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Adolescent varicocele: A large multicenter analysis of complications and recurrence in academic programs

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Keywords
Varicocele; Surgery; Laparoscopy; Hydrocele

Abbreviations
CPTCurrent Procedural Terminology; E&MEvaluation and Management; FPSCFaculty Practice Solutions Center; ICD-9International Classification of Disease 9th edition; PEpercutaneous embolization

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Summary

Objective
After varicocelectomy a wide range of recurrence rates have been reported from 0 to 18%, and rates of post-operative hydrocele formation between 0 and 29%. Controversy exists as to the appropriate approach for varicocele treatment, whether open, laparoscopic, or percutaneous embolization (PE) is best for young men. The literature on treatment of adolescent varicocele is limited to high-volume single surgeon, single institution, or small multi-institution series. Our goal was to evaluate the retreatment and complication rates from numerous institutions to determine more generalizable results.

Study design
The Faculty Practice Solutions Center database was queried to identify males under age 19 years with a diagnosis and/or treatment of varicocele between January 2009 and December 2012. Patients were followed until December 2013 (1–5 years follow-up) to determine if they had occurrence of outcome variables: retreatment, diagnosis, or treatment of hydrocele. Associations of the variables age, race, insurance type, geographical region, surgeon-volume, and surgical approach, with outcome variables were analyzed using a mixed-effects Cox proportional hazard model.

Results
Of 6,729 patients with a diagnosis of varicocele, 1,036 underwent open (405), laparoscopic (530), or percutaneous embolization (PE) (101) treatment by 213 physicians. Retreatment rates after open, laparoscopic, and PE treatments were 1.5%, 3.4% and 9.9%, respectively. Race, region, insurance type, and age were not independently associated with outcomes. The incidence of hydrocele after open, laparoscopic, and PE treatments was 4.9%, 8.1%, and 5%, respectively. No approach was independently associated with diagnosis or treatment of hydrocele. Young age was associated with a significantly higher rate of hydrocele formation. For each year of age, there was a 14% decreased rate of hydrocele formation.

Discussion
Although this series contains the largest cohort of patients, physicians, and institutions, we were limited by the inability to determine actual recurrence rates. Only patients receiving retreatment at the same institution within the 1–5 year follow-up period were captured. As such, the true rate of varicocele recurrence may be higher. The retreatment rate is influenced by the physician's threshold to retreat and the patient's desire to undergo another procedure. Despite its limitations, this is the first study to compare open, laparoscopic, and percutaneous approaches to varicocele treatment.

Conclusions
Percutaneous embolization has a significantly higher retreatment rate compared with either open or laparoscopic varicocelectomy. Retreatment and hydrocele formation after open and laparoscopic approaches were not significantly different. This supports a surgeon and family choosing an approach based on patient characteristics and surgeon preference.

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Introduction

Varicocele is the most common cause of male infertility and one of the most common surgically correctable urological abnormalities among adolescent males [1—3]. Between 15% and 30% of male adolescents have a varicocele [1,2,4—6]. The presence of varicocele can lead to testicular hypotrophy and long-term impact on spermatogenesis [7]. Varicocele presence has been associated with lower sperm density, motility, and changed morphology [8]. After repair of varicocele, studies have reported catch-up growth of the hypotrophic testicle in 40—100% of patients and improvement in sperm density and motility [8,9]. Hence, it is a potential source of infertility that is both identifiable and treatable in the prepubescent. Yet, only about 20% of boys with varicocele will experience long-term fertility effects [10]. In addition, the treatment of varicocele in adolescents and prepubescents is not without risk, including persistence or recurrence of varicocele, formation of hydrocele, and injury to the testicle.

After varicocelectomy a wide range of recurrence rates have been reported from 0 to 18%, and rates of postoperative hydrocele formation between 0 and 29% [1]. Variations in these reported rates could be a result of surgical approach, age, or length of follow-up in these studies. Controversy exists as to the appropriate approach for varicocele treatment. Multiple studies have been published regarding the operative technique, such as inguinal, subinguinal, lymphatic sparing, and artery sparing. More broadly, there is controversy over whether to approach varicocele through an open, laparoscopic, or percutaneous embolization (PE).

Despite the controversy, to our knowledge, all but one published series have been limited to single institutions and/or high-volume surgeons, limiting the ability to generalize results, and therefore, to help guide parents and patients in the question of whether to pursue an open, laparoscopic, or percutaneous approach [11]. In addition, few studies have compared the three broad categories of approaches. Therefore, our objective was to perform a multicenter analysis to determine the rates of recurrence and hydrocele formation after open, laparoscopic, and percutaneous treatment of varicocele to better counsel patients and parents. We hypothesize that these rates will not be equivalent to larger volume centers. To our knowledge, this study represents the first analysis of such magnitude and is the first to compare all three broad categories of treatment approaches on a large scale.

Materials and methods

To identify patients with a varicocele we queried the Faculty Practice Solutions Center (FPSC) database. FPSC was initiated by an alliance between the University Health System Consortium and the Association of American Medical Colleges in an effort to collect benchmarking data on academic clinical practices throughout the country. It involves more than 90 participating faculty practice plans with more than 60,000 physicians nationwide. Coding data analyzed include de-identified hospital and provider codes, patient date of birth, gender, race, physician specialty, CPT procedural billing codes, ICD-9 diagnosis billing codes, service date, region, and payer category. FPSC is unique not only for its large scale of data capture, but also for its role in tracking billing information which offers a more accurate reflection of practice patterns.

Male subjects under the age of 19 years with a diagnosis of varicocele based on an ICD-9 code of 456.4 for any visit between January 1, 2009 and December 31, 2012 were identified in the FPSC database to determine if they had treatment for varicocele with open surgery (CPT 55530), laparoscopic surgery (CPT 55550) or percutaneous embolization (PE) (CPT 37204, 75894, 36001, 37241, 36012, 36011, 36470, 36478, 37765, 37766, 37244, 35476, or 37799). There is no unique code for PE. Therefore, all potential CPT codes for percutaneous venous interventions in patients with ICD-9 diagnosis of varicocele were included for analysis of PE.

Type of intervention was analyzed by age at primary surgery, insurance type, race, region, and surgeon volume using a mixed-effects logistic regression model, fitted using the glmmPQL function in R [12]. The database was queried to determine if any patient had an admission or anesthetic within 48 h of the procedure.

To ensure a minimum of 1 year of follow-up, patients were followed in the database from the date of primary treatment (January 2009 to December 2012) through December 31, 2013 to discover any retreatment of varicocele, a new diagnosis of hydrocele (ICD-9 603.X), and/or treatment of hydrocele (CPT 55000, 55040, 55041, or 55500).

As the 5-year study was a prevalence analysis, a subset analysis was performed to determine treatment (incidence) rate. New patients seen by a urologist in the first 2 years of the study period (January 2009 to December 2010) were identified and followed to better define any treatment during the ensuing 3—5 years (until December 2013).

Time to retreatment was compared between surgical approaches, controlling for age at primary surgery, race, insurance type, region, and surgeon volume using a mixed-effects Cox proportional hazard model including random effects for surgeon and institution. Time to treatment for hydrocele from time of varicocele treatment was likewise compared between surgery types, controlling for age at primary surgery, surgeon volume and insurance type using a mixed-effects Cox model. Mixed-effects Cox models were fitted using the package coxme, version 2.2-3 in the statistical computing environment R, version 3.1.0. Time to retreatment of varicocele was plotted by primary surgical approach (without covariate adjustment) using Kaplan—Meier curves.

Results

The query identified 6,729 boys and young men with the diagnosis of varicocele of whom 1,006 received treatment, open (405), laparoscopic (530), and PE (101). Surgical patients were treated by 175 urologists and 38 interventional radiologists. Bilateral procedures were performed in only 46 open (11%), 27 laparoscopic (5%), and two PE (2%) patients, or approximately 7.5% of the patients. We found no occurrence of readmission or secondary anesthesia within 48 h of primary treatment.

Subset analysis for incidence

In the first 2 years of the study period, 1,330 patients were seen in consultation (new patient) for a diagnosis of varicocele. Of these, 305 (23%) underwent treatment within 3–5 years. Of these, 123 (40%) underwent open treatment, 165 (54%) underwent laparoscopic treatment, and 17 (6%) chose to undergo PE.

Table 1 shows patient characteristics (6,729 boys) by primary treatment type (1,006 primary procedures). The mean and median ages at surgery were not different between the three approaches. Multivariable mixed-effects logistic regression analysis showed no association of choice of surgical approach with patient age, race, or insurance type. Controlling for age at primary surgery, insurance type, and race, subjects in the West region were significantly more likely to be treated laparoscopically ($p = 0.04$) (Supplemental Table S1).

Retreatment

After 1 year, both laparoscopic and open approaches had an approximate 1% rate of retreatment compared with 10% for PE (Table 2). Fig. 1 shows the Kaplan–Meier plot of time to first retreatment by type of primary surgery.

Multivariable Cox proportional hazards analysis of time to retreatment showed no association of retreatment with surgeon volume, patient race, insurance type, or age. Controlling for surgeon volume, age at primary surgery, race, insurance type, and region, patients who had occlusion of the spermatic veins via PE had a significantly higher hazard of retreatment, nearly 6-fold, than patients who had open ligation of spermatic veins ($p = 0.01$), and PE showed a trend towards a higher hazard of retreatment (3-fold) compared with laparoscopic ligation ($p = 0.06$) (Supplemental Table S2). There was no statistically significant difference in retreatment rates between the laparoscopic and open approaches.

Hydrocele

The overall hydrocele diagnosis rate was between 5% and 8%, yet treatment of hydrocele was only 2%. Thus, only 28% of patients with a hydrocele diagnosis received treatment for their hydrocele within the 1–5 year follow-up period (Table 3). Controlling for other variables in the model, neither surgical approach nor surgeon volume was associated with hydrocele formation. On the other hand, increased age and having commercial insurance were associated with a significantly lower rate of hydrocele diagnosis (Table 4). For each year of age, there was a 14% decreased rate of hydrocele formation. Despite the apparent differences in hydrocele treatment, 12% after laparoscopic approach and 65% after open, when length of follow-up was analyzed, no patient or surgery characteristic was significantly associated with time to hydrocele treatment (Supplemental Table S3).

Discussion

To our knowledge, this is the largest evaluation of varicocele treatment, adolescent or adult, in the literature, capturing 6,729 boys of whom 1,006 received treatment from 213 physicians at 68 centers. Nees and Glassberg reported a large single-surgeon series of 400 patients evaluating hydrocele formation (15.4% overall) after various open and laparoscopic approaches with a median follow-up

Table 1 Patient characteristics and outcomes by primary surgery type.

	Open	Laparoscopic	PE	No surgery	All varicoceles
Patients (%)	405 (6.0)	530 (7.9)	101 (1.5)	5,693 (84.6)	6,729 (100)
Age at primary surgery					
Mean in years (SD)	14.7 (2)	14.7 (2)	15 (2.1)	n/a	n/a
Median in years	14.9	14.8	15.2	n/a	n/a
Race (%)					
White	106 (6.0)	117 (6.6)	58 (3.3)	1483 (84.1)	1764 (100)
Asian	3 (4.4)	4 (5.9)	2 (2.9)	59 (86.8)	68 (100)
Black	15 (4.3)	19 (5.6)	3 (8.8)	305 (89.2)	342 (100)
Hispanic	11 (4.1)	10 (3.7)	10 (3.7)	236 (88.4)	267 (100)
Native American	0	0	0	11 (100)	11 (100)
Other	8 (3.4)	24 (10.2)	1 (0.4)	202 (86.0)	235 (100)
Unknown	262 (6.5)	356 (8.8)	27 (0.7)	3397 (84.0)	4042 (100)
Insurance type (%)					
Commercial	302 (6.7)	375 (8.3)	87 (1.9)	3730 (83.0)	4494 (100)
Medicaid	61 (4.2)	107 (7.4)	9 (0.6)	1273 (87.8)	1450 (100)
Self pay	25 (8.3)	16 (5.3)	2 (0.7)	258 (85.7)	301 (100)
All other	17 (3.5)	32 (6.6)	3 (0.6)	432 (89.3)	484 (100)
Region (%)					
Midwest	115 (6.4)	70 (3.9)	10 (0.6)	1604 (89.2)	1799 (100)
Northeast	180 (8.0)	227 (10.1)	62 (2.8)	1782 (79.2)	2251 (100)
South	69 (4.3)	133 (8.2)	21 (1.3)	1392 (86.2)	1615 (100)
West	41 (3.9)	100 (9.4)	8 (0.8)	915 (86.0)	1064 (100)

Table 2 Retreatment rate and retreatment approach.

	Open	Laparoscopic	PE
Retreatment (%)			
No	399 (98.5)	512 (96.6)	91 (90.1)
Yes	6 (1.5)	18 (3.4)	10 (9.9)
Retreatment approach (%)			
Open	1 (17)	11 (61)	1 (10)
Laparoscopic	2 (33)	6 (33)	1 (10)
PE	3 (50)	1 (6)	8 (80)

Table 3 Rate of hydrocele formation after primary surgery.

	Open	Laparoscopic	PE
Diagnosis of hydrocele (%)			
No	385 (95.1)	487 (91.9)	96 (95)
Yes	20 (4.9)	43 (8.1)	5 (5)
Treatment of hydrocele (%)			
No	517 (97.5)	400 (98.8)	100 (99)
Yes	13 (2.5)	5 (1.2)	1 (1)

of at least 20 months [13]. Podkamenev et al. reported the largest overall case series in a single-center comparing open and laparoscopic approaches in 654 patients with a short median follow-up of 6 months. They reported recurrence rates of 3–8% with no significant difference between treatment approaches and a hydrocele formation rate of 1–4% [11]. Esposito reported on 161 boys at six high-volume pediatric centers after the laparoscopic approach [14]. The median follow-up was 30 months and they reported a 5.6% hydrocele incidence and a 2.4% rate of varicocele recurrence.

In a subset analysis we found that only 25% of adolescents referred for varicocele are treated within 3–5 years. This may be because of many pediatric urologists limiting treatment to patients with testicular hypotrophy or symptoms. In a practice pattern survey of 131 pediatric urologists by Pastuszak, only 19% of surgeons viewed "potential fertility problems" without other clinical signs or symptoms as an independent indication for surgery [15]. In the same survey, 50% of surgeons would never repair a sub-clinical varicocele found incidentally on ultrasound [15]. It has been our institutional experience that the majority of referrals are boys with grade 3 varicocele. Hence, very few adolescents with varicoceles are seen by urologists, and of those patients only a fraction are treated. We also noted that while this study cannot distinguish the grade of varicocele prior to treatment, the literature suggests that pretreatment grade of varicocele is unrelated to long-term outcome [1,10].

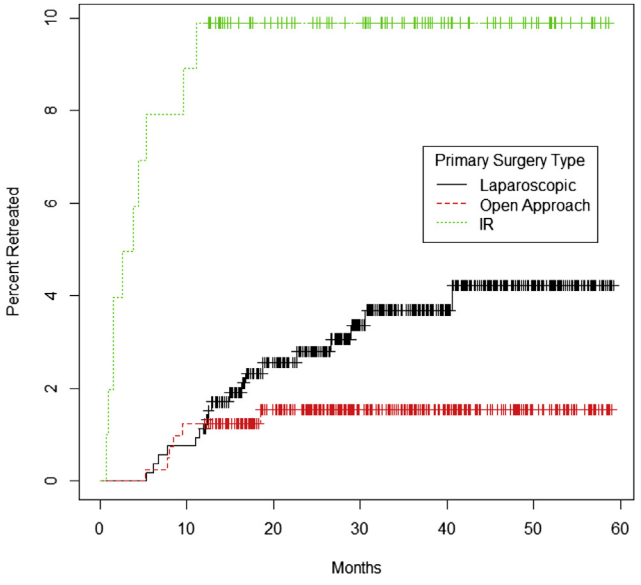

Figure 1 Kaplan–Meier plot of time to first retreatment by type of primary surgery.

Although this series contains the largest cohort of patients, physicians, and institutions, we were limited by the inability to determine actual recurrence rates. Only patients receiving retreatment at the same institution within the 1–5 year follow-up period were captured. As such, the true rate of varicocele recurrence may be higher. Along these lines, this database does not allow distinction between retreatment for persistence versus recurrence. The retreatment rate is influenced by the physician's threshold to retreat and the patient's desire to undergo another procedure. The perception of invasiveness may influence this choice by the patient and/or physician. This database also does not allow one to distinguish the details of the surgery, such as lymphatic or arterial sparing. Although the database does not allow for tracking complications, we did not identify any anesthesia, reoperation, or readmission encounters within 48 h of surgery. Although treatment at a different hospital is possible, with no occurrences at the primary institution, we believe the incidence of major complications was extremely low.

It is a known characteristic of the FPSC database that CPT codes are first and foremost for billing purposes. This does present some limitations. As discussed above, CPT codes in the varicocele and hydrocele context do not distinguish side or recurrence. We were unable to identify a recurrence versus a metachronous contralateral occurrence. However, in our own clinical practice we find there is a low likelihood of a patient to have been referred for varicocele and to have a hydrocele not recognized and/or

Table 4 Time to diagnosis of hydrocele: multivariable Cox proportional hazards analysis.

Covariate	Hazard ratio (95% CI)	*p*
Approach		
PE vs. open	1.01 (0.34–2.95)	0.991
Open vs. laparoscopic	0.70 (0.38–1.29)	0.250
PE vs. laparoscopic	0.70 (0.25–1.98)	0.503
Age at primary surgery	0.88 (0.80–0.97)	0.009
Insurance type: commercial vs. all other	0.52 (0.27–0.99)	0.047
Surgeon volume	1.00 (0.97–1.03)	0.835

treated by the surgeon at the same time. Similarly, there is a negligible amount of patients being treated in a staged fashion for bilateral varicocele such that a right-sided varicocele would be miscategorized as a recurrence. For example, in the largest single-surgeon series, 629 varicocelectomies in over 400 patients performed by Nees and Glassberg, only one case was for a right varicocelectomy after a left varicocelectomy [13]. As a benefit, FPSC is a database based on CPT billing codes. This is considered more accurate than other administrative databases because the CPT codes are generally assigned by certified abstractors and are audited by third-party payers with a vested interest in accurate coding.

Despite its limitations, this is the first study to compare open, laparoscopic, and percutaneous approaches to varicocele treatment. Although the use of percutaneous embolization has been held out as competitive with surgical approaches, in this series the risk of retreatment is nearly six times higher, while the rates of retreatment between open and laparoscopic approaches were equivalent [16–19]. This corresponds with prior analyses. Among 71 adolescents, Beutner found a 21% recurrence rate after PE compared with an 8% rate after laparoscopic treatment. In two meta-analyses, Barroso and Borruto found no significant difference in recurrence rates between open and laparoscopic approaches with rates of 3–4.4% and 5–9%, respectively [2,9]. This is consistent with a retreatment rate of less than 3% in the surgical groups in the present series consisting of 175 urologists in 68 institutions.

The literature offers little on retreatment. The pattern of retreatment we identified is new and interesting. For PE patients, 80% were retreated with PE. On the other hand, two-thirds of those who had secondary surgery after open and laparoscopic repairs were treated with a different approach from the primary surgery.

In the largest reported single-surgeon series, Nees and Glassberg found a hydrocele formation rate of 9% after the laparoscopic approach and 31% after the open approach [13]. A meta-analysis by Borruto found no significant difference in hydrocele rates after open (6.7%) and laparoscopic (9.5%) approaches [2]. The rates of hydrocele formation in the current analysis were similar for all three approaches. The higher rates of hydrocele detection by Nees and Glassberg may be because of the longer follow-up period. In their series, median time to hydrocele detection was approximately 2 years and median time to hydrocelectomy was 3.7 years [13]. At 1 year, they found an overall hydrocele incidence of 5.2%, which is similar to our reported incidence. In the Nees and Glassberg series, less than half the patients with hydrocele underwent hydrocelectomy. In the present series, we demonstrate that the difference between post-operative hydrocele detection and intervention can be generalized beyond a single surgeon and has a similar low rate (2%). The lower treatment rate suggests that most hydroceles detected are small and/or patients elect not to pursue treatment.

Interestingly, none of the large studies address the rate of hydrocele formation after PE. In a short retrospective series Storm et al. followed 21 adolescent patients for 9 months post-embolization from 2001 to 2009 and reported no hydroceles or recurrent varicoceles [20]. Of these, two patients failed PE because of technical issues and required subsequent open varicocele repair [20]. Hydrocele occurrence is almost unheard of among PE. In a meta-analysis of varicocele treatment choices in infertile adult men by Çayan, no study evaluated hydrocele occurrence after PE [21]. However, in a retrospective study of PE for varicocelectomy of painful varicoceles in 181 adult patients between 2007 and 2013, Puche-Sanz reported a 4.5% incidence of hydrocele diagnosis in a 39 month follow-up period [22]. The present series is consistent with Puche-Sanz in detecting a 5% rate of hydrocele detection after PE, which is equivalent to the 4.5% rate after open varicocelectomy. PE has been held out as the ideal lymphatic-sparing approach and therefore should not result in hydrocele formation. The formation of post-PE hydrocele suggests that the process for hydrocele formation caused by occlusion of venous drainage in addition to impairment of lymphatic drainage.

We were surprised to find that younger patients had a higher risk of hydrocele formation ($p = 0.009$). Of note, the analysis corrected for time so a longer follow-up of young patients was not a factor. There was a 14% decreased risk of hydrocele for each year of age at surgery. In other words, a 12-year old had a 68% higher risk than a 16-year old of forming a hydrocele after varicocele treatment. This could not be stratified by approach.

As expected, the analysis of such a large number of patients from 213 treating physicians afforded results quite different from series from single surgeons or high-volume centers, where there are both outcomes submission and publication bias. The results from this large multicenter trial appear consistent with meta-analyses, suggesting that these results may be generalizable. It is important to stress that this analysis was not able to distinguish between the many different techniques within each approach, that is subinguinal versus inguinal. As with all surgeries, individual results will vary between surgeons and specific techniques (e.g. sub-inguinal, Palomo, lymphatic sparing, etc.), yet the first question posed by the average patient is whether to proceed with open, laparoscopic, or percutaneous approach. These results provide a foundation for this discussion between patient, parent, and physician.

Conclusions

Percutaneous embolization has a significantly higher retreatment rate compared with either open or laparoscopic varicocelectomy. Retreatment and hydrocele formation after open and laparoscopic approaches were not significantly different. This supports a surgeon and family choosing an approach based on patient characteristics and surgeon preference.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jpurol.2015.05.003.

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