



Risk factors for urethrocutaneous fistula following hypospadias repair surgery in Indonesia

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Summary

Introduction

Hypospadias is one of the most common congenital malformations with a worldwide increasing trend over the years. Despite advancements in hypospadias repair, complications still occur. One of the most common complications of hypospadias repair surgery is Urethrocutaneous fistula. Studies attempting to analyze the association between the complication and risk factors are always beneficial, especially for studies performed in different areas of the world. We hypothesize that several evaluated risk factors among Indonesian hypospadias patients could be associated with the occurrence of urethrocutaneous fistula after the repair procedure.

Objective

To determine the risk factors associated with urethrocutaneous fistula after hypospadias repair surgery by collecting and analyzing data obtained from multiple centers in Indonesia.

Materials and methods

A nationwide, retrospective study with 12 hospitals in Indonesia of children with a diagnosis of hypospadias was conducted. The collected data, taken from patients admitted in 2018, from each center's medical records consisted of patient identity, repair technique used, neourethra length, percutaneous cystostomy, and splint size as independent variables speculated to be possible risk factors correlated to the presence of urethrocutaneous fistulae. Binomial logistic regression analysis was performed using SPSS

21.0 to determine the relationship between urethrocutaneous fistulae as a post-repair complication and possible risk factors.

Results

We collected 591 hypospadias cases from 12 centers in 9 cities in Indonesia. Most patients came when they were already at the age of more than four years old (60.4%). The chordee-only and failed urethroplasty groups are excluded from the analysis as they are not classified as true hypospadias. Most repairs were performed by using the Tubular Incised Plate (TIP) with Thiersch-Duplay technique (44.16%). Most of the reconstructed neourethra are 2–3 cm in length (32.13%). The 8 Fr urethral splint (46.41%) was mostly used during the operation. Most surgeons decided not to perform cystostomy throughout the procedure (61.03%) based on personal preferences. Urethrocutaneous fistula was found in 80 patients (15.27%) out of the total patients who underwent the surgery. The binomial logistic regression analysis shows that age (OR = 1.398, $p = 0.015$), the decision to not perform cystostomy (OR = 2.963, $p = 0.014$), and splint size (OR = 1.243, $p = 0.023$) are significantly associated ($p < 0.05$) with the development of urethrocutaneous fistula.

Conclusion

Age and splint size are significant risk factors for urethrocutaneous fistula after hypospadias repair in Indonesia, whereas performing percutaneous cystostomy during the repair decreases the risk for urethrocutaneous fistula occurrence.

Summary Table

	Age	Not performing Cystostomy	Neourethra Length	Splint Size	Urethroplasty Technique	Hypospadias Type
Odds Ratio (95% CI) for Urethrocutaneous Fistula Occurrence	1.398 (1.067–1.832)	2.963 (1.250–7.024)	1.411 (0.906–2.199)	1.243 (1.031–1.499)	0.879 (0.714–1.083)	2.124 (0.861–5.242)
	P = 0.015	P = 0.014	P = 0.128	P = 0.023	P = 0.226	P = 0.102

Background

In the world of Pediatric Urology, Hypospadias is considered to be one of the most common congenital malformation with a worldwide increasing trend over the years [1]. This increase of trend leads to advancements in hypospadias surgical repair, giving birth to many techniques such as Tubularized incised plate, Glandular approximation plasty Bracat, Preputial island flaps, among many others. Despite these advancements, complications still occur [2]. One of the most common complications of hypospadias repair surgery is Urethrocutaneous fistula with an incidence rate that varies in different countries [3]. In regard to the patient's quality of life, it is important to attempt to minimize the risk of developing complications after the surgery. Possible preoperative and intraoperative risk factors with various results between studies around the world have been identified in the past [4–6]. Therefore, more studies attempting to identify them will always be beneficial, especially in Indonesia where publications regarding the matter are limited. In this study, we aim to determine the risk factors associated with urethrocutaneous fistula after hypospadias repair surgery by collecting and analyzing data obtained from multiple centers in Indonesia. We hypothesize that several evaluated risk factors could be related to the occurrence of urethrocutaneous fistula after the repair procedure.

Materials and method

We conducted a nationwide, retrospective study with 12 hospitals in Indonesia of children with a diagnosis of hypospadias. This study was approved by the ethical committee of Sanglah General Hospital (179/UN.14.2/KEP/2016). Patient data was compiled from 18 Pediatric Urologists in each center to ensure competence and standard of management among cases. The clinical documentation from the patient's visits, operation, and follow-up visits was examined retrospectively. The collected data from each center's medical records consisted of patient identity, technique used, neourethra length, percutaneous cystostomy, and splint size as independent variables speculated to be possible risk factors correlated to the presence of urethrocutaneous fistulae as the dependent variable. Unfortunately, some of the data collected from the centers are incomplete as some patients were failed to be followed up after the procedure, thus a binomial logistic regression analysis is chosen instead of a multinomial logistic

regression to be performed using SPSS 21.0 to determine the relationship between urethrocutaneous fistulae as the dependent variable and possible associated risk factors as the independent variables with a defined confidence interval of 95% and significant value of $p < 0.05$.

Result

We collected 591 cases from 12 centers in 9 cities in Indonesia as shown in Table 1. The subject characteristics consisting of the possible risk factors for the complication are shown in Table 2. Some of the cases collected were not eligible for further analysis as several excluded patients failed to be followed up after the operation and some patients declined to provide further information after the procedure. Therefore, some subjects have incomplete data for age ($n = 588$), neourethra length ($n = 333$), cystostomy ($n = 349$), splint size ($n = 390$), and fistula occurrence ($n = 524$) among all the cases collected ($n = 591$). Out of the collected cases, most patients came when they were already at the age of more than four years old (60.4%). This age demographic shows that early awareness of the disease is still low. The chordee only and failed urethroplasty groups consisting of 24 cases will further be excluded from the analysis as they are not classified as true hypospadias. The types are categorized into proximal ($n = 264$) and distal ($n = 303$) for the analysis. A variety of different techniques were performed for the repair, however for most cases, Tubular Incised Plate (TIP) with Thiersch-Duplay technique (44.16%) was performed based on the preference of each surgeon. The decision to perform a certain type of technique is based on each surgeon's personal experience. All of the procedures in each center were performed by a pediatric urologist, thus ensuring a standard level of skill among different operators. Differences in neourethra length and splint size were also noted among the cases. Most of the reconstructed neourethra were 2–3 cm in length (32.13%). During the procedure, the 8 Fr urethral splint (46.41%) was mostly used. Amid the intraoperative differences in procedure, the decision to perform a urinary diversion was also divided, in which most surgeons decided not to perform one based on each individual's personal preference. During the follow up visits, urethrocutaneous fistula was discovered in 80 patients (15.27%) out of the total patients who underwent the surgery and came back to be evaluated. As mentioned previously, due to some incomplete data from a few centers, some parameters of the variables are missing their fistula occurrence data. The binomial logistic regression

performed using SPSS 24 disregards the missing data from certain several variables, ensuring a proper and accurate result. The result of the binomial logistic regression analysis in Table 3 shows that age (OR = 1.398, $p = 0.015$), the decision to not perform cystostomy (OR = 2.963, $p = 0.014$), and splint size (OR = 1.243, $p = 0.023$) are significantly associated ($p < 0.05$) with the development of urethrocutaneous fistula as a post-repair complication.

Discussion

An ideal hypospadias repair is expected to have low rates of complication which results in normal penis based on appearance and function, both urinary and sexually [7,8]. For pediatric urology surgeons, the topic of post-operative complications after hypospadias repair and their associated risk factors has always been an interesting subject matter to be studied and discussed [9]. Urethrocutaneous fistula, one of the most common post-repair complications, is a major burden for both the physician and the patient [10]. In this study, there are 15.27% patients who developed urethrocutaneous fistula after the repair as seen in Table 2. The incidence rate is somewhere in between the incidence estimated by previous studies, which is around 5%–10% [11–13]. Identifying modifiable risk factors in this study is still necessary to reduce the complication rate even further since, as of the publication of this study, there haven't been any studies in Indonesia focusing on this particular matter. The analysis of age, cystostomy placement, neourethra length, splint size, and urethroplasty technique as independent variables with the occurrence of urethrocutaneous fistula as the dependent variable generated interesting results. We classified the age of the patients into four different categories showing major differences in age in which the patients were brought to the Hospital. Ideally, pediatric genital surgery is performed at the age of 6–18 months based on the study conducted by The American Academy of Pediatrics [14]. Most infants develop good tolerance to anesthesia and surgery by the age of 6 months. By the age of 18 months, they are aware about their genitalia and are toilet trained. In some cases of hypospadias repair, some surgeons prefer to operate earlier at 4 months

of age because of faster healing time, fewer scars, and due to the belief, that it is easier for the infants to overcome the stress of surgery [15]. In this study, unsurprisingly most of the patients came when they were more than 4 years of age. In developing countries, the age of admission to hospital tend to be higher compared to developed countries due to ignorance, illiteracy, and financial issues. Therefore, the patients are operated whenever they are brought to the hospital, usually after the age of 4 years [16]. The direct implication of this situation can be seen in the binomial analysis, shown in Table 3, which shows that age is a significant ($p = 0.015$) factor for the development of urethrocutaneous fistula. As age increases, so does the risk of developing the post-operative complication (OR = 1.398). This finding is consistent with a study performed by Turan et al. which concluded that age of patient is a risk factor for urethrocutaneous fistula in hypospadias repair [17]. The development of fistula is influenced by hematoma, ischemia or necrosis of flap or graft, urinary extravasation, wound infection, technical error, and inadequate management after the surgery. By creating a urinary diversion using catheter to drain the bladder, percutaneous cystostomy could theoretically decrease the risk of urinary drainage to the neourethra, tissue reaction, stitch mobility, and risk of infection; hence, it would also decrease the risk of urethrocutaneous fistula [18]. Laura et al. claimed that performing cystostomy during the surgery reduces the risk of urethrocutaneous fistula [19]. This can be seen in this study, in which performing percutaneous cystostomy decreases the risk significantly (OR = 2.963, $p = 0.014$). In Indonesia, the decision to perform cystostomy is not yet determined as a standard part of the procedure. Currently, the choice is based on each surgeon's preference instead. The findings in this study could hopefully encourage pediatric surgeons to perform cystostomy during every hypospadias repair. Splint size is also a significant risk in developing the complication on all cases (OR = 1.243, $p = 0.023$). In theory, it is possible that a larger splint size, indicating a larger urethra, would increase the risk of post-repair hematoma and wound infection. However, an analysis of splint size as a possible risk has never been done previously in any studies, thus further studies on the correlation of splint size and the complication should be performed in the future. The correlation of neourethral length and urethrocutaneous fistula has never been studied; however, few studies have attempted to focus on the urethral defect length [20]. The possibility of the risk is high considering the low blood supply to anastomotic area with the original urethra and flap [21]. Nevertheless, the length of neourethra is not significant to the development of the complication in the analysis (OR = 1.411, $p = 0.128$). The findings of Huang et al., which analyzed the correlation of urethral length defect and the risk for complication, also resulted in an insignificant correlation [20]. More than a few procedures were designed for hypospadias repair and there is no single procedure which is suitable for all patients [11]. Chung et al. claimed that there is no correlation between urethroplasty technique and the complication [4]. With the advancement of surgical techniques and knowledge regarding proper technique to be used for each hypospadias cases, it is unsurprising that the urethroplasty technique used is not significantly correlated to the risk of developing

Table 1 Hypospadias cases distribution across multiple centers in Indonesia.

Hospital (City)	N (%)	%
Sanglah (Denpasar)	83	14
Cipto Mangunkusumo (Jakarta)	59	10
Hasan Sadikin (Bandung)	44	7.5
Saiful Anwar (Malang)	30	5.1
Sardjito (Yogyakarta)	28	4.7
Wahidin Sudirohusodo (Makassar)	27	4.6
Harapan Kita (Jakarta)	48	8.1
Fatmawati (Jakarta)	119	20.1
M. Djamil (Padang)	41	6.9
Dr. Soetomo (Surabaya)	56	9.5
Adam Malik (Medan)	25	4.2
Persahabatan (Jakarta)	31	5.3

Table 2 Risk Factors and Urethrocutaneous Fistula Occurrence Among Patients. All collected cases (n = 591); analysis performed on eligible patients: age (n = 588), neourethra length (n = 333), cystostomy (n = 349), splint size (n = 390), and urethrocutaneous fistula occurrence (n = 524).

Characteristics	N	%	Urethrocutaneous Fistula	
			Yes	No
Age				
0–1 years old	15	2.5	0	15
1–2 years old	39	6.6	4	33
2–3 years old	61	10.4	4	55
3–4 years old	118	20.1	19	90
>4 years old	355	60.4	53	248
Total	588	100	80	441
Hypospadias Type				
Distal				
Glandular	24	7.92	0	17
Sub-coronal	68	22.44	9	59
Penile	211	69.63	33	140
Total	303	100	42	216
Proximal				
Peno-scrotal;	171	64.77	22	136
Scrotal	76	28.78	13	57
Perineal	17	6.43	1	16
Total	264	100	36	209
Excluded from Analysis				
Chordee only	3	0.125	0	3
Failed Urethroplasty	21	0.875	2	16
Total	24	100	2	19
Urethroplasty Technique				
Chordectomy and Orthoplasty	17	2.88	0	12
MAGPI	25	4.23	1	23
Mathieu	16	2.71	4	10
Thiersch-Duplay TIP	261	44.16	41	183
Onlay Island Preputial Flap	88	14.89	11	72
Duckett	46	7.78	6	38
Dorsal Inlay Preputial Flap or Graft	35	5.92	6	28
Koyanagi	10	1.69	–	–
Two-Stage Technique	83	14.04	9	72
Fistulae Repair	10	1.69	2	6
Total	591	100	80	444
Neourethra length during Repair (cm)				
<1	28	8.41	1	27
1–2	79	23.72	9	70
2–3	107	32.13	21	86
3–4	83	24.92	8	75
>4	36	10.81	6	30
Total	333	100	45	288
Percutaneous Cystostomy During Repair				
Yes	136	38.97	20	116
No	213	61.03	29	184
Total	349	100	49	300
Urethral Splint Size (Fr)				
6	127	32.56	11	115
8	181	46.41	27	154
10	45	11.54	9	36
12	27	6.92	6	21
14	9	2.31	4	5
16	1	0.26	0	1
Total	390	100	57	332

Table 2 (continued)

Characteristics	N	%	Urethrocutaneous Fistula	
			Yes	No
Urethrocutaneous Fistulae				
Yes	80	15.27		
No	444	84.73		
Total	524	100		

Table 3 Binomial Logistic Regression Analysis of Urethrocutaneous Fistula occurrence.

Independent Variables	Odds Ratio (OR)	p-Value	CI 95%
Age	1.398	0.015	(1.067–1.832)
Not performing Percutaneous Cystostomy during the Procedure	2.963	0.014	(1.250–7.024)
Neourethra Length	1.411	0.128	(0.906–2.199)
Splint Size	1.243	0.023	(1.031–1.499)
Urethroplasty Technique	0.879	0.226	(0.714–1.083)
Hypospadias Type	2.124	0.102	(0.861–5.242)

the complication (OR = 0.879, $p = 0.226$). On the contrary, the types of hypospadias in this study are not significantly correlated to the development of fistula (OR = 2.124, $p = 0.102$) as opposed to Chung et al.'s study which shows that Distal hypospadias have better outcome and lower risk of fistula compared to proximal cases. We believe that as long as the proper technique out of the many possible techniques for the procedure was used to manage a certain type of hypospadias in a patient, the risk of developing a complication would be lowered. Further investigations regarding the matter are still needed as this nationwide study is limited due to the retrospective evaluation of risk factors and complication occurrence as opposed to a prospective cohort study. Another limitation is the limited follow-up of the patients; thus, the actual rate of complications out of the 591 patients is incomplete. This has been a problem that occurred multiple times in nationwide multicenter studies performed in a developing country. We hope that in the near future a massive nationwide project similar to this study could be carried out again to assess other questions surrounding the disease.

Conclusion

Age and splint size are significant risk factors for urethrocutaneous fistula after hypospadias repair in Indonesia. On the contrary, performing cystostomy during the repair decreases the risk for urethrocutaneous fistula occurrence.

Ethical approval

Ethical Approval to conduct this study was issued by the ethical committee of Sanglah General Hospital (179/UN.14.2/KEP/2016). The samples were taken from all hypospadias patients admitted to the centers in 2018.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

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