Comparative Outcomes of Single-Stage versus Two-Stage Laparoscopic Fowler-Stephens Orchidopexy: A Systematic Review snd Meta-Analysis

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Abstract

Introduction Intra-abdominal testis (IAT) remains a challenging and controversial subset within the management of cryptorchidism. While Fowler–Stephens orchidopexy (FSO) is still being advocated as the gold standard for the treatment of this entity, there is new and conflicting evidence on the comparative outcomes between single- or two-stage laparoscopic FSO (LFSO). The aim of the study is to investigate whether staging has benefits in children receiving LFSO.

Methods We searched the PubMed, Medline, Embase, and Cochrane Trials databases for studies comparing single- with two-stage LFSO in children from January 1, 1995 to December 31, 2023. We assessed the identified studies for quality and performed a systematic review and meta-analysis in accordance with the Preferred Reporting of Systematic Reviews and Meta-Analyses. The main outcome measures examined were success rate (in terms of the scrotal position of the testis) and testicular atrophy, which were analyzed using fixed effect models.

Results We included 17 eligible studies that involved a total of 499 operated testes. The overall success rates of single- and two-stage LFSO were 79.4 and 90.3%, respectively. The overall testicular atrophy rates of single- and two-stage LFSO were 17.3 and 11%, respectively. Fixed effect model analysis showed that two-stage LFSO is significantly superior to single-stage LFSO in overall success rate (odds ratio [OR: 2.57]; 95% confidence interval [CI]: 1.50–4.39, $p = 0.0006$) and testicular atrophy rate (OR: 0.48; 95% CI: 0.28–0.79, $p = 0.004$). There is no heterogeneity in the reports, and the funnel plot showed no publication bias.

Conclusions Two-stage LFSO remains the first choice of operation for children with a high IAT, with a significantly higher success rate and a lower testicular atrophy rate.

Keywords
- orchidopexy
- laparoscopic
- intra-abdominal testis

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Introduction

Cryptorchidism, or undescended testes, is the failure of testes to descend to their terminal scrotal position. Genetic, hormonal, and anatomical factors contribute to its etiology. Congenital abnormality occurs in 1 to 4.6% of full-term and 1.1 to 45.3% of preterm male neonates.[1] Spontaneous descent of testes is often seen in the first 3 to 6 months of life—0.7 to 1% remain undescended since the first year[2] and 23% remain cryptorchid without surgery.[3] It is reported that around 20% are impalpable, of which 30% are intra-abdominal,[4] making both diagnosis and treatment difficult.[5]

Timely diagnosis and treatment of undescended testes is crucial, as it may lead to fertility impairment and malignant transformation. Infertility and azoospermia rates were reported two times more for individuals with undescended testes than in normal individuals[6]; some studies have reported improved fertility after surgical correction.[7] Another important reason for treating an undescended testis is its increased risk of malignant transformation. The association between cryptorchidism and testicular germ cell tumors has been well documented, with cryptorchidism having a relative risk of 3.7 to 7.5 times higher than that of the normal population,[8] with intra-abdominal testis (IAT) at a 200-fold higher risk of malignant transformation.[9]

A variety of surgical modalities are available for managing undescended testes. The most common method is primary orchidopexy, during which the undescended testis is mobilized, brought down and fixated at scrotum. For low-lying IATs, which is defined as <3 cm from the deep inguinal ring, laparoscopic one-stage orchidopexy was advocated by a study as a suitable option with acceptable success rates.[10] For high-lying IATs, treatment modalities are still controversial, and the procedure is limited by the length of the testicular vessels. In 1959, Fowler and Stephen proposed a one-stage technique that involved the division of testicular vessels high from the testis to maintain collateral blood supply.[11] The method was modified by Ransley et al in 1984,[12] which involved a two-stage procedure with testes placement done after dividing the testicular vessels and anticipating collateral growth. The main controversies in the choice between single- and two-stage procedures lie in the potential better testis survival in two-stage Fowler–Stephens orchidopexy (FSO) as a result of more collateral blood supply via the medial vas-peritoneal flap.[13] On the other hand, single stage has its merits of obviating the need of a second general anesthesia, minimizing the exposure of testis in an unfavorable position intra-abdominally and avoiding potential inadvertent testicular injury due to challenging dissections in the second operation.[14,15] Other known surgical options for IAT include laparoscopic single-stage vessel intact orchidopexy and microvascular testicular autotransplantation.[16] Meanwhile, the recently described Shehata approach,[17] which utilizes controlled traction on testicular vessels, was reported in 2008, yet evidence of whether FSO or Shehata has better outcomes is still controversial.

Currently, there is new and conflicting evidence on the comparative outcomes of single- or two-stage laparoscopic FSO (LFSO). Some studies advocate that one-stage FSO has comparable benefits to two-stage FSO.[18] The current study is a systematic review and meta-analysis that aims to investigate whether staging has benefits in children receiving LFSO.

Methods

This systematic review and meta-analysis were conducted in accordance with the recommendations of the Preferred Reporting of Systematic Reviews and Meta-Analyses statement[19] and registered in PROSPERO (CRD42024535469).

Search Strategies

Comprehensive literature searches of PubMed, Medline, Embase, and Cochrane Trials databases were conducted using a four-component strategy: the population (e.g., MeSH terms "pediatrics" OR "pediatric population" OR "children" and language variations of these), the disease (e.g., MeSH terms "intra-abdominal testis" OR "undescended testis" and variations) and the intervention (e.g., ["Fowler-Stephens" OR "FSO" OR "F-S"] and ["single-stage" OR "one-stage" OR "stage"] and "laparoscopic" and variations). Google searches were also conducted using the aforementioned search terms. Reference lists from eligible studies were checked to ensure that further possibly eligible studies were included. The studies chosen included those published from January 1, 1995 to December 31, 2023. Only English language studies were included.

Eligibility Criteria

The titles and abstracts of the identified articles were analyzed. Their quality and eligibility for inclusion were assessed by two authors (A.C.H.F. and J.T.W.T.). Appropriateness and inconsistencies were resolved through discussions with the senior author (K.K.Y.W.). Studies in the final analysis must have included data on one-stage LFSO compared with two-stage LFSO in at least one clinically relevant outcome. Final analyses were run on outcome variables where data were sufficient across at least two studies to allow statistical analysis.

Inclusion and Exclusion Criteria

Clinical studies in which pediatric groups of patients had IAT and where patients either received single-stage or two-stage LFSO were deemed eligible. Patients' race, nationality, diagnosis, course of illness, and type of surgery received were not limited. Non-English literature, nonrandomized control trials, duplicate publications, literature from which complete data could not be obtained and studies with inappropriate design were excluded.

Data Extraction

Full texts were read, and relevant outcome data were extracted from each included study by two authors (A.C.H.F. and J.T.W.T.) from the final publication list. The data were integrated using Review Manager 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark) provided by the Cochrane Collaboration.

Outcomes of Interest

Two study groups were compared: patients receiving single-stage LFSOs and patients receiving two-stage LFSOs. The following study outcomes were measured in common among the 17 studies and extracted and analyzed: (1) success rate, as defined by the stable scrotal position of the operated testis during the follow-up period and (2) testicular atrophy, as defined by the reduction of the volume of operated testis on clinical examination from the intraoperative size. The crude odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated and pooled for each measured outcome.

Statistical Methods

Data from individual studies were pooled using a fixed effects meta-analysis. The study endpoints (success rate and testicular atrophy) were continuously distributed data and were thus pooled and analyzed using weighted mean differences. Variability in the data was assessed by determining the heterogeneity among the studies using the I^2 test. The presence of publication bias and related biases were examined with funnel plots. The results are presented as pooled ORs and 95% CIs. All analyses were performed using Review Manager 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark) provided by the Cochrane Collaboration.

Results

Studies Included

Electronic searches identified 153 publications from January 1, 1995 to December 31, 2023 using the keyword search strategy. After removing 13 duplicated articles, 140 publications were eligible for further screening. After the title and abstract screening, 80 publications were selected for full-text review, from which 63 articles were removed based on the exclusion criteria. The main reasons for exclusion were incorrect study design and incomplete data. We therefore identified 17 relevant studies (►Fig. 1).

Study Characteristics

The studies were conducted between 1998 and 2020 in Australia, Brazil, Canada, China, Egypt, Italy, Puerto Rico, the United Kingdom, and the United States. The date of the last database search was 2nd December 2023. Among the 17 studies, 15 were retrospective cohort studies, one was a prospective cohort, and one was a randomized controlled trial (RCT). Across the included studies, a total of 499 operated testes were included, with 237 operated by single-stage LFSO and 262 operated by two-stage LFSO. The ages of the included patients ranged from 3 months old to 18 years old. The study characteristics are summarized in ►Table 1. Funnel plots for all endpoints showed no evidence of asymmetry.

Success Rate

The data of 17 studies were extracted to compare the success rate of one-stage LFSO with two-stage LFSO and analyzed using a fixed effects model. The overall success rates of the one-stage and two-stage LFSOs were 79.4 and 90.3%, respectively. The meta-analysis revealed that, based on ORs, two-stage FSO achieved significantly better success rates than one-stage FSO (pooled crude OR: 2.57, 95% CI: 1.50–4.39; $p = 0.006$; $I^2 = 8\%$). The Egger tests indicated that the heterogeneity associated with the comparisons of the rates of success was very low and acceptable. The funnel plot of the success rate suggested a roughly symmetrical distribution around the mean effect, suggesting that there was no publication bias (►Fig. 2).

Testicular Atrophy

The data of 17 studies were extracted to compare the rate of testicular atrophy of one-stage LFSO with two-stage LFSO and analyzed using a fixed effects model. The overall rates of testicular atrophy in the one-stage and two-stage LFSOs were 17.3 and 11%, respectively. The meta-analysis revealed that, based on ORs, two-stage FSO achieved significantly lower testicular atrophy rates than one-stage FSO (pooled crude OR: 0.48, 95% CI: 0.28–0.79; $p = 0.004$; $I^2 = 21\%$). The Egger tests indicated that the heterogeneity associated with the comparisons of rates of testicular atrophy was very low and acceptable. The funnel plot of the testicular atrophy rate suggested a roughly symmetrical distribution around the mean effect, suggesting that there was no publication bias (►Fig. 3).

Discussions

Undescended testis is the most common disorder of sexual development in boys and affects 3.5% of male newborns.[2] It has been reported that 20% are impalpable, among which 30% are intra-abdominal. The condition is associated with higher risks of malignant transformation and infertility, with recent guidelines advocating orchidopexy by 18 months of age to minimize such risks. Chances of infertility and azoospermia were reported two times more often than in normal individuals,[6] with the literature reporting improvements in fertility after surgical correction.[7] For malignant transformation, the association between cryptorchidism and testicular germ cell tumors was well documented, with cryptorchidism having a relative risk of 3.7 to 7.5 times higher than that of the normal population.[8] While IATs are less common, they are associated with a significantly higher risk of malignancy and difficulty in localization and repair surgically when compared with inguinal testes. Hence, it is crucial to study the best corrective method.[9]

For IATs, surgery is limited by the length of the testicular vessels, whereas treatment modalities are still controversial. One-stage operative modalities include vessel intact laparoscopic-assisted orchidopexy, single-stage FSO and microvascular autotransplantation, whereas two-stage surgeries include two-stage FSO and the Shehata technique. The goal of FSO is to allow more extensive mobilization of testes by dividing the spermatic vessels, which was originally done in a single-stage manner.[11] There were reported increased risks of testicular atrophy; hence, a two-stage operation proposed by Ransley et al in 1984 was advocated,[12] in which the authors recommended high ligation of the spermatic artery to preserve and stimulate growth of the collateral channels between the vasal artery and the spermatic artery. However, a two-stage operation has the disadvantage of requiring patients to undergo general anesthesia twice within a 3- to 8-month period.[20] Furthermore, Rosito et al reported that histological changes in

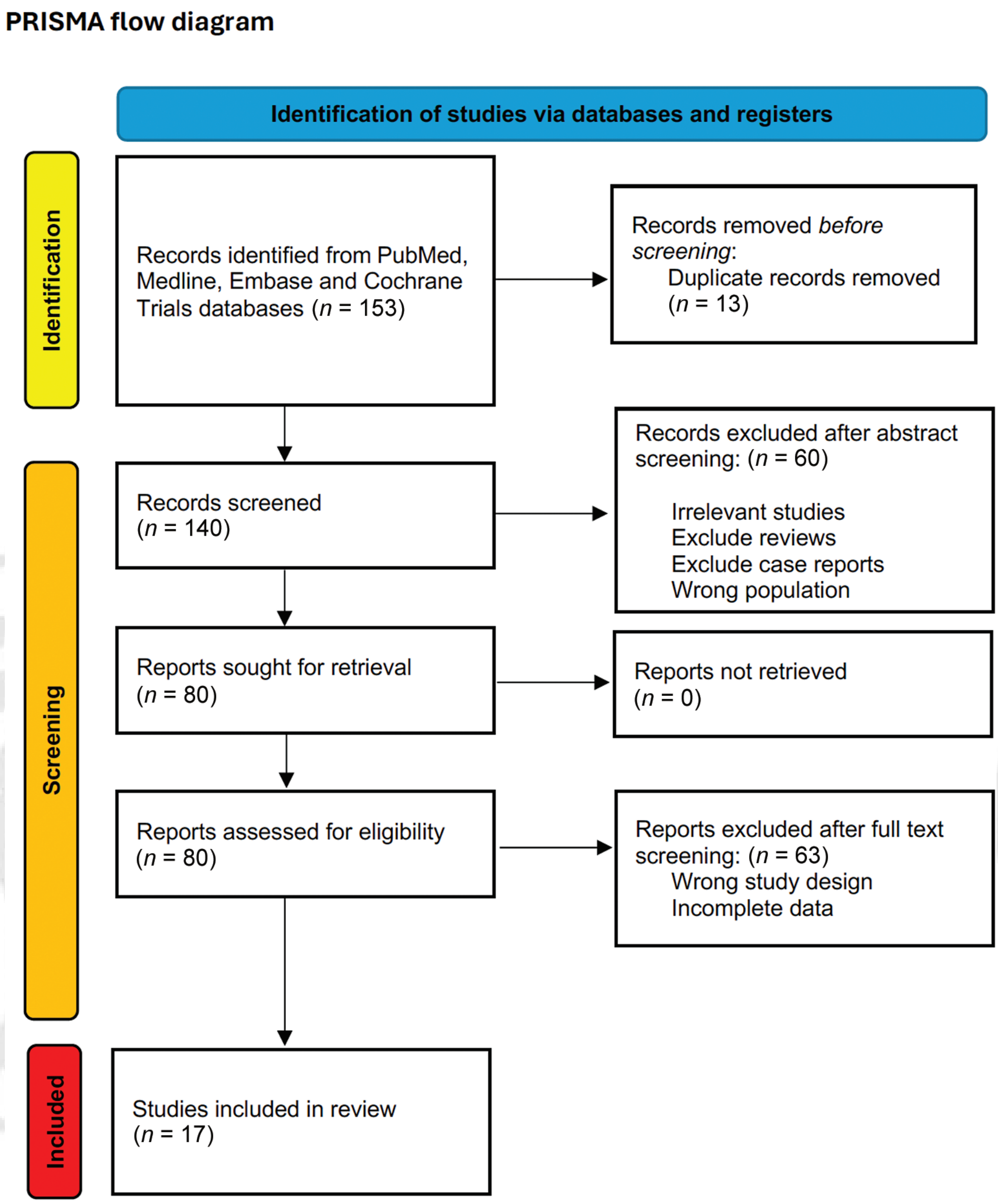

Fig. 1 PRISMA flow diagram. PRISMA, Preferred Reporting of Systematic Reviews and Meta-Analyses.

IATs were not caused by clipping or dividing spermatic vessels.[21] Instead, the 6-month interval between the two stages exposes the testes to a prolonged period of warm ischemia and inadequate venous return, as reported by Bianchi.[22] All these contributed to controversies on whether a staged procedure is beneficial. According to a survey supervised by the World Federation of the Association of Pediatric Surgeons (WOFAPS) in 2022, diversity in practice was noted for the management of IAT.[23] Hence, it is essential to study the outcomes of FSO and the significance of staging.

Evidence regarding the comparative outcomes of one-stage LFSO and two-stage LFSO is ample yet conflicting. Single-stage LFSO was reported to have a high success rate with comparable outcomes to two-stage LFSO in 2008,[18] whereas two-stage LFSO was found to be superior to one-stage LFSO in terms of success rates by a meta-analysis in 2018, with no statistical significance in atrophy rates reported.[24] On the other hand, some studies provide evidence of a higher success rate of two-stage FSO; however, the interpretation of the results is limited by the fact that a significant portion of open cases were included in the analysis instead of being purely laparoscopic.[13]

With the aim of determining the best corrective method for high-level IATs, this study provides the most updated systematic review and meta-analysis that focuses on the comparison of survival and atrophy rates between one-stage LFSO and two-stage LFSO, as aggregated from 17 studies involving 499 operated testes. While two retrospective cohort studies (Chang et al and Lindgren et al) reported higher success rates in one-stage LFSO group,[14,18] the remaining 15 studies consensually demonstrated better results in the two-stage LFSO group.[4,15,25–36] The overall success rates of

Table 1 Characteristics of included studies

Author	Year of publication	Country	Study design	Population (testes) (1-S/2-S)	Age scope	Outcomes measured
Alam et al[25]	2016	United States	Retrospective cohort	50/35	5–151 mo	Testicular atrophy Testis position
Baker et al[26]	2001	United States	Retrospective cohort	27/58	–	Testicular survival Testis position Hospital charges Operative time
Castillo et al[27]	2014	Puerto Rico	Retrospective cohort	6/1	8–84 mo	Testicular atrophy Testis position Complications
Chang et al[28]	2001	United States	Retrospective cohort	20/7	0.5–12 y	Testicular atrophy Success rate
Chang et al[18]	2008	United States	Retrospective cohort	35/10	–	Testicular atrophy Success rate
Clark and Borzi[29]	1999	Australia	Retrospective cohort	6/21	0.5–14 y	Testicular atrophy Testis position Complications
Denes et al[30]	2008	Brazil	Retrospective cohort	3/21	11 mo–22 y	Testicular atrophy Testis position Complications
Elzeneini et al[15]	2020	Egypt	Retrospective cohort	16/22	1–3.5 y	Testicular atrophy Testis position
Humphrey et al[20]	1998	United Kingdom	Retrospective cohort	2/10	0.5–3.5 y	Testicular atrophy Testis position Complications
Kaye and Palmer[31]	2008	United States	Retrospective cohort	2/2	7–52 mo	Testicular atrophy Testis position Complications
Lindgren et al[14]	1999	United States	Retrospective cohort	13/5	11–120 mo	Testicular atrophy Testis position
Merguerian et al[32]	1998	Canada	Retrospective cohort	3/3	5 m–18 y	Testicular atrophy Testis position Complications
Ostlie et al[33]	2015	United States	RCT	14/13	0.5–10 y	Testicular atrophy Testis position Complications
Papparella et al[34]	2020	Italy	Retrospective cohort	9/11	1–7 y	Testicular atrophy Testis position
Powell et al[35]	2013	United States	Retrospective cohort	8/16	0.25–13 y	Testicular Atrophy Testis position Operating room cost
Stec et al[36]	2009	United States	Retrospective cohort	8/11	3–167 mo	Testicular Atrophy Testis position
Wang et al[4]	2017	China	Prospective cohort	15/13	0.9–7 y	Testicular position Testicular volume Sex hormone levels

Abbreviation: RCT, randomized controlled trial.

one-stage LFSO and two-stage LFSO were 79.4 and 90.3%, respectively, with two-stage LFSO being significantly superior (OR: 2.57; 95% CI: 1.50–4.39, $p = 0.0006$). On the other hand, five studies (among which one is RCT) included in analysis showed lower testicular atrophy in single-stage LFSO group,[14,18,25,27,33] whereas the remaining 12 studies demonstrated better results in two-stage LFSO.[4,15,20,26,28–32,34–36] Overall testicular atrophy rates of one-stage LFSO and two-stage LFSO were 17.3 and 11%, respectively, with two-stage LFSO having a significantly lower atrophy rate (OR: 0.48; 95% CI: 0.28–0.79, $p = 0.004$). The results echoed a systematic review conducted by China in 2018,[24]

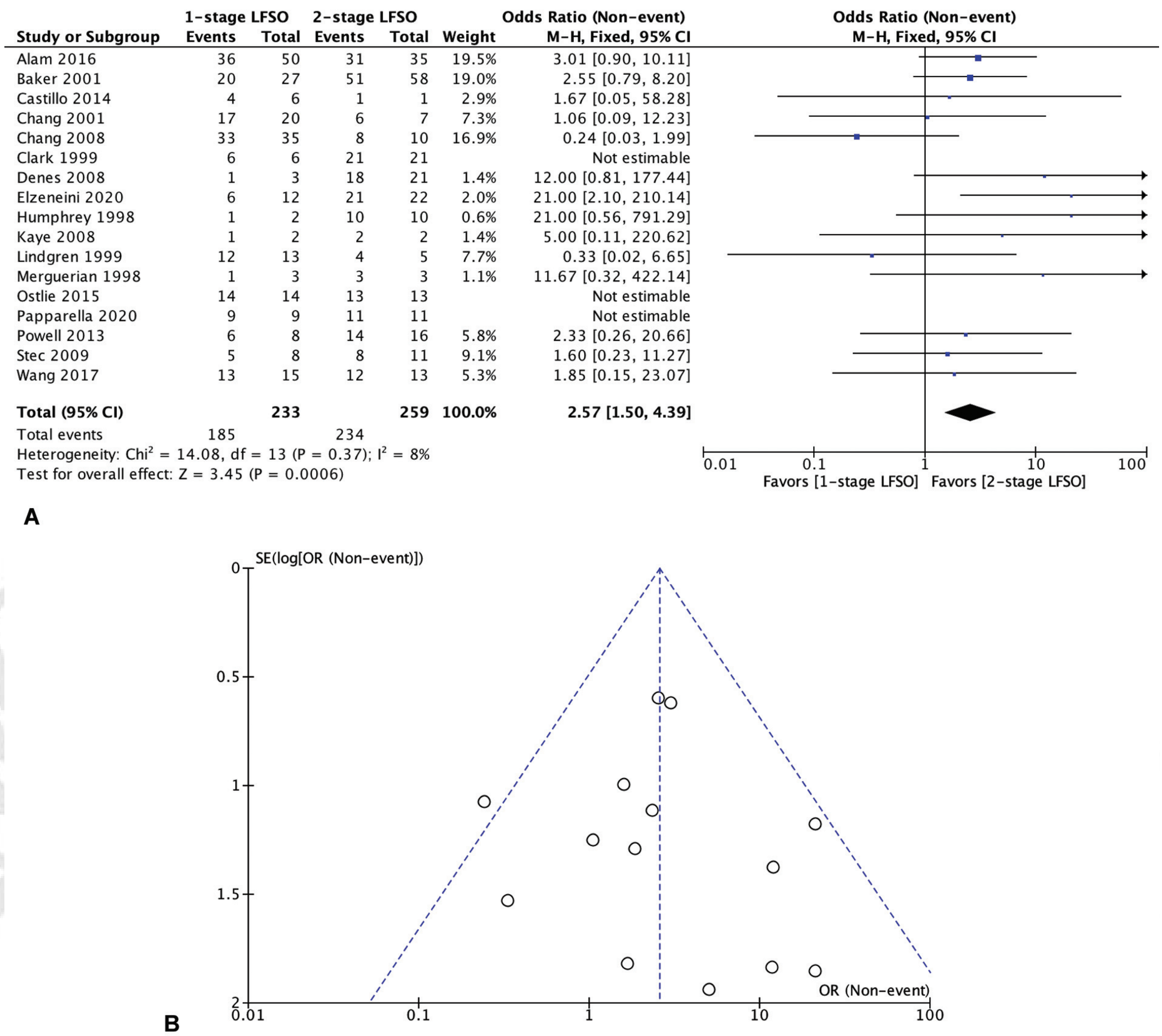

Fig. 2 (**A**) Forest plot of success rate. (**B**) Funnel plot of success rate. CI, confidence interval; LFSO, laparoscopic Fowler–Stephens orchidopexy; OR, odds ratio.

showing that two-stage FSO outperformed one-stage FSO in terms of success rate. However, it did not show statistically significant differences in atrophy rates, contrary to the findings of the present study. Our results are also consistent with the meta-analysis done in Ottawa, which showed a significantly higher success rate in the two-stage procedure.[13]

The results could be explained by the advantages of the two-stage technique when compared with the one-stage technique. It stimulates collateral circulation of the testes prior to scrotal placement and thus increases the chances of testicular survival. Meanwhile, LFSO can establish collateral circulation without causing excessive tissue damage with more precise dissection of the spermatic vessels when compared with open surgery, which contributes to its high success rate and low atrophy rate. Some centres did not report significant differences in atrophy rates. The atrophy rate was reported to be higher if there were previous surgeries or additional dissections around the vas deferens. Together with the patient's anatomy, these factors may contribute to heterogeneity in the comparison of atrophy rates in different centres. Meanwhile, the included studies have limitations, including a small sample size and a lack of objective methods for assessing testicular atrophy, such as orchidometry or Doppler ultrasound. All of these factors might have affected the reported testicular atrophy rates.

The current study provides an up-to-date appraisal of the best surgical option for IATs with the aim of updating pediatric urologists worldwide. This shows that two-stage LFSO is significantly superior to single-stage LFSO in terms of success and atrophy rates. It serves as a comprehensive systematic review with no detected publication bias. However, the strength of this study was limited by several factors. First, most of the included studies were retrospective studies. This systematic review only identified one RCT comparing the success rates of single- versus two-stage FSO, with the rest consisting almost entirely of retrospective cohort or case series. This might have led to inherent biases in selection of participants and reporting of results. The comparison of FSO procedures was also limited by the complexity of the intra- and postoperative parameters. For instance, testicular atrophy was not well defined in many of the included studies, and if defined,

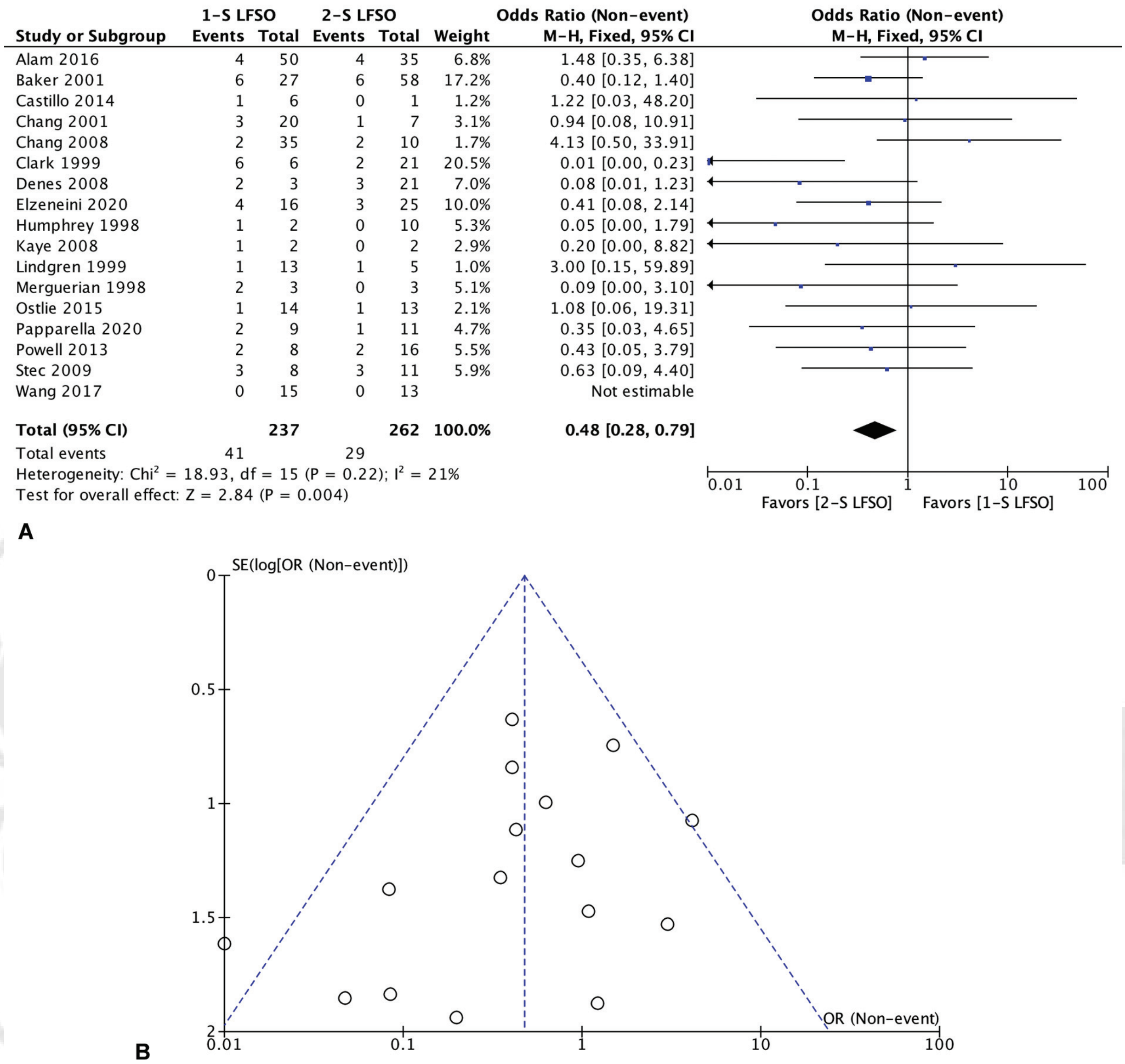

Fig. 3 (**A**) Forest plot of testicular atrophy rate. (**B**) Funnel plot of testicular atrophy rate. CI, confidence interval; LFSO, laparoscopic Fowler–Stephens orchidopexy; OR, odds ratio.

it showed a certain heterogenicity. A similar concern also applied to the differentiation of high- and lower-level IATs, with heterogenicity of definition noted in the included studies. Future adequately powered and well-designed trials with accurate definition and measures of outcomes are necessary to evaluate the clinical benefits of single- versus two-stage LFSO in children and make a conclusive comparison. Furthermore, the inclusion of only English language articles in our systematic review also potentially limited the generalizability of our review. Notwithstanding these potential pitfalls of our study, the significantly higher success rate and lower testicular atrophy rate achieved by two-stage LFSO in this systematic review and meta-analysis suggested that two-stage LFSO should remain the recommended standard of operation for children with IATs.

Recently, there have been proposed modifications to current surgical techniques, such as the Shehata technique, which involves traction rather than dissection of testicular vessels for high IATs, and testicular autotransplantation. Further research could focus on studying the effectiveness, success, atrophy rates, and long-term fertility rates for these modalities. Currently, RCTs exist (still in the recruitment phase) in comparing the best treatment modalities for IAT (NCT02936024, NCT05845515, and NCT04528381). It is clear that pediatric surgeons worldwide are paying attention to the best treatment strategy for children with IATs.

Conclusion

Two-stage LFSO significantly outperforms single-stage procedures in terms of success rates and reduced testicular atrophy for high IAT. These findings support the recommendation of two-stage LFSO as the preferred surgical approach for better clinical outcomes.

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Conflict of Interest
None declared.

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