Testicular Symmetry and Adolescent Varicocele—Does it Need Followup?

Ruslan Korets, Solomon L. Woldu, Shannon N. Nees, Benjamin A. Spencer and Kenneth I. Glassberg*

From the Division of Pediatric Urology, Morgan Stanley Children's Hospital of New York-Presbyterian, Department of Urology, Columbia University College of Physicians and Surgeons, New York, New York

Abbreviations and Acronyms

DDUS = duplex Doppler ultrasound

MVD = maximum vein diameter

PRF = peak retrograde flow

TA = testicular asymmetry

Study received institutional review board approval.

* Correspondence: Division of Pediatric Urology, Morgan Stanley Children's Hospital of New York-Presbyterian, 11th Floor, Department of Urology, Columbia University College of Physicians and Surgeons, 3959 Broadway, New York, New York 10032 (e-mail: kglassberg@aol.com).

Purpose: Appropriate management for adolescent varicocele with testicular symmetry is rarely discussed. We examined the natural history of varicocele in patients presenting with testicular symmetry to achieve better understanding of the clinical course.

Materials and Methods: Our varicocele registry was queried for adolescent boys who presented with varicocele in association with less than 15% testicular asymmetry and who underwent at least 1 testicular asymmetry assessment 12 or more months later. Patients were stratified into 2 groups based on an initial testicular asymmetry measurement of less than 10% vs 10.0% to 14.9%. Logistic regression modeling was used to analyze the association of Tanner stage, varicocele grade, peak retrograde flow and maximum vein diameter at presentation with increased testicular asymmetry at followup. Kaplan-Meier methodology was applied to compare testicular asymmetry progression rates.

Results: We identified 89 adolescents, of whom 52 (58.4%) and 37 (41.6%) presented with less than 10.0% and 10.0% to 14.9% testicular asymmetry, respectively. Of the patients 37 (41.6%) showed testicular asymmetry progression at a median 18-month followup. The overall 3-year testicular asymmetry progression-free rate was 48% while in patients with peak retrograde flow 30 cm per second or greater it was 23%. On multivariate analysis controlled for age, Tanner stage and varicocele grade a peak retrograde flow of 30 cm per second or greater was associated with worsening testicular asymmetry (OR 4.87, 95% CI 1.6–8.0).

Conclusions: Adolescents with varicocele and less than 15% testicular asymmetry are at risk for asymmetry during followup. Those with peak retrograde flow 30 cm per second or greater are at increased risk for early asymmetry while those with peak retrograde flow less than 30 cm per second may still show asymmetry but tend to do so after longer followup.

Key Words: testis, organ size, varicocele, disease progression, risk

In children the prevalence of varicocele increases with age from less than 1% in boys 10 years or younger to 15% during puberty and adulthood.[1] Of men evaluated for infertility 35% to 40% are diagnosed with a left varicocele.[2,3] While a clinically detectable varicocele in conjunction with abnormal semen analysis in an infertile couple is considered an indication for treatment, fewer than half of the men achieve paternity after the varicocele is surgically corrected.[4] Since fertility testing in children and adolescents is not routine, factors that may compromise testicular function or spermatogenesis are used to gauge the need for intervention.

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According to American Urological Association and American Society for Reproductive Medicine best practice guidelines any adolescent male with a unilateral varicocele should be considered a candidate for surgical repair if there is objective evidence of reduced testicular size ipsilateral to the varicocele. However, the guidelines do not clarify what represents objective evidence of reduced testicular size. Also, the guidelines suggest that adolescents with a varicocele but normal ipsilateral testicular size should be offered followup monitoring with yearly objective measurements of testicular size and/or semen analyses.[2] These guidelines are also nonspecific and state neither how long those with normal testicular size should be followed nor what factors should be considered if recommendations are made regarding followup duration.

Various cutoffs for testicular size discrepancy have been used to indicate clinically relevant asymmetry, most commonly 10%, 15% or 20%, or a 2 to 3 cc volume difference.[5–7] In addition to the controversy on the appropriate cutoff, there is debate on how long to follow adolescents with asymmetry before recommending surgery.[8,9] Diamond et al reported a higher incidence of a decreased sperm concentration and motility in patients with an ultrasound derived volume differential of as little as 10% and more severe abnormal parameters when asymmetry was greater than 20%.[10] They recommended varicocelectomy without observation when asymmetry greater than 20% was identified and persisted more than 1 year. Conversely Kolon et al suggested longer followup for patients with asymmetry since they found catch-up growth in 71% of boys with greater than 15% asymmetry at a mean of 3 years without any intervening surgery.[8]

However, little is known about whether patients with testicular symmetry, which we defined as less than 15% asymmetry, should be followed and, if so, for how long. We investigated the natural history of patients presenting with varicocele and testicular symmetry to identify predictors of asymmetry and determine the appropriate duration of surveillance.

MATERIALS AND METHODS

We retrospectively reviewed our institutional review board approved pediatric varicocele database, which included 734 adolescents who were evaluated by a single pediatric urologist between 1994 and 2009. Patients were excluded from analysis if they had 15% or greater initial asymmetry (415), underwent prior varicocelectomy (6) or inguinal surgery (13), did not undergo at least 2 testicular volume measurements a minimum of 12 months apart (161), had testicular volume measurements performed by different modalities (13), were younger than 12 or older than 18 years at first presentation (8) or had missing clinical information (29). Adolescents were stratified into 2 groups based on initial TA, including 10.0% or less vs 10.1% to 14.9%.

Testicular volume was measured preferentially by ultrasound using the Lambert equation, testicular volume = length $\times$ width $\times$ height $\times$ 0.71.[11] Percent TA was calculated using the formula, percent TA = [(right testis volume − left testis volume)/right testis volume] $\times$ 100.

DDUS measurements of retrograde venous blood flow were recorded in patients by a single ultrasonographer with the patients supine. As previously described, PRF and MVD were measured with the patient supine, and with and without the Valsalva maneuver for PRF and MVD, respectively.[12] DDUS has been our primary means of volume measurements since 2000 but previously we relied on Takihara ring orchidometry. Thus, in patients in whom scrotal ultrasound measurements were unavailable we used ring measurements. Only volumes obtained by the same modality in individuals were compared. For instance, initial measurements obtained by ring orchidometry were not compared against ultrasound measurements made at a later visit.

Logistic regression modeling was used to analyze the association of Tanner stage, varicocele grade, PRF and MVD at presentation with increased asymmetry at followup. The strength of association of various factors with worsening asymmetry is reported as the OR and 95% CI. TA progression-free rates were evaluated by the Kaplan-Meier method and differences between groups were compared by the log rank test. The predictive value of PRF velocity on new onset 10% or greater, 15% or greater and 20% or greater asymmetry was evaluated by the AUC of ROC curves. Accuracy was calculated for the best cutoff value, defined as the highest sum of sensitivity and specificity on the ROC plot, with PRF 30 cm per second or greater identified as the cutoff to be used in analysis. All statistical tests were 2-sided with $p < 0.05$ considered statistically significant. Statistical analysis was performed using Stata, version 9.0 (StataCorp®).

RESULTS

We identified 89 adolescents who presented with grade 1 to 3 varicocele with less than 15% TA and who were followed 12 or more months after the initial visit. Of these patients 52 (58.4%) presented with less than 10.0% and 37 (41.6%) presented with 10.0% to 14.9% TA (table 1). Mean $\pm$ SD age at presentation was 14.2 $\pm$ 2.7 years and median followup was 27 months. At last followup 38 (42.7%) and 14 adolescents (15.7%) had less than 10% and 10.0% to 14.9% TA, respectively. Of the boys with increasing asymmetry 13 (14.6%) had progressed to 15.0% to 19.9% asymmetry at a median followup of 19.4 months while 24 (27.0%) progressed to 20% or greater asymmetry after a median of 21.0 months of conservative management (table 2).

In the group with less than 10.0% initial asymmetry mean patient age was 14.0 $\pm$ 3.0 years. At a median followup of 28.8 months 26 patients (50%) maintained less than 10% TA while 5 (9.6%) showed