

SYSTEMATIC REVIEW

Perioperative Techniques and Long-term Outcomes in Hypospadias: A Systematic Review

Hery Poerwosusanta¹, Adam Rahardiyana Poerwosusanta¹, Elvira Esmeralda Poerwosusanta², Donny Aditia¹

¹ Department of Surgery, Faculty of Medicine, Universitas Lambung Mangkurat, Banjarmasin, South Kalimantan, Indonesia

² Emergency Department, Siaga Surgical Hospital, Banjarmasin, South Kalimantan, Indonesia

ABSTRACT

Introduction: Hypospadias is a condition when the urethra distal opens on the bottom of the penis and has a ventral penile curvature. Hypospadias is the second most frequent genital birth abnormality in boys after cryptorchidism. Surgery is the standard treatment of choice and has a significant risk problem. There are many surgical procedure complications, especially in appearance and function. This article discusses the appropriate operative management and the best long-term outcome. **Methods:** The data was culled and selected from the ten years of full-text English publication (2012-2022) utilizing the PubMed and Google Scholar databases. Meta-analyses (PRISMA) paradigm and PICO investigation of management techniques and long-term outcomes in clinical and randomized clinical trials. **Result:** From 149 search articles, 7 met the inclusion criteria. The gland penis size and the meatal location did not affect the outcome of the surgical technique. However, 58/432 patients required reoperation, and 61 (13%) had urethroplasty complications (UC), although not statistically significant (OR 0.8, 95% CI: 0.7-0.9). Testosterone is advised for small penises, narrow glands, thin urethral plates, and proximal hypospadias (67 vs. 87%). Preoperative antibiotics reduce the incidence of infection (17/150 repairs), tubularized incised plate (TIP), and the stent is recommended. **Conclusion:** The recommended strategies are good perioperative treatment, including antibiotics, testosterone treatment, surgery ages (6-18 months), tubularized incised plate (TIP) technique, and stent postoperative. *Malaysian Journal of Medicine and Health Sciences* (2023) 19(5):269-274. doi:10.47836/mjmhs19.5.35

Keywords: Congenital abnormality, Hypospadias, Surgical correction, Perioperative

Corresponding Author:

Hery Poerwosusanta, PhD

Email: herpoerwo@ulm.ac.id

Tel: +6282252658262

INTRODUCTION

Hypospadias occurs when the urethra and tip of the penis are not in the correct position at conception time. The urethra links the bladder and direction to the penis for urine exit (1,2). There is a lack of criteria to define and assess hypospadias. The meatal position is a criterion to determine the hypospadias degree but does not consider the amount of tissue dysplasia. The success criteria include penile size, length of the glans and urethral plate, the corpus spongiosum division degree, the curvature chord, abnormalities, and the abnormality of corpus spongiosum and scrotum location. The final classification is performed after the chord release (3).

In Europe, the incidence of hypospadias is roughly 18.6 times more likely to occur per 10,000 newborns. The hypospadias identified between 2001 and 2010 in all 23 EUROCAT registries remained steady according to the observed temporal patterns. The prevalence is lowest

in Asia, with 0.6–69 cases per every 10,000 births, while it is most remarkable in North America, with 34.2 patients per every 10,000 births (range: 6–129.8) (4-6). More than 90,000,000 newborns have been screened, but it is still impossible to assess the actual prevalence and trends due to many methodological variables. Hypospadias may significantly strain the resources of medical treatment. Due to increasing complications, many surgical procedures are being studied, especially in severe cases, with problems in appearance and function (4-7). This article discusses the hypospadias approach and its long-term outcome.

METHODOLOGY

Source

Consonance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) paradigm and eligibility, this systematic review was compiled.

Research question

The study aims to assess the management techniques and long-term outcomes in hypospadias using PICO investigation, including the main review aspects:

pediatric hypospadias (Population), perioperative management (Intervention), antibiotic medication, testosterone treatment, operation technic, age of surgery and stent postoperative (Comparison) and long-term outcome (Outcomes), to determine the research question: what are the best perioperative for longterm outcomes in pediatric hypospadias.

Eligibility Criteria

The systematic review data were from full-text English publications without clinical and randomized clinical trial comparisons.

Information Sources

The data utilized the PubMed and Google Scholar databases published in the preceding ten years (2012-2022). For a comprehensive review, the article references were also learned.

Search Strategy

This study initially input keywords into each database for this study, including the phrases “management”, “children with hypospadias”, and “long-term outcome”, which were used in the search. The keywords are “management”, “administration”, “child”, “hypospadias”, “long term” and “outcome”.

Selection Process

A total of 145 articles were obtained. From 2012-2022, there were 19 articles, Pubmed (4) and Google scholar (15). After screening, 10 articles were found that matched, 1 article was not found in full-text, 1 article review, and 1 case report. We get 7 articles that meet the requirements. The selection summary is shown in figure 1 and will be discussed during the discussion (Table I).

Quality appraisal

The quality of the systematic review was assessed using the PRISMA 2020 Checklist articles.

RESULTS

Bush et al. (8) reported that 432 major repairs (380distal(d)/19midshaft(mid)/33proximal(prox)) and 58 reoperations (28d/7mid/23prox) were performed on 490 boys (mean age: 1.5 years) who participated in the research. There was no correlation between age between 3 months and 10 years and glans size (R = 0.01, p = 0.18). 17 % had glans 14 mm. Urethroplasty Complication (UC) occurred in 61 (13 %) of the original TIP, 2-stage, and re-operative repairs. The study included 20/81 (25%) patients with short glans of 14 mm, in comparison to 41/409 (10%) patients with broader glans (p = 0.0003). Independent UC risk variables were a mid/proximal meatus (OR 3.1, 95% CI: 1.6-6.2), a small glans size (OR 3.5, 95% [CI]: 1.8-6.8), and reoperations (OR 3.0, 95% CI: 1.4-6.5). The surgery method, age, and UC risk were unrelated to gland penis size. Each additional mm of glans size was associated with a

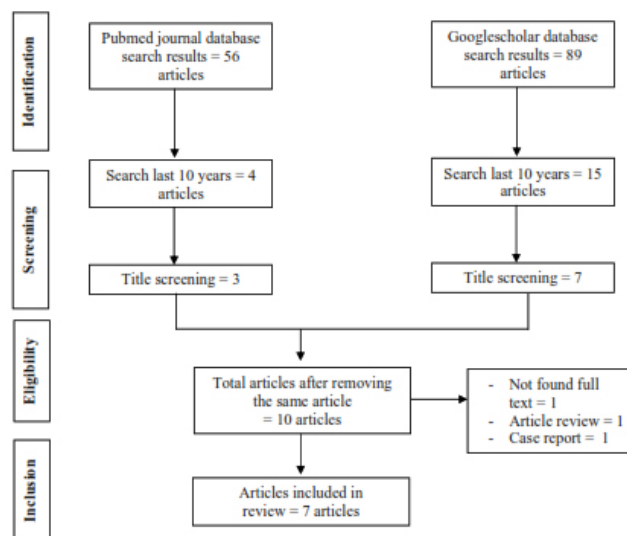


Figure 1: Article search flowchart

decreased incidence of UC (OR 0.8, 95% CI: 0.7-0.9).

The postoperative complications in both comparable groups were conical in shape (9/21 %), shallow (9/21 %), and grooved (24/57 %). Urethral Plate (UP) width comprised 26.62 % and 16.38 %, respectively. The UP lengths of 29 people ranged between 10 mm (12/41 %) and 15 mm (17/59 %). One prominent blood vessel (17 out of 41 %), two predominant (8 out of 19 %), an H-like form with two well-developed (6 out of 14 %), and a net-like structure with no predominant (11.2 out of 26 %). Penile size in 28 post-TIP patients below the 50th percentile (25/89%) (9).

Malik et al. carried out to 27 participants answered (53% response rate). Most North American respondents and the children had experience levels of less than 30 years. Compared to just 67 % of low-volume surgeons who take preoperative androgen, high-volume surgeons make up 87 % of those who take it. Testosterone was advised as a treatment option in cases of a small penis, a narrow glans, a thin urethral plate, and proximal hypospadias. The influence of testosterone was evaluated according to the penile appearance (59 %) (10).

The surgery complications include fistula, meatal stenosis, glans dehiscence, and urethral stenosis in varying group ages presented in treatment. A statistically significant increase in a fistula was the most result in patients aged 10 to 14 compared to younger groups (11). Due to a lack of follow-up, seven individuals were excluded from a research study after surgery. Antibiotics were administered to 62 of the 150 patients preoperative and reduced infection after repair in age, type of hypospadias, method of correction, and curvature were all comparable (12). The stented procedures significantly increase the use of preoperative antibiotics compared to non-use (82 vs. 52 %). There were two reports of wound infections (1 in the preoperative antibiotic and

Table 1: The literature included in this study

Author	Origin	Method	Sample Size	Period	Result
Bush, 2015 (8)	USA	Prospective study	490 boys	2009-2013	This research of prospective data collected from a standardized care regimen in 490 consecutive boys following hypospadias surgery includes the size of the glans as an independent risk factor for UC. The unknown is the most effective technique to alter this element. Our findings suggest that anyone researching hypospadias UC risk should assess glans width.
Silva, 2014 (9)	Brazil	Prospective study	42 boys	Not described	Glans shape, UP width, UP length, foreskin microcirculation, and phallic size do not affect distal TIP repair problems. Distal hypospadias is usually accompanied by mild hypogonadism.
Malik, 2014 (10)	USA	Cross-sectional	27 respondent	Not described	Although there are various practice patterns, most pediatric urologists use testosterone before hypospadias treatment. Patients with proximal hypospadias, a small penis, a decreased glans circumference, or a smaller urethral plate appear to be the only ones who can get testosterone treatment.
Yildiz, 2013 (11)	Turkey	Cross-sectional	307 childrens	2005-2011	Problems from hypospadias surgery become more likely as the patient gets older and different surgical techniques are used. However, correcting distal and mid-penile hypospadias in prepubertal patients using TIP is a risk-free procedure that may be performed at any age.
Baillargeon, 2014 (12)	USA	Retrospective study	157 case	March 2009-September 2012	Antibiotics are not recommended before having hypospadias surgery.
Zeiai, 2016 (13)	Sweden	Cross-sectional	113 case	Before March 2010	No data supports antibiotic prophylaxis for postoperative complications; as a result, clinical practice might vary considerably. However, according to the findings of our experiment, lower antibiotic dosages did not increase infections but did lessen consequences. Therefore, antibiotic prophylaxis with two doses is what we prescribe.
Chalmers, 2015 (14)	USA	Cross-sectional	89 infant	Not described	Infants' potential for complications following distal hypospadias surgery is low if a urethral stent is not placed in the urethra. In addition, when a stent is avoided, the risk of adverse events and the amount of short-term follow-up are reduced.

1 in the non-preoperative antibiotic group). Neither of the groups developed a symptomatic or culture-proven urinary tract infection (UTI). Neither group had significant outcomes in the infection and reoperation (17/150 repairs). Study limitations were a small sample size and a retrospective methodology (12).

The study included 113 Tubularized incised plates (TIP) with used stents. 17 out of 58 patients given continuous antibiotic prophylaxis ended up with infections, compared to only 9 out of 55 patients given 2-dose prophylaxis. Both constant and 2-dose prophylaxis was associated with an infection rate of 5 %. In contrast, the lower dosage antibiotics group pointed to a lower complication of infection (13). 89 patients without stents and 21 with stents were found to have an infection in 3 days (14). 4/89 (4.49%) stent-less patients required circumcision revision at 3 months, 1 patient had a urinary tract infection, and 1/21 (4.76%) postoperative stent patients needed meatal stenosis reoperation (13).

DISCUSSION

Hypospadias is a condition when the urethra is at the bottom and ventral penile curvature of penile and the second most genital birth disorder in boys after cryptorchidism and affects 1 in 200 boys born alive.

Surgical correction is the treatment of choice (2,15).

Systemic or topical dihydrotestosterone (DHT) and human chorionic gonadotropin (hCG) increase penis gland enlargement before surgery. Androgen treatment makes TIP better and reduces glans dehiscence. Topical and systemic testosterone are no guidelines for androgens treatment. Concerning the rising impact of testosterone on wound healing and blood loss during operations, there are no studies that using androgens preoperative can minimize glans dehiscence. An exhaustive investigation of the preoperative therapy revealed variations in the medications used, the amounts administered, and the results of hypospadias (10). 78% of urologists utilized testosterone therapy and stopped 1-2 months before surgery to reduce the risk of adverse effects either before or after surgery. A tiny-looking penis, a decreased glans diameter, a reduced urethra plate width, and proximal hypospadias are the indications for preoperative testosterone treatment. Penile appearance is the primary method of determining the effect of testosterone (59 %) (10). Most doctors (56 %) evaluated the penile appearance after administering testosterone and stopped prescribing after the treatment was over. 67 % of surgeons used intramuscular testosterone and began the treatment between 1-3 months before surgery. Intramuscular testosterone continues monthly and

ceases it 2 weeks before surgery. Topical testosterone use started during various periods before surgery and used a standardized dosage, and 83% stopped their medication a week before the operation (10).

Hypospadias repair has various surgical options, but none are specific. One-stage reconstruction is the best (16,17). Surgical aims to achieve a straight penis, a slit-shaped meatus at the glans apex, a conical reconfigured glans, a biologically male visual appeal, opts for preputial reconstruction, a complete and easily retractable foreskin, and an acceptable cosmetic outcome objectively.

Distal hypospadias surgery is complex and not a quick process. The position of the meatus isn't the sole consideration in reconstruction. Treating distal hypospadias is challenging because of its small glans, poor urethral plate, proximal spongiosis, and ventral curvature (VC). The surgical correction should only be performed by an experienced one who performs 40–50 procedures annually (16,17).

A circumcised penile appearance can be achieved with penile degloving, VC correction (orthoplasty), urethroplasty, vascularized covering, glanuloplasty, and cosmetic skin covers. It is essential to use magnification, sensitive instruments and sutures, minimal and non-traumatic tissue manipulation, meticulous hemostasis, and experienced surgical assistance for the best outcome (12,14).

Most surgical procedures use stents, and antibiotic dressings are not standardized. Variables depend on surgeon choice. Postoperative analgesia, caudal or dorsal penile nerve blocks are typically used. Further research must prove that caudal blocks increase the risk of urethral fistulas (12-14,18).

Cosmetic and normal functions are the goals of correction. Hypospadias is treated for spraying urine, inability to stand pee, curvature correction for difficulties during intercourse, reproductive concerns due to sperm deposition difficulties, and diminished genital appearance. Current standards recommend repairing hypospadias between 6 and 18 months, depending on the severity and necessity. Anesthetic risk, age-dependent tissue diameters, and genital surgery psychological impacts are essential to note (17,19).

Alarming data on anesthetic-induced neurotoxicity in developing rat CNS have been published, and methodological difficulties make applying these findings to humans unclear (20). Small glans and thin urethral plates are surgical anatomy difficulties characteristic (8,9). Mild penile development disturbance occurs in the first few years, penile size is rarely a limiting issue for hypospadias correction, and delaying surgery seems counterproductive. To enhance anatomical

proportions, some surgeons recommend testosterone supplementation in the microphallus (17,21).

Teens who didn't remember the operation were happier with their bodies and reduced mental stress (22). Genital awareness begins around 18 months because forgotten surgery and hospitalization are less desirable (17). Some studies imply that first hypospadias correction may cause additional difficulties later. Postoperative variables, including urethral secretions and nocturnal erections may cause infections, hematoma, and wound dehiscence (23,24). However, some studies showed no correlation between age at first surgery and the problems (25).

The hazards of anesthesia, the psychological influence, and the postoperative issues have led to discussion over the possibility of postponing surgery until the child is old enough to make decisions. Need for more research because most studies were retrospective from a single surgeon or location. Since its inception in 2010, "The Dutch Hypospadias Database" has compiled information on all repairs performed in the Netherlands. The database being implemented across Europe may provide insight into various problems, including the optimal treatment that should be performed (22).

There is a controversy that the elderly have more problems than the young (11,26). Potential surgical and medical treatment complications did not impact the function. Most studies recommend a waiting period of 6 to 18 months for surgery, and The American Academy of Pediatrics recommends that this period reduce psychological stress and behavioral disorders in toddlers.

Limitation

This study did not discuss in detail the degree and variations in operating techniques of hypospadias. However, they also did not address a guideline for giving preoperative hormonal therapy, antibiotics, or the postoperative stent catheter.

Recommendation

Detailed study of appropriate surgery according to the type of hypospadias, therapeutic hormone administration preoperative, antibiotic guidelines, and postoperative stent catheter is required.

CONCLUSION

Surgical is the treatment of choice for patients with hypospadias who has a significant risk of experiencing problems following surgery. Therefore, the perioperative management, including antibiotics, testosterone treatment, surgery ages (6-18 months), tubularized incised plate (TIP) technique, and stent postoperative, determined the best outcome.

REFERENCES

- van der Horst HJR, de Wall LL. Hypospadias, all there is to know. *Eur J Pediatr*. April 2017;176(4):435–41. doi:10.1007/s00431-017-2971-3
- McDougal WS; Wein AJ; Kavoussi LR; et al. *Campbell-Walsh Urology*. 4 ed. Philadelphia: Elsevier; 2016.
- Snodgrass W, Macedo A, Hoebeke P, Mouriquand PDE. Hypospadias dilemmas: a round table. *J Pediatr Urol*. April 2011;7(2):145–57. doi:10.1016/j.jpuro.2010.11.009
- Springer A, Van Den Heijkant M, Baumann S. Worldwide prevalence of hypospadias. *J Pediatr Urol*. 2016;12(3):152-e1. doi:10.1016/j.jpuro.2015.12.00
- Bouty A, Ayers KL, Pask A, Heloury Y, Sinclair AH. The Genetic and Environmental Factors Underlying Hypospadias. *Sex Dev Genet Mol Biol Evol Endocrinol Embryol Pathol sex Determ Differ*. 2015;9(5):239–59. doi:10.1159/000441988
- Bergman JEH, Loane M, Vrijheid M, Pierini A, Nijman RJM, Addor M-C, et al. Epidemiology of hypospadias in Europe: a registry-based study. *World J Urol*. Desember 2015;33(12):2159–67. doi:10.1007/s00345-015-1507-6
- Aulagne MB, Harper L, de Napoli-Cocci S, Bondonny JM, Dobremez E. Long-term outcome of severe hypospadias. *J Pediatr Urol*. Oktober 2010;6(5):469–72. doi: 10.1016/j.jpuro.2009.12.005
- Bush NC, Villanueva C, Snodgrass W. Glans size is an independent risk factor for urethroplasty complications after hypospadias repair. *J Pediatr Urol*. Desember 2015;11(6):355.e1-5. doi:10.1016/j.jpuro.2015.05.029
- da Silva EA, Lobountchenko T, Marun MN, Rondon A, Damiro R. Role of penile biometric characteristics on the surgical outcome of hypospadias repair. *Pediatr Surg Int*. Maret 2014;30(3):339–44. doi: 10.1007/s00383-013-3442-1
- Malik RD, Liu DB. Survey of pediatric urologists on the preoperative use of testosterone in the surgical correction of hypospadias. *J Pediatr Urol*. Oktober 2014;10(5):840–3. doi:10.1016/j.jpuro.2014.02.008
- Yildiz T, Tahtali IN, Ates DC, Keles I, Ilce Z. Age of patient is a risk factor for urethrocutaneous fistula in hypospadias surgery. *J Pediatr Urol*. Desember 2013;9(6 Pt A):900–3. doi:10.1016/j.jpuro.2012.12.007
- Baillargeon E, Duan K, Brzezinski A, Jednak R, El-Sherbiny M. The role of preoperative prophylactic antibiotics in hypospadias repair. *Can Urol Assoc J = J l'Association des Urol du Canada*. Juli 2014;8(7–8):236–40. doi: 10.5489/cuaj.1838
- Zeiai S, Nordenskjuld A, Fossum M. Advantages of Reduced Prophylaxis after Tubularized Incised Plate Repair of Hypospadias. *J Urol*. Oktober 2016;196(4):1244–9. doi:10.1016/j.juro.2016.04.083
- Chalmers DJ, Siparsky GL, Wiedel CA, Wilcox DT. Distal hypospadias repair in infants without a postoperative stent. *Pediatr Surg Int*. Maret 2015;31(3):287–90. doi:10.1007/s00383-014-3647-y
- Keays MA, Dave S. Current hypospadias management: Diagnosis, surgical management, and long-term patient-centered outcomes. *Can Urol Assoc J = J l'Association des Urol du Canada*. 2017;11(1-2Suppl1): S48–53. doi: 10.5489/cuaj.4386
- Snodgrass W, Bush NC. Re-operative urethroplasty after failed hypospadias repair: how prior surgery impacts risk for additional complications. *J Pediatr Urol*. Juni 2017;13(3):289.e1-289.e6. doi:10.1016/j.jpuro.2016.11.012
- Manzoni G, Bracka A, Palminteri E, Marrocco G. Hypospadias surgery: when, what and by whom? *BJU Int*. November 2004;94(8):1188–95. doi:10.1111/j.1464-410X.2004.05128.x
- McLorie G, Joyner B, Herz D, McCallum J, Bagli D, Merguerian P, et al. A prospective randomized clinical trial to evaluate methods of postoperative care of hypospadias. *J Urol*. Mei 2001;165(5):1669–72. doi:10.1016/S0022-5347(05)65228-7
- Riedmiller H, Androulakakis P, Beurton D, Kocvara R, Gerharz E. EAU Guidelines on Paediatric Urology1. *European urology*. 2001 Nov 1;40(5):589-99. doi: 10.1159/000049841
- McCann ME, Soriano SG. General anesthetics in pediatric anesthesia: influences on the developing brain. *Curr Drug Targets*. Juni 2012;13(7):944–51. doi: 10.2174/138945012800675768
- Wright I, Cole E, Farrokhhyar F, Pemberton J, Lorenzo AJ, Braga LH. Effect of preoperative hormonal stimulation on postoperative complication rates after proximal hypospadias repair: a systematic review. *J Urol*. Agustus 2013;190(2):652–9. doi: 10.1016/j.juro.2013.02.3234
- Carmack A, Notini L, Earp BD. Should Surgery for Hypospadias Be Performed Before An Age of Consent? *J Sex Res*. Oktober 2016;53(8):1047–58. doi: 10.1080/00224499.2015.1066745
- Dodson JL, Baird AD, Baker LA, Docimo SG, Mathews RI. Outcomes of delayed hypospadias repair: implications for decision making. *J Urol*. Juli 2007;178(1):278–81. doi: 10.1016/j.juro.2007.03.055
- Marrocco G, Vallasciani S, Fiocca G, Calisti A. Hypospadias surgery: a 10-year review. *Pediatr Surg Int*. Maret 2004;20(3):200–3. doi: 10.1007/s00383-004-1147-1
- Bush NC, Holzer M, Zhang S, Snodgrass W. Age does not impact risk for urethroplasty complications after tubularized incised plate repair of hypospadias in prepubertal boys. *J*

- Pediatr Urol. Juni 2013;9(3):252–6. doi: 10.1016/j.jpuro.2012.03.014
26. Lu W, Tao Y, Wisniewski AB, Frimberger D, Kropp BP. Different outcomes of hypospadias surgery between north america, europe and china: is patient age a factor? Nephrourol Mon. 2012;4(4):609–12. doi: 10.5812/numonthly.1853