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Prepubertal presentation of varicocele does not affect outcomes

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Summary

Introduction
Varicoceles in prepubertal boys are uncommon and little is known of the natural history. Historically, a large percentage of these boys have undergone surgical repair with the belief that such early presentation carried a worse prognosis, making assessment of longitudinal outcomes difficult.

Objective
While there may be concern that varicocele could represent a progressive disease and therefore prepubertal presentation would portend a worse prognosis, we hypothesized that there would be no difference between the prepubertal boys and other adolescents with varicocele.

Study design
We retrospectively reviewed a database of boys at a single institution with a documented left-sided varicocele between 1995 and 2011. Inclusion criteria were one or more of the following: 1. Clinician-documented Tanner 1 status, 2. Right testis orchidometric or ultrasound calculated volume of $\leq$3 cc's. Patients were drawn from a prospectively maintained database of all boys presenting to the outpatient urology clinic receiving a diagnosis of varicocele.

A cohort of adolescent boys was assembled by matching as closely as possible with respect to testis volume disparity and grade of varicocele. All matches were within 2% of volume difference. Volume was calculated using the length*-width*height*0.71 formula. Testis size disparity was set to a threshold of $\geq$20% using the Lambert formula: $(Volume_{Right} - Volume_{Left})/Volume_{Right}*100\%$. Our primary outcome was defined as hypotrophy or the need for surgery for hypotrophy at the termination of the study. We planned a single subgroup analysis of boys based on presentation with or without hypotrophy. The decision for surgery or observation was made by the individual clinician at the time of patient assessment.

Results
On presentation, the prepubertal cohort was younger (10.8 vs 14.1 years), and with smaller left (2.4 vs 11.6 cc) and right (2.4 vs 11.6 cc) testis volume. There were no significant differences with respect to varicocele grade and volume differentials at presentation. At the end of the study, 76% of the prepubertal cohort had neither hypotrophy nor the requirement for operation, compared with 83% of the matched cohort ($P = 0.71$, Fisher's exact test). Similarly, there were no significant differences in outcome when comparing prepubertal boys with initial symmetry or hypotrophy to their matched cohort of older adolescents.

Discussion
The prepubertal varicocele is a rare clinical problem for which little data exists to guide the clinician. In a review of Pubmed indexed English language manuscripts, we were only able to find five papers with information on Tanner stage; only 31 prepubertal boys have longitudinal data reported. This study approximately doubles the number of boys for whom such data is available in the literature.

Our chief limitation was sample size. A power analysis indicated that a final-analysis cohort of 90 prepubertal boys would be required to detect a 20% difference in outcome between that group and a matched cohort of pubertal or post-pubertal boys. We propose that given the lack of evidence for worse outcomes in prepubertal boys with varicocele that prepubertal status, in and of itself, not be considered an additional indication for correction of varicocele.

Conclusion
In our retrospective cohort of prepubertal boys with left testis varicocele and their matched cohort, we did not detect a difference in the rate of good outcomes, defined as the absence of hypotrophy and lack of need for surgical intervention. While we may have suspected, as have others, that prepubertal presentation would have conveyed a more pressing need to intervene, it is likely that these boys represent the very same patients that we see more commonly later in their adolescence, and should thus be managed in a similarly conservative fashion.

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Introduction

Varicocele is present in 11–29% of adolescent boys, but indications for intervention have not been firmly established. With respect to future infertility, interpretation of the role of varicocele is complex, as it is estimated that approximately 80% of adults with varicocele will be fertile [1]. The rare clinical problem of a left-sided varicocele presenting prior to the onset of puberty has been addressed by a few studies [2–6] and it has been suggested that perhaps a prepubertal presentation of varicocele might be more likely to result in hypotrophy or subfertility. While there may be concern that varicocele could represent a progressive disease and therefore, prepubertal presentation would portend to a worse prognosis, it was hypothesized that there would be no difference between the prepubertal boys and other adolescents with varicocele. To the authors' knowledge, this is the first controlled study examining longitudinal outcomes of prepubertal boys with varicocele using relative testicular volume as a primary endpoint.

Methods

A database of boys at a single institution with a documented left-sided varicocele between 1995 and 2011, with Institutional review board (IRB) approval, was retrospectively reviewed. Inclusion criteria were one or more of the following: 1) Clinician-documented Tanner 1 status, 2) Right testis orchidometric or ultrasound calculated volume of $\leq$3 cc. Patients were drawn from a prospectively maintained database of all boys presenting to the outpatient urology clinic receiving a diagnosis of varicocele.

Given the potential confounding by other conditions that may impact on testis volume, all patients were excluded with a history of: undescended testis, prior inguinal or scrotal procedures, documented scrotal trauma, presence of a hydrocele, chromosomal abnormalities, Prader–Willi syndrome, Kallmann syndrome, Cushing's syndrome, a history of malignancy or chemotherapy, chronic systemic disease, thyroid disease, hemochromatosis and diabetes mellitus.

A cohort of adolescent boys was assembled by matching as closely as possible with respect to testis volume disparity and grade of varicocele. All matches were within 2% of volume difference. Volume was calculated using the length*width*height*0.71 formula [7]. Testis size disparity was set to a threshold of $\geq$20% using the Lambert formula: $(Volume_{Right} - Volume_{Left})/Volume_{Right}*100\%$ [7]. The primary outcome was defined as hypotrophy or the need for surgery for hypotrophy at the termination of the present study. A single subgroup analysis of boys was planned based on presentation with or without hypotrophy. The decision for surgery or observation was made by the individual clinician at the time of patient assessment. Subjects were not included in the analysis if they underwent varicocelectomy for other indications, such as family preference, the presence of a large varicocele without hypotrophy, or physician preference without evidence of hypotrophy. Nine were excluded in the prepubertal group, and six in the matched group.

Statistical analysis was performed in JMP Pro, Version 10 (SAS Institute Inc., Cary, NC). Two-tailed values of $P < 0.05$ were considered to be statistically significant, with Fisher's exact test for binary data, Pearson's correlation for categorical data, and Wilcoxon rank-sum tests for continuous data.

Results

Thirty boys with prepubertal varicocele were studied; 30 boys were matched in the adolescent (pubertal and postpubertal) cohort. All boys had varicoceles of the left testis exclusively; there were no right-sided varicoceles and no bilateral cases. The descriptions of each cohort are shown in Table 1.

Table 1 Patient characteristics.

n	Prepubertal		Matched cohort		*P*
	n/median	[IQR]	*n*/median	[IQR]	
	21 (9 excluded)		24 (6 excluded)		
Age, years	10.8	[9.7, 11.8]	14.1	[12.6, 15.8]	<0.001[a]
Length of follow-up, years	3.1	[15.3, 4.7]	2.5	[1.7, 3.7]	0.57[a]
Volume presentation, cc					
Left	2.4	[1.1, 3.8]	11.6	[8.8, 11.6]	<0.001[a]
Right	2.4	[1.3, 3.5]	11.6	[8.9, 17.5]	<0.001[a]
Volume difference					
(Right–Left)/Right *100%	0	[−4.7, 11.9]	1.24	[−3.5, 21.9]	0.51[a]
Left varicocele grade					
Large (III)	10		16		0.37[b]
Medium (II)	9		6		
Small (I)	2		2		

[IQR] = Interquartile range.
[a] Wilcoxon Rank Sum.
[b] Pearson chi-square.