Chapter

Controversies in the Laparoscopic Treatment of Varicocele in the Pediatric Population

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Abstract

At present, treatment of varicocele is still controversial in adolescents for at least three reasons. Firstly, the long-term outcome of treatment is not known in the absence of spermiogram support and in terms of long-term follow-up. Secondly, it is still uncertain which is the best type of operation for children/adolescents. Thirdly, the principle that if a technique is designed for adults, it can also be safely performed in adolescents cannot be applied. A recent systematic literature review and meta-analysis demonstrated that open and laparoscopic techniques appear to yield better results with a microsurgical approach compared with laparoscopy. However, laparoscopic techniques that preserve the lymphatic vessels appear to have a clear advantage by preventing postoperative hydrocele. At present, the evaluation and choice of treatment for adolescent varicocele patients are based not on objective fertility criteria (paternity) but on indirect evidence that testicular function or spermatogenesis and thus ultimately also fertility may be compromised. In the absence of sufficient data regarding the treatment of varicocele at a pediatric age, the choice of the technique appears to depend largely on the experience and preferences of the surgeon rather than on a shared option.

Keywords: varicocele, laparoscopy, microsurgery, fertility, adolescents, children

1. Introduction

The incidence of varicocele is approximately 10–15% in children and adolescents [1]. Approximately 10% of young males exhibit asymptomatic varicocele, of whom approximately 16% have reduced sperm counts based on sperm examination, and approximately 30% exhibit significant abnormalities in their semen. A recent European study that included over 7000 patients found a 15.7% rate of varicocele in young males with a median age of 19 years [2]. The prevalence of varicocele in prepubescent boys younger than 10 years of age is much lower, at <1%. In 2000, Akbay et al. reported a 0.8% prevalence in boys aged 2–6 years, 1.0% for those 7–10 years, 7.8% for those 11–14 years, and 14.1% for those 15–19 years of age [3]. These data suggest that varicoceles are progressive and increase in prevalence as boys approach puberty, which may be ascribed to the testis enlargement and the increase in blood supply to the testis [4].

2. Clinical evaluation

Children and adolescents suspected of having varicoceles should undergo a thorough assessment of their medical history, as well as a physical exam including an examination of the scrotum in the standing and supine position in a warm environment. The grading scale for varicoceles ranges from subclinical to grade III, depending on the severity, as depicted in **Table 1**. Subclinical varicoceles are only detected with ultrasound imaging. Dubin and Amelar developed a scale for varicocele comprising grades I through III in the early 1970s [1].

Grade I varicoceles are only palpable with Valsalva. Grade II varicoceles are visible with Valsalva pressure and palpable without Valsalva pressure, while grade III varicoceles are visible without Valsalva pressure and are historically correlated with the pathognomonic 'bag of worms' appearance. Depending on the scrotal skin thickness and room temperature, the 'bag of worms' is not always readily apparent even with grade III varicocele. In general, grade II and III varicoceles are readily identifiable by physical examination and are commonly referred to a urologist.

Testicular growth is typically considered to be inversely negatively affected by the varicocele grade. However, other studies have not observed a relationship. Therefore, some authors argue that the varicocele grade alone is not an indication for surgery in the majority of patients [5].

Testicular volumes can be more accurately assessed with ultrasound in pediatric patients rather than by physical examination alone, and serial ultrasound imaging can be utilized for active monitoring of the impact of varicocele on testicular growth. While ultrasound is a better method for accurate measurement of testicular volumes, an orchidometer is a reasonable alternative.

The development of US imaging and particularly the introduction of high-frequency probes associated with the color-Doppler US has led to widespread use of this diagnostic method in the search and characterization of varicocele. The examination evaluates the diameter of the venous vessels as well as colorimetric and blood flow changes.

The most commonly applied US classification systems are those proposed by Sarteschi et al. and Chiou et al. [6, 7].

The classification system proposed by Sarteschi et al. divides varicocele into five grades on the basis of color-Doppler US findings obtained with the patient at rest and during the Valsalva maneuver (**Table 1**). Other US classification systems comprise those proposed by Hoekstra, Hirsh, Oyen, and the recent system proposed by Iosa et al. [8, 9].

The testes of a normal patient should be symmetrical in size and consistency. An orchidometer can be a reliable device to assess testicular size, with good interobserver variability. However, compared with ultrasonography (US), it may lack sufficient accuracy to distinguish a testis volume differential of less than 50%.

Subclinical	**Not visible or palpable by physical examination; only discernible by ultrasound**
I	Not visible; palpable by physical examination only with Valsalva
II	Visible with Valsalva, palpable by physical examination without Valsalva
III	Visible without Valsalva

Table 1.
Grades of varicocele.

Two formulas are used to calculate testicular volume on the basis of dimensions obtained via US: the Lambert formula and the volume-of-rotational-ellipsoid formula. The Lambert formula is as follows:

- Testicular volume = Length × width × depth × 0.71

Two variations exist for the volume-of-rotational-ellipsoid formula:

- Testicular volume = Length × width × depth × 0.52
- Testicular volume = Length × $width^2$ × 0.52

Hsieh et al. studied the reliability of these formulas and found that the Lambert formula was more accurate than both of the volume-of-rotational-ellipsoid formulas and more precise than the second of the two volume-of-rotational-ellipsoid formulas.

A size difference of more than 3 cm^3 is considered significant. The average volume of the male testis is 23 ± 3 cm^3 [10–12].

A comprehensive analysis of US data on varicocele diagnosis is available from the review of Lotti et al. The authors indicate that there is no international consensus for the assessment of different ultrasonography parameters. An agreement between world societies would be useful in this case [13].

3. Hormonal studies

Hormone profile studies may be beneficial in the workup of a varicocele in pediatric and adolescent male patients, as is the case with the adult population. The presence of varicocele has been associated with higher serum levels of basal follicle-stimulating hormone (bFSH) and basal luteinizing hormone (bLH) in patients with pathologic semen analysis with lower inhibin B levels.

On the other hand, Romeo and colleagues found that inhibin B was decreased but all other hormones (LH, FSH, testosterone) were normal and there was no correlation with semen parameters [14]. There is currently no consensus on the utilization of hormone profile laboratory values in the workup of this population [15–17].

Another important factor is represented by sperm nuclear DNA fragmentation, which occurs in adolescent varicocele even when there are no changes in sperm quality as assessed by conventional seminal analysis. Bertolla et al. found the presence of DNA sperm fragmentation in adolescent varicocele even in the presence of normal sperm [18].

This is probably due to both increased oxidative stress and temperature. DNA sperm fragmentation could become an essential additional diagnostic test to be recommended for patients with clinical varicocele [19, 20].

4. Spermiograms in the pediatric population

Among the most important points to consider regarding varicocele in the pediatric population are the reliability of spermiograms, the ethical implications, and the

reliability of the results. The age at which men start producing spermatozoa; whether spermatogenesis and accessory gland secretions start on one certain day; and the time required for stabilization of the production, maturation, and the release of spermatozoa have not been clearly established. One of the problems encountered relates to the method used to obtain samples for semen analysis. The requirement that adolescents have to masturbate can cause a degree of conflict with the moral and ethical values of some sectors of society, although it has been pointed out that masturbation has no effect on health [5]. On the other hand, varicocele usually increases around adolescence and is rarely reported to occur later in adult men. Patients are commonly referred to a urologist either after detection of a scrotal mass, classically described as a "bag of worms", after detection of a difference in testicular size during childhood, or following a sport-related physical examination or for flank/testicular pain even when in some cases they are completely asymptomatic. Kurtz et al. concluded that the total testis volume and the testicular volume differential are associated with semen analysis outcomes in adolescents with varicocele. A testicular volume differential greater than 20% doubles the odds of a low total motile sperm count. A total testis volume of less than 30 cc quadruples the odds of a low total motile sperm count [21].

A useful criterion could be that proposed by Dabaja (2014). The authors consider it is appropriate to request semen specimens by masturbation from teenagers at one year and six months after the onset of puberty. The age of puberty onset plus 1.5 years is an important predictor of ejaculation. Any adolescents around this age who have experienced ejaculation should be considered candidates for self-stimulation for the collection of a semen sample [22].

One of the first studies in this regard is that of Laron et al. [23].

The authors introduce the term "oigarche" as the age of first conscious ejaculation, in analogy with female menarche. Despite a wide range in the chronological age at the occurrence of the first conscious ejaculation, the mean bone age in all groups, including that with delayed puberty, was 13.5 ± 0.5 years (SD), ranging from 12.5 to 15.5 years.

An important observation regarding semen analysis is that proposed by Chu et al. The authors found that two-thirds of Tanner Stage V boys with uncorrected varicocele and normal testicular volumes achieve a normal total motile count irrespective of the varicocele grade or age. Despite Tanner stage V development, 47% of those with an initial "poor" SA will improve to normal status without surgery, and only a small subgroup of patients will have a persistently poor total motile count [24].

Therefore, some authors argue that the varicocele grade alone is not an indication for surgery in the majority of patients [14].

5. Treatment

For centuries, treatment of varicocele has been associated with correction of the scrotum swelling and ultimately also the pain.

Varicocele surgery dates back to the first century AD. According to Hotchkiss, Cornelius Celsus (25 BC–ca. 50 AD) performed the first documented ligation and cauterization of a varicocele. In 1541, Ambroise Paré provided the most poetic and effective definition of varicocele. He described a condition of "compact groups of vessels filled with melancholic blood and often growing in men of melancholy temper". "Melancholic" probably refers to slow and "toxic" blood, and one can, therefore,

assume that Paré was aware of blood stasis in varicocele veins. Only in the past century has treatment of varicocele entered the age of modern evidence-based medicine, and varicocele surgery has finally progressed beyond merely providing relief of scrotal pain and swelling. The first studies to document an improvement in semen quality and an increase in pregnancy rates following treatment of varicocele were by Barwell in 1885, Bennett in 1889, and Macomber and Sanders in 1929. William Selby Tulloch (1913–1988) was the first surgeon to repair a varicocele for the treatment of infertility. His initial report described an infertile man with bilateral varicoceles and testicular biopsy-proven maturation arrest. This patient was able to attain an increase in sperm concentration and give rise to a natural pregnancy after their varicocele was repaired. Tulloch's report contributed to the worldwide acceptance of the role of varicocele in male infertility [25–28].

Coming to the modern era, the common principle that rules the modern treatment of varicocele in the pediatric population is the closure of refluxing veins and sparing of lymphatic vessels and arteries. Naturally, no specific procedure has been conceived specifically for this particular population. Rather, all treatment options have originated from the practice of adult male infertility. These comprise standard open surgery, microsurgical-assisted techniques, laparoscopy/robot-assisted surgery, and percutaneous embolization.

In 2015, the European Society for Pediatric Urology and the European Association of Urology formulated the following recommendations for management of varicocele in children and adolescents:

The recommended indication criteria for varicocelectomy in children and adolescents are varicocele associated with a small testis:

- a volume difference of ≥2 mL or 20%;
- an additional testicular condition affecting fertility;
- bilateral palpable varicocele;
- pathological sperm quality (in older adolescents);
- symptomatic varicocele.

These recommendations have been reaffirmed in the European Association of Urology document of 2022 [29].

Inguinal exploration has been a standard procedure for many years, with ligation of all venous vessels as described by Bernardi and Ivanissevich [30, 31].

Palomo retroperitoneal ligation of arteries and veins above the internal inguinal ring was proposed in 1949. The technique has a high success rate and a low risk of testicular atrophy. As stated in Palomo's publication, the blood supply of the testis is preserved mainly by the integrity of the cremasteric and deferential arteries [32].

With the advent of laparoscopy, Palomo ligation has become the most common operation feasible in a short time by use of two or three trocars or by single-incision laparoscopic surgery (SILS) [33].

Indeed, at present, the two techniques that have gained worldwide acceptance for use in children/adolescents are laparoscopy and subinguinal microsurgery.

As for venous embolization, according to some authors, venous embolization has the advantage of being a minimally invasive procedure with a faster return to normal

activities and a considerably lower cost. The most common technique utilizes a combination of thrombogenic fibered metal coils and a liquid sclerosant to ensure occlusion of both large and small veins. However, other materials such as biological glues and vascular plugs may also be utilized. Coils are the most commonly used embolization agent due to their safety features, easy handling, and low cost. Complications associated with coil insertion such as migration to the heart or pulmonary arteries and infection are rare but potentially serious. Moreover, the use of X-rays can be considered a disadvantage [34, 35].

6. Laparoscopy

Sanchez De Badajoz et al. reported the first laparoscopic varix ligation in 1988 [36, 37].

In 1991, Aaberg reported the first experiences of Palomo performed by laparoscopy with the use of clips [38]. In 1992, Hagood et al. and Donovan et al. [39, 40] reported laparoscopic varicocelectomies with sparing of the spermatic artery. They reported that a laparoscopic camera provided a good level of magnification of the vascular structures. The arteries could readily be visualized after a papaverine drip, and the internal spermatic veins were identified and clipped without difficulty. Donovan reported a mean operating time of 101/153 minutes. As of the early 1990s, laparoscopic surgery has increasingly been utilized by pediatric surgeons [41, 42].

The principle of laparoscopic varicocele ligation is based on the following steps: peritoneal approach; opening a small window on the posterior peritoneum at a distance of 1–2 cm from the inner inguinal ring; isolation of the vessels and their ligation or sealing "en bloc"; or exclusion of the artery and the lymphatics. The procedure is facilitated by the magnifying effect of the laparoscopic lens, which allows for excellent visualization of the structures of the vascular bundle. To achieve better visualization of the lymphatics, recent findings have shown that intra-dartos/intra-testicular injection of isosulfan blue is significantly better than the previously described intra-dartos injection, thereby allowing identification of lymphatic vessels in 100% of the cases in our series [43–46].

With time lymphatic/artery sparing technique has taken over from Palomo while still maintaining the same laparoscopic approach. Laparoscopic varicocele ligation can also be performed by SILS. The ligature of the vessels can be achieved by using a simple absorbable thread, by clips (absorbable or not absorbable), or by LigaSure™ [47–50].

A further improvement in terms of success and prevention of complications in laparoscopy of varicocele appears to be the high ligation of the venous plexus above the linea terminalis. This aspect is highly innovative and should be pursued (**Figures 1**-**4**) [51].

7. Microsurgery

In 1985, Marmar et al. proposed combined microdissection of the spermatic cord at the external inguinal ring, ligation of the dilated veins, and controlled sclerosis of small cross-collateral veins (Polidocanol 3%, 2–3 ml) [52]. The procedure was performed with an operating microscope and microsurgical instruments. Out of 71 cases, there were no post hydroceles and two palpable (0.28%) recurrences. In this initial report, the semen parameters demonstrated statistically significant improvement,

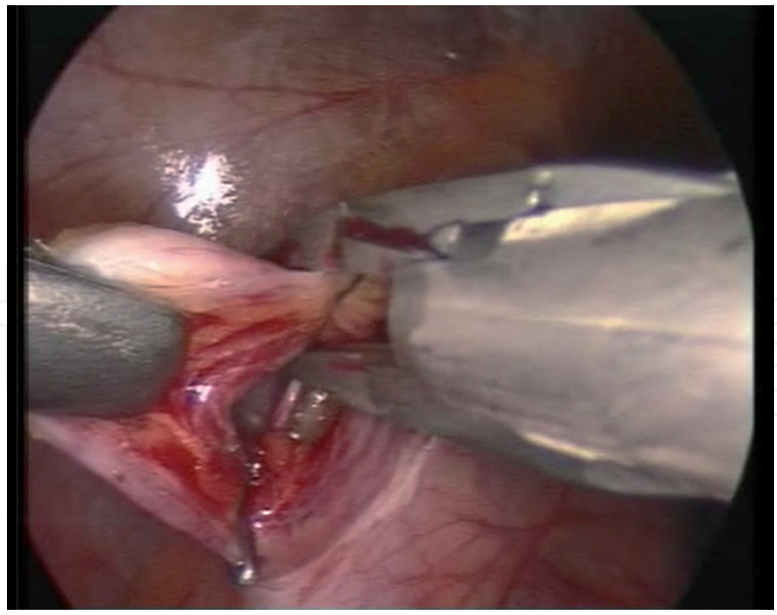

Figure 1.
Laparoscopic clips varicocelectomy.

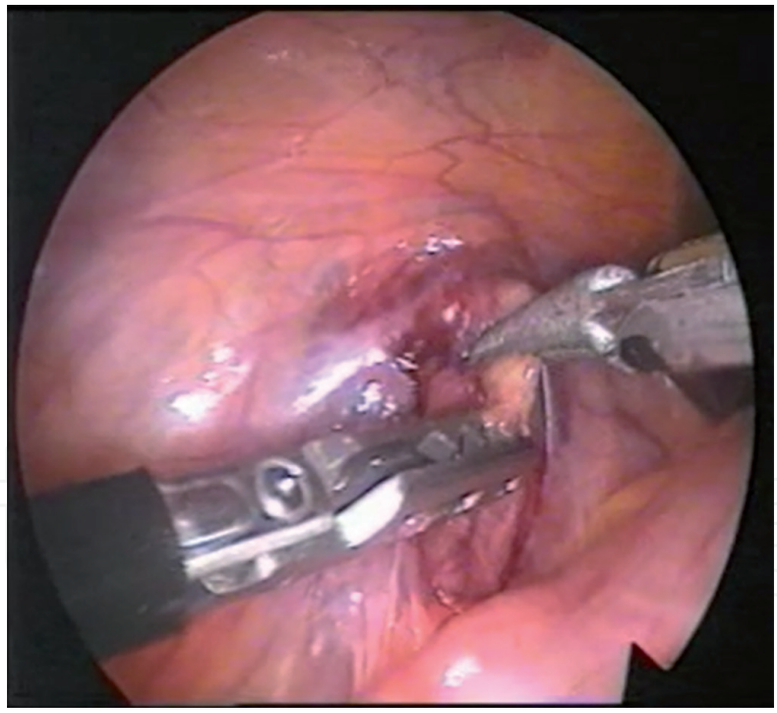

Figure 2.
Laparoscopic LigaSure™ vessel-sealing varicocelectomy.

and the pregnancy rate was 29.9%. However, in 1994, Marmar and Kim reviewed their experience with 466 subinguinal microsurgical varicocelectomies. There was only one permanent hydrocele, a palpable recurrence rate of 0.82%, and a one-year pregnancy rate of 35.6% [53]. In 1992, Goldstein modified the microsurgical subinguinal varicocelectomy, taking a more aggressive approach with arterial and lymphatic microsurgical dissection and venous ligation by an arterial and lymphatic sparing technique that involved the delivery of the testis and ligature of gubernacular veins. The authors

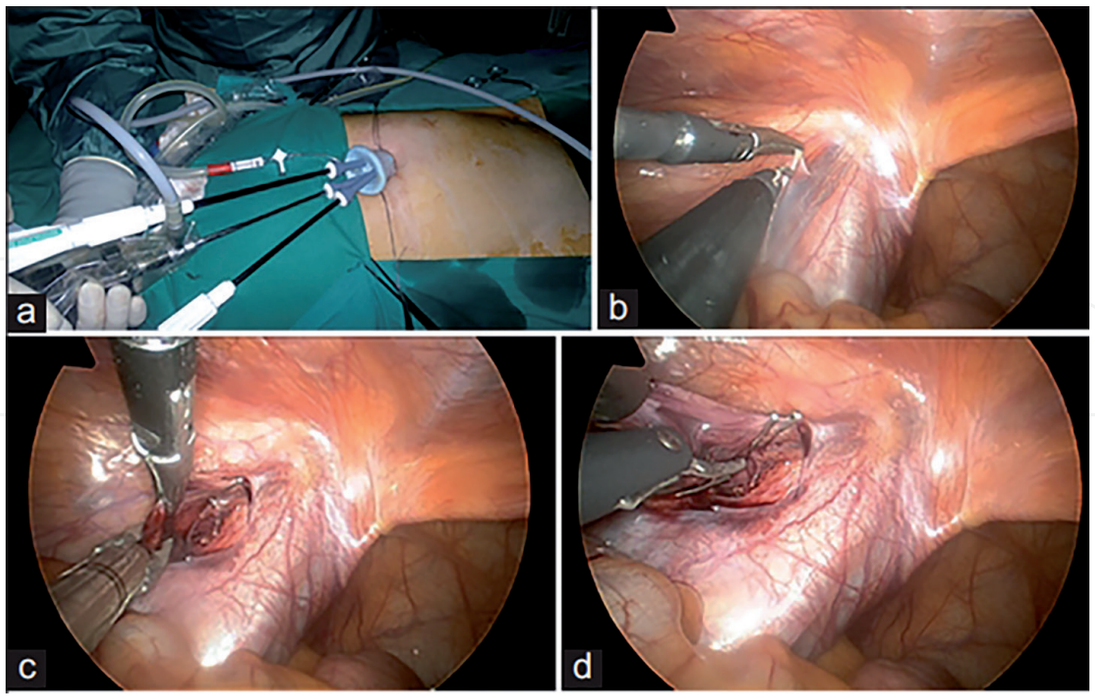

Figure 3.
Single-incision laparoscopic varicocelectomy. Isolation of the bundle and clips application.

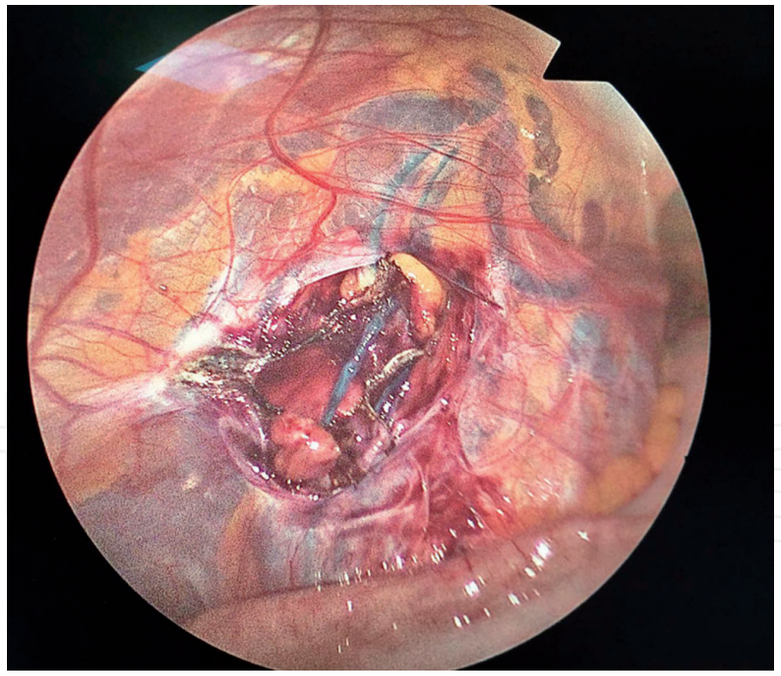

Figure 4.
Lymphatic sparing laparoscopic varicocelectomy with isosulfan blue dye injection into the testicular vaginalis. Lymphatics are colored in blue.

reported a failure rate of 0.6% for all of the procedures, and a pregnancy rate per couple of 43% within 6 months [54].

A microsurgical approach in pediatrics was proposed in the late 80s, although for many authors there is a prevalence of the use of selective laparoscopic ligation [55].

Over time, other investigators have questioned the need to deliver the testicle as part of a microsurgical inguinal varicocelectomy. For example, Ramasamy and

Schlegel in their comparative study in adults demonstrated that there were no varicocele recurrences with either procedure and that delivery of the testis did not provide any beneficial effects on the semen quality or pregnancy rates after varicocelectomy. On the other hand, Spinelli and coauthors reported in a randomized controlled trial, a case series of seventy adolescents suffering from varicocele and reduction of the ipsilateral testicular volume greater than 20%, that lymphatic vessel and arteriole-sparing microsurgical inguinal varicocelectomy with delivery and ligature of all collateral and gubernacular veins of the testis resulted in significantly higher left testicular catch-up growth compared to non-delivery of the testis. Unfortunately, pediatric urologists are less likely than andrologists to use the microscopic approach due to limited experience and concern over post-varicocelectomy ipsilateral testicular atrophy, which is a rare but devastating occurrence [56, 57].

However, a recommendable use of the microsurgical approach should be previous operations for inguinal hernia or cryptorchidism, in which laparoscopic ligation can induce testicular ischemia. Any future vasectomy interventions, with sectioning of the deferential artery, can also lead to testicular atrophy as this is one of the vicariant arteries of testicular vitality [58, 59].

Cayan et al. in 2017 performed a meta-analysis that included 20 studies. The authors considered artery sparing, hydrocele, recurrence, morbidity, and reoperation rates. The results were as follows:

> Laparoscopy: Hydrocele 2–15%, Recurrence1–15%, Reoperation 2–4%.
> Microsurgery: Hydrocele 0–3%, Recurrence 0–3%, Reoperation 0%–0.1%.
> Radiologic embolization: Hydrocele 0–5%, Recurrence 15–20%, Reoperation 5%–9.9% [60].

A recent review by Macey in 2018 found that the most common surgical approaches to varicocelectomy were laparoscopic (38%), subinguinal microsurgical (28%), inguinal (14%), and retroperitoneal (13%). These studies suggest a lack of consensus regarding diagnosis, management, and operative approaches for pediatric and adolescent varicoceles among pediatric urologists. Moreover, this degree of heterogeneity limits the development of standardized guidelines in this population (**Figures 5** and **6**) [61].

8. Conclusion

Given the current status of the literature, we can confidently state that, from a scientific perspective, the treatment of varicocele in the pediatric population is a typical example of epistemic uncertainty. While active treatment of varicocele in the pediatric and adolescent population is controversial, it is clear that some untreated patients will suffer symptoms later in life, while overtreatment remains a concern for this large and vulnerable population [61].

One of the most complete studies on the current trends regarding varicocele is a scientometric study undertaken in 2022, performed by analysis of data retrieved from the Scopus database presented by Agarwal et al. [62]. They considered 1943 original human studies on varicocele, published between 1988 and 2020. The authors found that studies of adolescents were underrepresented compared with studies of adults. Published reports on varicocele in adolescents included 355 (n = 18.3%) articles, with the highest yearly trend of publications in 2013 (n = 21). All of the remaining

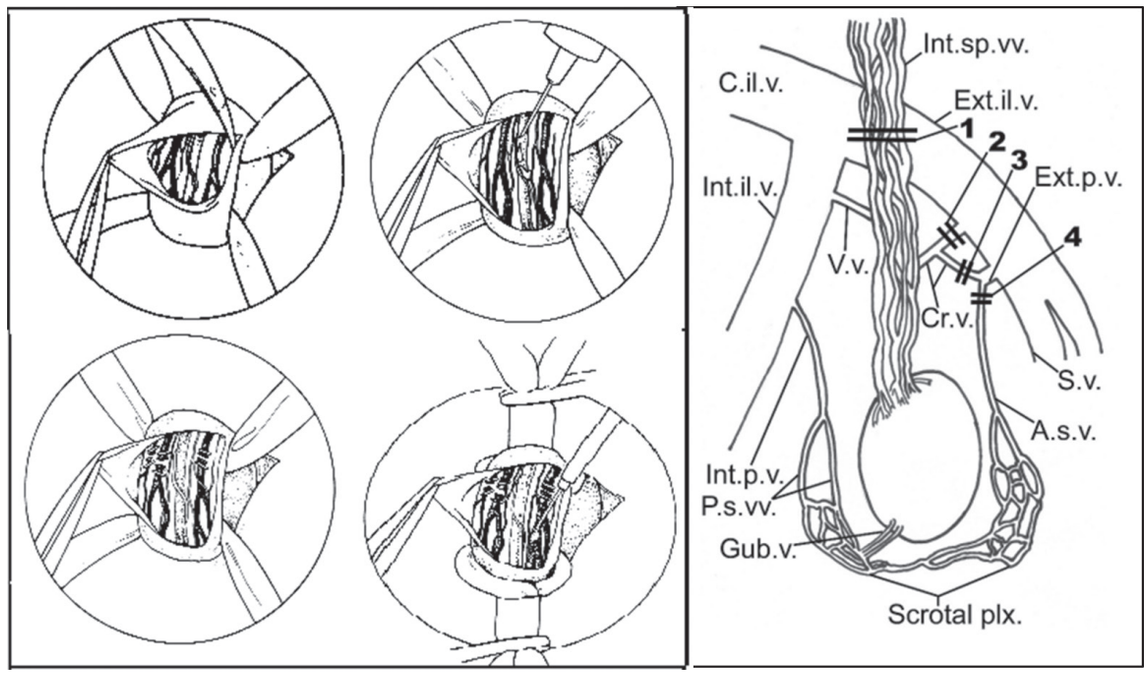

Figure 5.
Drawing of microsurgical varicocelectomy according to Marmar's technique (right) and Goldstein's technique (left).

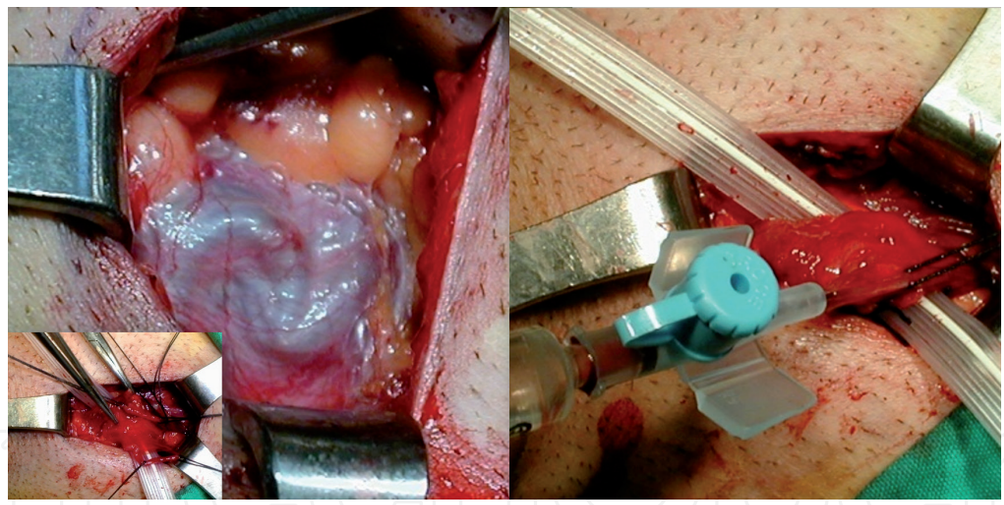

Figure 6.
Marmar's technique.

manuscripts (n = 1588; 81.7%) focused on adults. Studies on diagnostic and prognostic aspects of varicocele were more numerous than studies on varicocele prevalence, mechanistic studies, and studies focused on etiological and risk factors. Varicocele surgery was investigated more than non-surgical approaches. Furthermore, adolescent varicoceles are usually diagnosed incidentally, and the presentation of symptomatic cases may differ during pubertal development. In addition, the collection of semen samples from post-pubertal patients is not always feasible, and there are no reference standards for the interpretation of semen analysis in this population. The study has shown a higher interest by scholars (88.9%) in choosing surgical rather than non-surgical options (20.5%) in the management of varicocele. From the overall analysis of multicenter studies, it appears that pediatric surgeons are more familiar

with the laparoscopic approach, although this does not mean that laparoscopy is the most effective technique. The current trend demonstrates a progressive shift towards the microsurgical technique, even though the studies in the pediatric population remain limited compared with those for adults. Solid data on the impact on paternity rates are still lacking. However, it has been shown that when an intervention is performed, the lymphatic sparing techniques have a distinct advantage.

At present, the evaluation and choice of treatment for adolescent varicocele patients is based not on objective fertility criteria (paternity) but on indirect evidence that testicular function or spermatogenesis and thus ultimately also fertility may be compromised [63]. Finally, from the analysis of the literature, the choice of the technique appears to depend largely on the experience and preferences of the surgeon rather than on a shared option.

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