospermia.
- Patients with infertility due to causes other than varicocele.

Based on these criteria, men with primary infertility (PI) ($n = 22$) and secondary infertility (SI) ($n = 28$) who underwent varicocelectomy at the Republican Specialized Scientific Practical Medical Center of Urology between January 2021 and December 2022 were included in the study. Participants were divided into two groups: 22 men with PI (ages 21 to 33) formed group I, and 28 men with SI (ages 24 to 46) formed group II.

Intervention (Procedure)

All patients underwent microsurgical subinguinal or inguinal varicocelectomy, performed by experienced surgeons. In the subinguinal approach, a 2–4 cm incision was made below the external inguinal ring, while in the inguinal method, the incision was made above the inguinal canal. The spermatic cord was isolated, with veins carefully separated from arteries, lymphatic vessels, and the vas deferens, and ligated under high magnification using surgical loupes or a microscope.

Statistics

Statistical analysis was performed using MS Office Excel 2019. All numerical data were presented as mean $\pm$ standard deviation (SD). The significance of differences between group means was tested using Student's t -test, with significance considered at $p < 0.05$. Pearson's correlation coefficient (r) was applied to assess correlations between variables.

Results

The analysis demonstrated that the mean age of patients in group I was significantly lower compared to those in group II ($p < 0.001$), indicating that men with primary infertility tend to be younger than those with secondary infertility. Additionally, the mean duration of infertility in group I was notably shorter than in group II ($p < 0.01$), suggesting a more prolonged period of infertility among patients with secondary infertility. These differences in age and duration of infertility between the two groups highlight the potential influence of age and infertility duration on treatment outcomes (see Table 1 for detailed statistics).

Furthermore, the majority of patients in this study were diagnosed with left-sided varicocele, with 43 out of 50 patients (86 %) exhibiting this condition. Left-sided varicocele is generally more common due to anatomical differences in venous drainage, which may contribute to higher susceptibility in the left testis. This predominance of left-sided varicocele across the sample aligns with findings in previous studies, which report a similar distribution pattern (Table 1).

In terms of body mass index (BMI), the analysis showed varied distributions across the patient group. A total of 18 patients (36 %) had a BMI slightly above the normal range (25.0–30.0), classifying them as pre-obese. Another 9 patients (18 %) had a BMI significantly above the normal range (> 30.0), which qualified them as obese. Meanwhile, 23 patients (46 %) had a BMI within the normal range (18.5–25.0), indicating a healthy weight [14]. Consequently, over half of the patients (27 out of 50, or 54 %) fell into either the pre-obese or obese categories.

The following table (Table 2) presents a statistical comparison of the primary semen parameters of patients in both groups prior to surgery. This baseline assessment includes parameters such as semen volume, sperm concentration, total sperm count, percentage of progressively motile sperm, total motility, and total motile sperm count. These values were crucial for evaluating the initial reproductive health of the patients and for later assessing the impact of varicocelectomy across the two groups.

As shown in Table 2, no statistically significant differences were observed in the initial semen parameters between the two groups. This lack of significant variation suggests that both groups had comparable baseline semen characteristics, allowing for a more reliable comparison of varicocelectomy outcomes.

Table 3 presents the preoperative and postoperative semen parameters for both groups, enabling a thorough evaluation of varicocelectomy efficacy. This table facilitates comparison not only of changes within each group before and after the procedure but also between the groups. By examining these parameters postoperatively, we aim to assess the improvements in semen quality attributable to varicocelectomy and determine if the outcomes differ based on the type of infertility (primary vs. secondary).



Table 1. Key features of group of patients

Groups	Age M ± m	Anthropometric data			Varicocele in abs. (and in %)*						Duration of infertility (in months) M ± m
		Height	Weight	BMI**	Side			Grade			
					Left	Right	Bilateral	I	II	III	
First	27.4 ± 0.6	1,7	81.2	26.8	20 (91)	—	2 (9)	8 (29)	19 (68)	1 (3)	28.7 ± 4.6
Second	31.0 ± 0.6	1.7	79.9	26.5	23 (82)	1	4 (5)	5 (23)	15 (68)	2 (9)	51.8 ± 5.6
P	< 0.001	—	—	—	—	—	—	—	—	—	< 0.01
Total	—	—	—	—	43 (86)	1 (2)	6 (12)	8 (20)	34 (68)	3 (6)	—

* data are given in absolute numbers and in % (in brackets) in relation to the group.

** body mass index.

Table 2. Main preoperative semen parameters of both groups

Groups	Semen volume, ml M ± m	Sperm concentration (M/ml) M ± m	Total sperm count (M) M ± m	Sperm with progressive motility (%) M ± m	Total sperm motility (%) M ± m	Total motile sperm count (M) M ± m
First	3.4 ± 0.3	62.2 ± 8.7	213.6 ± 35.9	11.4 ± 2.3	30.8 ± 3.6	76.7 ± 17.1
Second	3.7 ± 0.3	47.2 ± 8.6	171.9 ± 33.5	13.5 ± 2.6	35.1 ± 4.6	76.3 ± 19.2
p	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

Table 3. Assessment of pre- and postsurgical main semen parameters of both groups

Groups	Semen volume, ml M ± m	Sperm concentration (M/ml) M ± m	Total sperm count (M) M ± m	Sperm with progressive motility (%) M ± m	Total sperm motility (%) M ± m	Total motile sperm count (M) M ± m
First ¹	3.4 ± 0.3	62.2 ± 8.7	213.6 ± 35.9	11.4 ± 2.3	30.8 ± 3.6	76.7 ± 17.1
First ²	3.4 ± 0.2	93.5 ± 10.0	341.8 ± 46.6	20.0 ± 3.1	46.1 ± 4.5	163.4 ± 27.8
p ³	> 0.05	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05
Second	3.7 ± 0.3	47.2 ± 8.6	171.9 ± 33.5	13.5 ± 2.6	35.1 ± 4.6	76.3 ± 19.2
Second	3.9 ± 0.3	65.7 ± 10.2	246.9 ± 40.8	28.0 ± 5.2	46.0 ± 6.0	132.7 ± 31.3
p	> 0.05	> 0.05	> 0.05	< 0.05	> 0.05	> 0.05
p ⁴	> 0.05	> 0.05	> 0.05	< 0.01	> 0.05	< 0.01

¹ preoperative period; ² postoperative period; ³ statistically significant changes; ⁴ statistically significant differences between groups.

In the postoperative period, the following average changes were observed in the semen parameters for both groups:

- Semen volume remained largely unchanged in both groups ($p > 0.05$).
- Sperm concentration showed a significant increase in group I (by 50 %, $p < 0.05$), while in group II, the increase was not statistically significant (by 39 %, $p > 0.05$).
- Total sperm count rose by 60 % in group I ($p < 0.05$), whereas in group II, this parameter increased by 44 %, but without statistical significance ($p > 0.05$).
- The percentage of sperm with progressive motility increased more substantially in group II (by 107 %, $p < 0.05$) than in group I (by 75 %, $p < 0.05$), with a significant difference between the groups ($p < 0.01$).
- Total sperm motility showed a significant rise in group I (by 50 %, $p < 0.05$), while in group II, this parameter

also increased but without statistical significance (by 31 %, $p > 0.05$).

- Total motile sperm count increased more significantly in group I (113 %, $p < 0.01$) compared to group II (74 %, $p < 0.05$ vs. $p > 0.05$ respectively).

As shown above, statistically significant differences emerged between the groups in changes to some postoperative semen parameters. For patients in group I, varicocelectomy led to significant improvements across all semen parameters. In contrast, among patients in group II, a statistically significant improvement was observed only in the percentage of sperm with progressive motility, which showed a greater increase than that in group I.

Additionally, a notable discrepancy was found between the groups in the correlation coefficient (r) between initial and postoperative percentages of sperm with progressive motility. In group I, there was no correlation ($r = -0.02$),



whereas in group II, the correlation was direct and strong ($r = 0.71$). Overall, the difference in mean correlation coefficients between initial and postoperative semen parameters was not statistically significant ($r = 0.4$ for group I and $r = 0.5$ for group II).

Discussion

Varicocele remains the most common surgically treatable cause of male infertility. Although substantial research supports the beneficial impact of varicocele repair on sperm parameters, the actual effect of surgery on testicular function is still a matter of debate [3, 4, 15]. Despite this uncertainty regarding the precise relationship between improvements in semen parameters and varicocelectomy, a meta-analysis of randomized controlled trials (RCTs) by Agarwal et al. reported significant enhancement in semen parameters following varicocelectomy [15], which aligns with our study's findings. Interestingly, greater improvements were observed in patients with primary infertility and varicocele compared to those with secondary infertility and varicocele, though positive effects were also noted in the latter group.

Several studies have examined the relationship between initial semen parameters and the efficacy of varicocele repair. These reports suggest that men with higher baseline semen parameters may experience more pronounced improvements after varicocelectomy [16, 17]. Our study partially supports this hypothesis, as a moderate association was found between preoperative and postoperative semen parameters.

It is also noteworthy that, as some studies indicate, the average age of men with secondary infertility tends to be higher, which is consistent with our findings. However, while these studies report no significant differences in the duration of infertility between groups, our research identified a notable disparity in this parameter [10, 17, 18]. Additionally, the aforementioned authors highlight differences in baseline semen parameters among patients with secondary infertility, though our analysis found no statistically significant differences in initial semen characteristics between men with primary and secondary infertility.

Research by Bozhedomov et al. and others suggests that varicocele is slightly more prevalent in men with secondary infertility than in those with primary infertility, with a small difference of +3.5 % ($p < 0.05$). They also report that patients with primary and secondary infertility are of comparable age, a finding that contrasts with our results [1].

Another ongoing question is the actual influence of infertility type and other factors on varicocelectomy outcomes. Some recent studies suggest that infertility type may adversely impact varicocelectomy success, particularly in the context of age and infertility duration differences between patient groups [17]. Other researchers, however, have concluded that infertility type does not significantly influence the success of varicocele repair [19–23].

A primary limitation of our study was the relatively small sample size, which contributed to differences in mean age and duration of infertility between the two groups. Patients in the secondary infertility group were generally older and had a longer history of infertility compared to those in the primary infertility group. Despite these limitations, the results still provide valuable insights into the effectiveness of varicocelectomy for primary and secondary infertility. The observed improvements, especially in patients with primary infertility, align with previous research and underscore the significance of varicocelectomy as a treatment option. Further studies with larger sample sizes and matched age and infertility duration across groups are recommended to clarify these effects and strengthen the findings.

Conclusions

Patients with secondary infertility and varicocele were older and had a longer infertility duration compared to those with primary infertility. Varicocelectomy significantly improved main semen parameters in patients with primary infertility, while in those with secondary infertility, only the percentage of progressively motile sperm showed significant improvement. A positive correlation was observed between initial semen quality and varicocelectomy efficacy, with higher baseline parameters linked to better surgical outcomes. These findings suggest that the type of infertility may influence the effectiveness of varicocelectomy, but only in the context of differences in age and duration of infertility between these groups.

Declarations

Ethics approval and consent to participate

The study was approved by the Republican Specialized Scientific and Practical Medical Center of Urology ethics committee (№ 8/21 from January 25, 2021).

Consent for publication

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