Hypospadias

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1. Introduction

Hypospadias is a congenital defect of the penis, with an arrest in penile and urethral development. It is the most common congenital malformation of the penis and presents on a spectrum of severity. Epidemiological studies suggest a rise in the incidence of hypospadias, though the etiology of hypospadias is not fully elucidated. The surgical management of hypospadias is a common source of discussion amongst pediatric urologists and a wide array of surgical approaches have been developed to correct hypospadias.

2. Definition

Hypospadias is a congenital defect characterized by an insufficient development of the ventral face of the penis. It is usually defined by 3 clinical findings: 1- an ectopic urethral meatus proximal to the mid glans on the ventral aspect of the penis. 2 - In the majority of cases, there is an absence of foreskin on the ventral aspect of the glans, also referred to as a dorsally hooded foreskin. 3 - **Chordee**, ventral curvature of the penis, generally occurs with hypospadias and its severity generally correlates with the degree of the urethral defect.

3. Risk Factors and Pathophysiology

3.1 Normal development of the penis and urethra

The penis (and clitoris) derives from the genital tubercle, which is ventrally curved. The male urethra forms by fusion of the genital folds under the influence of androgens, between 8 to 14 weeks gestation. **Testosterone** is synthesized by the fetal testes (**Leydig cells**). In adults, pituitary gonadotropins stimulate testosterone synthesis. In contrast, **fetal testosterone secretion is under the influence of placental hCG during 8-14 weeks of gestation**. Testosterone is converted to the more potent androgen, **dihydrotestosterone** (**DHT**), by the enzyme, **5-alpha-reductase**, in the fetal external genitalia.[1] The pendulous male urethra is a derivative of the urogenital sinus (UGS) and has pseudostratified and stratified columnar epithelium in the penile portion and a non-keratinizing, stratified squamous epithelium lining the glanular portion. Its formation results from the tubularization of the urethral plate from proximal to distal according to a double zipper manner.[2] Regarding the distal urethra, there are two proposed mechanisms of glans urethral development: ectodermal ingrowth cannulating the glans[3] versus UGS tubularization to the tip of the glans.[4] Similar to the urethra, the prepuce forms laterally and fuses ventrally as the urethra forms. Hypospadias is in most cases due to **arrested development** with failure of ventral urethral and preputial fusion and a degree of corporal ventral curvature.

3.2 Risk factors for hypospadias

The normal development of the male urethra requires appropriate maternal and fetal hormone levels during a critical window of morphogenesis. Multiple factors may influence this delicate interaction of hormones, receptors and tissues. **Placental health** is a major risk factor for hypospadias. **Human chorionic gonadotropin is released by the placental syncytiotrophoblast, and hCG peaks in the first trimester of pregnancy stimulating fetal testosterone production from fetal Leydig cells leading to normal male genital development.** [5] **Peycelon et al noted that proximal hypospadias was associated with a significantly higher level of hCG than distal hypospadias**[6] Intra Uterine Growth Restriction is more frequent in hypospadias patients than normal boys, especially in posterior forms.[7] In twins, the boy with hypospadias is usually the one with the lower birth weight.[8] Gestational length is reduced in boys with hypospadias compared to controls. Low placental weight and placental infarctions are also more frequent in boys with hypospadias. **Other potential risk factors include** maternal nutrition (vegetarian diet and phytoestrogens), maternal body index (and subsequent hyper-oestrogenia), parity, age, twinning, paternal fertility and assisted reproductive techniques (ART). **A recent systematic review found no significant difference in the risk of urogenital tract malformation, including hypospadias and cryptorchidism, between in vitro fertilization and intracytoplasmic sperm injection technologies.** [9] It is possible some medications and seasons may influence the hormonal milieu and/or the process of urethral masculinization.

3.3 Pathophysiology of hypospadias

Hypospadias is a multifactorial defect that is at the crossroad of genetic, hormonal and environmental factors.

Genetic mutations are identified in less than 30% of cases while the vast majority of cases remain unexplained.13 Genes of the genital tubercle development such as HOX genes, bone morphogenetic proteins (BMP genes), sonic hedgehog (SHH), fibroblast growth factors (FGF genes) may be altered but mutations remain rarely identified in human. Molecular defects responsible for hypovirilization are more frequent. They may be due to 1. testicular dysgenesis, 2. androgen biosynthesis defects or 3. androgen resistance. Testicular dysgenesis may induce hypospadias due to an insufficient secretion of testosterone during the window of masculinization. This includes patients with heterozygous mutations of Wilms Tumor 1 (WT1) who may exhibit severe hypospadias associated with other genital abnormalities[10] Mutations of genes encoding for transcription factors implicated in the testicular determination such as SOX9, DMRT1 and GATA4 are also associated with 46,XY DSD, including severe hypospadias. Androgen biosynthesis defects may include LH receptor defects and subsequent Leydig cell hypoplasia and severe hypospadias. Mutations of the 5-alpha reductase gene are associated with decreased synthesis of DHT and induce similar phenotypes. MAMLD1 may also be implicated in testosterone synthesis and MAMLD1 mutations are reported in patients with posterior and anteior hypospadias. Last the Androgen Receptor gene (AR) on the X chromosome mediates the biological effects of gonadal androgens. AR is expressed during the development of the penis and urethra. Several mutations of AR have been reported in hypospadiac patients, mostly with posterior forms, micropenis and normal or elevated plasma testosterone. Several other gene and single nucleotide polymorphims have been linked to hypospadias by genome-wide association study (GWAS) (DGKK, MID1) but their clinical implications remains to be determined since they explain only 9% of the liability of developing hypospadias.[11]

Hypospadias is also associated with multiple syndromes including WAGR (Wilms tumor, aniridia, genitourinary malformations and mental retardation), Denys Drash (genitourinary malformations, renal failure and Wilms tumor), Smith-Lemli-Opitz (ocular hypertelorism, asymmetry of the skull, and laryngoesophageal defects), Robinow, and other Differences in Sex Development[12]

Fetal exposure to xenoestrogens and antiandrogens could augment a child's inherent predisposition to hypospadias and that could explain the increasing incidence of the disorder[13] This exposition induces the testicular dysgenesis syndrome that connects the rising incidence of hypospadias, micropenis, fertility trouble and testis cancer in

some parts of the world. These substances are called endocrine disrupting chemicals which are known to antagonize the effects of androgens and to simulate the effects of estrogens by both genomic and non-genomic mechanisms. They are reported in many environmental pollutions. Some parental professions for instance may be at risk for hypospadias in children, especially those exposed to endocrine disrupting chemicals[14] Some studies provide conflicting results and further confirmation is needed.

4. Epidemiology

Hypospadias has historically had an incidence of **1/125-1000 live male births**. Numerous studies have revealed the increasing prevalence of hypospadias in a wide range of countries. This trend was first detected in the late 60s then later in Hungary and the United Kingdom[15] followed by Oceania, North America[16] and the Scandinavian countries[17] Recent data from the United States has shown an apparent doubling of the rate of hypospadias to **1/125-250 male births**. The incidence of hypospadias in non-whites is also increasing.[16]

These data have nevertheless been questioned.[18] For instance, in Europe, Dolk et al identified no significant variation of the rate from 1980 to 1999 in the population followed by the European Surveillance of Congenital Anomalies.[19] In the United States, the New York State Congenital Malformations Registry showed that the prevalence of hypospadias tended to decrease over a 20-year period, according to the study of Fisch et al;[20] and the California Birth Defects Monitoring Program found similar results from 1984 to 1997.[21] **Much of this data is complicated by reporting criteria**. These discrepancies may be due to a greater awareness of hypospadias among pediatricians today and the more frequent request for surgical correction from families, even in mild forms. As minor hypospadias makes up 75% of the cases, the definition of phenotypes in the studies is also a major point and may explain the contradictory results. Last, the differences between countries are important (eg, 1% in Denmark vs 0.3% in Finland), as are there may be ethnic/population differences.

However, international birth defect surveillance programs participating in the International Clearinghouse for Birth Defects Surveillance and Research do demonstrates that the prevalence of hypospadias is increasing internationally.[22] The familial aggregation of hypospadias is well recognized with about 10% of patients having an affected relative.[23] Male siblings of affected patients have a 10% risk of developing hypospadias.[24] It is equally passed through maternal and paternal sides, with heritability estimated to be 57-77%.[25] When compared to singletons, the prevalence of hypospadias is higher among members of male-male twin pairs and lower in male-female pairs. Severe hypospadias is more often seen in sporadic cases, whereas milder variants are more often familial (odds ratio [OR] = 10.4). [26] Familial history of genital defect is probably underevaluated.[27]

5. Diagnosis and Evaluation

History may search for familial hypospadias and undescended testis, risk factors for hypospadias (see above), ventral deflection of urinary stream and straightness of erection. Hypospadias is rarely associated with extra-urogenital anomalies, chromosomal defects and congenital malformation syndromes, as well as differences of sex development (DSD). Most boys with hypospadias have no other health problems and are considered to have "isolated" hypospadias **although Ludorf et al recently noted that 12.7% of cases with hypospadias and without known syndromes had at least one additional birth defect**.[28] The physical examination will demonstrate absence of the ventral foreskin and a proximal meatus. The real degree of severity of hypospadias is determined by the level of the division of the corpus spongiosum. The position of the meatus and the presence of a urethra with thin, translucent overlying skin may be misleading. Other attributes that should be noted include ventral penile curvature, bifid scrotum and penoscrotal transposition. The clinical exam should also include the evaluation of the length of the penis and the position of the testis. The ano-genital distance may be reduced. A variant of hypospadias, **megameatus with intact prepuce**, demonstrates a large, fish-mouth meatus sometimes extending below the corona. It is usually found after or during neonatal circumcision or in an older child when the foreskin retracts. **There is no gold standard tool that standardizes the way hypospadias is classified although a recent study by Fernandez et al demonstrated a promising machine learning model to increase the objectivity of hypospadias recognition and classification.**[29]

Bladder and kidney imaging are not necessary unless the child has a relevant malformation syndrome.[30] Undescended testes are associated with hypospadias. The incidence increases with severity of hypospadias.[31-32] The association may be due to similar risk factors of prematurity and low birth weight. **Difference of sex development (DSD)** should be considered when hypospadias is associated with undescended testis (especially if bilateral or non-palpable) or with micropenis, or if severe. In such cases a karyotype and a hormonal work-up should be considered. **In a recent cohort study of 60 boys with proximal hypospadias who underwent endocrine/genetic evaluation, 28% had genetic abnormalities and 15% had differences/disorders of sexual differentiation.**[33] **Of note, 3 of 9 patients with a DSD condition had bilaterally descended testes and all 9 patients had a bifid scrotum and/or penoscrotal transposition.**[33]

6. Treatment

The goal of hypospadias repair is to create a straight penis with an orthotopically placed, slit-like meatus, allowing the patient to void in the standing position. A wide variety of surgical approaches have been described for the correction of hypospadias.[34-35-36] Management strategies depend on the **location of the meatus**, **quality of the urethral plate and spongiosum**, **size of the glans**, **degree of ventral curvature**, and **quantity and quality of skin**. While distal hypospadias may not impact voiding, sexual function or fertility, many parents will elect to correct hypospadias to improve the cosmetic appearance. More severe hypospadias and chordee can compromise a child's ability to void standing up, deliver sperm and have sexual intercourse.

6.1 Timing of Surgery

Consideration of surgical timing in children is due to psychosocial aspects related to separation anxiety from parents, intervention prior to walking and potty training, quality of healing as well as decreased recollection of the surgery. If a two-stage surgery is required, the first intervention should be performed at an age that is young enough to allow the second stage procedure, typically delayed by 6-9 months, to be completed prior to an age relevant to the same concerns listed above.

Many authors reference the 1996 Action Committee for the American Academy of Pediatrics - Section of Urology, which recommended surgery between 6-12 months based on anesthetic risks, psychosocial factors and technical aspects of the repair.[37] While Korvald et al. observed a lower complication rate in surgeries performed at 1 year old versus 5 years old.[38] Lee and Kurzrock et al evaluated outcomes of 5,236 boys after repair. Each additional year of patient age at distal repair was associated with a 15% increased risk of requiring secondary cystoscopy and a 21% increased risk of requiring urethral dilation/incision.[39] Manzoni et al. recommend avoiding surgery between 18 months and three years old as this is the onset of genital awareness and represents a phase of difficult and uncooperative behavior in the child's development.[40] While some raise the question of later surgery to include the patient in the decision process, Garnier et al. have observed an increased complication rate with increasing age, noting age above 2 years old as a significant predictor of complications, when they extended the analysis beyond complications requiring intervention to include healing problems, infections, lower urinary tract symptoms and dysfunctional voiding.[41]

6.2 Parental perspective

Recent studies in the hypospadias literature have focused on the parents' perspective regarding hypospadias decision-making. Chan et al described a four-stage process including processing the diagnosis, synthesizing information, processing emotions and concerns and finalizing the decision [42] about surgery. Anxiety and confusion are present throughout their experience and parents re-visit these stages in cyclic fashion as they synthesize information from a variety of sources and develop trust in their child's urologist.[42] A recent systematic review by Vavilov et al noted a mean overall prevalence of decisional regret 62.5% of parents who chose hypospadias surgery for their sons with moderate to severe regret in 20.3%.[43] Several authors have found an association between preoperative decisional conflict and postoperative decisional regret.[44-45] In a recent survey of parents of hypospadias patients, 20% reported that the "surgeon did not spend enough time" with them to answer questions and address their concerns.[46] Parents wanted more information regarding etiology, treatment options, and expected results from surgery, including no surgery options. Chan et al recently developed a

parent-centered, web-based decision support tool to address these issues by delivering high-quality, timely information and clarifying values[43-47-48-49] and preferences related to hypospadias. Evidence-based tools that support shared decision-making can improve informed decisions thereby reducing decisional conflict and improving patient knowledge, satisfaction, and engagement with care.[50-51]

6.3 Glans Size

A small glans width has been proposed to be an independent risk factor for complications after hypospadias repair. Bush et al. have measured glans size in their series of hypospadias repair and report an increased complication rate in glans width <14 mm.[52] However, other authors, Faase et al., have also prospectively recorded glans size and did not observe an increased complication rate associated with glans size.[53]

6.4 Pre-Operative Hormonal Stimulation

The exact place of hormonal stimulation remains unclear. Since a glans that is small may increase tension on the glans closure, increasing risks of glans dehiscence and/or fistula formation, some authors proposed a frequent use of stimulation. Koff and Jayanthi reported that the use of preoperative human chorionic gonadotropin (hCG) led to simpler repairs due to increased penile size and length, decreased hypospadias severity in regards to meatal position and associated curvature, as well as increased vascularity and thickness of proximal corpus spongiosum.[54] However, the use of pre-operative hormone therapy remains controversial and the use of hormones have been alternatively reported to increase the complication rate[55] orto lower it in a prospective randomized trial for patients with distal hypospadias.[54]

The use of hormones for severe hypospadias and/or micropenis is more widely accepted **and pre-operative hormone use is more commonplace in proximal repairs**. Although, hCG, testosterone or dihydrotestosterone can be used, variability exists in formulations, route of therapy (parenteral vs. transdermal), timing of therapy, and duration of therapy (**Table 1**).[30-56] **Penile growth is enhanced irrespective of administration route**. A period of time between the end of stimulation and surgery may reduce the risk of post-operative complication.

Table 1: Preoperative hormone stimulation and its effect on penile size

Study	n	Hormone	Route of Administration	Dosage	Protocol	Mean Increase in penis length (mm)	% increase	Mean Increase in glanular circumference (mm)	% increase
Sakakibara et al. (1991)[57]	15	Testosterone	Topical cream	NR	Daily for 3 weeks	NR	NR	NR	NR
Koff and Jayanthi (1999)[58]	12	Human chorionic gonadotropin	Parenteral	250 IU (<1 year) 500 IU (1-5 years)	Twice weekly for 5 weeks starting 6–8 weeks before surgery	133	77	NR	NR
Luo et al. (2003)[59]	25	Testosterone enanthate	Parenteral	25 mg	Monthly for 3 months before surgery	40	20	104	38
Ishii et al. (2010)[60]	17	Testosterone enanthate	Parenteral	25 mg	Monthly up to 3 times	101	NR	NR	NR
Chalapathi et al. (2003)[61]	13	Testosterone enanthate oil	Topical	NR	Twice a day for 3 weeks before surgery	118	59	NR	NR
Chalapathi et al. (2003)[61]	13	Testosterone enanthate	Parenteral	2 mg/kg	Weekly for 3 weeks before surgery	126	68	NR	NR
Nerli et al. (2009)[62]	10	Testosterone	Topical Cream	Manufactured sachets	Daily for 3 weeks	38	18	100	36
Nerli et al. (2009)[62]	11	Testosterone enanthate	Parenteral	2 mg/kg	Monthly for 3 months before surgery	38	18	102	37
Gorduza et al. (2010)[55]	21	Human chorionic gonadotropin	Parenteral	1,500 IU	6 doses every other	NR	NR	NR	NR
Gorduza et al. (2010)[55]	25	Testosterone enanthate	Parenteral	100 mg/m2	2-6 monthly injection	NR	NR	NR	NR

NR - not reported

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View Image.

6.5 Surgical Technique

Given the variability of glans size, location of meatus, penile size and degree of curvature, no one technique is appropriate for all repairs. In general, the surgery entails five steps: **orthoplasty** (penile straightening), **urethroplasty**, **meatoplasty with glanuloplasty**, **scrotoplasty** and **skin coverage.**[34]

Historically, repairs have been categorized into (i) **urethral plate tubularization**, (ii) **urethral plate augmentation** (perimeatal or dorsally-based skin flaps), and (iii) **urethral plate excision and replacement** with skin or buccal tube (one or two stage). Very few studies have systematically compared outcomes for the different repairs.[63-64-65] Surgical decision-making often will depend upon degree of ventral curvature and health of the urethral plate.[66]

6.6 Ventral Curvature

75% of patients with penile curvature can be corrected with degloving of the ventral skin to the penoscrotal junction. After degloving, curvature can be assessed with a proximal tourniquet and injection of saline or vasoactive drugs into the corporal body. If the erect penis can be straightened with gentle pressure with a finger or below 30 degrees, dorsal, midline permanent plication sutures will be sufficient to correct the curvature.[10] Small ventral releasing incisions (fairy cuts) may be sufficient or used to augment the dorsal plication. Aggressive use of dorsal plication sutures may lead to penile shortening or recurrent curvature.

For curvature greater than 30 degrees, some authors advocate mobilizing the urethral plate.[67,68] Alternatively, severe curvature may be corrected with division and proximal mobilization of the urethral plate. Severe curvature may represent a disproportion between the dorsal and ventral aspects of the corpora cavernosa. This can thus be corrected with a ventral lengthening procedure, transversely incising the ventral tunica albuginea at the point of the greatest curve. The defect is then patched using a dermal graft, a tunica vaginalis flap or commercially available single ply small intestine submucosa.

6.7 Urethroplasty

One goal of hypospadias repair is to advance the meatus to the orthotopic location on the glans. For **distal** (glanular or coronal) hypospadias, such correction may be achieved with **meatal advancement procedures** including the urethromeatoplasty, meatal advancement and glansplasty (MAGPI), Mathieu or flip-flap, Koff procedure or meatal inverted V glansplasty.[34]

Mid-shaft and distal hypospadias may be approached with a tubularization of the urethral plate, the **Thiersch-Duplay repair**. Developed nearly 140 years ago, it is the basis of many surgical approaches including the currently popular TIP procedure in which incising the urethral plate allows it to be hinged for urethral tabularization. Narrow urethral plates that previously were not adequate for a Thiersch-Duplay repair could now be utilized in the TIP approach or dorsal inlay graft.[69]

Alternatively, the preputial onlay island flap can be used to augment the urethral plate.[34-36] In this approach, an inner-preputial flap, based on a vascular pedicle from the dorsal skin, is transferred ventrally and sewn to the urethral plate.[70] For severe ventral curvature, the urethral plate may be completely resected and a transverse island tube repair performed to recreate the urethra. Similar to the onlay flap, inner preputial skin on a dorsal vascularized pedicle is rolled into a neourethra. This repair carries higher risks of urethral diverticulum and proximal stricture and some surgeons favor a two-stage approach[34-70] in which the urethral plate is excised in the process of correcting ventral curvature. Dorsal excess foreskin is then transferred ventrally in the form of Byar's skin flaps or inner prepuce graft. After a period of healing usually around 6 months, the skin flap or graft is tubularized to create the neourethra in a second surgery.

Buccal and labial mucosa has become a popular graft used in urethral reconstruction. While commonly used in failed repairs, it is also utilized in primary repairs and 2-stage repairs.[36-71] After penile straightening and resection of scarred urethra, buccal and labial mucosa, harvested from inner cheek or lip, is grafted to the ventral bed, with possible healing retraction. A second surgery is performed for tubularization and skin coverage.[36] Several approaches have incorporated buccal grafting in one-stage repairs for proximal, perineal and scrotal hypospadias.[72]

6.8 Urethroplasty Coverage

In addition to spongioplasty, a second layer of well-vascularized tissue is often employed to cover the urethroplasty. De-epithelialized subcutaneous dartos flaps can be raised from the ventral, dorsal or lateral skin for coverage of the repaired neourethra.[35] Alternatively, tunica vaginalis or scrotal de-epithelialized flaps can be used as a second layer of coverage especially for proximal hypospadias.[73-74] Vascularized tissue coverage has been shown to decrease overall complication and fistula rates.[69-75-76-77]

6.9 Complications

Common-post surgical complications include meatal stenosis, urethrocutaneous fistula, diverticulum, urethral stricture, dehiscence, persistent ventral curvature, proximal position of urethral meatus and poor cosmetic outcome (**Table 2**).[77] While post-operative urinary drainage has been shown to influence complication rates, the type and duration of urinary diversion, catheter size, dressing type, and anesthetic choice do not appear to significantly influence outcomes.[77] Reoperative surgery also is known to increase complications rates and Snodgrass and Bush report a two-fold risk for subsequent complications over primary repair, increasing to 40% with three or more operations.[78] They support prior theories that successive surgeries can compromise vascularity of penile tissues.

Not surprisingly, **complication rates rise with degree of hypospadias**, **from 10% for distal to 70% for proximal repairs**. Using a hospital consortium database, Lee and Kurzrock observed a 9% secondary surgery rate for distal hypospadias repairs.[79] In this population-based study of over 5,000 patients, increased patient age was associated with secondary endoscopic intervention, while low surgeon volume independently increased risks for repair of fistula, stricture, or diverticulum.[79] A recent large, retrospective cohort study noted complication rates of 10.7%, 18.8% and 53.8% for distal, mid-shaft and proximal hypospadias repair respectively.[80] The median time to complication for all repair types was 69.2 months.[80] Given that fewer than half of the complications presented within the first year postoperatively,[80] the authors recommended long-term follow up for all patients undergoing hypospadias repair. This follow-up evaluation should include uroflowmetry after toilet training and a final evaluation at puberty to assess for voiding issues and recurrent chordee.

6.10 Patient-reported Outcomes

There is growing recognition of the importance of patient-reported outcomes (PROs) after hypospadias repair. Bhatia et al presented a conceptual framework for Hypospadias Specific Quality of Life (HRQoL), which posited 5 domains including penile appearance, voiding function, social function, psychological/behavioral function, and pubertal/sexual health.[81] Current generalized measures for PROs, however, lack relevance to the experience of hypospadias patients, and disease-specific measurements focus primarily on penile appearance and to a lesser degree on puberal development/sexual health.[81] Wilcox and Snodgrass reported that up to 40% of men with a history of severe hypospadias will report some level of voiding problems, while 20% will have sexual problems.[82] **In a cross-sectional survey of 193 adolescent and young adult men (ages 16-21) born with hypospadias, Tack et al noted that the psychosexual outcome was most influenced by the number of surgeries and the patients' satisfaction with their penile appearance. In a small cohort of adolescents (≥14 years) with penoscrotal to perineal hypospadias who underwent urethroplasty from 1996-2005, 44% were dissatisfied with penile length and all patients were 'satisfied' or 'very satisfied' with meatal position and shape although it was often slightly retracted.**[83]

Table 2: Overview of Complications in hypospadias failure

Complication	Prevalence	Clinical presentation	Diagnostic tools	Treatment options (success rate)
Recurrent curvature	9-32%[84]	Curved penis during erection	Clinical assessment; photos; erection test	No treatment if <30° (NR); corporoplasty (93-96%);[85-86] urethral substitution (NR)
Preputial dehiscence or secondary phimosis	2-20%[87]	Tight or open prepuce	Clinical assessment	Circumcision (100%)[88]
Glans dehiscence	0-8%[89]	Meatal regression to coronal sulcus	Clinical assessment	No treatment (NR); redo distal urethroplasty (70-95%)[90-91]
Urethral fistula	4-28%[92]	Double stream	Clinical assessment (number, size, and location); calibration of distal urethra	Simple closure (75-100%);[93] closure with flaps (90-100%)[93-94]
Urethral breakdown	NR	Recurrent hypospadias	Clinical assessment	Retubularization (74-81%);[95-96] augmentation urethroplasty (76-85%);[96-97] substitution urethroplasty (62-66%)[96-98]
Meatal stenosis	0-14%[92]	Weak stream; other lower urinary tract symptoms	Clinical assessment; calibration; retrograde and voiding urethrography and cystoscopy if stricture suspected	Meatotomy (100%)[92] meatal
Urethral stricture	6-12%[99]	Weak stream; other lower urinary tract symptoms	Clinical assessment; meatal calibration; retrograde and voiding urethrography and cystoscopy if stricture suspected	Urethral dilatation (21-40%);[99] endoscopic incision (NR); augmentation urethroplasty (53-100%);[99] substitution urethroplasty (NR)
Urethral stricture owing to BXO*	4-16%[100-101]	Weak stream; other lower urinary tract symptoms	Clinical assessment; meatal calibration; retrograde and voiding urethrography and cystoscopy if stricture suspected	Substitution urethroplasty with oral mucosa graft (NR)
Urethral diverticulum‡	4-12%[102]	Urethral ballooning during micturition	Clinical assessment; calibration of distal urethra; retrograde and voiding urethrography	Urethral tapering (100%)[102]
Hairy urethra	5-15%[103]	Recurrent urinary infections and urethral stones	Urethroscopy	Ablation of hairs and their follicles (NR); substitution urethroplasty (NR)
Abnormal skin configuration	55%[85]	Abnormal appearance	Clinical assessment	Skin reconfiguration (NR)
Skin deficiency	5%[104]	Trapped penis	Clinical assessment	Free skin grafts (NR); skin expanders (NR)

* After repair incorporating a preputial skin flap.
‡ Only after tube repair.
BXO – balanitis xerotica obliterans
NR – not reported

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View Image.

7. Costs

While the costs of hypospadias repair have decreased with the transition from inpatient to outpatient surgery, few studies have formally assessed the financial burden of hypospadias management.[105,106,107] Pohl et al. estimated that $8 million was incurred in national inpatient expenditures in 2000, with the average cost of hospitalization exceeding $5,389 per patient. [105] **Insurance expenditures for hypospadias in the first three years of life totaled $5,431 per patient from 2004-2016.**[108] The overall health care costs for the treatment of hypospadias are certainly more when considering the number of patients affected, increasing incidence and management of long-term complications. Some of this might be mitigated by increased specialization.

8. Clinical Care Pathway

See **(Figure 1)**

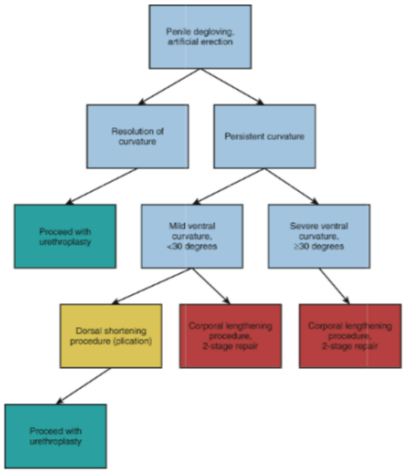

Figure 1 (From Campbell's Urology, Figure 45.7): Algorithm for management of penile curvature. Once the penis is degloved, artificial erection is performed. If the curvature is resolved, the urethroplasty can be completed. If there is persistent penile curvature, we use a measurement of 30 degrees as the defining measurement for performing a dorsal plication or a corporal lengthening procedure. If the surgeon is concerned about the quality of the ventral shaft skin in spite of curvature of less than 30 degrees, a corporal lengthening procedure can be considered.

Videos

Proximal Hypospadias - 1 Stage Repair

Second Stage Hypospadias Repair with Dorsal Inlay BMG

Harvesting a Lower lip Bucal Mucosal Graft

PROXIMAL HYPOSPADIAS REPAIR UTILIZING STAGED STAGED AUTOGRAFT [STAG] TECHNIQUE

PROXIMAL HYPOSPADIAS REPAIR URETHROPLASTY FOLLOWING STAGED STAGED AUTOGRAFT UTILIZING THIERSCH DUPLAY TECHNIQUE

Distal Hypospadias Repoart with Thiersch Duplay Technique (TIP)

Presentations

Hypospadias Presentation 1

References

† Wilson JD, Griffin JE, Russell DW. Steroid 5 alpha-reductase 2 deficiency. Endocrine reviews 1993;14:577-93

1 Impairment of 5 alpha-reductase enzyme causes variable phenotypic manifestations of disorders of sexual development, most commonly ambiguous genitalia. Mutations in the steroid 5 alpha-reductase 2 gene are the cause.

2 Baskin et al, Differentiation. 2018 Sep-Oct;103:74-85. doi: 10.1016/j.diff.2018.08.001. Epub 2018 Aug 23)

† Glenister TW. The origin and fate of the urethral plate in man. Journal of anatomy 1954;88:413-25.

After examining histologic stains of fetal urethras the author made several conclusions including: the urethral plate is an outgrowth of the urogenital sinus, the spongy urethra and proximal portion of the glandar urethra are derived from the urethral plate, the distal portion of the glandar urethra is derived from the surface ectoderm.

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