Microsurgical Subinguinal Varicocele Repair of Grade II–III Lesions Associated with Improvements of Testosterone Levels

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Key Words
Hypogonadism • Microsurgery • Varicocele repair • Testosterone

Abstract
Introduction: The results of reports on the association between varicocele repair and testosterone levels were conflicting. The aim of the present study is, therefore, to investigate the impact of varicocele repair on testosterone levels.

Materials and Methods: The study is based on 20 men who experienced microsurgical subinguinal varicoceles repair because of chronic dull scrotal pain. All hormonal profiles available in the clinical records were reviewed. Follow-up evaluation was done at 1 and 12 months after surgery. Men were classified into groups based on the preoperative testosterone levels: euogonadal (serum levels of testosterone > 12 nmol/l), hypogonadal men (serum levels of testosterone ≤ 12 nmol/l).

Results: Microsurgical subinguinal varicocele repair was associated with a significant improvements of testosterone levels at 1 and 12 months after surgery as compared to the preoperative levels (13 nmol/l vs. 18 nmol/l, p = 0.03; 13 nmol/l vs. 15 nmol/l, p = 0.01). The same trend was seen in men who were classified as being hypogonadal (7.0 nmol/l vs. 15 nmol/l, p = 0.01; 7.0 nmol/l vs. 10 nmol/l, p = 0.02). No significant improvements in testosterone levels were observed in euogonadal men (p > 0.05).

Conclusion: Microsurgical subinguinal varicocele repair was associated with a significant improvements of testosterone levels in men with grade II–III lesions and low preoperative testosterone values.

Introduction

Varicocele defined as dilatation of the pampiniform plexus of veins surrounding the testis is observed in 10–15 % of the general male population, in 20–40 % of the infertile men [1], and in 2–14 % of men with scrotal pain [2, 3]. Several studies have reported significant improvements in semen quality and pregnancy rate [4, 5], and scrotal pain [6–8] following repair of clinical varicoceles.

The association between clinical varicocele and hypogonadism has been accepted, although the exact pathophysiology of the process remains uncertain. However, the primary hypotheses involved hyperthermia, venous pressure, toxin substances, and apoptosis [9–12]. Moreover, the results of reports on the association between varicocele repair and testosterone levels were conflicting, indicating no association [13–16] or a positive association [17–21]. This contradictory could be attributed...
to the different methods of classification of men based on their preoperative testosterone levels among different studies. Many studies that failed to demonstrate a positive association between varicocele repair and testosterone levels did not characterize patients with low preoperative testosterone levels.

The aim of the present study is to investigate the impact of microsurgical varicocele repair on testosterone levels based on data from 20 men who had the microsurgical subinguinal varicoceles repair because of chronic dull scrotal pain. All hormonal profiles available in the clinical records were reviewed.

**Materials and Methods**

The present study was based on 20 men who had the microsurgical subinguinal varicoceles repair because of chronic dull scrotal pain from April 2014 to August 2014 at the Department of Urology, Ystad hospital. Preoperative evaluation was including detailed medical history; assessment of scrotal pain; scrotal examination including measurement of testicular size using orchidometer, assessment of the epididymis with respect to its consistency and any pain on palpation, and evaluation of the spermatic cord for the presence of varicocele and its location (left, right, bilateral). Varicoceles were assigned to grades I–III during examination while the patients in a standing position according to the criteria [22] as follow: grade I, palpable only with Valsalva; grade II, palpable without Valsalva; and grade III, visible from distance.

Patients who had other causes of scrotal pain such as testicular trauma, testicular torsion, epididymitis, prostatitis, and sexually transmitted diseases were excluded. Only patients with clinical varicocele and chronic dull scrotal pain were included and were scheduled for microsurgical subinguinal varicocele repair. None of the men were taking hormonal or other kinds of treatment for male infertility or hypogonadism.

Our technique of microsurgical subinguinal varicocele repair was previously described [7]. All hormonal profiles available in the clinical records including testosterone, luteinizing hormone (LH), sex-hormone-binding (SHBG), and testosterone/SHBG ratio were reviewed. Testosterone was obtained before 10 a.m. Follow-up was done at 1 and 12 months after surgery.

**Statistical Analyses**

Statistical analyses were done using the SPSS software version 16 (SPSS, Inc; Chicago, IL). For the comparison of the preoperative and postoperative levels of LH, testosterone, SHBG, and testosterone/SHBG ratio paired-sample t tests were used. In order to estimate factors that could affect testosterone changes after surgery, the analyses were stratified for varicocele grade (grade II vs. grade III) and the age of men (< 40 vs. ≥ 40 years). Thereafter, men were classified according to the preoperative testosterone values into 2 groups: euogonadal (serum levels of testosterone > 12 nmol/l) and hypogonadal men (serum levels of testosterone 12 nmol/l), based on the cutoff level set by [23], and postoperative changes in testosterone levels were compared to the preoperative values using paired-sample t tests. P-values less than 0.05 were considered statistically significant.

**Results**

Descriptive statistics of the study population is presented in table 1. Overall, microsurgical subinguinal varicocele repair was associated with a statistically significant higher levels of testosterone at 1 and 12 months after surgery as compared to the preoperative levels (13 vs. 18 nmol/l, p = 0.03; 13 vs. 15 nmol/l, p = 0.01). The same trend was found regarding serum levels of LH (3.0 vs. 5.0 IE/l, p = 0.01; 3.0 vs. 5.0 IE/l, p = 0.04). On the other hand, no significant differences were found when comparing the postoperative serum levels of SHBG and testosterone/SHBG ratio with the preoperative values (p > 0.05). Postoperative testicular volume did not differ significantly when compared with the volume measured before surgery (p > 0.05) (table 2).

When stratified by the clinical grade of varicocele and the age of subjects, no significant difference was found in the mean preoperative testosterone levels among the 2 grades (Grade II and III) or the age of subjects (< 40 years vs. ≥ 40 years) (p > 0.05) (table 3).

For the euogonadal men, no significant improvements in testosterone levels were observed at 1 and 12 months after surgery as compared to the preoperative values (p > 0.05). When looking to the hypogonadal men, testosterone levels were significantly improving following varicocele repair at 1 and 12 months after surgery as compared to the preoperative values (7.0 vs. 15 nmol/l, p = 0.01; 7.0 vs. 10 nmol/l, p = 0.02) (table 4).

| Table 1. Descriptive statistics of the study population |
|----------------|----------------|
| **Variables**  | **Value**      |
| Number of patients | 20             |
| Age (years)       | 35 (18–66)     |
| Testicular volume (ml) | 19 (15–25)   |
| Varicocele grade  |                |
| I                | 0 (0%)         |
| II               | 8 (40%)        |
| III              | 12 (60%)       |
| Varicocele laterality |            |
| Unilateral       | 20 (100%)      |
| Left             | 19 (95%)       |
| Right            | 1 (5.0%)       |
| Bilateral        | 0 (0%)         |
Discussion

Based on 20 men who had undergone microsurgical subinguinal varicocele repair of grade II-III lesions because of chronic scrotal pain, varicocele repair was associated with a significant improvements of testosterone levels in men with low preoperative testosterone levels. Therefore, microsurgical subinguinal varicocele repair may benefit patients with grade II-III lesions and low testosterone levels.
A growing body of evidence suggests that varicocele adversely affects Leydig cell function and testosterone production. Tanrikut et al. [20] measured testosterone levels in 325 men with clinical varicoceles and in 510 men without clinical varicoceles who served as a comparison group. Men with clinical varicoceles had significantly lower testosterone levels than the comparison group, the difference persisted when analysed by age of men. In the same line, Hurtado et al. [24] reported significantly lower testosterone levels in 36 infertile men with unilateral left varicocele and 33 age-paired fertile controls. Luo et al. [25] studied the morphology and function of Leydig cells in the rat testis between 40 male Sprague-Dawley rats which were divided into 2 groups: the experimental group underwent surgery to create a left varicocele, and the control group underwent a sham operation. The mean apoptosis index of Leydig cells in the experimental group was significantly higher than that in the control group after 4 or 8 weeks. Steroidogenic acute regulatory (StAR) protein mRNA levels in the Leydig cells of the experimental group were significantly lower compared to those of the control group. The authors suggested that varicocele impairs Leydig cell function by increasing apoptosis and suppressing the expression of the StAR protein.

Sirini et al. [26] analysed testosterone levels in 200 infertile men with clinical varicoceles who were divided into two groups, 100 men with clinical varicoceles who had microsurgical varicocele repair and 100 age-matched men with clinical varicoceles who underwent assisted reproduction procedures served as the control group. Testosterone levels improved significantly after varicoceles repair as compared to the control group. Abdel-Meguid et al. [17] recently reported significant improvements in testosterone levels after varicocele repair in men with low preoperative levels. A similar significant change was observed by others [27, 28]. In accordance, we demonstrated significant improvements in testosterone levels following repair of clinical varicoceles in men with low preoperative testosterone levels.

In an attempt to elucidate factors that could affect changes in testosterone levels after surgery, we considered varicocele grade and age of the men as determining factors. However, neither the varicocele grade nor the age of the men seems to determine the improvement in testosterone levels in our study and others' [17, 19, 28]. We believe, therefore, that varicocele grade and the age of patients are not predicting factors for how testosterone changed following varicocele repair.

Zohdy et al. [21] reported that serum LH decreases significantly following varicocele repair in the hypogonadal patients and this may be attributed to improvement in Leydig cell function. We failed to observe such changes in our study in accordance with previous reports [28]. We were not able to explain this contradictory.

Our study has some limitations; the study is retrospective in design and based on a small number of selected group, namely men who undergone varicocele repair because of chronic dull scrotal pain and testosterone improvement was a secondary outcome. Therefore, our results might not representing men from the general population and/or men under infertility assessment. However, our results are still valid and support the nation that varicocele repair associated with improvement of testosterone in men with low preoperative testosterone values. Our study did not involve patients with grade I varicocele and/or patients with bilateral varicocele. Therefore, we could not make a conclusion whether repair of small varicocele and/or bilateral varicocele can improve testosterone levels.

In conclusion, our results have shown that microsurgical subinguinal repair of varicocele grade II-III was associated with a significant improvements of testosterone levels in men with low preoperative values. Therefore, microsurgical varicocele repair may benefit men with grade II-III lesions and low preoperative testosterone values.
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