

The validity of testicular catch-up growth and serum FSH levels in the long-term postoperative assessment of laparoscopic varicocele correction in adolescents

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Abstract

Background: Postoperative assessment after varicocele surgery in adolescence is commonly centred around catch-up growth of the testis. There is paucity of evidence on the correlation of catch-up growth with underlying testicular function in these patients.

Aims: To assess the reliability of catch-up growth of the testis as an indicator of normalization of testicular function and the utility of serum FSH levels in the long-term postoperative assessment of varicocele surgery in adolescence.

Materials and Methods: Prospective cohort study of young adults (18-27 years) who had laparoscopic varicocele correction in adolescence (11-16 years). Evaluation included serum FSH levels, scrotal ultrasonography and semen analysis.

Analysis: Anatomical and functional parameters of participants with equal and normal testicular size were compared to those of participants with persistent testicular hypotrophy or hypertrophy. Sensitivity and positive predictive value of postoperative serum FSH levels were estimated and elevated levels of serum FSH were checked for association with suboptimal outcomes of varicocele correction.

Results: The serum FSH levels of participants with unequal testicular sizes ($n=6$, median 6.65 IU/l), which included testicular hypertrophy ($n=3$, median 7.2 IU/l) and persistent testicular hypotrophy ($n=3$, median 6.1 IU/l), were significantly higher than the group with equal testicular sizes ($n=8$, median 3.5 IU/l; $P=0.014$, Mann-Whitney U test). Postoperative elevated serum FSH levels were significantly associated with suboptimal outcomes of varicocele surgery ($P=0.015$, Fisher's exact test). The test also had a high positive predictive value.

Conclusions: Testicular catch-up growth may not be a reliable postoperative assessment criterion by itself. Serum FSH levels may be of value in detecting suboptimal outcomes of varicocele surgery in adolescents.

Key Words: Varicocele, follow-up, adolescent, testicular hypertrophy, testicular function

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INTRODUCTION

Varicoceles are common in adolescence with a reported prevalence ranging from 7 to 24%.^[1,2] Surgical correction is recommended when they are associated with ipsilateral testicular hypotrophy in adolescents due to the long-term risk of subfertility.^[3-5]

Postoperative assessment is commonly carried out using tests for anatomical parameters alone. Clinical examination and ultrasonography are performed to rule out recurrence and to confirm ipsilateral testicular catch-up growth.^[3,5-11] Confirmation of normalization of underlying testicular function has to be assumed since tests which assess the true underlying function of the testes; i.e. serum FSH and semen analysis, are rarely employed.^[12,13]

This is a prospective study which examines the accuracy of anatomical and functional assessment of testicular function in the long-term follow-up of varicocele surgery in adolescents.

Aims

In young adults, who have undergone laparoscopic varicocele correction in adolescence (11-16 years), we aim

- to assess the reliability of testicular catch-up growth as an indicator of normalization of testicular function
- to evaluate the accuracy of serum FSH levels in detecting suboptimal outcomes

MATERIALS AND METHODS

A prospective follow-up study plan was set up for young adults who underwent laparoscopic varicocele correction (LVC) in adolescence, which was approved by the Human Research Ethics Committee of the Children's Hospital at Westmead.

All young adults who had undergone LVC between 11 and 16 years of age at our hospital from 1993 to 2006 were eligible to participate in this study provided they were more than 18 years at the time of assessment. Patients with associated endocrine disorders were excluded from the study.

The subjects were recruited to this follow-up plan by means of a letter sent out in early 2006. They attended an outpatient clinic where they were clinically examined between June 2006 and March 2007.

Details of their past treatment were recorded. They were then requested to undergo the following tests:

1. Scrotal ultrasonography and Doppler examination.
2. Hormonal tests- serum FSH (normal <6.1 IU/l), LH and testosterone levels.
3. Semen analysis – A single semen analysis was performed at a tertiary level fertility center.

Surgical technique

Our practice is to use a Doppler flow transducer vascular access device, "Smart Needle" (Escalon Medical Corp, New Berlin, WI) during laparoscopic varicocele correction to identify and

preserve the testicular artery. This enables us to divide the veins only, preserving the artery. The lymphatic network to the testis can often be better seen and attempts were made to preserve the same wherever possible.

The following data were collected- indication for surgery, date of surgery, length of follow-up, occurrence of a postoperative hydrocele, Tanners stage at the time of follow-up, size of the testes at follow-up as measured by ultrasonography, presence of persistent hypotrophy (difference >2 ml), presence of hypertrophy (difference > 2 ml), recurrence as defined by the presence of a palpable mass with evidence of increased flow during Valsalva manoeuvre, either clinically or on ultrasonography, serum FSH, LH and testosterone levels, sperm count and motility.

Analysis

The first part of the analysis was carried out by dividing the patients into three groups:

Group 1: Normal and equal testicular size at follow-up.

Group 2: Left testis smaller than right (difference >2 ml), and

Group 3: Left testis larger than right (difference >2 ml).

Postoperative anatomical (recurrence of varicocele, hydrocele) and functional (serum FSH levels) parameters were compared. The difference in the serum FSH levels in two groups- with equal testicular sizes and unequal testicular sizes was checked for statistical significance using the Mann-Whitney U test.

For the purpose of the second part of the analysis, the patients were divided into two groups as follows:

Group A: normal serum FSH levels at follow-up (<6.1 IU/l), and

Group B: high FSH levels at follow-up (≥ 6.1 IU/l).

A difference of more than 2 ml in testicular volume, a recurrence of varicocele and sperm density below 20 million/ml were considered as suboptimal outcomes of surgery as measured at the time of follow-up. Sensitivity, specificity and positive predictive value of serum FSH as a test to diagnose suboptimal outcomes were estimated. The strength of association between high serum FSH levels and suboptimal outcomes was checked using Fisher's exact test.

RESULTS

Demographics

A total of 16 patients responded to the letter of recruitment from a total eligible sample of 55 patients (29%; median age 21 years). Two participants dropped out of the study for personal reasons prior to any tests being performed. All had undergone transperitoneal LVC with preservation of testicular artery in

their adolescence by a single surgeon. The median duration of the follow-up was eight years (range 5-12 years). All the patients had a Grade 2 or Grade 3 varicocele preoperatively (Dubin and Amelar grading system). The indications for surgery in the group were left testicular hypotrophy ($n=13$), hypotrophy and pain ($n=2$) and pain only ($n=1$). All participants were requested to undergo semen analysis. However, only seven participants agreed, - three had equal testicular sizes at follow-up, two had hypertrophy and two had persistent hypertrophy. Table 1 summarizes the follow-up findings of the study population.

Catch-up growth and serum FSH levels

A total of 11 participants demonstrated postoperative catch-up growth (hypertrophy in three). Four participants had an elevated serum FSH level [Table 2]. The group with persistent hypotrophy and the group with hypertrophy both had higher median levels of serum FSH than the group with equal testicular sizes at follow-up [Table 3]. The serum FSH levels for the group with equal testicular sizes ($n=8$, median 3.5 IU/l, range 1.7-5.8 IU/l) were significantly lower than those for the group with unequal testicular sizes (including hypertrophy) at follow-up ($n=6$, median 6.65 IU/l, range 4.0-9.7 IU/l; $P=0.014$, Mann-Whitney U test). The serum LH and testosterone levels were unremarkable in the study population.

Suboptimal outcomes and serum FSH levels

Four participants in the study had a high serum FSH level at the time of follow-up [Table 3]. All these patients had suboptimal outcomes (positive predictive value = 100%). Two patients with a normal serum FSH had a suboptimal outcome while eight patients with a normal serum FSH did not have any abnormality at follow-up (sensitivity = 67%, specificity = 100%, negative predictive value = 80%). There was a significant statistical association between high serum

FSH levels and suboptimal outcomes ($P=0.015$, Fisher’s exact test).

DISCUSSION

There is growing evidence that surgical correction is beneficial to adolescents who present with a varicocele that is associated with an ipsilateral testicular hypotrophy. This is because the varicocele exerts a progressive deleterious effect on the testis leading to subfertility in some of these patients.^[4,14]

The significance of increase in size of the testis in the postoperative period appears to be overstated. This phenomenon has been extensively reported in adolescents after correction of varicocele as an important criterion of postoperative evaluation.^[3,5-11] However, very few papers have correlated this with the underlying testicular function and even fewer have focussed on left testicular hypertrophy – where the left testis attains a size larger than the right testis. We noticed this phenomenon of ‘hypertrophy’ in three of our early patients. This appears to be first reported in 1999 by Gershbein *et al.*^[8] but they could not pinpoint the exact cause of this. Kocvara *et al.* have reported the findings of a similar nature that they attributed to destruction of testicular lymphatics during the surgical procedure.^[13] Their claims are well substantiated by testicular biopsy results. All patients with hypertrophy in our series also developed a hydrocele. The relationship between intraoperative damage to testicular lymphatics and postoperative hydrocele is well established.^[15] It is also interesting that testicular hypertrophy is associated with higher levels of serum FSH in our study. Hence we are in agreement with Kocvara *et al.* that testicular hypertrophy is a result of damage to testicular lymphatics. This claim has been challenged by other authors but they do not have better alternative explanations for the cause of ipsilateral hypertrophy in their patients.^[16] In our opinion, ipsilateral

Table 1: Summary of the follow-up findings of the study population

Study factor	Total (n = 14)
Catch-up growth	11 (79)*
Recurrence	3 (21)
Post-op hydrocele	3 (21)
Abnormal serum FSH (>6.1 IU/l)	4 (29)
Abnormal semen analysis	3/7 (43)

*Hypertrophy in 3, Figures in parentheses are in percentage

Table 3: Correlation between high serum FSH and suboptimal outcomes at the time of follow-up (n = 14)

	No. of “suboptimal” outcomes				Total
	0	any number (1 or 2)	1	2	
Normal FSH	8	2	1	1	10
High FSH	0	4	2	2	4
Total	8	6	3	3	14

Fisher’s exact test: $P = 0.015$

Table 2: Summary of anatomical outcomes at follow-up (catch-up growth, recurrence and hydrocele) (n = 14)

	Description	Recurrence	Post-operative hydrocele formation	Median serum FSH levels (IU/l) (normal < 6.1 IU/l)
Catch-up growth	Left = right (n = 8)	0	0	3.5 (2.1 – 6.1)
	Left > right (hypertrophy) (n = 3)	0	3	7.2 (5.1 – 9.7)
No catch-up growth	Persistent hypotrophy (n = 3)	3	0	6.1 (4.0 – 8.9)

testicular hypertrophy when associated with a hydrocele may be associated with a subnormal testicular function. Furthermore, testicular function appeared to be the best when the two testes were equal in volume at follow-up.

Serum FSH levels may have a role in postoperative assessment of varicocele surgery since they are a sensitive indicator of spermatogenesis in adolescents and young adults.^[17] Besides, it is obvious from our study that anatomical parameters, when used in isolation, can be misleading. Although there have been conflicting reports regarding the utility of preoperative FSH levels to identify those adolescents with varicocele who are at risk of testicular damage, they have been reported to be a reliable test in the postoperative assessment by Kaneko *et al.*^[7,12,13] Our findings also suggest that serum FSH levels seem to successfully predict suboptimal outcomes of surgery (positive predictive value = 100%). Serum FSH level is a test that is easily available and ethically acceptable in all age groups. Hence, clinicians should be encouraged to incorporate this test in the postoperative assessment of varicocele surgery.

This study, however, has several limitations. The response rate was poor, possibly due to the very mobile and independent nature of the people in that age group, that could lead to a selection bias. A single semen analysis is not always reliable and hence we have tried not to base our conclusions on the results of a single semen analysis. Testicular biopsies were not possible due to ethical considerations.

Nevertheless, this study provides a good platform for research aimed at studying if testicular hypertrophy is a phenomenon which could lead to progressive worsening of testicular function or whether it is a self-limiting one. The findings of our study can also lead to more elaborate studies aimed at defining the precise role of serum FSH levels in the routine follow-up of varicocele surgery in adolescence.

In conclusion, we would like to state that

- Contrary to popular opinion, increase in testicular size is not a reliable follow-up parameter in itself. This is because when associated with a hydrocele after successful LVC, it appears to be associated with a subnormal testicular function.
- Elevated postoperative serum FSH levels appear to be highly predictive of the suboptimal outcomes of varicocele surgery.

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