INTRODUCTION

Hypospadias is a condition where the urethral meatus is located on the ventral of the penis and is commonly associated with chordee. It is the second most common congenital abnormality among male children. Hypospadias repair is one of the most common surgical procedures pediatric urologists perform, as surgical reconstruction becomes the mainstay treatment option for hypospadias. The primary purposes of reconstruction are to create a vertical slit of the orthotopic meatus, straighten the curvature of the penis, and establish an excellent cosmetic result, including the glans penis.

Snodgrass et al. described a technique for distal hypospadias repair referred to as the tubularized incised plate (TIP) technique that has been widely used. Meanwhile, in different studies, parameatal flap-based urethroplasty, or the Mathieu procedure, is another commonly used technique with a complication rate of less than 4%. However, the meatus would have a horizontal and circular shape, which is cosmetically less favorable than the vertical slit meatus resembling normal anatomy.

Innovative techniques in distal hypospadias surgery and modifications of previously used techniques are continuously introduced to reduce complication rates and to achieve better functional and cosmetic outcomes. Previous studies have reported that combining a distal urethral plate incision and a meatal-based flap technique yielded an excellent postoperative complication profile and improved the cosmetic aspect. However, a high level of evidence pertinent to the combined distal urethral plate incision and meatal-based flap known as the Mathieu with plate incision technique and the standard TIP urethroplasty are yet to be established. This study aimed to compare the outcome of postoperative complications between the Mathieu with plate incision technique and the standard TIP technique in patients with distal hypospadias.
METHODS

Study Design
The study population in this review is pediatric patients with distal hypospadias, with the intervention of Mathieu with plate incision or standard TIP technique. This research was conducted by referring to the protocol described in The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and following the rules and requirements elaborated in the Handbook for Systematic Reviews of Interventions from Cochrane.

Systematic Search Strategy
The search process for relevant studies was conducted online in well-known databases, i.e., PubMed and ScienceDirect. The primary outcomes evaluated in the analysis are postoperative complications in the respective intervention group. The protocol of this study has been registered on PROSPERO (ID: CRD42022341745).

Eligibility Criteria
Eligibility of the study was determined on several criteria, which include a randomized controlled trial (RCT), clinical trial, and retrospective study design; a minimum of two or more treatment arms comparing different techniques of urethroplasty, including Mathieu with plate incision and standard TIP; the intended patient population of distal hypospadias in the course for the first procedure. Eligible studies report the occurrence of postoperative complications after each procedure, with the incidence of meatal stenosis and fistula or urethrocutaneous fistula (UCF) among the outcome of interest. Potential articles were excluded if the study designs were not as mentioned, i.e., case series. Studies on animals, non-English articles, and abstract-only were also excluded.

Data Extraction and Quality Assessment
Two independent reviewers completed the data extraction process by filling in the criteria required in the research protocol. Any differences in data extraction outcome will be discussed with a senior reviewer for the final decision. The data extracted from the studies included in the study are summarized in the table characteristics of obtained articles and postoperative complications outcome. The quality of each study and the risk of bias was assessed using the Cochrane Risk of Bias Tool 2.0 for randomized studies. A thorough evaluation was performed for each included study, following the algorithm provided with the instrument. Quality assessment data is summarized in the form of a table with five domains of valuation.

The characteristics of obtained articles, including operative characteristics with postoperative complications outcome of each study, are summarized in the form of data tabulation. Pooled studies were analyzed quantitatively and qualitatively according to the study outcome parameters. Measures of effect were presented as odds ratio (OR) with a 95% confidence interval (95% CI). Heterogeneity between the studies was analyzed using the I² index and heterogeneity test. The I² value of < 50% and heterogeneity p-value > 0.05 denoted that the included studies exhibited low heterogeneity; therefore, the fixed-effects model will be utilized. Otherwise, the random-effects model will be used for significant heterogeneity. The analysis results will be presented as forest plots, and the publication bias will be assessed using a funnel plot, giving a sufficient number of studies. All analyses will be conducted using statistical software Review Manager 5.4.1 (Cochrane Collaboration).

RESULTS

Systematic Search Results
The review process was represented by the PRISMA flow diagram shown in Figure 1. An initial literature search on PubMed and ScienceDirect databases yielded 127
articles. The keywords used for search strategy are “Mathieu”, “paramesal flap”, “perimesal flap”, “Snodgrass”, “tubularized incised plate”, “tubularised incised plate”, “TIP”, “plate incision”, and “hypospadias”. As many as 27 duplicates were removed, with further screening through titles and abstracts leaving only 42 retrievable articles. Exclusion on eligibility phase was made due to unavailable full-text and specifically inappropriate population, inappropriate comparison, review article type, and non-English articles. Three final articles were obtained for qualitative and quantitative analysis.

Study Characteristics
The characteristics of each included study are shown in Table 1. The author of the study, time of publication, and country of origin were enlisted. Included studies are all RCTs published from 2008 to 2017. Distal hypospadias was varied as ventrally located meatus of coronal, subcoronal, and distal penis. No intervention of distal hypospadias alongside urethroplasty using Mathieu with plate incision and standard TIP technique was compared. The mean age of the study population is between 25.3–87.72 months. Among the postoperative complications as the endpoint of studies was the incidence of meatal stenosis, narrow stream, and fistula formation.

Risk of bias assessment
The overall assessment generated a low risk of bias in all three studies. Evaluated indicators include any concern arising from the randomization process, deviation from the targeted intervention, missing outcome data, outcome measurement, and selective reporting. One study by Aminsharifi et al. presented some concerns in the first domain, of which they did not explain the manner of randomization used. No particular domains indicated serious bias risk. The study quality based on the risk of bias assessment is shown in Figure 2.

Meta-analysis result on meatal stenosis
The incidence of meatal stenosis in patients with distal hypospadias who underwent urethroplasty is significantly lower in the Mathieu with plate incision group compared to the standard TIP group (OR: 0.08 CI 0.01-0.41 p = 0.003). The forest plot comparison is shown in Figure 3. Heterogeneity between the pooled studies was insignificant (I²: 0%; p = 0.99), which justifies the fixed-effects model for analysis.

Meta-analysis result on narrow stream
The narrow stream incidence rate of patients with distal hypospadias who underwent urethroplasty was significantly lower in the Mathieu with plate incision group compared to the standard TIP group (OR: 0.09 CI 0.02-0.49 p = 0.006). The forest plot comparison is shown in Figure 4. The fixed-effect model was applied due to the low level of heterogeneity between studies (I²: 0%; p = 0.97).

Meta-analysis result on fistula formation
Endpoint analysis showed a significantly lower fistula occurrence rate in patients with distal hypospadias who underwent urethroplasty using Mathieu with plate incision technique compared to the standard TIP technique (OR: 0.28 CI 0.08-0.96 p = 0.04). The forest plot comparison is shown in Figure 5. The fixed-effect model was used for analysis as heterogeneity between studies was not significant (I²: 0%; p = 0.47).

DISCUSSION
This study compared the postoperative complication outcomes of the different approaches used for distal hypospadias repair: the standard TIP technique and the modified technique incorporating plate incision to the Mathieu procedure. To the best of our knowledge, this is the first review study of Mathieu with plate incision versus standard TIP technique for distal hypospadias repair. Complications are the primary concern for evaluation in the follow-up of urethroplasty, as it determines the need for subsequent repair.13 The pooled analysis resulted in meatal stenosis that was significantly higher in the standard TIP group compared to the Mathieu with plate incision group (OR: 0.08 CI 0.01-0.41 p = 0.003; I²: 0%).

All included studies in the meta-analysis reported no meatal stenosis occurrence among patients in the
Mathieu with plate incision group. In this instance, studies on Mathieu with plate incision are very limited, and the available evidence is mainly comparing the original Mathieu with the TIP technique. A large retrospective analysis documented a similar success rate and low complication rate between Mathieu and TIP techniques.\(^{14}\)

A systematic review comprising a series spanning two decades reported that the Mathieu technique is consistently associated with lower meatal stenosis incidence than TIP.\(^{15}\) A recent meta-analysis also estimated that the meatal stenosis rate was significantly lower with Mathieu than with the TIP technique.\(^{16}\)

Nguyen and Snodgrass correlated meatal stenosis after the use of TIP technique with technical factors, such as too distal tubularization of the urethral plate.\(^{17}\) Other studies suggest that the natural configuration of the urethral plate plays an important role. A narrow, flat urethral plate is more prone to meatal stenosis even though the incision and tubularization are not too distal.\(^{18}\) In contrast, these were not the contributing factors in the Mathieu procedure, which does not depend on the urethral plate characteristics. It allows for the creation of a neourethra with a greater circumference, while the width of the existing urethral plate limits the neourethra in TIP repair.\(^{15,19}\)

Mathieu technique incorporated with incision of the urethral plate allows re-establishment of the urethral meatus in slit-like form. It is an essential surgical step to create a vertical-shaped meatus, which is more cosmetically preferable than the rounded shape yielded from the original technique.\(^{9,20}\) Moreover, an interesting

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**Figure 2.** Risk of bias assessment using risk of bias tool (ROB) for randomized trial.

**Figure 3.** Forest plot comparison of meatal stenosis incidence.

**Figure 4.** Forest plot comparison of narrow stream incidence.

**Figure 5.** Forest plot comparison of fistula formation.
result in the use of the Mathieu technique was reported in patients with deep fissures in the urethral plate, of which a vertical meatus was created in approximately one-third of the population.9-20 On the other hand, the healing of incised urethral plate after the TIP procedure could form a deep narrow groove or a linear scar resulting in stenosis.21

The postoperative narrow stream event after application of the two techniques showed a significantly higher rate among the standard TIP group (OR: 0.91 CI 0.02-0.49 p = 0.006; I²: 0 %). As with the meatal stenosis rate, the absence of postoperative narrow stream events was obtained in the entire population of included studies treated using the Mathieu with plate incision technique for distal hypospadias repair.22-24 A study by Naeem also reported a higher occurrence of narrow steam among patients who underwent TIP compared to the Mathieu repair.25 It warrants attention that in a study focusing on urinary flow measurements, Winberg et al. revealed a significant difference in Qmax and curve patterns in favor of the Mathieu group after the two procedures.26 However, another long-term follow-up study found that Qmax improved in all patients regardless of the repair technique.27 Despite not often reported narrow stream events could be a useful indicator associated with other complications following distal hypospadias repair.

Fistula formation was hypothesized to correlate with meatal stenosis and narrow stream outcomes. A significantly higher incidence of fistula in the standard TIP group compared to the Mathieu with plate incision group was observed (OR: 0.28 CI 0.08-0.96 p = 0.04; I²: 0 %). Urethral plate characteristics were also regarded as the most significant factor of postoperative fistula with TIP repair. The narrow and flat urethral plate was more susceptible to fistula formation, regardless of deep incision and plate tubularization.8 Even in distal hypospadias with less than 14 mm glans width, Mathieu with plate incision was associated with a lower rate of urethrocuteanous fistula (UCF), meatal stenosis, and also glans dehiscence.28 However, a previous meta-analysis of RCTs comparing Mathieu and TIP techniques reported a similar risk of UCF, but a significantly lower risk of urethral stricture in Mathieu repair.29 These could highlight the advantage of the Mathieu with plate incision technique of which fistula formation was lower among included studies.22-24 A modified technique incorporating glans augmentation also showed a promising result in reducing meatal stenosis, UCF, and overall complications, especially in patients with shallow urethral grooves when TIP is not preferable.30

The quality of the study was represented by the risk of bias appraisal utilizing the Cochrane Risk of Bias Tool 2.0 since only RCTs were included in the meta-analysis. The included studies presented a low risk of bias across all domains. This could be a favorable aspect of this study, considering the analyses were generated out of domains with minimal bias; therefore, the findings are presumed to be robust. However, the current assessment was performed on outcomes that were limited to postoperative complications, even if it is regarded as the primary measure for successful distal hypospadias repair. A subsequent review study on this subject is expected to report a more comprehensive evaluation of the success and benefits of the Mathieu with plate incision technique compared to standard techniques such as TIP urethroplasty, including cosmetic outcomes.31

This review provides insight into the comparison of postoperative complications between the standard TIP technique as the current technique of choice for distal hypospadias repair and the modified technique of Mathieu with plate incision. Hopefully, this study will contribute to a clinical consideration for urologists in determining the preferred technique for repairing distal hypospadias. Among the limitation of this study, the lack of extensive studies which compares the Mathieu with plate incision to standard TIP technique stands out. Multicentre randomized studies with robust methodology in larger sample sizes are required to obtain more substantial internal and external validity. Opportunities in investigating novel surgical techniques are widely available, considering either standard or modified urethroplasty techniques for hypospadias have been vastly proposed to date. Innovative techniques are expected to provide the best possible outcome with the lowest complication rate.

CONCLUSION
The incidence of meatal stenosis, narrow stream, and fistula formation is lower in patients with distal hypospadias who underwent Mathieu with plate incision procedure compared to the standard TIP urethroplasty. More complementary investigations regarding the complication of both techniques are needed in future studies to get a comprehensive safety picture of the distal hypospadias repair technique.

CONFLICTS OF INTEREST
The authors declare that they have no conflict of interest.

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None.

ETHICS COMMITTEE APPROVAL
This systematic review and meta-analysis do not require an ethical approval.

AUTHOR CONTRIBUTION
• Muhammad Arif Hakim Jamhari (M.A.H.J.) is involved in the concept and project design, materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.
• Ilham Akbar Rahman (I.A.R.) is involved in the materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.
• Muhammad Rifki Setiawan (M.R.S) is involved in the materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.
• Sirin Salsabila (S.S.) is involved in the materials, literature search, data collection and/or processing, analysis
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- Johan Renaldo (J.R.) is involved in the concept and project design, supervision, resources, materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.

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REGISTRATION OF RESEARCH STUDY

- Name of the registry: PROSPERO
- The unique identifying number or registration ID: CRD42022341745
- Hyperlink to registration: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=341745

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