



# Current Issues in Adolescent Varicocele: Pediatric Urological Perspectives

Jae Min Chung<sup>1,2</sup>, Sang Don Lee<sup>1,2</sup>

<sup>1</sup>Department of Urology, Pusan National University School of Medicine, <sup>2</sup>Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Yangsan, Korea

While varicocele is the most common cause of surgically correctable infertility in adult males, with repair resulting in improved semen parameters in 60% to 80% of men and a higher likelihood of conception in up to 60% of men, the rationale for varicocele repair in the pediatric population is less clear. Additionally, prepubertal varicoceles are much less common and their management is controversial. Adolescents with a varicocele are often in the midst of a progressive disease process. Despite the high prevalence of varicocele and its association with progressive disease processes, the indications for adolescent varicocele repair and the effects thereof on paternity have been persistently challenging to study. This review will briefly present some of the current issues regarding adolescent varicocele from a pediatric urological point of view, including the evaluation of adolescent varicocele, the optimal surgical indications, the optimal choice of surgical intervention to be performed, and outcomes.

**Keywords:** Adolescent; Diagnosis; Infertility; Therapeutics; Treatment; Varicocele

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## INTRODUCTION

Testicular varicocele is a dilation of the veins of the pampiniform plexus draining the testicle, and is the most commonly seen urological condition in postpubertal boys. Varicoceles are found in 15% of all men, including 19% to 41% of men with primary infertility and 80% of men with secondary infertility, and are recognized as the most common surgically correctable cause of male infertility [1,2]. Although varicoceles are rarely seen in prepubertal boys, they are relatively common in adolescent males, as in adults [3]. Varicoceles are found in <1% of prepubertal boys [4], but are

diagnosed in 5% to 30% of postpubertal 12- to 18-year-old males [5,6].

The vast majority of adolescent varicoceles are asymptomatic, left-sided, and incidentally noted by a primary care provider. Varicocele is one of the most important causes of atrophy/hypotrophy of the testis, which raises concerns regarding future fertility [7]. While abundant studies have investigated varicocele in the adult population, comparatively little data exist on varicocele in young males. The management of adolescent varicocele has evolved over the past several decades. Despite this, over the past half-century, there has been widespread debate and disagreement among

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**Correspondence to:** Sang Don Lee <https://orcid.org/0000-0001-9459-3887>

Department of Urology, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, 20 Geumo-ro, Mulgeum-eup, Yangsan 50612, Korea.

**Tel:** +82-55-360-2671, **Fax:** +82-55-360-2164, **E-mail:** [lsd@pusan.ac.kr](mailto:lsd@pusan.ac.kr)

clinicians regarding the benefits of varicocele repair [8]. Adolescents with varicocele are heterogeneous, have rapidly changing hormonal levels, and may present at different stages of physical and pubertal development [9]. For this reason, a standard approach for evaluation, management, and outcome assessment in these patients may not be possible, and considerable debate remains regarding these issues. Therefore, the current challenges in the management of varicocele lie in determining which patients to treat, when to initiate the treatment, and what type of treatment is the best [3,10].

This review briefly presents some of the current issues regarding adolescent varicocele from a pediatric urological point of view, including the evaluation, the optimal surgical indications, the optimal choice of surgical intervention to be performed, and outcomes.

## EVALUATION

Typically, adolescent varicoceles are asymptomatic, although some patients present with complaints of chronic fullness or swelling in the scrotum or inguinal area. Approximately 90% of varicoceles are left-sided and 3% are clinically palpable bilaterally. Subclinical, contralateral varicoceles have been described in up to 30% of males with a unilateral varicocele [11]. The presence of an isolated right-sided varicocele or prepubertal varicocele is extremely rare. Unlike adult varicoceles, which are mainly identified in physical examinations as part of an infertility evaluation, most adolescent varicoceles are detected during routine medical examinations for local clinics, school, or sports [3], or by testicular self-examination, as most boys are asymptomatic, with ultrasonography used to confirm the diagnosis and to more objectively assess testicular size and peak retrograde flow (PRF) [12].

### 1. Physical examination

Physical examination still represents the gold standard for diagnosing clinically significant varicocele. It should be performed in a supine and standing position, and especially while standing, patients should be asked to perform a Valsalva maneuver to accentuate a small varicocele. The scrotum should be visually inspected and then examined by palpation, and the patient should be asked to perform a Valsalva maneuver. Varicoceles can be appreciated as a plexus of veins with a consistency of a 'bag of worms' adjacent to the

testis, which typically decompresses when the patient is supine [3,12]. Varicoceles are graded according to the system of Dubin and Amelar [13] as follows: grade 0, subclinical varicocele (not detectable on clinical examination; identified on scrotal ultrasound [US] or venography); grade I, small varicocele (palpated only during the Valsalva maneuver); grade II, moderate size (readily palpable without the Valsalva maneuver); and grade III, large size (readily visualized).

An important part of the physical examination is the assessment of varicocele grade, testicular volume, and testicular consistency. Varicocele grade, however, has not proven to be a reliable indicator of future asymmetry [14]. Diamond et al [15] could not identify any difference in semen parameters or testicular volume differentials between varicocele grades. Testicular volume can either be measured in the office setting with orchidometers comprised of comparative ovoids (Prader), cut-out ellipses (Rochester or Takahara), or with scrotal US. A softer consistency of the involved testis is noted in a small percentage of boys, and is typically associated with decreased volume [12].

Appropriate caution should be taken to ensure that patients who are prepubertal, have an isolated right-sided varicocele, or have a varicocele that does not decompress in the supine position should undergo US due to suspicion of having a retroperitoneal or renal mass [16]. The European Society for Pediatric Urology guidelines recommend performing a renal US examination in such boys, as the extension of a Wilms tumor into the renal vein and inferior vena cava may be associated with a secondary varicocele [17,18].

### 2. Orchidometric measurement

Various clinically useful markers of future infertility have been studied. Semen analysis (SA) may be the most accurate predictor of future fertility. However, some physicians have raised ethical concerns regarding obtaining semen samples, especially in adolescent patients. For this reason, the most important factor in deciding to treat a varicocele in adolescence is testicular volume. Varicoceles may be associated with testicular atrophy and histologic abnormalities of the testis. Testicular volume measurement using an orchidometer and/or US offers a non-invasive method of gauging future fertility potential. In general, it has been demonstrated that US is more accurate than orchidometry in volume measurement in both adults [19] and adoles-

cents [20]. However, in clinical practice, orchidometers are still reliable tools to measure testicular volume, since there is a close relationship between US-derived and orchidometer-derived testicular volume, and this procedure can be performed very easily during a physical examination. In addition, orchidometers are inexpensive, less invasive, less time-consuming, and more cost-effective. Until recently, both Prader orchidometry and Rochester (or Takahara) orchidometry have been popular methods of measuring testis volume, and orchidometric evaluation of the testis has been proposed as a cost-effective alternative to measurement of the testis with high-frequency linear US.

In clinical practice, Rochester orchidometry in general appears to overestimate testis size, and its low sensitivity (33%) means that a 20% testis volume differential would be missed in approximately 2 out of 3 boys screened with orchidometry alone [21]. Besides, little is known about the effectiveness of orchidometry in the clinical setting in large series of adolescents with varicocele. Therefore, appropriate caution should be exercised when relying solely on orchidometric evaluation of the testis, and US should be performed annually to evaluate testicular volume in adolescent males with varicocele.

### 3. Doppler ultrasound

Possible indicators of future infertility include varicocele grade, asymmetric testicular growth, total testicular volume, and the Doppler US parameters of maximum vein diameter and PRF [14]. Although the diagnosis of a varicocele is usually made primarily by a physical examination, scrotal US is indicated for the evaluation of a questionable physical examination of the scrotum because it allows accurate measurements of testicular volume and a precise assessment of spermatic vein status. While it is recognized that US is more objective than an orchidometer, its routine use is not recommended because of its higher cost and operator bias. While all guidelines recommend physical examination as the cornerstone of varicocele diagnosis, the European Association of Urology (EAU) guidelines state that it should be complemented with color duplex US [22]. In a 2014 questionnaire study of the assessment of adolescent varicocele by pediatric urologists, 131 (54%) of 242 pediatric urologists responded to the survey. Most physicians used US or Doppler US to aid in the diagnosis of varicoceles, and half of the physicians stated that they would not repair incidental find-

ings of varicocele on US. A more recent survey study examined the approach to asymptomatic grade 2 and 3 varicocele by pediatric urologists. In this study, in which the response rate was 28% (74 of 267 surveys), Coutinho et al [23] found that 49% of respondents used US to evaluate testicular size, with 38% continuing to use orchidometers. In a recent survey conducted in Korea in 2016, 32 respondents (86%) used US and/or Doppler US for the diagnosis of varicocele, with most of those respondents (n=25, 68%) using US in 76% to 100% of all cases. Twenty-nine respondents (78%) used objective US criteria, including testicular volume discrepancy, as well as venous dilation and/or backflow, but 8 respondents (22%) answered that US findings did not influence their decision-making process [24].

### 4. Semen analysis

SA may be the most accurate predictor of future fertility. However, based on the currently available data, the role of SA in the evaluation of adolescent varicocele remains unclear. In Tanner V adolescents, SA can be considered as an additional way to assess testicular function. However, ethical concerns have arisen regarding obtaining semen samples in postpubertal patients. In addition, it is difficult to interpret semen analyses in adolescents because there are currently no standard norms for interpreting semen parameters in this population. The natural history of semen parameters in patients with asymptomatic Tanner V adolescent varicocele shows a regression to the mean for previously poor SA results in subsequent SA. Using serial SA as a surveillance tool rather than testicular volumetrics, Chu et al [25] demonstrated that repeated SAs are necessary in the management of these patients, as nearly half of the patients with an initially poor total motility count (TMC) showed normalized semen parameters on the second SA. A subpopulation of high-risk patients, however, had persistently poor TMCs. These findings suggest that patients with adolescent varicocele who have normal semen parameters should be followed conservatively with annual or biannual SAs. An abnormal SA should always be confirmed by at least a second SA [26].

### 5. Endocrine parameters

The presence of varicocele has been postulated to affect testosterone production and, in turn, the hypothalamic-pituitary-gonadal axis. However, in terms of endocrine evaluation, the utility of obtaining a baseline

hormonal evaluation for identifying adolescents at risk for infertility has not yet been demonstrated, and the significance of testosterone changes pre- and post-intervention remains unclear [27]. Multiple recent studies support a relationship between varicocele and the development of hypogonadism and androgen deficiency, potentially providing an impetus for early varicocele repair [28,29]. In contrast, some investigators believe that the duration of exposure to varicocele has a direct impact on the worsening of testicular function [17].

## MANAGEMENT

The management of adolescent varicocele has evolved over the last 30 years, but remains one of the most interesting and controversial topics in pediatric urology. The purpose of treating varicocele in adults is to improve patients' current fertility status [30]. In contrast, in most cases, the goal of treatment for adolescent varicocele is to prevent testicular injury and maintain testicular function for future fertility [3]. The management options of adolescent varicocele are limited to observation with follow-up, percutaneous embolization of the gonadal veins, or surgical intervention [3]. Some authors have recommended early surgical interventions to preserve fertility [31], whereas in other series, non-operative management was preferred based on reported testicular 'catch-up' growth during development [32]. However, while numerous studies have sought to define the timing and necessity for intervention based on testicular size, few have reported the natural progression of testicular growth associated with adolescent varicocele. The American Urological Association (AUA) and the American Society of Reproductive Medicine (ASRM) recommended that all adolescents with reduced ipsilateral testicular growth should be offered varicocele repair, and that adolescents who do not show any changes in testis size should be followed until such a change in testis size becomes apparent [26,33]. In a 2014 questionnaire study of pediatric urologists, only 3% of respondents operated on varicoceles at diagnosis, whereas 14% observed them, and 83% based their treatment plan on further indications. Varicocelectomy is most commonly performed for decreased ipsilateral testicular size (96%), testicular pain (79%), and altered SA parameters (39%), with the mean age for varicocelectomy being 12.5±3.1 years. The most common surgical approaches to varicocelectomy were laparoscopic (38%),

subinguinal microsurgical (28%), inguinal (14%), and retroperitoneal (13%), and most physicians used loupes for these procedures. Recently, Lee et al [24] surveyed pediatric urologists to determine the current practices for the diagnosis and management of pediatric and adolescent varicoceles in Korea. Ten respondents (27%) chose to operate on varicoceles, whereas 9 (24%) chose to observe them, and 18 (49%) decided upon the treatment strategy depending on the clinical situation. These surveys noted significant variations in the decision to treat and operative approaches among pediatric urologists [34].

### 1. Conservative management (observation with follow-up)

Early surgical intervention for varicocele aims to resolve testicular hypotrophy and to ensure catch-up growth. The question of reversibility of function with early surgical intervention often arises. Decastro et al [35] studied testicular catch-up growth following spermatic vein ligation in 163 boys aged 10 to 24 years. They found no difference in the prevalence of catch-up growth as a function of Tanner stage or age, with a good response even into the 20-year range. A recent study of the impact of patient age on semen parameters following varicocelectomy comparing young adults (18–25 years) with older patients (26–35 years and >36 years) found no difference in outcomes [36]. These studies suggest that there appears to be little evidence that waiting for a few years to correct adolescent varicocele results in worse functional outcomes. Although varicocele is detected in 35% of primary infertile men, nearly 80% of adults with varicocele are asymptomatic and fertile [10,12]. It has been shown that fertility problems will arise later in life in approximately 20% of adolescents with varicocele, which can be interpreted as evidence in favor of performing an early intervention to avoid disease progression [37].

An observational approach to adolescents with a varicocele is based on the inability to predict the effect of the varicocele on fertility. At the first sign of varicocele-related testicular dysfunction, as manifested by a change in testicular size, especially in the absence of a SA or an abnormality on SA, varicocele repair should be offered. Limited evidence has been published on the natural history of semen parameters or testicular size discrepancy in adolescent varicocele. The recent EAU guidelines published in 2012 highlight the risk of

overtreatment [38]. The AUA guidelines for varicocele recommend that adolescents who have a varicocele with normal ipsilateral testicular size should be offered follow-up monitoring with annual objective measurements of testicular size and/or SA [12]. The ASRM also recommended that men with varicocele and normal semen parameters should be followed conservatively with annual or biannual SAs [33].

In a recent study by Bogaert et al [39], 85% of adolescents with uncorrected varicoceles managed with observation achieved paternity, which was a proportion similar to the 78% of men whose varicoceles were repaired. They suggested that treatment of the varicocele at diagnosis did not appear to improve later chances of paternity. They also emphasized that if all adolescent males with a varicocele underwent surgery, 80% would undergo an unnecessary operation. This finding is consistent with some previous observational data on adolescent varicocele [12]. Furthermore, Moursy et al [31] examined semen parameters in adolescent patients with no testicular size differences who were managed conservatively, with 59 of 60 patients demonstrating normal parameters on serial SA. In the most recent study by Chu et al [25], two-thirds of Tanner V boys with an uncorrected varicocele and normal testicular volumes achieved a normal TMC regardless of varicocele grade or age. Despite Tanner V development, 47% with an initial 'poor' SA improved to normal status without surgery. These studies support the conservative management of adolescent varicocele in the form of active surveillance with serial SA. However, in a recent study, Van Batavia et al [40] described 115 boys aged 9.5 to 20.0 years who were followed over a mean of 11.7 months via US. They noted that up to 63 boys (55%) presented with >15% asymmetry from the start, and 21 boys (33%) experienced a resolution of testicular asymmetry, but 22 of the 45 boys (49%) without asymmetry worsened to >15% asymmetry with time. A small subgroup of patients can be expected to have a persistently poor TMC. In conclusion, semen parameters and/or testicular asymmetry can improve over time, and SA should be followed and repeated at least once in symptomatic Tanner V boys with varicocele.

Taken together, many studies recommend that adolescents with varicocele should be observed for testicular disproportion for at least 1 year to allow for potential spontaneous catch-up growth prior to surgical intervention, and be followed annually with an objec-

tive assessment of testicular size and/or SA.

## **2. Interventional approach (surgery or venous embolization)**

Various studies have shown adverse effects of adolescent varicocele on testicular volume, and a correlation between varicocele and the regression of testicular development has been demonstrated [37,41,42]. In several studies, repair of varicocele resulted in increases in serum testosterone in most men to eugonadal levels, independently of varicocele grade, over the course of several months of follow-up. These findings support a relationship between varicocele and the development of hypogonadism and androgen deficiency, potentially providing a rationale for early varicocele repair [28]. Furthermore, varicocele repair results in testicular growth that correlates with increased serum testosterone, supporting a link between testicular 'catch-up' growth and a rise in serum testosterone. Therefore, because untreated varicocele may result in androgen deficiency even in younger men, early varicocele repair should be promptly reconsidered in current management practices [43].

### **1) Surgical indications**

Among a small proportion of adolescents, varicocele has a detrimental effect on testicular growth and can lead to irreversible testicular damage. Thus, the most important issue in the management of adolescent varicocele is to appropriately select patients who actually need treatment [3]. A number of studies have attempted to characterize the clinical progression of adolescent varicocele and to identify criteria to select those who might benefit from surgical intervention. Several indications for varicocele repair have been reported in various studies. Varicocele grade, testicular disproportion, and the potential for 'catch-up' growth during adolescence have all been previously proposed as criteria for adolescent varicocele repair. Mehta and Goldstein [10] emphasized that deterioration in semen parameters, significant and persistent ipsilateral testicular hypotrophy in adolescents who are unable to provide a semen sample, or classic varicocele-associated pain should be used as the primary indications for surgical intervention.

Taken together, while the indications for surgical intervention in these patients are controversial, many experts, especially pediatric urologists, advocate for varicocele repair in adolescents with a persistent testicular size discrepancy of greater than 20%, abnormal

SA if obtainable, and painful varicocele [12].

## 2) Choice of surgical intervention

One of the most important problems in the treatment of adolescent varicocele is to determine the varicocelelectomy method. The ideal surgical approach for adolescent varicocelelectomy represents another area of debate and is usually dependent on the surgeon's preference. Currently, the best procedure for the treatment of adolescent varicocele has not been established; instead, multiple methods exist for the treatment of varicocele that produce consistent results. Surgical options include the traditional inguinal (Ivanissevich) or high retroperitoneal (Palomo) approaches, laparoscopic repair, and microsurgical repair via an inguinal or subinguinal incision [12]. Alternatively, sclerotherapy or embolization can be used as a non-surgical option. All surgical repairs involve the ligation of the spermatic veins, with the main differences between the techniques involving the surgical approach to the testicular vessels, the level of the ligation (proximal or distal) and whether the testicular artery and lymphatic vessels are spared or ligated along with the veins [12]. The 2 methods of varicocelelectomy that have gained the most popularity among pediatric urologists in the United States are the Palomo repair with high inguinal *en bloc* ligation and the laparoscopic approach [44]. Pediatric urologists are less likely than andrologists to use the microscopic approach (only 1% of adolescent varicocelelectomies in a recent national survey) because of limited experience with it and the fear of the quite rare incidence of post-varicocelelectomy ipsilateral testicular atrophy [6,44]. According to the 2001 United States practice survey, the most common surgical approach was inguinal (36%), followed by subinguinal (30%), retroperitoneal (Palomo; 21%), and laparoscopic (10%). However, in a 2014 survey of 131 pediatric urologists, Pastuszak et al [34] reported that the preferred surgical approaches were laparoscopic (38%), subinguinal microsurgical (28%), inguinal (14%), and open Palomo (13%). They noted that the management of pediatric varicocele appeared to have remained stable over the past decade, with a shift toward increasing use of the laparoscopic technique. This reflects the fact that laparoscopic surgery has gained popularity in the United States over time. Contrary to the United States survey, in the Korea practice survey, the most common surgical approach for pediatric and adolescent varicocele was subinguinal microsurgical

(51%), followed by inguinal (24%), laparoscopic (14%), and open retroperitoneal (Palomo) (11%) [24].

## OUTCOMES

### 1. Catch-up growth

Since SA cannot be performed as a form of postoperative evaluation in pediatric patients, testicular catch-up volume is the most important parameter for evaluating the outcomes of varicocelelectomy [6]. Although the actual benefit of varicocele treatment in children and adolescents is still debatable, several studies have reported testicular catch-up growth after varicocelelectomy in 60% to 90% of boys with preoperative asymmetry, and in many studies, recovery of testicular hypertrophy has been reported after varicocelelectomy [41,45-48]. Sinanoglu et al [47] followed 39 adolescents with varicocele at 3-month intervals after varicocelelectomy by calculating testicular volumes. During an average follow-up of 39 months, they reported catch-up growth in 90% of cases with ipsilateral testicular atrophy. In the report of Fast et al [49], the incidence of catch-up growth following lymphatic non-sparing laparoscopic varicocelelectomy was 71%, in contrast to 80% after lymphatic-sparing procedures, and 83% following lymphatic- and artery-sparing procedures [49].

The concept of catch-up growth is complex. In the setting of testicular asymmetry, varicocele repair appears to result in catch-up testicular growth and improvements in sperm count [37]. Catch-up growth has been shown to occur after varicocele ligation, independently of the patient's Tanner stage or age, but can occur spontaneously in a significant proportion of adolescents with unrepaired varicocele [10,12]. A large meta-analysis encompassing 14 studies and 1,475 patients that evaluated the effects of varicocelelectomy on testicular catch-up growth in adolescents with a testicular volume discrepancy  $\geq 10\%$  showed a significant reduction in the volume differential after varicocelelectomy, although SA data were absent [50].

One of the most important problems in the treatment of adolescent varicocele is to determine the varicocelelectomy method and the optimal age of surgery that will achieve the highest catch-up growth rate [12]. However, in studies performed on the impact of the surgical method on the catch-up growth rate, no effect of the surgical method on the testicular catch-up rate could be detected. Recently, Shiraishi et al [51] performed subin-

guinal and high-ligation microsurgical varicocelectomy and reported catch-up growth rates of 70% and 78%, respectively, during 24 months of follow-up. However, they were not able to detect a statistically significant difference between these methods. Atassi et al [52] compared 36 patients who underwent artery-preserving varicocelectomies (n=36) with those who underwent the Palomo procedure during a follow-up period of 22 months, and when compared with preoperative values, the left testicular volume increased from 73% to 91% in patients undergoing artery-preserving surgery, while in patients who underwent the Palomo procedure, the average increase was from 73% to 91%, without any statistically significant intergroup difference. Regarding testicular artery sparing, Fast et al [49] also evaluated the effect of testicular artery sparing on catch-up growth, and they found that there was no difference between the artery-sparing group and non-artery-sparing groups.

## 2. Semen parameters

The outcome of varicocele repair has been analyzed from a multitude of angles [53]. Relatively few studies have evaluated the effects of varicocele on semen parameters in young men. A recent meta-analysis investigated the natural history of varicocele in terms of the effects of varicocele and varicocelectomy on semen parameters in males 15 to 24 years old, finding that across 10 studies encompassing 357 varicocele and 427 control patients, varicocele was associated with decreases in sperm density, motility, and normal morphology [54]. In 10 additional studies encompassing 379 treated and 270 untreated men with varicocele, significant improvements in sperm density and motility were observed in treated men. Together, these results suggest that varicocele has similar effects in adults and young men with respect to fertility, with similar benefits from treatment [55]. Regarding paternity outcomes, Pajovic and Radojevic [56] reported a 75% conception rate in men who had undergone varicocelectomy between ages 15 to 19 for abnormal semen parameters. The above evidence suggesting beneficial effects of varicocele repair for improving natural fertility in men with clinical varicocele and abnormal semen parameters support the current guidelines issued by the AUA, ASRM, and EAU [22].

## 3. Varicocele-associated pain

Several studies have demonstrated the successful resolution of varicocele-associated pain following vari-

cocele ligation in between 50% and 90% of patients, depending on the definition used [10,57-60]. Varicocele grade [57], preoperative duration of pain [58], and quality of pain [59] have been found to be predictors of post-varicocelectomy pain resolution in different series.

## CONCLUSIONS

There is no current consensus on the diagnosis and management of pediatric and adolescent varicocele among pediatric urologists throughout the world. Based on the evidence available in the literature, adolescent varicocele remains one of the most interesting and controversial topics in pediatric urology. Adolescents with varicocele have rapidly changing hormonal levels and may present at different stages of physical and pubertal development. For this reason, it may not be possible to apply a standard approach to adolescent patients. The standard clinical follow-up protocol, the optimal indications for surgical intervention, and the optimal choice for the intervention method continue to be debated. Therefore, an individualized approach should be used in which all parameters, including pain, testicular asymmetry, semen parameters, endocrine parameters, and abnormal color Doppler parameters, should be considered. Besides because most studies were retrospective, single-operator, single-institute studies with a small sample size, and most of the recommendations were derived from nonrandomized clinical trials, retrospective studies, and expert opinion due to the paucity of robust data, we strongly recommend well-conducted prospective, randomized, controlled multicenter trials to investigate surgery versus observation in the pediatric population.

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## Disclosure

The authors have no potential conflicts of interest to disclose.

## Author Contribution

Research conception & design: Lee SD. Data acquisition: all authors. Data analysis and interpretation: all authors. Drafting

of the manuscript: Chung JM. Critical revision of the manuscript: Chung JM. Receiving grant: Lee SD. Approval of final manuscript: all authors.

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