Comparison of the efficacy and safety of dorsal inlay graft urethroplasty (DIGU) method with tubularized incised plate urethroplasty (TIPU) method in primary distal hypospadias repair: a systematic review and meta-analysis

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ABSTRACT

Introduction: Tubularized Incised Plate Urethroplasty (TIPU) is a technique that is widely used in distal hypospadias repair. The advantages possessed by this technique are better cosmetics, the meatus is at the tip of the penis, and the phallus is straight. Some researchers believe that a urethral plate with a size of less than 8 mm is unsuitable for the TIPU technique so augmentation with a graft using the dorsal inlay graft urethroplasty (DIGU) technique is needed. To date, there have been no systematic reviews and meta-analyses that have directly compared the efficacy and complications of DIGU and TIPU. Therefore, this study aimed to compare the effectiveness and complications of these two modalities for repair in primary distal hypospadias patients.

Methods: This study is a systematic review study and meta-analysis. The protocol for conducting and compiling this study was based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. A systematic search was performed on six databases: PubMed, Scopus, Web of Science, ProQuest, Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov. The risk of bias in the study will be analyzed using the Cochrane Risk of Bias Tools for Randomized Trials version 2 (RoB 2).

Results: Six studies that met the inclusion criteria were included in the meta-analysis with a total of 381 samples. The success rates (OR 1.46, 95% CI 0.74-2.87, p = 0.28) and urine output (OR 2.54, 95% CI 0.63-10.20, p = 0.19) were not significantly different, while the mean operating time (SMD 1.96, 95% CI 1.10-2.82, p < 0.0001) was significantly shorter in TIPU (P < 0.05). The incidence of meatal stenosis was significantly more in TIPU than DIGU significantly (OR 5.11, 95% CI 1.46-17.92, p = 0.01), while fistula (OR 2.93, 95% CI 0.92-9.35, p = 0.07) and dehiscence (OR 3.05, 95% CI 0.81-11.45, p = 0.10) was not significantly different between the two techniques.

Conclusion: TIPU has the advantage of shorter operating time but a higher incidence of meatal stenosis than DIGU.

Keywords: tubularized incised plate urethroplasty, dorsal inlay graft urethroplasty, primary distal hypospadias.


INTRODUCTION

Hypospadias is a congenital anatomical malformation of the male external genitalia. It is characterized by abnormal development of the urethral fold and ventral prepuce of the penis leading to abnormal positioning of the urethral meatus.1 Hypospadias is the second most common congenital anomaly of the human male reproductive system. It is found in one out of every 250 males born.2 In hypospadias, the external urethral meatus may show varying degrees of malposition and may be found with a ventral curvature of the penis. Depending on the location of the abnormality, patients may have other genitourinary malformations, such as undescended testes.3,4 In addition to the abnormal location of the meatus, there is a classic triad of hypospadias, including ventral curvature of the penis (chordee), abnormal prepuce that is excessive on the dorsal part (dorsal hood).5 At least 90% of hypospadias cases are distal hypospadias, where the meatus is “glanular” or near the glans. The remaining cases are proximal hypospadias, where the meatus is located deep behind the shaft of the penis, penoscrotal, inside the scrotum, or in the perineum.6

The overall success rate in hypospadias surgery is usually no more than 60%. There are many methods described in the medical literature for hypospadias surgery.
However, numerous complications occurred postoperatively. However, numerous postoperative complications occurred with these techniques. This can cause confusion for young surgeons as they do not know which method works best.

Tubularized incised plate urethroplasty was the most widely used urethroplasty technique in distal hypospadias repair. TIPU technique was introduced by Warren Thomas Snodgrass in 1994. This technique has many advantages, such as better cosmetics, the meatus being at the tip of the penis, and the phallus being straight. The most common complications of this technique are urethro-cutaneous fistula, meatus stenosis, and glans dehiscence. This can be explained by the inflammatory reaction and granulation tissue formation on the incised urethral plate, where fibroblasts differentiate into fibromyoblasts and cause wound contraction until the wound surface is covered with urothelium tissue, causing progressive tension and fistulas in the wound.

Many researchers argue that urethral plates with a size of less than 8 mm are not suitable for TIPU technique urethroplasty, requiring augmentation with a graft, also known as the dorsal inlay graft urethroplasty technique or also known as the Snodgrass technique. The addition of a dorsal inlay graft to the urethral plate is suggested to accelerate the healing process and may improve surgical outcomes. Previous cohort studies have found that the TIPU procedure accompanied by a graft has better results than the classic TIPU procedure when applied as the procedure of choice for all cases of hypospadias, ranging from glanular to proximal penis. However, large-scale studies are still needed to strengthen these findings. This technique effectively reduces the risk of complications from the meatus or neourethra in hypospadias cases with narrow and flat glans and can provide a vertical slit-like neourethra meatus at the tip of the penis.

There had been no meta-analysis comparing the DIGU urethroplasty method to the TIPU method in repairing primary distal hypospadias prior to the publication of this study, so the authors conducted a systematic review and meta-analysis to determine the comparison.

**MATERIALS AND METHODS**

**Study design and protocol registration**

This systematic review and meta-analysis were performed in accordance with the Cochrane Handbook for Systematic Reviews and Intervention, in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Figure 1).

**Literature search strategy and eligibility criteria**

Two independent reviewers systematically searched for relevant articles through PubMed, Scopus, Web of Science, ProQuest, Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov databases from their inception up to May 2023 using MeSH* related to “hypospadias”, “urethroplasty”, “DIGU”, “preputial graft”, “plate graft”, “snodgrass”, and “TIPU”. The titles and abstracts were screened using pre-specified eligibility criteria. All randomized controlled trials (RCTs) which evaluated patients with distal primary hypospadias, comparing the DIGU and TIPU techniques, and reported the outcome of success rate, mean operative time, urinary stream, meatal stenosis, fistula, and gland dehiscence incidence were eligible for inclusion in this meta-analysis. Animal studies, unpublished articles, and non-English articles were excluded.

**Data collection and quality assessment**

Two independent reviewers collected data using a standardized data collection form. Additional reviewers solve any dispute between the reviewers, voting will be performed to justify any disagreement. The piloted form comprised of the first author’s name, study design, intervention protocol, total participants, participant’s age, urethral plate size, operator number, follow-up duration, and the outcomes included in the meta-analysis. This study’s primary outcome was the procedure’s success rate, which refers to the success rate of surgery without complications. Secondary outcomes of this study were the mean operative time urinary stream, meatal stenosis, fistula, and gland dehiscence incidence. The bias was evaluated by using Cochrane Risk of Bias Tools for Randomized Trials version 2 (RoB 2).

**Data synthesis**

Outcomes with dichotomous data were analyzed using odds ratio (OR) with Confidence interval (CI) at 95% and p-value below 0.05 was considered statistically significant. Continuous data will be analyzed using mean difference (MD) and standard deviation (SD). Heterogeneity between studies was calculated using $I^2$, if $I^2$ > 50% it was considered statistically high heterogeneity and a random-effect effects model was applied. If $I^2$ < 50%, then the fixed-effects model will be applied to this meta-analysis. Statistical analysis will use RevMan 5.4 for Windows software which will be presented in the form of forest plots and descriptive narratives.

**RESULT**

**Systematic Search Result**

A total of 486 studies were obtained from the systematic search. Out of the obtained studies 180 duplicates were removed. Primary screening resulted in 17 articles, which were further evaluated for eligibility. The final results obtained 6 studies that were included in this study. A summary of this systematic screening process is shown in the PRISMA flowchart (Figure 1).

**Study Characteristics**

All inclusion studies were RCTs with 381 primary distal hypospadias patients. The interventions performed were divided into two, using the DIGU and TIPU techniques. The mean age of the patient population ranged from 12.4 months to 41 months. The outcomes analyzed in each study were success ratio, mean operative time, stenosis, fistula, wound dehiscence, urine output. The characteristics of the studies are displayed in table 1.

**Risk of Bias**

According to Cochrane Risk of Bias (ROB) version 2.0 tools, overall bias of included studies was low, which only two studies had some concern. Studies by El Shazly et al. and Helmy et al. had a moderate risk of bias. The study by Helmy (2018) has missing outcome data bias and selection.
Comparison of DIGU and TIPU procedures on success rate
There were six articles with 381 hypospadias patients to evaluate the success rate parameter. The success rate of TIPU procedure was not significantly different from the DIGU technique (OR 1.46, 95% CI 0.74-2.87, p = 0.28) (Figure 3).

Comparison of DIGU and TIPU procedures on mean operative time
A total of five articles with 337 hypospadias patients comparing the mean operative time of the two techniques. Patients undergoing the TIPU procedure had a significantly faster mean operative time compared to the DIGU technique (MD 1.96, 95% CI 1.10-2.82, p<0.0001) (Figure 4).

Comparison of DIGU and TIPU procedures on the incidence of meatal stenosis
Five studies reported the incidence of meatal stenosis. The pooled odds ratio was 5.11 (95% CI 1.46-17.92, p = 0.01), TIPU had a significantly higher incidence of meatal stenosis compared to DIGU (Figure 6).

Comparison of DIGU and TIPU procedures on the incidence of fistula
A total of six studies compared the fistula incidence between two procedures. TIPU and DIGU had no significant difference in the incidence of fistula (OR 2.93, 95% CI 0.92-9.35, p = 0.07) (Figure 7).

Comparison of DIGU and TIPU procedures on the incidence of dehiscence
A total of five studies reported the incidence of dehiscence. TIPU and DIGU had no significant difference in the incidence of dehiscence (OR 3.05, 95% CI 0.81-11.45, p = 0.10) (Figure 8).

DISCUSSION
Due to its high success rate in the correction of hypospadias, Warren Thomas Snodgrass’s 1994 introduction of the TIPU technique for urethroplasty has become widely used around the world. The TIPU technique has advantages including better cosmetics, the meatus is at the tip of the penis, and a straight phallus.

Urethra-skin fistulas, meatus stenosis, and dehiscence may result from an inflammatory reaction and the creation of granulation tissue on the incisional urethral plate, where fibroblasts convert into fibromyoblasts and compress the wound until urothelial tissue covers it, causes progressive tension and fistulas in wounds.

Many researchers suggest that urethral plates smaller than 8 mm in size are unsuitable for urethroplasty TIPU procedure, necessitating graft augmentation, also known as DIGU technique or Snodgraft technique. Previous cohort studies found that the TIPU procedure accompanied by a graft had better results than the classic TIPU procedure, when applied as the procedure of choice for all cases of hypospadias, ranging from glanular to proximal penis.

Our findings for mean operative time are favoring TIPU, which concludes TIPU is faster dan DIGU. The study by Omran et al. also showed the same result as this review which DIGU took longer operative
### Table 1. The characteristics of the included studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Country</th>
<th>Study Type</th>
<th>Group</th>
<th>Subjects (n)</th>
<th>Age in months (Mean±SD)</th>
<th>Urethral Plate width before Procedure (mm)</th>
<th>Numbers of operator</th>
<th>Follow up</th>
<th>Control</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouravas, 2014</td>
<td>Greece</td>
<td>RCT</td>
<td>DIGU</td>
<td>23</td>
<td>41</td>
<td>No data</td>
<td>2</td>
<td>2-5 years</td>
<td>TIPU</td>
<td>DIGU</td>
<td>Success Rate, MOT, Meatal Stenosis, Fistula, Wound Dehiscence</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TIPU</td>
<td>24</td>
<td>38</td>
<td>No data</td>
<td>2</td>
<td>2-5 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helmy, 2018</td>
<td>Egypt</td>
<td>RCT</td>
<td>DIGU</td>
<td>30</td>
<td>40 ± 15</td>
<td>&lt;8mm</td>
<td>1</td>
<td>Every 3 months</td>
<td>TIPU</td>
<td>DIGU</td>
<td>Success Rate, MOT, Meatal Stenosis, Fistula, Wound Dehiscence</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TIPU</td>
<td>30</td>
<td>40 ± 15</td>
<td>&lt;8mm</td>
<td>1</td>
<td>Every 3 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eldeeb, 2020</td>
<td>Egypt</td>
<td>RCT</td>
<td>DIGU</td>
<td>30</td>
<td>13 (5-24)</td>
<td>Median 6 mm</td>
<td>1</td>
<td>2 weeks, 3 months, 1 year</td>
<td>TIPU</td>
<td>DIGU</td>
<td>Success Rate, MOT, Meatal Stenosis, Fistula, Wound Dehiscence</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TIPU</td>
<td>30</td>
<td>12 (6-24)</td>
<td>Median 5 mm</td>
<td>1</td>
<td>2 weeks, 3 months, 1 year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>El-Shazly, 2020</td>
<td>Egypt</td>
<td>RCT</td>
<td>DIGU</td>
<td>23</td>
<td>37.8 ±48.9</td>
<td>Mean 7.6 mm</td>
<td>TD</td>
<td>2 weeks, 6 months</td>
<td>TIPU</td>
<td>DIGU</td>
<td>Success Rate, MOT, Fistula, Wound Dehiscence, Urinary Stream</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TIPU</td>
<td>24</td>
<td>23.0 ±14.8</td>
<td>Mean 8 mm</td>
<td>TD</td>
<td>2 weeks, 6 months</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Zeina, 2021</td>
<td>Egypt</td>
<td>RCT</td>
<td>DIGU</td>
<td>30</td>
<td>11.40 ±3.10</td>
<td>3.5-7 mm, Mean 4.57 ±0.75</td>
<td>TD</td>
<td>Every in 1 month, 3 months, 6 months</td>
<td>TIPU</td>
<td>DIGU</td>
<td>Success Rate, MOT, Meatal Stenosis, Fistula</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TIPU</td>
<td>30</td>
<td>12.6 ±3.64</td>
<td>4-7 mm, Mean 4.85 ±0.75</td>
<td>TD</td>
<td>Every in 1 month, 3 months, 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ahmed, 2021</td>
<td>Egypt</td>
<td>RCT</td>
<td>DIGU</td>
<td>53</td>
<td>33.6 ± 39.4</td>
<td>7.6 ±1.8</td>
<td>3</td>
<td>2 weeks, 1 month, 3 months, 6 months</td>
<td>TIPU</td>
<td>DIGU</td>
<td>Success Rate, MOT, Meatal stenosis, Wound Dehiscence, Fistula, Urinary stream</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TIPU</td>
<td>54</td>
<td>23.1 ± 14.6</td>
<td>8 ± 0.96</td>
<td>3</td>
<td>2 weeks, 1 month, 3 months, 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sample totals</strong></td>
<td></td>
<td></td>
<td></td>
<td>381</td>
<td></td>
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</tbody>
</table>
time with an average of 85-110 minutes compared with other approaches.\(^9\) Other studies also explained that TIPU took a shorter operative time with an average of 92 minutes while DIGU took 115 minutes. DIGU is indicated for more complicated cases with the shallowest incision.\(^9\) While DIGU required more operational time of this procedure seemed to not result in an improved aesthetic, success rate, or urine flow rate. The additional operational time for DIGU compared to TIPU from the pooled analysis is calculated to be around two minutes, which is clinically insignificant despite being statistically significant.\(^1\)

A comparison of complications between TIPU and DIGU was assessed from the incidence of meatal stenosis, fistula, and dehiscence. Analysis of the incidence of meatal stenosis obtained significant results. TIPU has a greater incidence of meatal stenosis than DIGU. Zeina et al., states that meatal stenosis is the most common postoperative complication of hypospadias repair tips. This complication occurs due to a technical error in urethral plate tubularization that is performed too distally.\(^2\) The DIGU technique provides more surface area on the urethral plate so that it is expected to prevent granulation and contraction underlying stenosis.\(^1\) Stenosis can also occur if the incision made in TIPU is too shallow, this is what is tried to be overcome with the DIGU technique that minimizes incisions that are too shallow.\(^9\) We propose that the difference in the incidence of meatal stenosis is attributable to differences in technique. TIPU has a higher risk of stenosis because it is easier for too shallow or too distal incisions to occur than DIGU.

This meta-analysis found no significant differences in success rate, urine emission, fistula incidence, or dehiscence between DIGU and TIPU groups. In 2020, Eldeeb and Ahmed found success rates comparable to the DIGU and TIPU groups.\(^8\),\(^9\) Ahmed's study assessed hypospadias success using the HOSE score. The HOSE score objectively evaluates hypospadias surgery results. Ahmed observed that DIGU performed similarly to TIPU.\(^9\) Glans dehisens is a concern of hypospadias correction due to their tiny size.\(^2\)-\(^2\) As mentioned in the literature, hypospadias correction aims to create a straight urine stream. DIGU and TIPU treatments can improve primary distal hypospadias, providing a good urine stream with 87 to 91.3 percent success.\(^1\),\(^2\) Fistula is the second most frequent

**Figure 2.** Risk of bias using Cochrane Risk of Bias (ROB) version 2.0.

**Figure 3.** Forest plot comparing DIGU and TIPU procedures on success rate.

**Figure 4.** Forest plot comparing DIGU and TIPU procedures on mean operative time.

**Figure 5.** Forest plot comparing DIGU and TIPU procedures on urinary stream.

**Figure 6.** Forest plot comparing DIGU and TIPU Procedures on the Incidence of Meatal Stenosis.
Table 1. Forest plot comparing DIGU and TIPU procedures on the incidence of fistula.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TIPU</th>
<th>Total</th>
<th>DIGU</th>
<th>Total</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed 2021</td>
<td>55</td>
<td>54</td>
<td>12.2%</td>
<td>9.91 [0.52, 188.76]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eldib et al. 2020</td>
<td>30</td>
<td>28</td>
<td>10.7%</td>
<td>3.39 [0.17, 68.77]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>El shazly 2020</td>
<td>30</td>
<td>28</td>
<td>10.7%</td>
<td>3.04 [0.14, 68.77]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helmy 2018</td>
<td>30</td>
<td>28</td>
<td>10.7%</td>
<td>5.39 [0.25, 116.31]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mouras 2014</td>
<td>23</td>
<td>21</td>
<td>10.6%</td>
<td>0.99 [0.06, 16.25]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>189</td>
<td>192</td>
<td>100.0%</td>
<td>2.33 [0.62, 9.30]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>10</td>
<td>3</td>
<td></td>
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</tbody>
</table>

Test for overall effect: Z = 1.81 (P = 0.07)

CONCLUSIONS

According to the findings of this meta-analysis, the researchers contend that the TIPU approach is preferable in terms of the average amount of time spent operating and the percentage of patients who experience mental stenosis. The TIPU approach is more effective than the DIGU technique in reducing the time spent in operation and the risk of developing mental stenosis complications.

CONFLICT OF INTEREST

All author declares there is no conflict of interest regarding publication of this study.

PROTOCOL REGISTRY

The protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO CRD42023403164).

REFERENCES