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REVIEW

Does bilateral undescended testis have worst testicular function than unilateral cases? A meta-analysis of adult orchidopexy patients

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Summary ***Introduction: Cryptorchidism, or undescended testis (UDT), is a congenital anomaly linked to an increased risk of infertility. The laterality of UDT, whether unilateral or bilateral, may influence post-orchidopexy outcomes. This meta-analysis compares testicular function and azoospermia rates between patients with bilateral and unilateral UDT post-orchiopexy.***

Materials and methods: A comprehensive literature search was performed using PubMed, ScienceDirect, and Google Scholar databases up to March 2025. Statistical analyses were conducted using Review Manager (RevMan).

Result: Ten eligible studies were included in the analysis, comprising 563 bilateral UDT post-orchidopexy and 1259 unilateral UDT post-orchidopexy cases. Populations post bilateral orchidopexy have significantly higher FSH level (MD: 3.77 UI/L [95% CI: 1.65 - 5.89]), significantly higher LH level (MD: 1.27 UI/L [95% CI: 0.27 - 2.26]), lower inhibin B level (MD: -44.86 pg/mL [95% CI: -69.58 - -20.15]), and higher frequency of azoospermia (OR 2.3 [95% CI: 1.57 - 3.37]) compared to unilateral UDT post orchidopexy.

Conclusions: Bilateral UDT post-orchidopexy exhibit poorer testicular function with significantly higher FSH and LH levels, reduced inhibin B levels, and a greater incidence of azoospermia compared to unilateral UDT post-orchidopexy

KEY WORDS: Bilateral; Unilateral; Undescended testis; Post-orchidopexy; Testicular function.

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INTRODUCTION

Cryptorchidism or *undescended testis* (UDT) is a common congenital malformation in pediatric urology caused by an incomplete descent of the testis. It can be divided into palpable or non-palpable testis according to the location of the testis (1). Based on laterality, in one-third of cases, UDT is unilateral (2).The prevalence of undescended testis is 1.6%-9% at birth and 0.9-1.8% at age 3 months (3). Undescended Testis is related to an increased risk of Infertility associated with testicular atrophy and tumors, particularly germ cell tumors (3).

Standard current treatment for cryptorchidism is orchiopexy (4). Early treatment by orchidopexy is the definitive procedure for cryptorchid patients with an undescended testis (4). The mainstay of treatment for cryptorchidism is to perform the treatment as soon as possible, preferably before 12 months and no later than 18 months, to decrease the chance of testicular atrophy (1). However, fertility after orchidopexy may be adversely affected. One factor influencing fertility potential after orchidopexy is the laterality of the undescended testis. Some studies indicate differences in testicular function between patients with unilateral and bilateral UDT post-orchidopexy, with better outcomes observed in unilateral UDT (5, 6). However, another study suggests that there is no significant difference in testicular function between unilateral and bilateral UDT (4, 7).

As far as we know, no comparative meta-analysis regarding bilateral and unilateral UDT in testicular function exists. The primary objective of our meta-analysis is to compare bilateral and unilateral UDT post-orchiopexy in terms of their FSH, LH, Inhibin B, and azoospermia rates. This finding will help guide clinical decision-making for surgical strategies for UDT.

METHODS

Study design

This study is a systematic review and meta-analysis to evaluate testicular function following orchidopexy in bilateral and unilateral UDT.

The study followed the *preferred reporting items for systematic reviews and meta-analyses* (PRISMA) guidelines to ensure comprehensive research.

The literature search was conducted using *PubMed*, *Google Scholar*, and *Science Direct* databases until March 2025. The search strategy for the articles included [("*adult*") OR ("*post-pubertal*")] AND [("*orchidopexy*") OR ("*orchiopexy*")] AND ("*bilateral*") AND ("*unilateral*") AND [("*fertility*") OR ("*testicular function*") OR ("*semen analysis*")]. All search results will be screened for duplicates and assessed based on title and abstract relevance. Full-text articles are retrieved for detailed evaluation and the references of the selected studies are manually reviewed to identify additional relevant articles.

The studies comprised RCTs and observational studies to assess the post-orchidopexy outcome. Original research

articles were included if they met following criteria: (a) diagnosis of undescended testis that underwent orchidopexy for the definitive treatment, (b) state the bilateral or unilateral condition of the testis before orchidopexy, (c) assessesment of FSH, LH, Inhibin B levels, and azoospermia rate post-orchidopexy. The exclusion criterias were: (a) review article, letter to the editor, animal study, commentary, or consensus document, (b) study not focusing on undescended testis.
The study protocol was registered in the international prospective register of systematic review (PROSPERO) to ensure transparency and adherence to established standards (PROSPERO CRD420251010333).

Data extraction and synthesis

The data extraction was conducted with two independent reviewers. The discrepancies of the reviewers were resolved through discussion and consultation with a third reviewer. All extracted data included were extracted and pooled using the Excel program, including study characteristics such as author, year of publication, sample size, laterality of UDT, values of FSH, LH, Inhibin B, and Azoospermia rate. Risk of bias was assessed using Newcastel-Ottawa Scale.

Statistical analysis

Primary outcomes in this study are post-orchidopexy FSH, LH, Inhibin B levels, and azoospermia rate, as these serve as key indicators of testicular endocrine function. We conduct the meta-analysis using *Review Manager* (RevMan) to synthesize the results of the included studies and, using I^2 statistic and Chi^2 test, to perform the heterogeneity assessment. A fixed-effects model was used when I2 was < 50%, whereas, when I^2 was > 50%, a random-effects model was chosen. In the fixed-effects model, population effect sizes were assumed to be the same for all studies. In contrast, the random-effects model attempted to generalize the results beyond the included studies by assuming that the selected studies were random samples from a larger population. If there was statistical heterogeneity in the results, a further sensitivity analysis was performed to determine the source of heterogeneity. A sensitivity analysis was performed to assess the robustness of the findings by excluding studies with a high risk of bias or those with extreme outlier results.

Meta-regression may also be employed to explore potential moderators affecting testicular function outcomes post-orchidopexy.

Results

Data retrieval

The literature review identified 3945 studies as potentially relevant to this investigation. After removing duplicates, 1821 studies were eliminated. The titles and abstracts of 2134 studies were then screened, and 39 were selected for eligibility assessment. Of these, 29 studies were excluded due to being review letter, commentary or editorial; incomplete data; not focusing on the hormonal outcome. Finally 10 studies were included in this systematic review and meta-analysis.
Figure 1 presents the PRISMA flow chart for the study selection process.

Study characteristics

Data from 10 studies are summarized in Table 1 and were stratified by laterality into unilateral and bilateral. There were 563 patients who underwent orchidopexy for bilateral UDT and 1259 patients who underwent orchidopexy for unilateral UDT. The study outcomes included in this study are *follicle-stimulating hormone* (FSH), *luteinizing hormone* (LH), inhibin B levels, and azoospermia rate.
Table 1. Studies characteristics of bilateral and unilateral UDT post-orchidopexy.

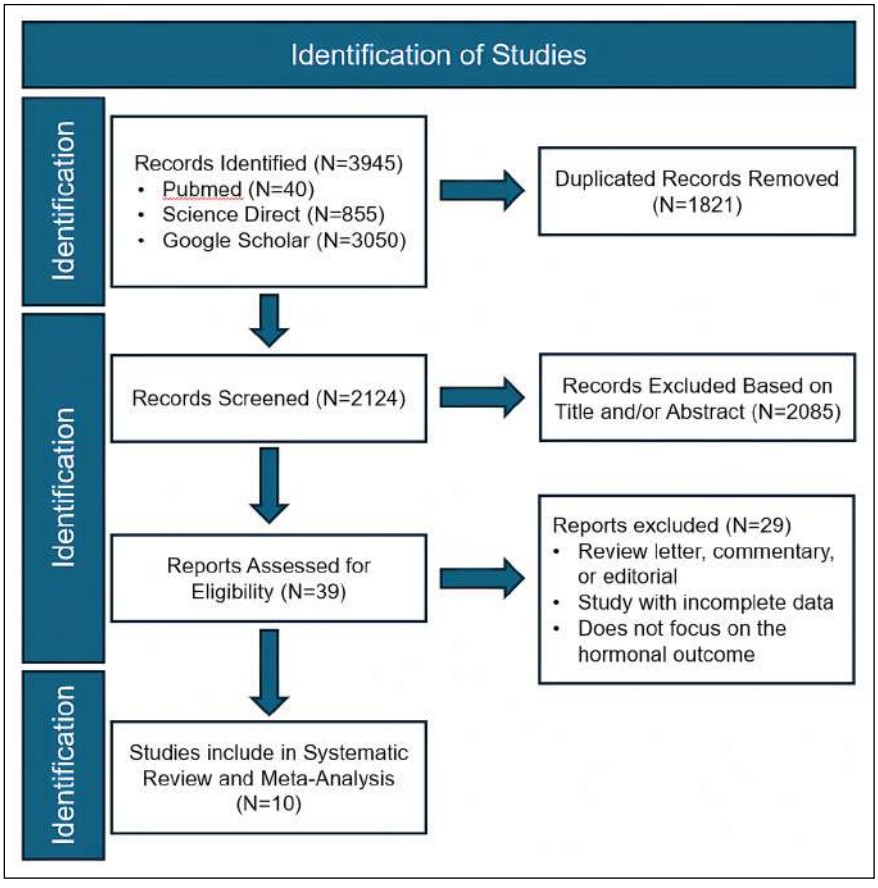


Figure 1.
PRISMA flow chart.

Table 1.
Studies characteristics of bilateral and unilateral UDT post-orchidopexy.

Study	Bilateral					Unilateral				
	Patients	FSH	LH	Inhibin B	Azoospermia	Patients	FSH	LH	Inhibin B	Azoospermia
Chiba et al. (2009) (8)	10	23.2 ± 5.6	6.8 ± 1.7	-	10	10	-	-	-	5
Lee et al. (2001) (9)	88	17.4 ± 14.3	7.1 ± 2.4	59.8 ± 50.6	-	609	6.7 ± 4.6	4.6 ± 3.1	112.5 ± 57.6	-
Trsinar et al. (2009) (7)	19	5.9 ± 3.3	-	119 ± 106.2	2	49	4.8 ± 3.9	-	164 ± 65.4	2
Rusnack et al. (2003) (10)	11	10.27 ± 4.34	7.24 ± 2.93	-	-	25	5.56 ± 2.56	6.59 ± 3.2	-	-
Ozan et al. (2019) (5)	86	28.19 ± 12.4	-	-	-	62	22.71 ± 11.86	-	-	-
Rohayem et al. (2016) (11)	135	15.5 ± 11.9	6.3 ± 5	-	62	222	11.9 ± 10	5.3 ± 3.3	-	62
Fan et al. (2024) (4)	43	7.19 ± 3.06	4.84 ± 1.74	-	23	56	7.15 ± 2.92	4.26 ± 1.81	-	19
Barbotin et al. (2019) (12)	145	21.3 ± 12.1	-	67.0 ± 26.5	-	80	19.3 ± 10.5	-	91 ± 38.9	-
Van Brakel (2012) (6)	7	8.2 ± 7.4	-	182.5 ± 90.8	-	55	4.8 ± 3.9	-	288.0 ± 133.0	-
Kraft et al. (2012) (13)	19	9.70 ± 4.19	6.35 ± 3.36	-	-	91	5.48 ± 3.58	5.17 ± 2.73	-	-

Study	Selection (Max 4)	Comparability (Max 2)	Outcome (Max 3)	Total (Max 9)	Risk of Bias
Chiba et al. (2009) (8)	4	1	2	5	Moderate
Lee et al. (2001) (9)	4	2	3	9	Low
Trsinar et al. (2009) (7)	4	2	3	9	Low
Rusnack et al. (2003) (10)	3	1	2	6	Moderate
Ozan et al. (2019) (5)	3	1	2	6	Moderate
Rohayem et al. (2016) (11)	4	2	3	9	Low
Fan et al. (2024) (4)	4	2	3	9	Low
Barbotin et al. (2019) (12)	4	2	3	9	Low
Van Brakel (2012) (6)	4	2	3	9	Low
Kraft et al. (2012) (13)	3	1	2	6	Moderate

Table 2.
Risk of bias assessment using Newcastle-Ottawa scale for each included study.

Risk of Bias

We included 10 studies in this meta-analysis, 5 of which are retrospective cohorts, 3 prospective cohorts, and 2 cross-sectional studies. Each study's risk of bias assessment is presented using the Newcastle Ottawa Scale, as shown in Table 2. Six studies have a low risk of bias, and the other four studies have a moderate risk of bias.

Follicle-stimulating hormone (FSH)

Nine studies were included In the meta analysis of FSH value. The forest plot revealed that post-orchidopexy FSH values in bilateral UDT were significantly higher compared to FSH values after unilateral UDT, with a mean difference (MD) of 3.77 UI/L (95% CI: 1.65-5.89, p = 0.0005) and significant heterogeneity (I^2 = 86%, p < 0.00001) (Figure 2).

Luteinizing hormone (LH)

Five studies were included in the meta-analysis of LH value. Post-orchidopexy LH values after bilateral UDT were significantly higher compared to LH values after unilateral UDT, with a *mean difference* (MD) of 1.27 UI/L

Figure 2.
Forest plot of FSH value.

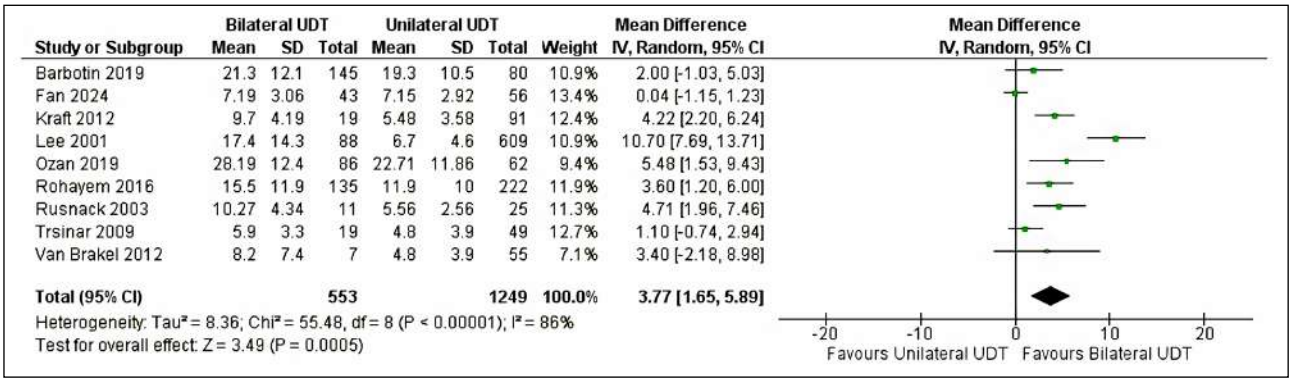


Figure 3.
Forest plot of LH value.

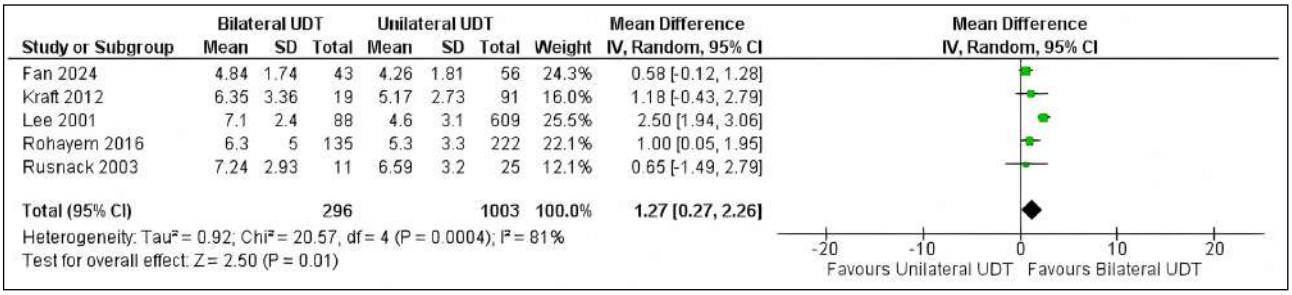


Figure 4.
Forest plot of Inhibin B value.

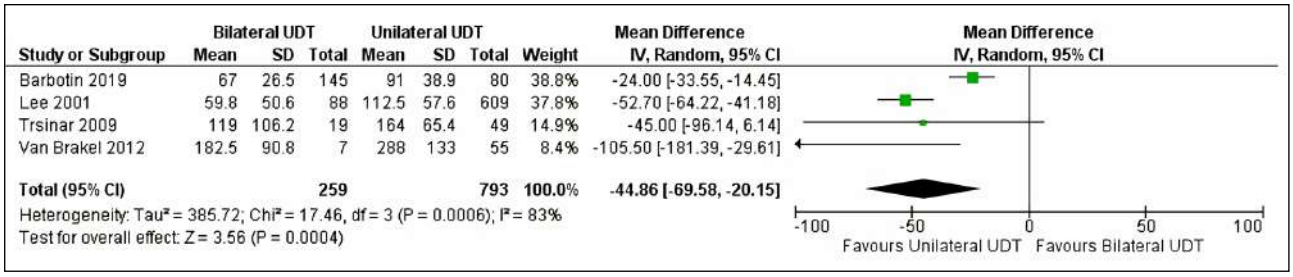
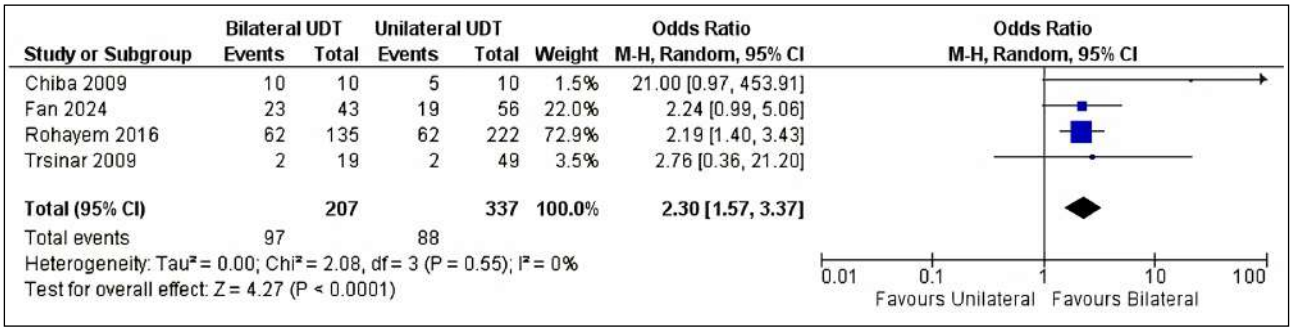


Figure 5.
Forest plot of azoospermia rate.



(95% CI: 0.27-2.26, p = 0.01) and significant heterogeneity (I^2 = 81%, p = 0.0004) (Figure 3).

Inhibin B

Meta analysis of Inhibin B value included four studies. Inhibin B levels post-orchidopexy in bilateral UDT were significantly lower compared to Inhibin B levels after unilateral UDT, with a mean difference (MD) of -44.86 pg/mL (95% CI: -69.58 - -20.15, p = 0.0004) and significant heterogeneity (I^2 = 83%, p = 0.0006) (Figure 4).

Azoospermia

Four studies were included in the meta-analysis of azoospermia rate.

The frequency of azoospermia was significantly higher in post-orchidopexy after bilateral UDT compared to unilateral UDT, with an *odds ratio* (OR) of 2.3 (95% CI: 1.57-3.37, p < 0.0001) and low heterogeneity (I^2 = 0%, p = 0.55) (Figure 5).

Discussion

This meta-analysis involved ten studies comprising 563 post-orchidopexy cases for bilateral UDT and 1259 post-orchidopexy cases for unilateral UDT. It was shown that patients with bilateral *undescended testis* (UDT) have significantly poorer post-orchidopexy testicular function compared to unilateral UDT. We find significantly elevated FSH and LH, and reduced inhibin B, which suggests some degree of primary testicular failure in bilateral UDT patients. These hormonal findings are backed up by significantly increased incidence of azoospermia.

Various other studies have found that bilateral UDT has a worse outcome than unilateral UDT. *Lee et al.* found that patients with bilateral UDT had significantly higher FSH and LH, and lower inhibin B than cases with unilateral UDT (9). *Trsinar et al.* and *Ozan et al.* also found a significant difference between unilateral and bilateral UDT (5, 7).

Our meta-analysis found that the risk of azoospermia was

more than twofold higher in bilateral UDT than unilateral UDT (OR 2.3). These findings backed up by various studies with similar results. A study by *Van Brakel et al.* found that sperm concentration is significantly lower in the bilateral UDT (6). Studies by Rohayem et al, also find that 49% of the patients with history of bilateral UDT with azoospermia and only 27% of the unilateral UDT had azoospermia (11), FSH, inhibin B, and LH represent the functions of the Sertoli and Leydig cells, respectively. FSH enhances T action by maintaining the supporting function of Sertoli cells on spermatogenesis (3). Serum levels of inhibin B are strictly related to the germinative epithelium status and reflect the Sertoli function (14). Inhibin B and FSH are biomarkers for the integrity of the seminiferous tubules. Damage to the seminiferous tubules are suggested by the elevation of FSH and low Inhibin B levels (9). On the other hand, LH works in the Leydig cell and helps stimulate the production of T, which is the cornerstone of effective spermatogenesis (3). Earlier study found elevated FSH and decreased inhibin B are a good markers of decreased sperm production (9, 15). This is also consistent with this study, which found that the risk of developing azoospermia is significantly higher in patients with bilateral UDT, who exhibit poorer results in FSH and inhibin B levels compared to those with unilateral UDT.

This shows that laterality of UDT is one of the critical factors for testicular functions after orchidopexy, along with the timing of surgery. Additionally, for adult patients presenting with infertility and a history of cryptorchidism, the laterality should be a critical component of the clinical assessment.

Our study has limitations inherent to retrospective data synthesis. Additionally, heterogeneity was moderate to high for endocrine markers (FSH, LH, inhibin B), likely due to variation in study design, patient age at surgery, timing of hormonal assessment, and laboratory methods. Although we used a random-effects model to account for this variability, residual confounding cannot be excluded. Future studies should stratify outcomes based on surgical technique and pubertal status, with a focus on long-term fertility endpoints.

Conclusions

This meta-analysis provides strong evidence that bilateral UDT is associated with significantly poorer testicular function outcomes following orchidopexy compared to unilateral UDT. Patients with bilateral UDT exhibited markedly elevated levels of FSH and LH, reduced levels of inhibin B, and a more than twofold increased risk of azoospermia. These findings suggest greater Sertoli and Leydig cell dysfunction in bilateral cases, highlighting the long-term implications of testicular maldescent on reproductive endocrinology.

Despite heterogeneity in hormone assay timing and surgical timing across studies, the consistency of trends across multiple parameters strengthens the validity of our findings.

Future prospective studies with standardized protocols and longer follow-up are warranted to explore the impact of laterality on fertility outcomes in greater depth, particularly when combined with variables such as age at surgery and testicular histopathology.

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Declarations

Ethical approval: *Ethical approval was not crucial for this study, as it did not involve directly patients, and all included data were previously published.*

Availability of data and material: *Availability of data and materials used in our study are available to access by request.*

Competing interests: *The authors declare that they have no competing interests.*

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Authors' contributions: *AANKA, investigation, writing – original draft, perform statistical analysis; MHWP, investigation, writing – original draft, perform statistical analysis; GWKD, conceptualization, supervision, writing-review and editing, validation. All authors read and approved the final manuscript.*

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