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TITOLO DELLA TESI:

**FUNCTIONAL AND COSMETIC OUTCOMES
AND THEIR PSYCHOLOGICAL IMPACT
IN ADULT PATIENTS WHO UNDERWENT
AN URETHROPLASTY FOR HYPOSPADIAS REPAIR
IN THE PAEDIATRIC AGE. PRELIMINARY DATA.**

Settore scientifico-disciplinare: **MED/38**

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Ai miei Genitori

Pilastri della mia vita e della mia conoscenza

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SUMMARY

Introduction: Hypospadias is a penile congenital malformation characterized by an ectopic localization of the external urethral meatus alongside the ventral face of the penile shaft or even within the scrotum, a preputial ventral cleft, and different degrees of penile curvature. It is a multifactorial disease, caused by genetic and environmental factors (1). Surgery is needed for three reasons: Functional, Sexual and Esthetical. Surgical techniques for the repair of hypospadias have been evolving during the last years, but the aims have remained the same: to obtain a straight penile shaft with the external urethral meatus on the apex of the glans, acceptable both esthetically and functionally (3). Surgery for the repair of hypospadias has a long and steep learning curve to obtain acceptable results. Proximal hypospadias is the most complex and challenging condition, and may be treated both with a single-stage and a staged procedure (4). There is not a technique considered as the gold standard, and pediatric urologists who want to treat hypospadias have to deal with a wide variety of techniques (5).

The primary aim of the project was to determine the overall complication rate whereas the secondary aim was to determine the long term functional, cosmetic results and the psychological impact of urethroplasty for hypospadias repair in the adult patients.

Material and Methods: Our study group included consecutive cases from two Italian high volume and experienced Paediatric Urology Institutions (Milan and Padua). The overall inclusion period of the study was between January 1st 1984 to January 1st 2002. *Inclusion criteria:* Adult men (older than 18 years) who underwent a urethroplasty for hypospadias repair before 18 years old, were included. *Exclusion criteria:* All the patients younger than 18 years old at the beginning of the study and patients treated in other centre than Milan and Padua.

All of the collected data were included in the descriptive analysis, whereas some variables were excluded for the statistical analysis, due to the fact that they were not related to the outcomes of the study. Data of the included patient were presented as categorical data (nominal, divided in binomial or multinomial or ordinal) and as ratio data. Variables were described and reported in tables (summarised in

categories, numbers, percentage). Data were analysed using IBM® SPSS® Statistics Base version 25.0 (SPSS Inc., Chicago, IL, USA).

Results: This paper reports preliminary data of the ongoing study. 942 patients were identified from paper or electronic medical records and from retrospective or prospective database. Excluding the patients of whom there was not an updated telephone number; 359 patients met the inclusion criteria. 77 patients (21%) completed the psychological and sexuological tests, 94 (26%) questionnaires about penile perception and only 52 (15%) the urological evaluation.

After a median follow-up of 21 years (18-35), we found an overall complication rate of 30%: 7 patient (9%) reported ventral dehiscence, 4 patients (6%) presented meatal/neourethral stenosis, 6 patients (8%) developed a urethrocutaneous fistula, 2 (2%) a recurrent ventral curvature and 4 (5%) skin defects. In addition to these complications reported by the patients, during the urological evaluation, should be take into account the 5 complication diagnosed at the urological evaluation.

Thus, recalculating the overall complication rate, it is 36% with a higher rate of stenosis 8 (10%) and fistula 7 (9%).

Starting from the analysis of the cosmetic results (SIGHT questionnaire), the satisfaction with the appearance of the penis, detected in our patients, was about 77% and the subjects who believe that their penis is normal was 71. Regarding penis size satisfaction, it was 59% of cases apparently lower if compared with the result of the other aspects assessed by the questionnaire. About patient satisfaction with the sexual function of their penis 78% was satisfied or very satisfied. Not less important was the proportion of patients who complained of the need to hide their penis on public occasions (30%) and with fear of being laughed because of the appearance of their penis (15%), data are consistent with study from the group of Padua (70).

The HOSE questionnaire investigates the aspect of the penis reported by the patient as objectively as possible, the position of the external urethral meatus was distal in 95% of cases, and the shape is reported as vertical in 61% of cases, again in line with what has also been seen in other studies (71). The patients also declared to perceive their penis as straight with complete absence of curvature in 67% of cases, and with a slight curvature in less than 10° and therefore not to be considered

clinically significant in 28% of cases. Approximately 5% of patients report a moderate or severe residual curvature. The patients who declared themselves satisfied from the point of view of their urinary function were 53%, this is consistent with the literature where 40% of patients complain with micturition (41).

Finally, the absence of urethrocutaneous fistulas was reported by most of the patients (93%).

We also evaluated the functional outcome performing uroflowmetry. On uroflowmetry the maximal urinary flow rate is widely accepted as a useful parameter for assessing an individual's voiding function. Median Qmax was 17,9 (9,2-26,2) ml/sec; median Qaverage was 8,95 ml/sec (4,5-17,6); median voided volume was 225 (130-620). A significant post-voiding residual was found in none of the patients. Uroflowmetry curve shape was evaluated by the F.I. and was Tower in 0 patient, bell in 17 (33%) and Plateau 35 (67%).

Analyzing the SF-36 questionnaire, twenty-one (27%) defined their health excellent, 36 (47%) very good and 15 (20%) good. Only five. (6%) defined their status of health as "fair" none poor.

The BDI-II that should outline case and grade of depression, (not as a diagnostic tool), confirms a good overall state of mental health with a minimal depression in 3 patients (4%) and moderate depression in 3 patients (4%). Severe depression in described in only one patient.

A mild grade of anxiety was outlined in one third of patients with both STAI-Y1 and STAI-Y2.

The SCL-90 with its multiple fields of investigation underline in the mayor percentage of the population a normal condition without pathological condition. These data need to be correlate to the other questionnaires and with a psychological investigation.

In the MAST only 7 patients (9%) seems to show a pathological tendency to suicide but this data are only indicative of a possible discomfort which must be confirmed by a specialist in the phycological field.

The prevalence of erectile dysfunction (ED) in ours study was (15%) with mild grade in 3 patients (12%) and in one severe (3%).

Preliminary data about MSQ questionnaire seems to show a low anxiety to approach sexual aspects and an overall normal sexuality in our population.

In our apparent male sexual health population, MSHQ questionnaire, outline that more than half of the subjects are satisfied by the quality of their sexual life but there was an high number of young patients (14%) that need a medications to achieve an erection. Two patients are not able to get an erection without using drugs, six (8%) had this problem in less than half of the time and 4 (5%) in about half of the time. Anejaculation is reported by 5 patient.

Conclusion: The overall complication rate seems to be slightly higher than those reported in literature. This could be due to the long follow-up reported in the study, unique in the literature. Preliminary data show a low anxiety to approach sexual aspects and more than half of the subjects are satisfied by the quality of their sexual life. Our study highlighted a good satisfaction rate for the cosmetic result, in more than half patients, consistent with the data reported in the literature. We also conclude that uroflowmetry remains a useful tool in screening and prevent complication in a long term follow-up after hypospadias surgery.

ABSTRACT

Introduction: Hypospadias is a penile congenital malformation. Surgery is needed for three reasons: Functional, Sexual and Esthetical. The primary aim was to determine the overall complication rate whereas the secondary was the long term functional, cosmetic results and the psychological impact of urethroplasty for hypospadias repair in the adult patients.

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Results: 942 patients were identified, 359 patients met the inclusion criteria. 77 patients (21%) completed the psychological and sexuological tests, 94 (26%) questionnaires about penile perception and only 52 (15%) the urological evaluation. After a median follow-up of 21 years (18-35), we found an overall complication rate of 30%: 7 patient (9%) reported ventral dehiscence, 4 patients (6%) presented meatal/neourethral stenosis, 6 patients (8%) developed a urethrocutaneous fistula, 2 (2%) a recurrent ventral curvature and 4 (5%) skin defects. Uroflowmetry curve shape was bell in 17 (33%) and Plateau 35 (67%). Analysing the questionnaires 1/3 of patients defined their health excellent with a good overall state of mental health with a minimal depression and mild grade of anxiety. The prevalence of erectile dysfunction (ED) was (15%) with mild grade in 3 patients (12%) and low anxiety to approach sexual. In the HOSE q patients declare themselves satisfied of the appearance of their penis.

Conclusion: The overall complication rate seems to be slightly higher than those reported in literature. Preliminary data show a low anxiety to approach sexual aspects and more than half of the subjects are satisfied by the quality of their sexual life. Our study highlighted a good satisfaction rate for the cosmetic result, in more than half patients, consistent with the data reported in the literature. We also conclude that uroflowmetry remains a useful tool in screening and prevent complication in a long term follow-up after hypospadias surgery.

1. INTRODUCTION

Hypospadias is a penile congenital malformation characterized by an ectopic localization of the external urethral meatus alongside the ventral face of the penile shaft or even within the scrotum, a preputial ventral cleft, and different degrees of penile curvature.

It is a multifactorial disease, caused by genetic and environmental factors (1).

Its prevalence is 1/125 newborn males: hypospadias is in fact one of the most common congenital malformations (2).

Surgery is needed for three reasons:

- *Functional reason.* Reconstructing the urethra and replacing the external meatus on its correct position, the patient will have no more difficulties during micturition.
- *Sexual reason.* To allow a satisfying erection, especially if hypospadias is associated with penile curvature.
- *Esthetic reason.* To eliminate the patient's discomfort due to the abnormalities of his penis.

Surgical techniques for the repair of hypospadias have been evolving during the last years, but the aims have remained the same: to obtain a straight penile shaft with the external urethral meatus on the apex of the glans, acceptable both esthetically and functionally (3). Surgery for the repair of hypospadias has a long and steep learning curve to obtain acceptable results.

Proximal hypospadias is the most complex and challenging condition, and may be treated both with a single-stage and a staged procedure (4). There is not a technique considered as the gold standard, and pediatric urologists who want to treat hypospadias have to deal with a wide variety of techniques (5).

1.1 Historical aspects

Hypospadias derives from the ancient Greek *υπο*, which means under, and *σπαδόν*, which means hole. Galenus (130-199 A.D.) was the first mentioning of the term hypospadias (6).

Although his anatomical knowledge was limited, Galenus wrote about difficulties during a sexual intercourse due to penile curvature (“chordee”), and about fertility problems due to sperm difficulties in reaching the uterus. At that time other physicians proposed glans amputation in order to obtain an apical urethral orifice. One thousand five hundred years after, in 1556, Amatus Lusitanus treated a boy with peno-scrotal hypospadias by creating a canal from the hypospadiac meatus to the penile fossa. From that time on, progresses about anatomical knowledge have been made, and from the 19th Century about 300 techniques for the surgical repair of hypospadias have been described (6).

1.2 Epidemiology

Prevalence ranges from 0,26 cases in 1000 newborn in Mexico to 2,11 in Hungary and 2,6 cases in 1000 newborn in Scandinavia. This prevalence has been incrementing in the last decades (2) (7) (8).

There is not a known cause for this growing prevalence, but probably an interaction between genetic predisposition and environment is involved.

Low weight at birth, hypotrophic placenta, low weight for gestational age, high maternal BMI, twin pregnancy are considered risk factors (9) (10); a diet poor in meat and fish, and in vitro fertilization are also considered, but with variable results (11) (12).

1.3 Aetiology

Hypospadias is a multifactorial condition, caused by both genetic and environmental factors. However, the real cause is still unknown.

Genetic factors

A familiar clustering in 25% of affected patients strongly suggests that genetic factors are involved in the pathogenesis of hypospadias. An affected relative is the main risk factor, with the risk growing with the severity of hypospadias (9). A big

number of genetic mutation has been found, especially in patients with proximal hypospadias, but their function remains uncertain in the majority of cases.

All the involved genes are determinant in the embryonic development of male gonads: WT1 (Wilms Tumor 1), SF1 (NR5A1 o Steroidogenic factor 1), FSHR (Follicle Stimulating Hormone Receptor), LHCGR (Luteinizing Hormone / Choriogonadotropin Receptor), AR (Androgen Receptor), 17 β -HSD (17beta hydroxysteroid dehydrogenase), SRD5A2 (5alfa reductase) (13) (14).

Environmental factors

Several studies have addressed chemical substances as altering the endocrine system with an antiandrogenic mechanism (15). Use of oral contraceptives during the first part of pregnancy results in an exposition to estrogens, but there are no strong proves to support this correlation (1).

1.4 Embryology

Sex is defined at three levels (Figure 1):

- Chromosomes X and Y define the chromosomal sex;
- Testicles and ovaries define the gonadal sex;
- External genitalia and secondary sexual characters define the phenotypic sex.

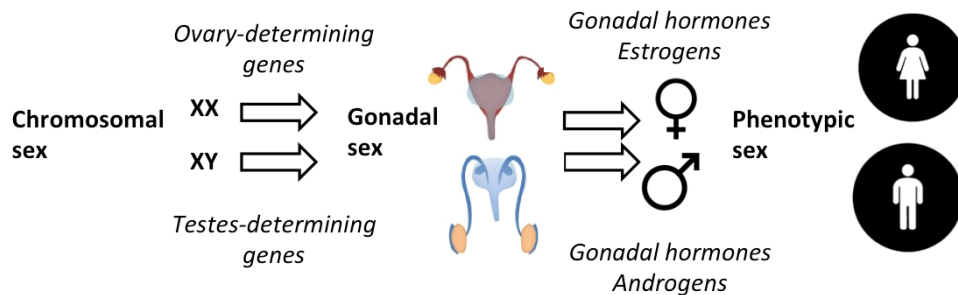


Fig. 1. Chromosomal, gonadal, and phenotypic sex.

Normal sexual development

Until the sixth week of gestation, the embryo has undifferentiated gonads, with the potentiality to become both male and female. The chromosomal sex determines the successive development of the gonads (16). The Y chromosome contains the sex determining region (SRY). This gene codes for a protein which is a transcriptional factor that starts a genes cascade resulting in the differentiation into testicles. Genes duplications or deletions are associated with disorders of sexual development (DSD) (17). Gonadal differentiation into testicles depends on SOX-9 gene (SRY-box 9), which is in turn regulated by SRY. SOX-9 activates SF-1 and other genes responsible for the differentiation into testicles, and inhibits WNT4, which instead induces the differentiation into ovaries. Without SRY and in presence of two X chromosomes, ovaries develop (18) (Figure 2).

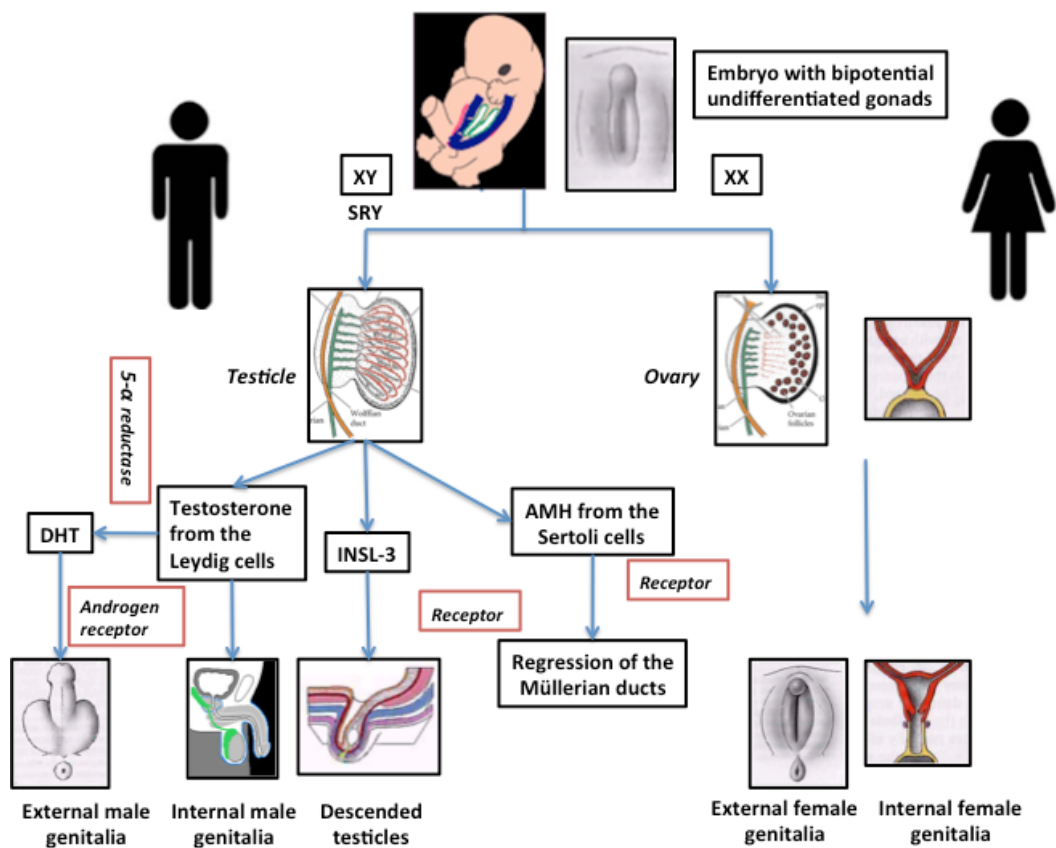


Fig. 2. Normal sexual development.

Internal genitalia develop from Wolffian ducts in males, and from Müllerian ducts in females, whereas external genitalia develop from the same structures both in males and females.

Testicles produce the necessary hormones for a normal male development.

Testosterone is produced by Leydig cells and partially converted into DHT by 5 α -reductase. Testosterone stimulates the development of internal genitalia from Wolffian ducts, while DHT is necessary for the development of external genitalia. Sertoli cells produce the anti-müllerian hormone (AMH), which induces the regression of the Müllerian ducts (19) (Figure 3).

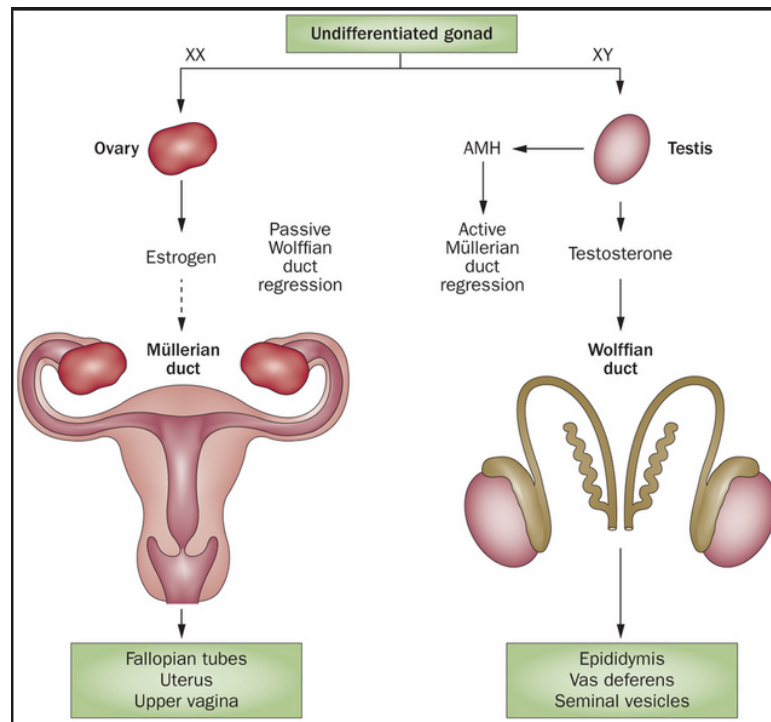


Fig. 3. Differentiation of internal genitalia.

Testicles also produce INSL-3, an hormone that induces the descent of the testicle from the abdomen into the scrotum (16). Female internal genitalia development is induced by estrogens produced both by ovaries and by maternal placenta (20).

External genitalia derive from cloacal folds, and remain identical in males and females until the end of the sixth week. Cloacal folds fuse cranially to form the

genital tubercle, whereas caudally they divide into urethral and anal folds. At the same time, genital folds become visible, and will develop into scrotal folds in males and into labia majora in females.

In male sexual development, androgens also induce the genital tubercle lengthening to the phallus. Urethral folds follow the lengthening, and form the urethral cleft to the tip of the glans. Urethral plate develop by the end of the third month, with the urethral cleft being covered by an epithelial coating. Distal urethra, including the external orifice, develop more lately, during the fourth month. It is believed that ectodermal cells from the tip of the glans migrate internally to form an epithelial chord and then a lumen. Scrotal folds move downward and become separated by a septum, resulting in the scrotum.

In females, from the genital tubercle derive the clitoris, the labia minora and the labia majora.

The cloaca

The cloacal membrane is the membrane that covers the embryonic cloaca during the development of the urinary and reproductive organs. It is formed by ectoderm and endoderm coming into contact with each other. As the embryo grows and caudal folding continues, by the end of the seventh week, the cloacal membrane disrupts, and the urorectal septum divides the cloaca into a ventral urogenital sinus and dorsal anorectal canal (20) (Figure 4).

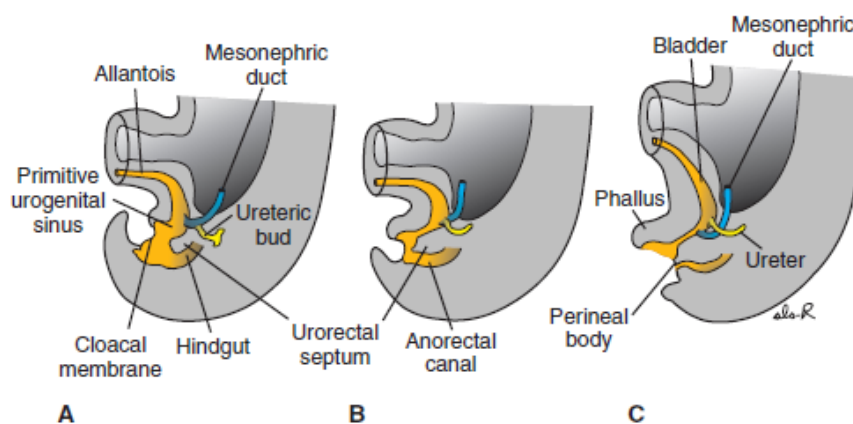


Fig. 4. Division of the cloaca.

Three portions can be distinguished in the urogenital sinus. The most cranial one develops into the urinary bladder. Initially it is in continuity with allantois, but then the allantois obliterates, and its remnant – the uracus – remains as a fibrous chord which joins the apex of the urinary bladder with the umbilicus. The following portion of the urogenital sinus is a straight canal from which originate the prostate and the membranous urethra. The last portion gives birth to the phallus (20).

During the differentiation of the cloaca, ureteral buds – which originate from the mesonephric ducts – enter into bladder wall. As a result of the kidneys ascent, ureteral orifices move cranially, whereas those of the mesonephric ducts get closer and enter into the prostatic urethra and become ejaculating ducts (20). As ureteral buds have a mesodermal origin, also the bladder trigone is covered by a mucosa of mesodermal origin. The mesodermal covering of the trigone is substituted by endodermal epithelium over time. Urethral epithelium has an endodermal origin. By the end of the third month, it begins proliferating, and from these buds originate the prostate in males, and urethral and paraurethral glands in females (20) (Figure 5).

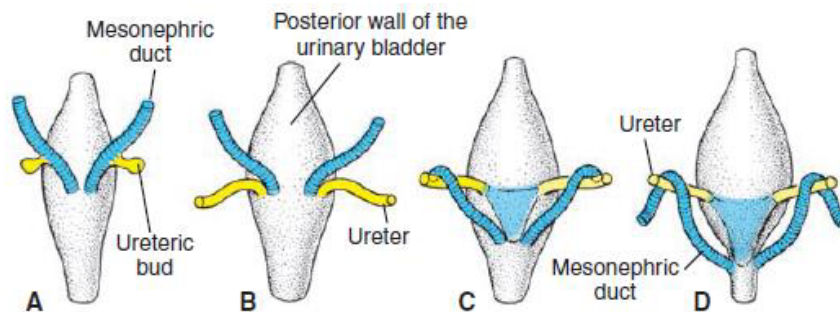


Fig. 5. Ureter and mesonephric duct during development.

Differentiation of the external genitalia

This process occurs between the seventh and the seventeenth week of gestation (21).

During the fifth week, cloacal folds form mesenchimal cells that migrate to the perineum, and accumulate along the medial line to form the genital tubercle (22).

The genital tubercle is cranial to the median opening of the urogenital sinus, called urogenital ostium. The urogenital ostium is sided by the urogenital folds and the labioscrotal folds. It is believed that epithelial endodermal cells from the urogenital sinus invade the genital tubercle to form the urethral plate (21).

Labioscrotal folds fuse along the medial line to form the scrotum in males, whereas they remain separate in females and form the labia majora.

In males, androgens induce the lengthening of the genital tubercle to form the penis. In females, the absence of androgens makes the genital tubercle minimally grow and develop into clitoris.

During the lengthening of the urethral plate to the tip of the genital tubercle, a cleft forms along the ventral surface of the genital tubercle, sided by the urethral folds. Those urethral folds fuse along the medial line, converting the urethral cleft into penile urethra.

If the urethral folds do not correctly fuse, hypospadias results (22).

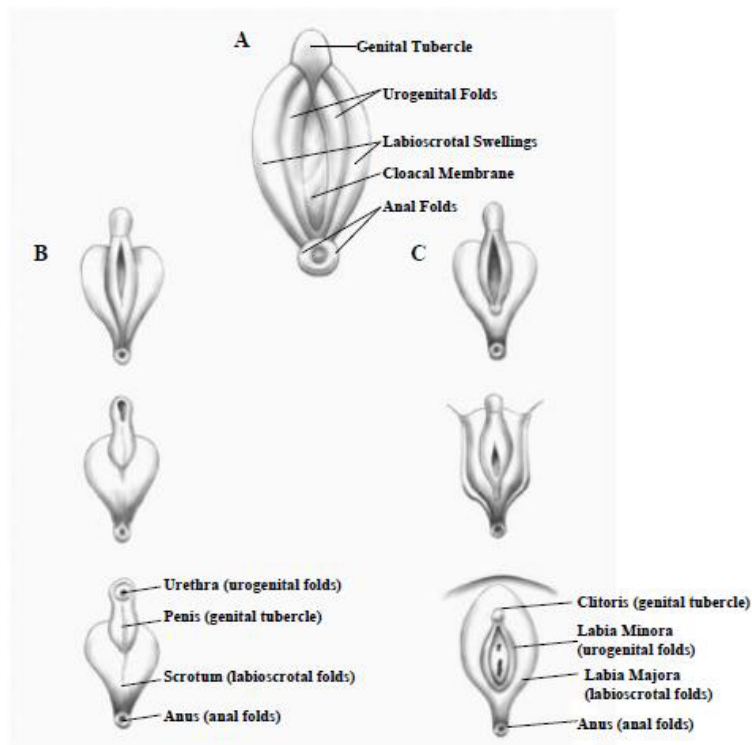


Fig. 6. Differentiation of the external genitalia.

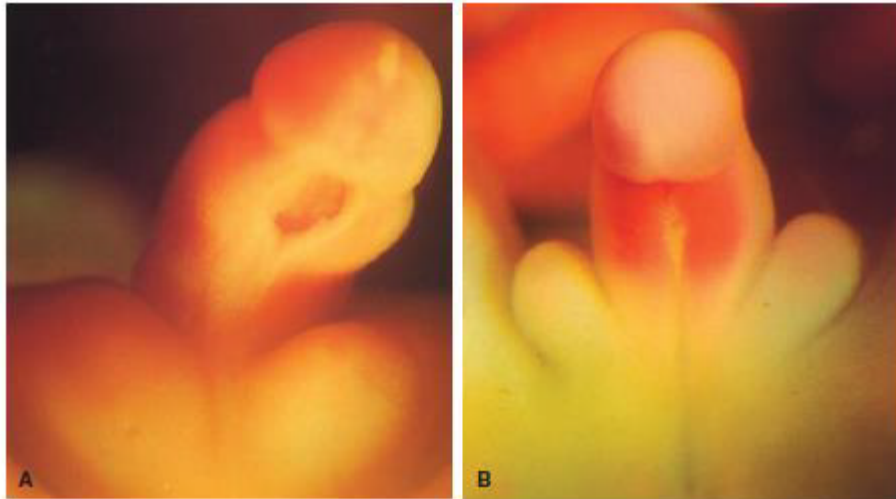


Fig. 7. Picture of the external genitalia of a male fetus at 12 weeks and of a female fetus at 11 weeks.

Disorders of sexual development (DSD)

DSD is a generic term to define congenital conditions of atypical development of the chromosomal, gonadal or phenotypic sex (23).

The anomaly may concern the development of the gonads, a dysfunction of the gonads, or defects in the target organs (17).

Males with DSD present with a phenotypic spectrum which varies from female external genitalia to apparent male genitalia. The virilization grade depends on androgen levels and responsiveness to androgens (Figure 5). Diagnosis is made at birth, but some conditions are diagnosed at puberty. According to the new classification system, DSD is divided in DSD of the sexual chromosome (for instance 47,XXY, Klinefelter syndrome), DSD 46,XY (for instance CAIS) and DSD 46,XX (as in gonadal development disorders) (23) We will focus our attention on XY DSD associated with hypospadias.

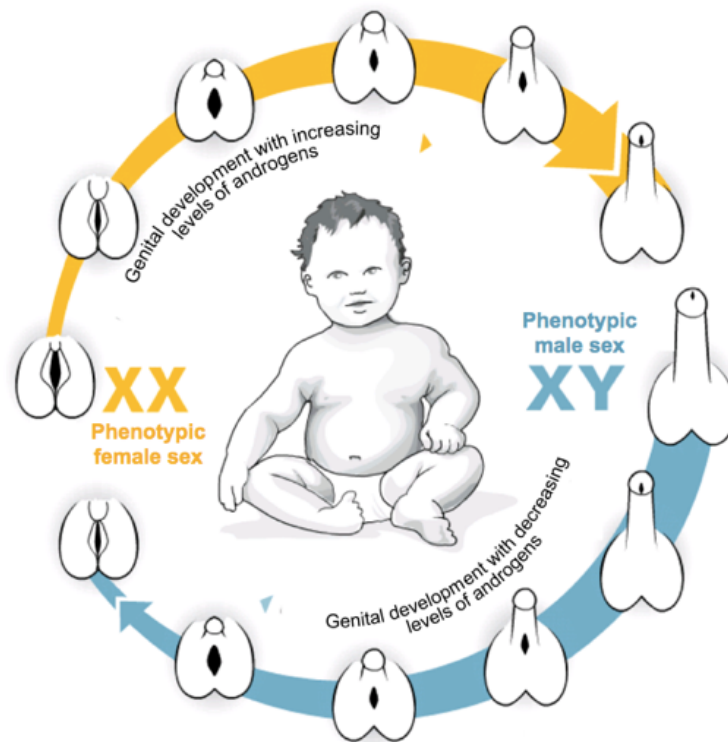


Fig. 8. Genital development according to androgens levels.

Complete androgen insensitivity syndrome (CAIS) is a form of DSD dependent on the loss of number or affinity or function of androgen receptors (17). It is caused by inactivating mutations of the gene coding for the androgen receptor (AR), located on the X chromosome. It is therefore an X-linked condition: 46, XY individuals are affected. A partial insensitivity (PAIS) provoke an incomplete masculinization with, for instance, hypospadias, cryptorchidism or infertility.

A deficiency of the 17β -hydroxysteroid dehydrogenase, the enzyme that converts the androstenedione into testosterone, may cause under-masculinization of the external genitalia and even severe hypospadias.

A deficiency of 5α -reductase, the enzyme that converts the testosterone into DHT, influences the development of the external genitalia resulting in a phenotypic spectrum that varies from feminine external genitalia to a small penis with hypospadias (24).

Partial Gonadal Dysgenesis is caused by an abnormal gonadal differentiation during the embryonic life. According to the grade of the dysfunction, the child presents different grades of under-masculinization (17).

The ovotestis DSD is a particular form of gonadal dysgenesis with both ovaric and testicular tissue in the same gonad or in the contralateral one. The clinical presentation depends on the amount of testicular tissue producing testosterone, with different grades of virilization.

1.5 Anatomy of the penis

The penis

The penis is composed of paired corpora cavernosa, each with a proximal prolongation - the crus - attached to the pubic arch, the corpus spongiosum and its proximal part - the bulb of the penis – and the glans, an expansion of the corpus spongiosum.

The shaft of the penis is surrounded by five layers.

The skin over the penis is the most superficial layer, and it is particularly moveable and expandable to accommodate erection.

The superficial fascia or dartos fascia, is a part of the membranous layer of the superficial fascia of the groin and perineum or Colles' fascia. Imbedded in it are the superficial penile arteries and the superficial dorsal vein.

Beneath the dartos fascia and Colles' fascia lies a very thin connective tissue layer, the tela sub-fascialis.

A deep layer of the fascia is the Buck's fascia. It is a heavy elastic layer that encloses not only the two corpora cavernosa, but, in a somewhat separate compartment, the corpus spongiosum as well. It also encloses the deep dorsal vein and the dorsal arteries and nerves. Buck's fascia has a dense structure, in contrast to the loose superficial fascia of the penis; it is composed of longitudinally running fibers and is firmly attached to the underlying tunica albuginea.

The deepest layer is the tunica albuginea, forming a thick white coat set in a fibro-areolar matrix. This layer encloses the corpora cavernosa and the corpus spongiosum. It is composed of an outer longitudinal coat and an inner circular coat. The tunica albuginea becomes thicker ventrally and it forms a groove for the corpus spongiosum.

The two corpora cavernosa are separated in the sagittal plane by a dense tunica albuginea layer that passes between them as the intercavernosous septum. The septum is incomplete distally, being perforated on its dorsal margin by vertically orientated openings in the pectiniform septum that provide free vascular communication between the corpora.

Continuous with the inner surface of the tunica albuginea within the corporeal bodies are numerous flattened columns or sinusoidal trabeculae, composed of fibrous tissue, elastin fibers, as smooth muscle surrounding the endothelial-lined sinusoids or cavernous spaces. In addition, a row of structural trabeculae arises near the junction of the three corporal bodies, the corporal junction, and inserts on the wall of the corpora about the midplane of the circumference.

The tunica albuginea covering the corpus spongiosum is about half as thick as that over the corpora cavernosa and contains smooth muscle fibers that may contract during ejaculation.

The caliber of the corpus spongiosum is uniform throughout its penile segment, but it, along with the contained urethra, widens proximally where it is covered by the bulbo-spongiosus muscle to form the urethral bulb.

The crus of the corpus cavernosum is encased in an ischio-cavernosus muscle. The paired muscles arise from the inner surfaces of the ischial tuberosities beside each crus and insert into their medial and inferior surface. They do not completely envelop the crura, being deficient on the side against the bone.

The corpus spongiosum is covered by the bulbo-spongiosus muscle, which invests the bulb of the corpus spongiosum including the bulbar urethra. The bulbo-spongiosus forms a thin muscular coat that runs obliquely on each side of the corpus to surround the bulb and insert in the midline inferiorly. The ischio-cavernosus and bulbo-spongiosus muscles are attached to the underlying layer of Buck's fascia by their investing fascia (25) (26). (Figure 9)

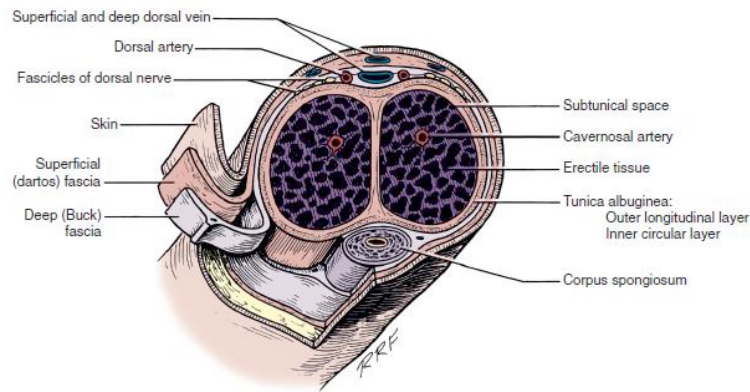


Fig. 9. Cross-section of the penile shaft.

Male urethra

Male urethra is divided into four parts: prostatic, bulbo-membranous, bulbo-spongy, and penile.

The bulbo-membranous is a 2 cm segment lying in the urogenital diaphragm and within the striated urethral sphincter, plus the proximal few centimeters of the bulbous urethra.

The bulbo-spongy urethra extends from within a few centimeters of the anatomic membranous urethra distally to the level of the suspensory ligament. Its lumen widens to form the urethral bulb.

The penile urethra is about 15 cm long, running from the suspensory ligament to the meatus. It lies within the corpus spongiosum throughout its length. The lumen of the urethra, although dilated as it passes through the bulb, is otherwise of uniform caliber except at the fossa navicularis, where it widens out before narrowing into the vertical slit of the urethral meatus.

The membranous urethra is involved in urinary continence and control of ejaculation. The remainder of the urethra serves to allow the free passage of the urine during micturition, and to assist the expulsion of semen during ejaculation.

To this end, it is surrounded by specialized tissue, the corpus spongiosum, that is normally relaxed for the free passage of urine, whereas when it is engorged, it provides bulk against which the compressive action of the bulbo-spongiosus can act to evacuate the semen (21).

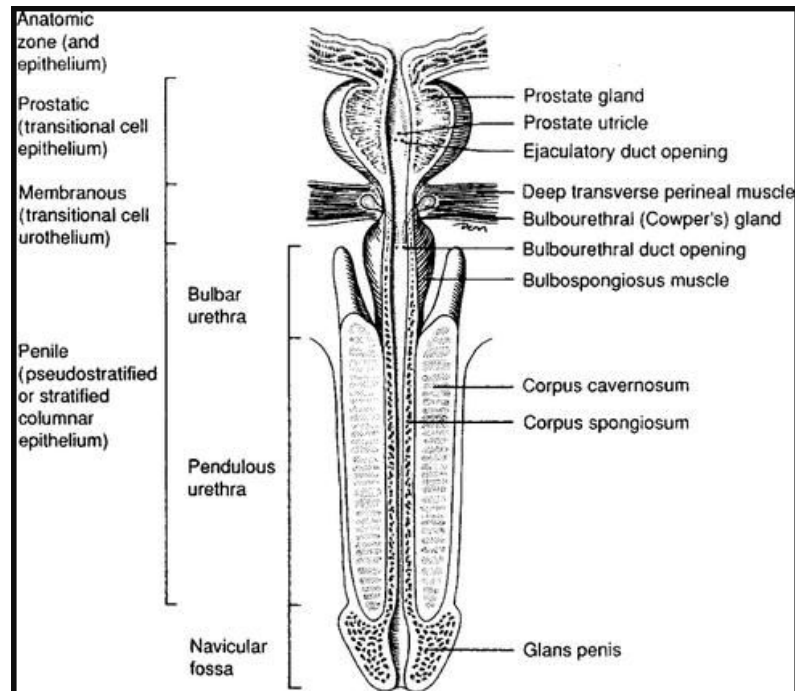


Fig. 10. *Anatomy of the male urethra.*
Arterial blood supply

The superficial arterial supply to the penile skin and prepuce lies in the superficial layer of the superficial fascia of the penis. The two superficial penile arteries arise from each inferior external pudendal artery, a branch of the femoral artery. They divide on each side, usually into a dorsolateral and a ventrolateral branch. At intervals, these vessels give off fine branches to the skin.

The only point of connection between the deep and superficial systems is an anastomosis at the coronal sulcus, where the superficial vessels circle back dorsally to join the dorsal artery of the penis.

The anterior branch of the internal iliac artery divides to form the inferior gluteal artery and the internal pudendal artery. The latter passes beneath the sacrospinous ligament and over the sacro-tuberous ligament and bifurcates into the perineal artery and continues as the penile artery, which runs under the superficial transverse perineal muscle and the symphysis.

The penile artery pierces the urogenital diaphragm along the medial margin of the inferior ramus of the ischium behind the superficial transverse perineal muscle near the bulb of the urethra, and divides into three branches: the bulbourethral artery (to the bulb of the urethra, the corpus spongiosum and the glans), the cavernous artery (to the corpus cavernosum), and then terminates as the dorsal artery of the penis (along the dorsolateral surface of the penis, to the glans) (21).

The cavernous artery gives off multiple short terminal branches, the helicine arteries, most of which open directly into the sinusoids; a few of the helicine arteries end in capillaries that provide a second system of circulation that nourishes the trabeculae.

The circumflex arteries from the dorsal artery send penetrating branches through the tunica albuginea. These divide into helicine arteries and spread among the trabeculae to enter the sinusoids.

Venous drainage

Three systems drain the penis: superficial, intermediate, and deep.

The superficial system for the prepuce, skin, and subcutaneous tissue is carried in multiple superficial veins that run randomly on the dorsolateral surface of the penis under the superficial penile fascia. These join a single or double superficial dorsal vein that drains into either saphenous vein.

An intermediate system drains the glans penis, the corpus spongiosum and the distal two-thirds of the corpora cavernosa. Many small veins leave the glans penis via the retro-coronal plexus to enter the deep dorsal vein that runs in a groove at the junction of the two corpora. Emissary veins from the corpora join the circumflex veins. These communicate with each other and with corresponding veins on the opposite side and are joined by lateral veins, ultimately becoming multiple trunks running under Buck's fascia before emptying into the deep dorsal vein.

The deep dorsal vein passes through a space in the suspensory ligament and between the puboprostatic ligaments to drain into the prostatic plexus.

The deep drainage system is composed of the cavernous veins, the bulbar veins and the crural veins. The cavernous veins unite between the crura into one or two large

main cavernous veins, which in turn run between the bulb and the crus to drain into the internal pudendal vein, then to the internal iliac vein. Crural veins arise from the dorsolateral surface of each crus and unite to drain into the internal pudendal vein. The bulb itself is drained by the bulbar veins, which empty into the prostatic plexus (21).

Innervation of the penis

The somatic nerve supply comes from spinal nerves S2, S3, S4 by way of the pudendal nerve. The pudendal nerve passes through the Alcock's canal, where it gives off the perineal nerve and the rectal nerve. It continues as the dorsal nerve of the penis as it runs over the surface of the obturator internus and under the levator ani. The dorsal nerve runs on the deep layer of the urogenital diaphragm, where it gives off a branch to the crus. It then passes through the deep transverse perineal muscle to course on the dorsum of the penis.

The main cutaneous nerve supply to the penis and scrotum comes through the dorsal and posterior branches of the pudendal nerve, but the anterior portion of the scrotum and the proximal part of the penis are supplied by the ileo-inguinal nerve.

The sympathetic nerves arise from the lumbar nerves L1, L2, and the parasympathetic nerves from sacral nerves S2,S3,S4.

White rami communicates from L1 and L2 pass to ganglia in the lumbar sympathetic chain. From the ganglia, the third and fourth lumbar splanchnic nerves join the superior hypogastric plexus that lies over the aortic bifurcation, the left common iliac vein and the promontory of the sacrum. From each side of this plexus, the right and left hypogastric nerves descend medial to the internal iliac artery to the right and left pelvic plexuses. The pelvic plexus contains also parasympathetic fibers derived from the sacral pelvic splanchnic nerves. The anterior part of each pelvic plexus constitutes the vesical plexus; the lower part makes up the prostatic plexus, the nerves from which supply the prostate and ejaculatory ducts, seminal vesicles, membranous and penile urethra, and the bulbourethral glands.

The cavernous nerve leaves the pelvis between the transverse perineal muscles and the membranous urethra before passing beneath the arch of the pubis to supply each

corpus cavernosum. Two branches may be found. One is the lesser cavernous nerve that supplies the erectile tissue of the corpus spongiosum as well as the penile urethra. The other branch, the greater cavernous nerve, stays beneath the prostatic venous plexus to be distributed to the erectile tissue of the corpora cavernosa (21) (22).

1.6 Diagnosis

Prenatal

Hypospadias may be associated with other abnormalities (neural tube, heart, urogenital and anorectal tract) or may be part of a syndrome. In the majority of the cases, however, it remains an isolated manifestation. Therefore, only an accurate analysis of the genital morphology by means of ultrasound (US) allows a correct prenatal diagnosis.

The principle characteristic US sign is the presence of a ventral curvature of the penis and its brevity. Meizner described the so called “tulip sign” in case of severe hypospadias, corresponding to a very short and ventrally curved penis associated with a peno-scrotal transposition. Moreover, it may be observed that the distal part of the penis appears rounded, due to the abundance of the prepuce on the dorsal surface (27).

Post-natal

Clinical evaluation

The clinical evaluation at birth is sufficient for the diagnosis. It should include:

- Position, shape and length of the external urethral orifice
- Presence of an hypoplastic urethra with a division of the corpus spongiosum
- Aspect of the glans and prepuce
- Dimensions of the penis
- Curvature of the penis during erection.

It should be also evaluated the position of the testicles: in case of cryptorchidism, it should be excluded a DSD by means of hormonal exams. Some Authors

recommend a routinely hormonal assessment in case of proximal hypospadias, independently from the position of the testicles.

Symptoms

Children with hypospadias generally present a normal urinary flow. Only in a small percentage of cases there is a stenosis of the hypospadic meatus, causing successive difficulties in bladder emptying.

The clinical presentation is in each case related to the severity of hypospadias: distal forms may only cause esthetic discomfort, whereas patients with proximal hypospadias may have problems with peeing standing up and with sexual intercourses due to the penile curvature (28).

Karyotype

Karyotype may be useful for the correct assessment of hypospadias in case of other associated abnormalities. The principle aim is to exclude a DSD, especially in case of concomitant cryptorchidism (2).

Imaging

There are no studies supporting the necessity of performing imaging to detect abnormalities of the urinary tract associated with an isolated hypospadias. Imaging is therefore reserved only to patients with a diagnosed syndrome or DSD (25).

1.7 Clinical characteristics

Anatomy of the hypospadic penis

Meatus: its position defines the severity of hypospadias. It may be located at every level of the penile shaft, from the glans to the perineum. The more lately occurs the growth arrest during the gestation, the more distal will be the hypospadias (Figure 11).

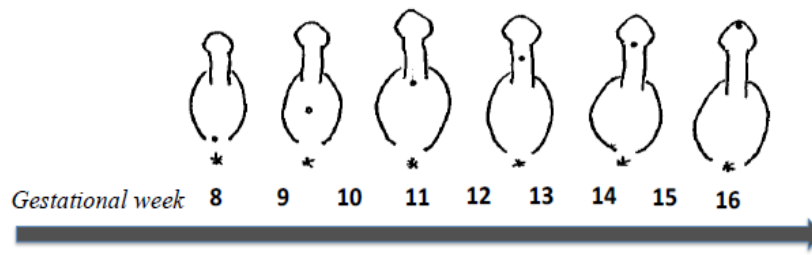


Fig. 11. Position of the meatus according to the gestational week.

Glans: according to the characteristics of the urethral groove, it could be cleft, incomplete cleft, flat.

Prepuce: it is generally hypoplastic on the ventral surface and superabundant on the dorsal surface; there may also be dysmorphisms of the raphe.

Urethral plate: it represents the dorsal aspect of the urethra. A correct assessment is possible only in the operating room, and it defines the surgical strategy. (Figure 12).

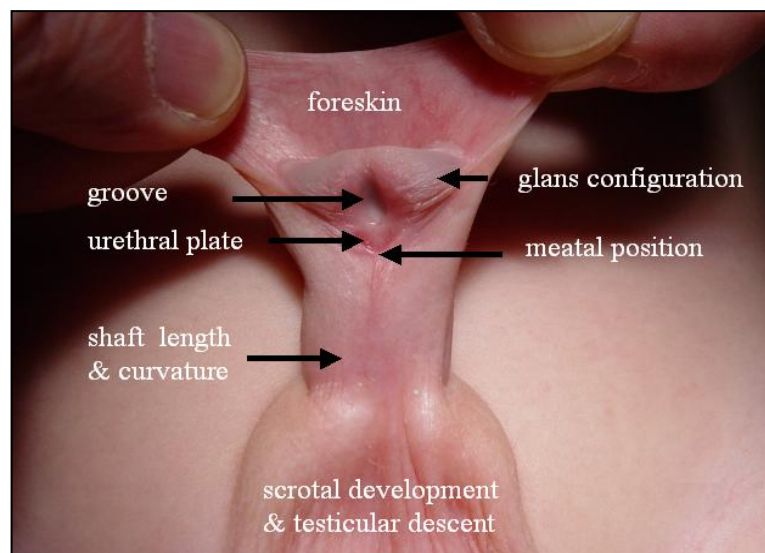


Fig. 12. Anatomical characteristics of an hypospadiac penis.

Ventral curvature of the penis: it could be due to cutaneous abnormalities or to corporal/urethral hypoplasia (Figure 13). It is more frequent in the proximal forms of hypospadias, but could also manifest independently from hypospadias. Studies

on fetuses have led to the comprehension that curvature is a normal phase of the penile development. It is therefore normal that fibrosis (known as chordee) is not always associated with curvature (18) (29). Snodgrass et al (30) supported this theory analyzing biopsies of the urethral plate: they documented the presence of a well vascularized connective tissue composed of smooth muscular cells and collagen, without fibrous or dysplastic tissue. (30) Baskin et al (29) found well vascularized connective tissue underneath the epithelial surface of the urethral plate in a 33 weeks fetus with distal hypospadias.

Devine and Horton described three types of “chordee” without hypospadias. In type I, the most severe defect, corpus spongiosum is hypoplastic from the apex of the curvature to the glans, and urethral mucosa is subtle. In type II, corpus spongiosum is normal, but the covering layers (Buck’s fascia and dartos) are not. In type III, only dartos fascia is abnormal.



Fig.13. *Ventral curvature of an hypospadiac penis.*

Length of the penile shaft: it is frequently documented a short penis [normal dimensions of a neonatal penis are between 3.1 and 4.7 cm] (Figure 14).



Fig.14. *Brevity of the shaft.*

Hypoplasia of corpus spongiosum: as for the urethra, it results incomplete, divergent, and ventrally open. The apex of the divergence may be at the level of the meatus or even more proximally. In the most severe cases, a peno-scrotal transposition may be associated. (Figure 15).



Fig.15. *Peno-scrotal transposition.*

Classification of hypospadias

Hypospadias is classified according to the severity of the malformation, that corresponds to the position of the external urethral orifice: distal (60-65%), mid shaft (20-30%), proximal (10-15%)³⁰ (28) (Figures 16-17).

Smith 1938	Schaefer 1950	Avellan 1975		Browne 1938	Duckett 1996	Hadidi 2004	
1st degree	Glanular	Glanular		Glanular	Glanular	Glanular	
				Sub-coronal	Sub-coronal	Sub-coronal	
				Distal penile	Distal penile	Distal penile	Distal
2nd degree	Penile	Penile		Mid shaft	Mid shaft	Mid shaft	
				Proximal penile	Proximal penile	Proximal penile	
				Penoscrotal	Penoscrotal	Penoscrotal	
				Midscrotal	Midscrotal	Midscrotal	
3rd degree	Perineal	Perineal		Perineal	Perineal	Perineal	Perineal
		Penoperineal					
		Perineal					
		Perineal w/o Bulb					
					Scrotal	Scrotal	
					Perineal	Perineal	
						Proximal	

Fig.16. Classification of hypospadias according to the position of the external urethral orifice.



Fig. 17. Clinical classification of hypospadias: a) distal b) mid shaft c) peno-scrotal d) scrotal e) perineal

This classification system, however, does not consider the quality of the urethral plate, the eventual division of the corpus spongiosum, and the grade of curvature.

A complete evaluation of all these characteristics can be done only in the operating room (21) (Figure 18).

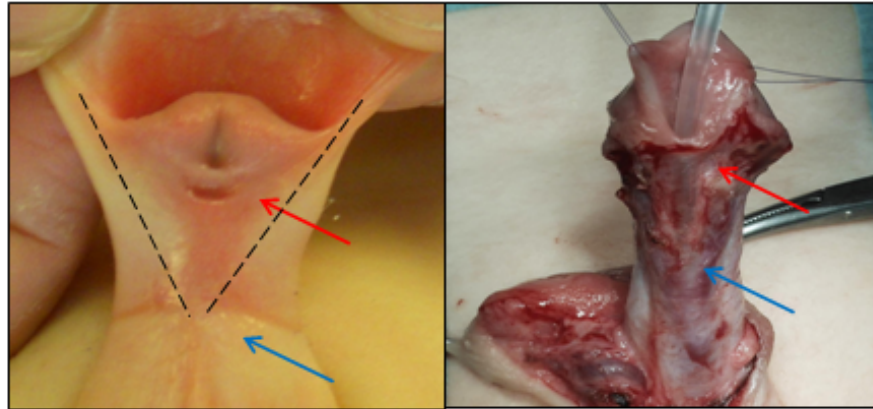


Fig. 18. Intra-operative evaluation. Blue arrow = divergence of the corpus spongiosum. Red arrow = hypospadiac meatus.

Associated abnormalities

8 - 10% of newborn with hypospadias presents an undescended testis, whereas 9 - 15% has an inguinal hernia. In case of proximal forms of hypospadias, the rate of associated cryptorchidism is up to 32%. The incidence of chromosomal anomalies is higher (22%) in this group of patients than in patients with isolated hypospadias (5-7%) or cryptorchidism (3-6%).

Prostatic utricle

Prostatic utricle is a structure that originates cranially from the müllerian ducts, and caudally from wölfian ducts and from the urogenital sinus. Children with hypospadias frequently present a dilated utricle, that may alterate the urinary flow, with consequent infections of the lower urinary tract, stones, pseudo-incontinence. Devine et al. Demonstrated, by means of cystoscopy, that 57% of patients with perineal hypospadias, and 10% of patients with peno-scrotal hypospadias, had a dilated prostatic utricle.

Disorders of sexual development (DSD)

Though hypospadias is considered a form of arrest in the masculinization process, it is distinguished from DSD. Defects in testosterone production, or in its conversion into DHT, or in AR activity, may be found in patients with hypospadias. In presence of both hypospadias and cryptorchidism, the risk of DSD is higher. Kaefer and colleagues reported a DSD in 50% of patients with hypospadias and non-palpable testis. The most frequent finding is a myxth gonadal dysgenesis, followed by ovotestis DSD, incomplete androgens insensibility, deficiency of 5 α -reductase type 2 and testicular dysgenesis. The concomitance of hypospadias and cryptorchidism may be also explained by low weight at birth and premature delivery, as documented in a Swedish study.

1.8 Peri-operative considerations

Choice of the correct timing for surgery

This is still a debated matter. Factors to be taken into account are the risks related to general anesthesia, the dimensions of the penis, and the psychological impact.

After six months, anesthesiologic risk doesn't change with age. There are no indications to operate children with hypospadias younger than six months.

Penile growth is very slow in the first years of life. This therefore doesn't represent a reason to wait.

Children usually begin to be aware of their genitalia at about 18 months; moreover, after this age, children are also more active and less collaborative (31). Despite these considerations, a study didn't demonstrate any difference in terms of psychological impact among children who underwent surgery before or after 18 months (32). Children usually don't remember events happened before three years of age, so they won't remember the operation if this will be performed before that period.

Moreover, nowadays attention is paid to reduce hospitalization time, in order to let the child come back home earlier with his parents. Successive follow-up is conducted in an outpatient setting (31).

Actual tendency in Italy is to recommend surgery between 12 and 18 months of age.

Further studies are needed to augment our knowledge about the best timing for surgery.

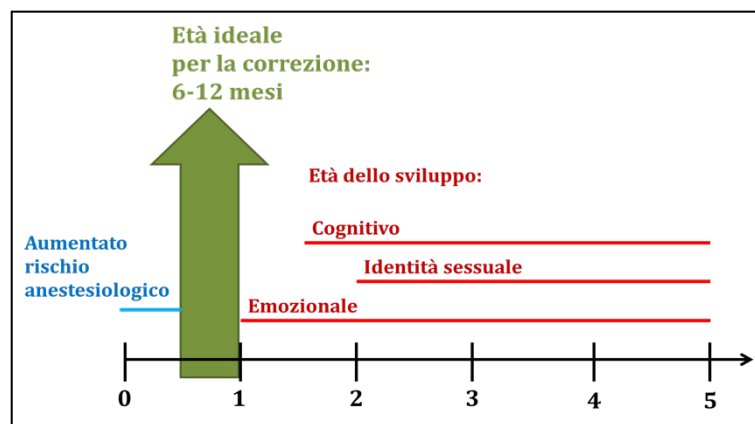


Fig. 19. Choice of the best timing for surgery.

Hormonal therapy

If an hormonal stimulation before surgery is needed, is another debated matter. Data in literature are still lacking.

Stimulation with androgens is usually offered to children with a very short penis, or in case of complex re-operation, with the aim not only to augment the dimensions of the penis, but also its tropism, to ameliorate surgical outcomes.

Testosterone can be administered with intramuscular injections as testosterone enantate, or topically as testosterone propionate. Studies didn't demonstrate any difference between the two modalities in terms of surgical outcomes (33).

1.9 Surgical techniques

The aim of surgery is to obtain a penis with a normally functioning urethra, without curvature, and with the urethral orifice at the apex of the glans (34).

Many techniques have been described, but none of them is considered the gold standard, as the decision is made according to the severity of hypospadias and the surgeon's preference.

Surgical steps for the repair of hypospadias are the following:

1. Degloving of the penile shaft and evaluation of the urethral plate
2. Evaluation of the corpus spongiosum
3. Evaluation and correction of penile curvature
4. Urethroplasty
5. Covering layers
6. Meatoglanuloplasty
7. Scrotoplasty
8. Skin reconfiguration

Correction of the curvature: this step is fundamental, since it represents the key for the surgical success. After the degloving of the penile shaft, an artificial erection is induced, as described by Gittes and McLaughlin in 1974 (Figure 20): it allows the correct evaluation of any residual curvature and its entity, in order to better choose the surgical technique for the repair of hypospadias (35). Ventral curvature may be corrected by liberation of an hypoplastic corpus spongiosum, by section of the urethral plate, or by correction of corporal curvature.

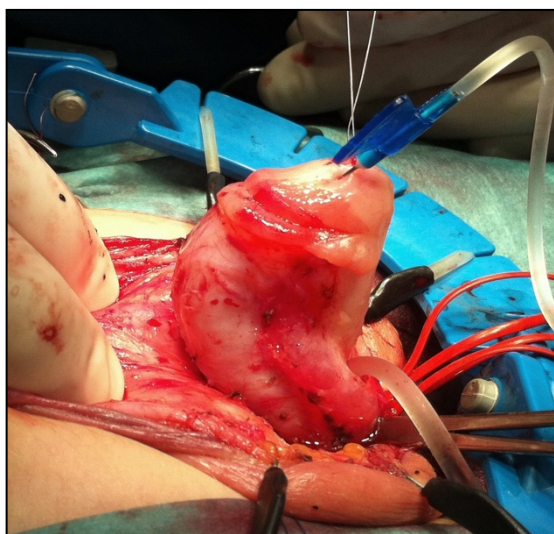


Fig. 20. Intra-operative artificial erection.

Principal techniques for the correction of penile curvature are:

Nesbit: an Allis clamp is applied at the point of maximum curvature to straighten the erect penis. An ellipse of tunica albuginea of 1 mm per 10° curvature is excised.

TAP (Tunica Albuginea Plication): parallel incisions on the tunica albuginea are made, then sutured with absorbable stitches.

Dorsal midline plication sec. Baskin: multiple plications of the tunica albuginea are made at twelve o'clock.

Urethroplasty: surgical technique is chosen according to the precise location of the meatus after correction of the penile curvature, and the quality of the urethral plate. Urethral plate can be tubularized or widened, with a single-stage or a staged surgery.

Glanduloplasty and meatoplasty: the aim is to obtain a meatus at the apex of a conical-shaped glans.

Skin reconfiguration: in order to allow a correct wound healing, the reconstruction of the subcutaneous and cutaneous layers of the penile shaft is of crucial importance. If feasible, a spongioplasty is recommended to cover the neo-urethra. It should be utilized vital and well vascularized skin, eventually with the Byars flaps technique.

About three hundred techniques for urethroplasty have been described. We will mention the most utilized ones in our Institution.

TIP (Tubularized Incised Plate) sec. Snodgrass. It is applied to distal forms of hypospadias. Longitudinal incision of the urethral plate along the midline allows the widening and the successive tubularization of the urethral plate on a catheter. The incision starts at the level of the ectopic meatus, and extends distally to the presumptive location of the neo-meatus. In case of curvature requiring an extended

liberation of the urethral plate, TIP should be performed with caution, in order to avoid any damage to the vascularization of the urethral plate (Figure 21).

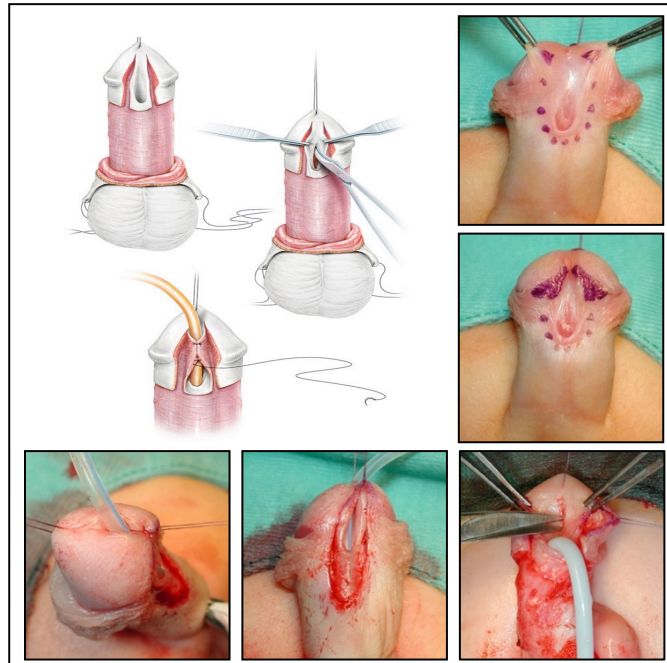


Fig. 21 Snodgrass technique.

Tubularized incised plate with dorsal inlay graft (Snodgraft). It is a variant of the classical Snodgrass technique described by Ferro, in those cases when the urethral plate results non sufficiently wide to be tabularized. Both prepuce and buccal mucosa can be utilized as a graft to cover the defect and allow the urethral plate widening (Figure 22).

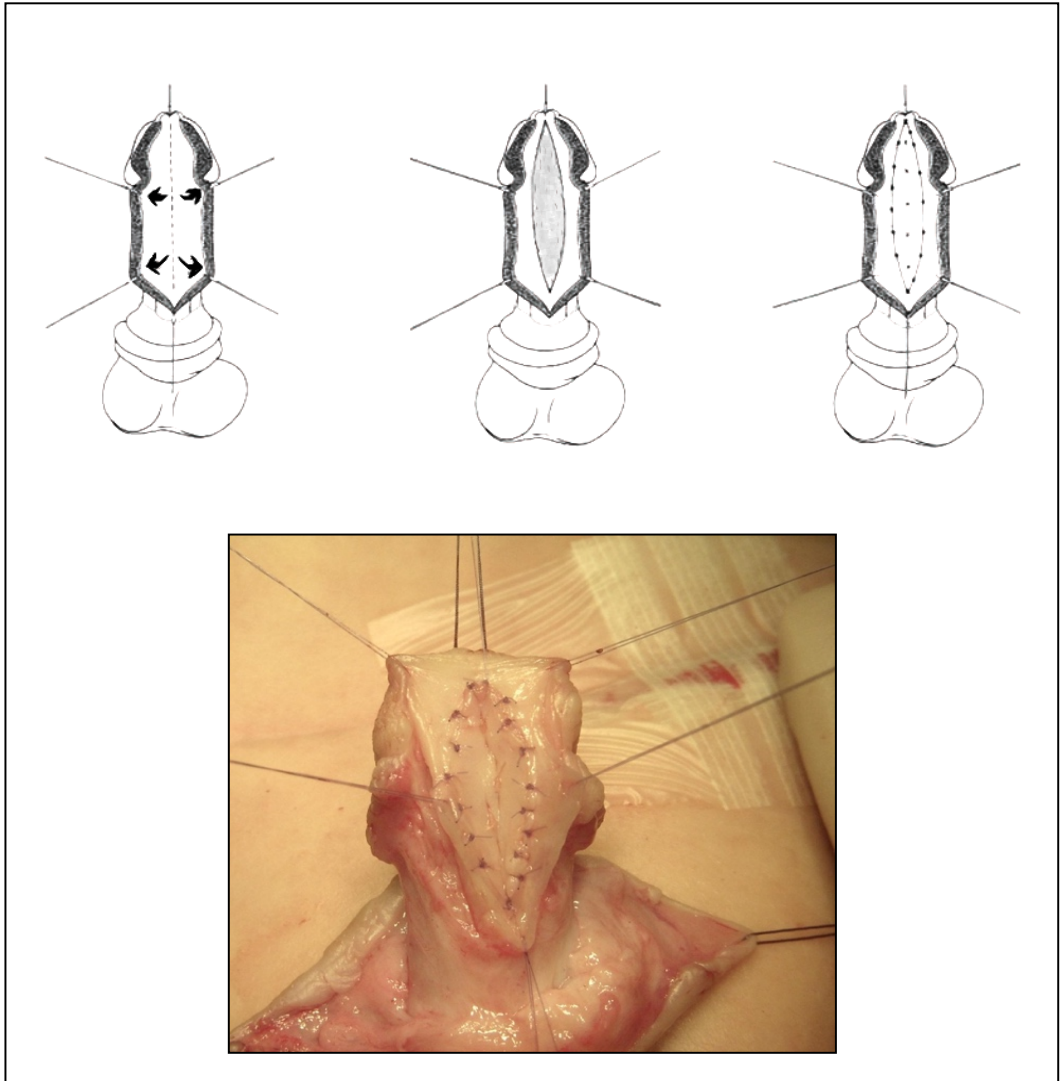


Fig. 22 Snod-graft technique.

Onlay island flap. This technique consists in ventral trans position of a preputial flap to constitute the roof of the neo-urethra (Figure 23).

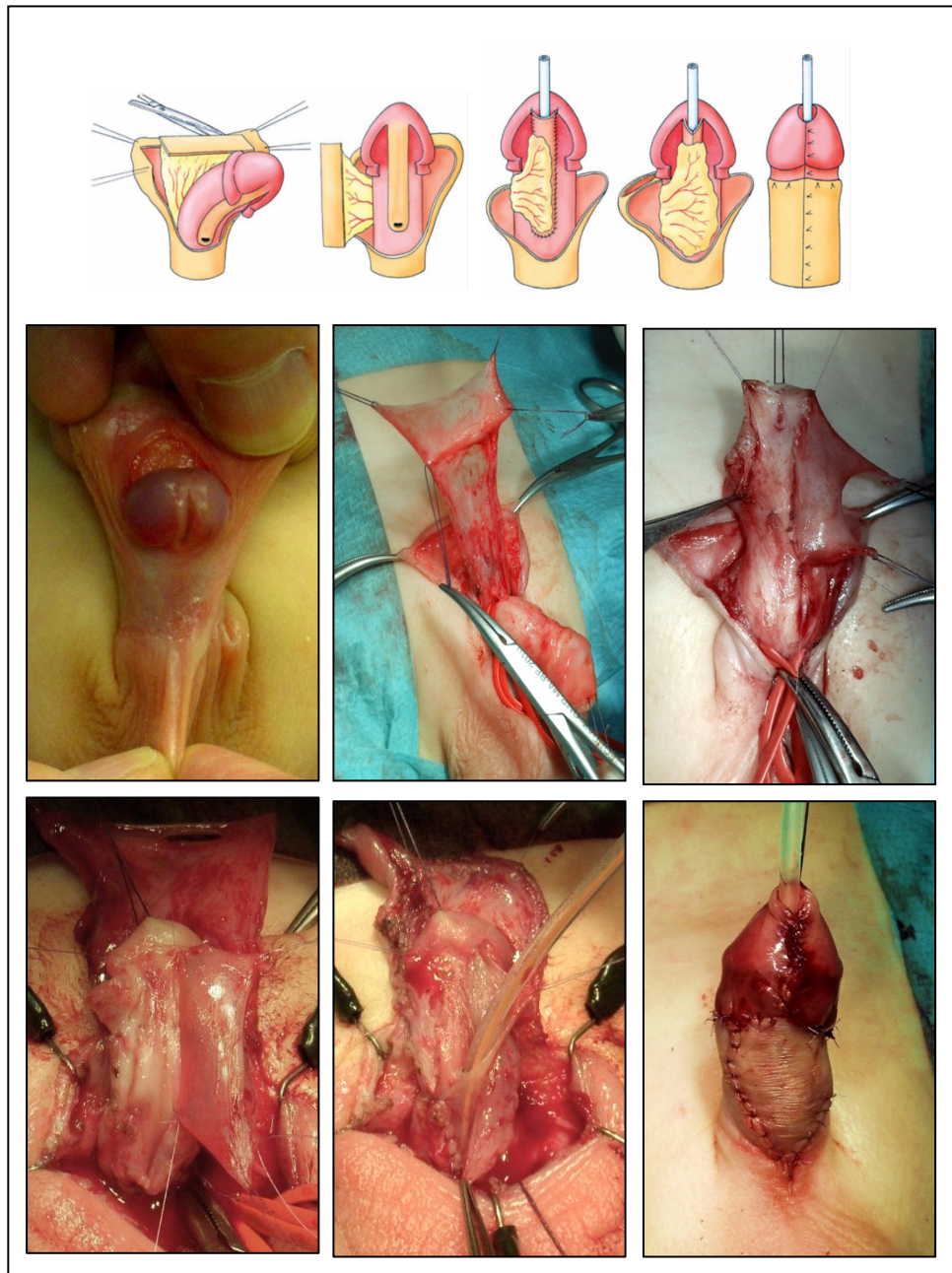


Fig. 23 Onlay island flap technique.

Onlay on albuginea. A preputial flap is directly sutured on the tunica albuginea surrounding the corpora cavernosa.

Double faced onlay. When the skin over the penile shaft is not sufficient to warren a good result of the cutaneous ventral plasty, dorsal prepuce can be preserved with the respective tubularized mucosa, and together ventrally transposed, so without the need of a cutaneous ventral plasty.

Bracka two-stage urethroplasty. In case of severe hypospadias with notable curvature, a complete resection of the urethral plate and its entire substitution may be necessary. Single-stage techniques have a too high complication rate, so, in latest eighties, Bracka modified the two-stage technique initially described by Nové-Josserand.

During the first stage, curvature is corrected, the urethral plate is incised and widened by means of apposition of a preputial or buccal mucosal flap (Figure 24).

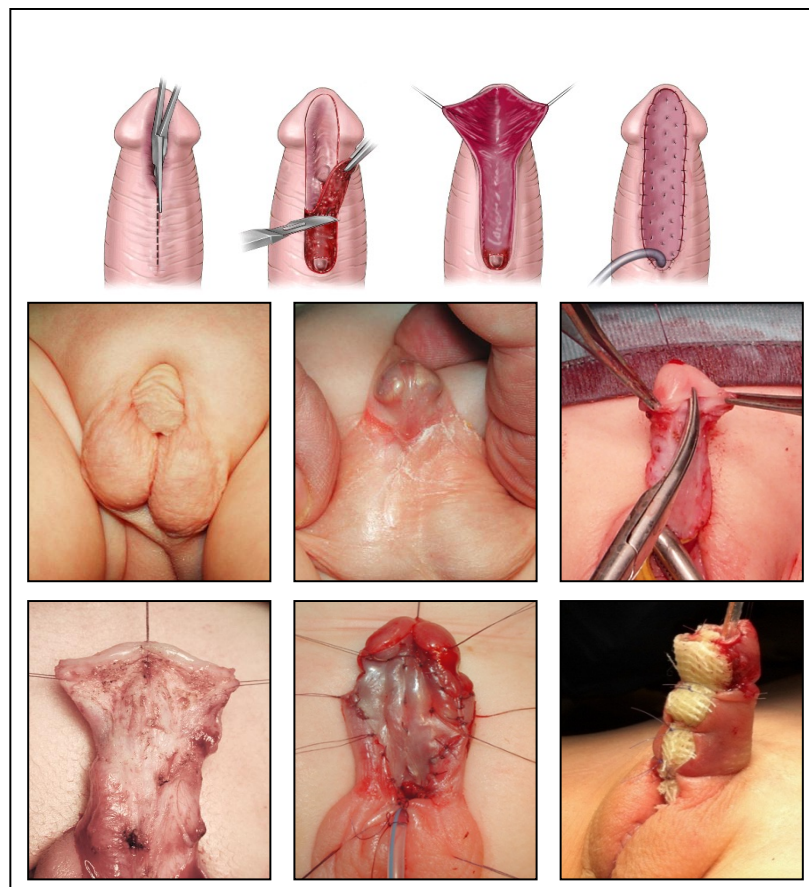


Fig. 24 First stage of Bracka urethroplasty.

An adequate engraftment is fundamental for the second stage to be successful, and 4-6 months are needed. In the second stage, urethral plate is laterally incised, and then tubularized (Figure 25).

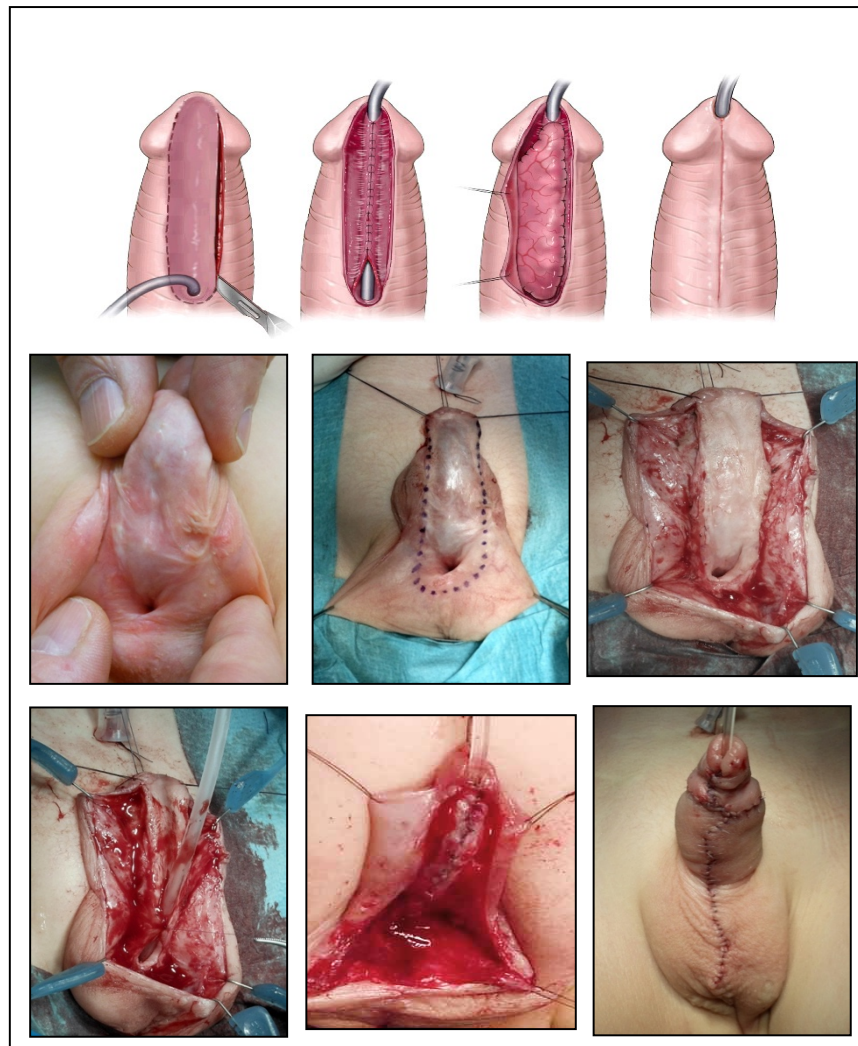


Fig. 25 Second stage of Bracka urethroplasty.

1.10 Surgical results

Complications

Infections are rare after surgery for hypospadias. A single dose antibiotic prophylaxis is given to all patients with an indwelling catheter.

Obstruction of the catheter, or bladder spasms may occur.

The most frequent complications are: urethro-cutaneous fistula, stenosis of the neomeatus, urethral stenosis with a distal urethral diverticulum, glans dehiscence, a not satisfying esthetic result. They may require a re-operation (35).

Urethro-cutaneous fistula is the most common complication after hypospadias repair (Figure 26). Its incidence ranges from 0,5 and 20%, according to the surgical technique. Once fistula occurs, 6-12 months generally pass before a re-operation is performed. Fistulas are commonly excised, sutured and covered by several layers (7) (36).

The second most frequent complication is stenosis (meatal or urethral), even if surgical advances have significantly reduced its incidence. Stenosis may also occur due to Lichen Sclerosus, manifesting with difficulties in bladder emptying, infections and incontinence. Clinical examination, uroflowmetry and ultrasound generally lead to a correct diagnosis.

Urethral dilation or diverticula, less common complications, may also be due to the presence of a distal stenosis (37).



Fig.26 *Urethro-cutaneous fistulas.*

Other post-operative problems, like dehiscence (Figure 27), persistence or recurrence of curvature, and a not satisfying esthetic result, may require a re-operation (36).



Fig.27 Dehiscence.

An adequate evaluation of the post-operative complications is not so easy, since studies generally involve a small number of patients, or compare different techniques, or have a short follow-up (36). Although complications generally occur in the first post-operative months, data from Gent demonstrated that 25% of patients needed a re-operation, with only a 47,37% of them during the first post-operative year, indicating the necessity of a longer follow-up (36).

Esthetic result

Along with surgical advances, esthetic results have been ameliorating over time, but patients and parents satisfaction still remains a problem (37) (38). In several studies lack of satisfaction, especially regarding penile length and curvature, is reported (39) (40). Il follow-up e la valutazione del risultato cosmetico sono quindi cruciali. Several attempts to objectivate surgeons, parents and patients evaluation of the cosmetic result have been done (41) (42). There are two scoring systems: the Hypospadias Objective Scoring Evaluation (HOSE) (43), and the Hypospadias Objective Penile Evaluation (HOPE) (44).

The HOSE score evaluates the location of the meatus, its shape, urinary stream, erection, eventual presence of fistula; each domain is given a score (1-2 or 1-4), with a final score ranging from 5 to 16. A final score ≥ 14 is considered an acceptable result if the location of the meatus is glandular, if there is a single urinary stream, and if the penile shaft is straight during erection (44).

The HOPE score is a validated instrument that includes all the surgically reparable elements, i.e. the location of the meatus, its shape, glans shape, penile skin and penile shaft. A urologist compares the surgical result with the image of a penis taken as reference (44).

Also patient's satisfaction is important. Weber et al. Developed and validated an instrument to evaluate patients satisfaction about the esthetic result, both for children (pediatric PPS) and for adults (Penile Perception Score, PPS) (43) (45). The score system is composed of four elements: meatal position and shape, glans shape, skin surrounding the penile shaft, general aspect of the penis.

Functional result

Even though some studies about functional results after urethroplasties have been published in the last years, data are still lacking (36).

Patients with hypospadias generally show abnormal uroflowmetries, compared to age-adjusted nomograms defined by the International Children's Continence Society (ICCS).

Some studies underline the importance of post-operative functional studies, showing a tendency toward improvement over time.

A recent systematic review recommends to perform a uroflowmetry after the achievement of continence. Children with obstructed or borderline flows should be followed up until adulthood (36).

Neither the position of the hypospadiac meatus nor the surgical technique are considered a negative prognostic factor for the recovery of a good urinary function. The severity of penile curvature, instead, seems to be correlated to functional outcomes (36).

Sexual function and quality of life

This is a very awkward topic, difficult to be evaluated.

There are some studies comparing patients with hypospadias to a control group about psycho-sexual aspects, such as sexual desire, erection quality and duration, penile general aspect, dimensions and curvature, ejaculation, masturbation and sexual intercourses with a partner, general satisfaction with sexual life. These data show that patients who underwent surgery for hypospadias, generally have a satisfactory sexual life (36).

However, there are some differences among patients and controls. In particular, patients who underwent surgery for the repair of hypospadias, are generally worried about their penile aspect and dimensions. The more severe hypospadias is, the more unsatisfying the long-term result is, and a better sexual life seems to be related to a better esthetic result (36). Recent data show a relatively high incidence of erectile dysfunction and premature ejaculation.

Generally speaking, these studies underline the importance of a long-term follow-up until young adulthood.

Transitional Hypospadiology

For many adult urologists, during their residency, pediatric urology and transitional urology should part of their training, but the exposure to these field is always quite limited. Reconstructive urology fellowships, focus primarily on restoring urologic functions that have been compromised by congenital, traumatic and iatrogenic conditions. Reconstructive urologists as pediatric urologist learn skills in bladder augmentation, creation of continent catheterizable channels, methods of urinary diversion and in urethral surgery.

Hypospadias is usually treated early in life, if not it will persist into adulthood, causing varying degrees of bother ranging from none at all to severe decrements in sexual and quality of life. Patients with a history of surgery for hypospadias can present to adult urology clinics with numerous issues and the most common of which are lower urinary tract symptoms or sexual dysfunction do to urethral

stricture, urethrocutaneous fistulas, persistent ventral curvature. Management of urethral strictures, urinary tract fistula, erectile dysfunction, penile curvature and acquired buried penis amongst other conditions should be always referred to high volume reconstructive urology.

These patients are reluctant to leave their pediatric facilities, multidisciplinary clinics, and trusted surgeons who have cared for them throughout the course of their lifetime. When they need to refer to adult urologist or try to, they have to find a tertiary referral center and it is the first major barrier given to the limited number of center in each country. This first barrier and others numerous ones, over the course of their lives, are the reason why they prefer to leave the follow-up.

This study come from the need to report long-term follow-up data concerning the adult population who underwent a urethroplasty in pediatric age because long term outcomes are still full of lack in the literature (41).

2. MATERIALS AND METHODS

The present study is a national multicentre retrospective observational study.

2.1 Study population

Institutions involved in the study

Our study group included consecutive cases from two Italian high volume and experienced Paediatric Urology Institutions: the Division of Pediatric Urology, IRCCS Ca' Granda Foundation, Policlinic of Milan and the Division of Pediatric Urology, University of Padua.

Timing of data collection and overall inclusion period

The principal investigator, between June 1st 2021 to October 1st 2022, retrospectively collected variables, in a database designed before the beginning of the study and approved by the local ethics committee (n°5716). The overall inclusion period of the study was between January 1st 1984 to January 1st 2002.

Data collection

Variables were collected retrospectively, by the principal investigator, from patient's paper or electronic medical records and from retrospective or prospective database or by patient's interview.

The investigator is accountable for the data collection and their accuracy.

Inclusion and Exclusion criteria

Inclusion and exclusion criteria were decided before data collection and they were applied on the collected data before statistical analysis was performed.

Inclusion criteria

Adult men (older than 18 years) who underwent a urethroplasty for hypospadias repair before 18 years old, were included. We decided to use 18 years old subjects, as maximum age to be included in the study, because MEDLINE® uses the range of "birth-18" to define a patient as "Child".

Patients were selected upon all the type of urethroplasty performed in the two centre for primary hypospadias repair.

Exclusion criteria

We exclude all the patients younger than 18 years old at the beginning of the study and patients treated in other centre than Milan and Padua.

For statistical analysis we exclude patients who answered incomplete to the questionnaires.

2.2 Study protocol

A prior study protocol with a time-line and a database to collect variables were wrote and discussed at the beginning of the PhD protocol.

Assessment of risk of bias

The risk of selection bias, as in every retrospective study, were the difficult to: find the exposed subject, find telephone numbers or e-mails and the poor motivation to participate in the study.

The first risk of bias of this study was the difficult to find all the exposed subject due to the possible lack in data from paper or electronic medical records.

The most important risk of bias of this study was the difficulty in finding patient contacts.

Furthermore, the risk of selection bias, as in any study based on the administration of questionnaires, may be due to the fact that patients in a condition of well-being are less motivated than those with problems or dissatisfaction with the aesthetic result to respond to questionnaires and to present themselves for the follow-up clinical visit.

In the way to ensures that selection bias were avoided, selection criteria were well defined from the beginning of the study and subjects were motivated to perform both a medical and psychological consultation on a date and time most suited to them.

Ethical approval

In all the European country all studies which will involve people as participants need a research ethics committee review. Retrospective research is conducted on already available data and/or biologic material, but ethics approval is necessary. The main criteria to be considered are that data must be anonymous for statistical analysis, ethics committee must approve the study, and if there is a contact with the subjects, family doctor and patients must be informed. Patients have to sign a consents at the beginning of the study.

Following the Italian law an ethics committee approval was obtained in Milan with the protocol number: 5716.

Documents are available in the Hospital website: www.policlinico.mi.it.

Dataset

Patients were selected consecutively, by the principal investigator, from paper or electronic medical records and from retrospective or prospective database available in the two centre.

Available data were collected in the database.

Phone numbers or e-mails were searched with considerable difficulty in the online hospital and regional database.

First contact (telephone contact)

The respective parents or caregivers or patients were contacted by telephone and informed about the studies.

The parents/caregivers/patients who consented to the study by providing an e-mail address subsequently received an email with the link for the questionnaires, presented in a Google form format, to be filled independently by the patient, after having read the information and given informed consent to data processing.

A short interview was conducted by telephone in order to obtain as many variables as possible.

All the documentation available was also requested to be sent by e-mail or brought to the clinical examination.

On-line Validated Questionnaires

Validated questionnaires were selected to investigate aspects as quality of life, sexual function and penile perception.

Questionnaires about quality of life

Short Form Health Survey 36 (SF-36)

The Short Form Health Survey 36 (SF-36) is a 36-item, patient self-reported survey about health status (46). The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. The lower the score the more disability. The higher the score the less disability i.e., a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability.

The eight domain of health are :

- Limitations in physical activities because of health problems.
- Limitations in social activities because of physical or emotional problems
- Limitations in usual role activities because of physical health problems
- Bodily pain
- General mental health (psychological distress and well-being)
- Limitations in usual role activities because of emotional problems
- Vitality (energy and fatigue)
- General health perceptions.

Beck Depression Inventory (BDI-II)

The Beck Depression Inventory (BDI) is a 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression. It is one of the most widely used psychometric tests for measuring the severity of depression.

The BD I-II was a revision of the BDI (47). The BDI-II was revised in 1996 to be more consistent with DSM-IV criteria for depression.

The BDI-II is widely used as an indicator of the severity of depression, but not as a diagnostic tool, and numerous studies provide evidence for its reliability and validity across different populations and cultural groups.

BDI-II contains 21 questions, each answer being scored on a scale value of 0 to 3. Higher total scores indicate more severe depressive symptoms. The standardized cutoffs used differ from the original:

- 0–13: minimal depression
- 14–19: mild depression
- 20–28: moderate depression
- 29–63: severe depression.

State Trait Anxiety Inventory Form Y (STAI-Y1 e STAI-Y2)

The State Trait Anxiety Inventory (STAI) is a commonly used measure of trait and state anxiety consisting of 40 self-report items (48).

It can be used in research or clinical settings to diagnose anxiety and to distinguish it from depressive syndromes.

The Form Y 1-2 is the most recent version and it has 20 items for assessing trait anxiety and 20 for state anxiety. State anxiety (S-anxiety) can be defined as fear, nervousness, discomfort, etc. and the arousal of the autonomic nervous system induced by different situations that are perceived as dangerous. This type of anxiety refers more to how a person is feeling at the time of a perceived threat and is considered temporary.

Trait anxiety (T-anxiety) can be defined as feelings of stress, worry, discomfort, etc. that one experiences on a day to day basis. This is usually perceived as how people feel across typical situations that everyone experiences on a daily basis.

All items are rated on a 4-point scale. Higher scores indicate greater anxiety. The STAI requires a sixth grade reading level.

Symptom Checklist-90-R (SCL-90-R)

The Symptom Checklist-90 (SCL-90) is a 90-item questionnaire self-report psychometric instrument used to assess psychological problems. The Symptom Checklist-90-Revised (SCL-90-R) is the revised version of the questionnaire. The revised version is almost identical (2 questions with slightly different wording). It is designed to evaluate a broad range of psychological problems and symptoms of psychopathology. It is also used in measuring the progress and outcome of psychiatric and psychological treatments or for research purposes and It is one

of the most widely used measures of psychological distress in clinical practice and research.

It consists of 90 items and takes 12–15 minutes to administer, yielding nine scores along primary symptom dimensions and three scores among global distress indices. The three indices are global wellness index, hardiness, and symptom free (49).

Multi Attitude Suicide Tendency Scale (MAST).

The Multi-Attitude Suicide Tendency Scale (MAST) was designed to assess suicidal tendencies in youth. This 30-item scale has four types of attitudes: attraction to life, repulsion by life, attraction to death, and repulsion by death. (50)

Questionnaires about sexual activities

The International Index of Erectile Function: (IIEF-15)

The 15 questions International Index of Erectile Function (IIEF) questionnaire is a validated, multi-dimensional, self-administered investigation that is used in the clinical assessment of erectile dysfunction and treatment outcomes in clinical trials. The IIEF addresses the relevant domains of male sexual function:

- erectile function (A,1-5, 15),
- orgasmic function (B,9,10),
- sexual desire (C,11,12),
- intercourse satisfaction (D,6-8),
- overall satisfaction(E,13,14).

A score of 0-5 is awarded to each of the 15 questions. Analysis of the questionnaire should, therefore, be viewed as an adjunct to, rather than a substitute for, a detailed sexual history and examination. The following guide-lines may be applied:

- Patients with low IIEF scores (<14 out of 30) in Domain A (Erectile Function) may be considered for a therapy unless contraindicated.
- Patients demonstrating primary orgasmic or ejaculatory dysfunction (Domain B) should be referred for specialist investigation.

- Patients with reduced sexual desire (Domain C) require testing of blood levels of androgen and prolactin.
- Psychosexual counselling should be considered if low scores are recorded in Domains D and E but there is only a moderately lowered score (14 to 25) in Domain A (51) (52).

Multidimensional Sexuality Questionnaire (MSQ)

The Multidimensional Sexuality Questionnaire (MSQ) was designed to measure psychological tendencies associated with sexual relationships. MSQ is a self-report instrument designed to measure 12 aspects of the sexual self-concept. The MSQ included those tendencies measured previously by the Sexuality Scale and the Sexual Awareness Scale, and it included several new subscales designed to assess control-related aspects of the sexual self-concept (e.g., personal sexual control, powerful-other sexual control, chance/luck sexual control). Factor analysis and reliability analyses confirmed the adequacy of the psychometric properties of the Multidimensional Sexuality Questionnaire (MSQ) (53).

Male Sexual Health Questionnaire (MSHQ)

The Male Sexual Health Questionnaire (MSHQ) is a 25-item self-administered questionnaire for assessing erection, ejaculation, and satisfaction in men. It was designed to be culturally sensitive and age appropriate. The MSHQ assesses sexual function and satisfaction in men also with urogenital symptoms of LUTS and sexual dysfunction. This new instrument has excellent psychometric properties and is well suited for use in clinical and research settings (54).

Questionnaires about penile perception

Hypospadias Objective Scoring Evaluation (HOSE)

The Hypospadias Objective Scoring Evaluation (HOSE) is a validated scoring system that incorporates the evaluation of meatal location and shape, urinary stream, straightness of erection, presence and complexity of urethral fistula (43).

Meatal location was described as being predominantly in the distal glans, proximal glans, coronal or more proximally on the penile shaft, and scored from 4 to 1. Meatal shape was classified as either a vertical slit or circular, and scored 2 or 1. Urinary stream, assessed with the child voiding, was described as either a single stream or spray, and scored 2 or 1. Erection was gauged after an erection witnessed by the assessor or based on a parental evaluation using the following guidelines: straight, mild angulation ($<10^\circ$), moderate angulation ($>10^\circ$ but $<45^\circ$), and severe angulation ($>45^\circ$), with corresponding scores from 4 to 1. Finally, any fistula was documented and further classified as sub-coronal or more distal, proximal or multiple/complex, with scores from 4 if absent to 1 if multiple or complex.

The minimum total score is 5, and the maximum total score is 16. The point score is graded as either acceptable or not. Inter-observer variation using the HOSE system was minimal, supporting its use as an objective outcome measure after hypospadias surgery, and facilitating an impartial evaluation of operations used in correcting hypospadias.

HOSE - Hypospadias Objective Scoring Evaluation

Assessor:

Patient:

Date:

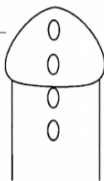
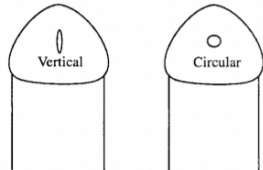
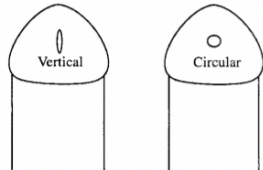
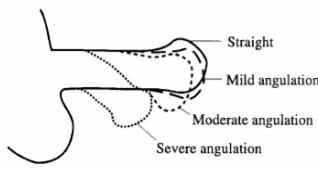
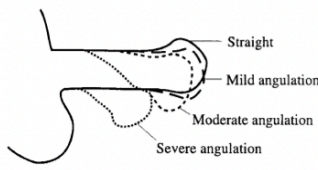
Variable	Score	Diagram
1. Meatal location		
Distal glanular	4	
Proximal glanular	3	
Coronal	2	
Penile shaft	1	
2. Meatal Shape		
Vertical slit	2	
Circular	1	
3. Urinary Stream		
Single stream	2	
Spray	1	
4. Erection		
Straight	4	
Mild angulation (<math>< 10^\circ</math>)	3	
Moderate angulation ($> 10^\circ$ but <math>< 45^\circ</math>)	2	
Severe angulation ($> 45^\circ$)	1	
5. Fistula		
None	4	
Single - subcoronal or more distal	3	
Single - proximal	2	
Multiple or complex	1	
Total		

Fig.28 The HOSE assessment form.

The Pediatric Penile Perception Score (PPPS)

The Pediatric Penile Perception Score (PPPS) is a reliable instrument to assess penile self-perception in children after hypospadias repair, and for appraisal of the surgical result by parents and uninvolved urologists (45). The PPPS was developed and evaluated in a cross-sectional study on the psychosexual development and health-related quality of life of children and adolescents with hypospadias because no instrument was available before to objectively assess the surgical outcome and self-perception after hypospadias repair. Patient express their satisfaction for every single item according to a 4-point Likert scale, which included the ratings of very dissatisfied (0 points), dissatisfied (1), satisfied (2) and very satisfied (3). The PPPS

was calculated by adding the scores of the items meatus, glans, shaft skin and general appearance.

APPENDIX 1

		very satisfied	satisfied	dissatisfied	very dissatisfied
Interview child					
We will talk about several aspects of your penis. Please tell me how satisfied you are with these. There are four possible answers: Very satisfied, satisfied, dissatisfied, very dissatisfied. Please tell me which one is the most appropriate for you.					
a	Length of your penis	<input type="checkbox"/> (3)	<input type="checkbox"/> (2)	<input type="checkbox"/> (1)	<input type="checkbox"/> (0)
b	Position and shape of your urethral opening	<input type="checkbox"/> (3)	<input type="checkbox"/> (2)	<input type="checkbox"/> (1)	<input type="checkbox"/> (0)
c	Shape of your glans	<input type="checkbox"/> (3)	<input type="checkbox"/> (2)	<input type="checkbox"/> (1)	<input type="checkbox"/> (0)
d	Shape of your penile skin	<input type="checkbox"/> (3)	<input type="checkbox"/> (2)	<input type="checkbox"/> (1)	<input type="checkbox"/> (0)
e	Penile axis (straightness upon erection)	<input type="checkbox"/> (3)	<input type="checkbox"/> (2)	<input type="checkbox"/> (1)	<input type="checkbox"/> (0)
f	General appearance of your penis	<input type="checkbox"/> (3)	<input type="checkbox"/> (2)	<input type="checkbox"/> (1)	<input type="checkbox"/> (0)

Fig.29 The PPS assessment form.

Satisfaction In Genital Hypospadias Treatment (S.I.G.H.T.)

The Satisfaction In Genital Hypospadias Treatment (SIGHT) is a validated scoring system, with 9 items, which investigate the patient's satisfaction with the result of the surgery, the appearance of his penis, the functionality of his penis and the size of his penis (55). The SIGHT investigated whether the patient believes that his penis is normal, if he feel limited in his masculinity and sexuality, if he hide his penis on public occasions (e.g. gym locker rooms), if he is afraid of being laughed for the appearance of his penis. Answers are given using a scale of 1 (complete disagreement) to 5 (complete agreement). The first five questions are positive, the second four negative. The points are assigned inversely in the four negative questions to calculate a score the higher the more positive the result. The three final

additional questions concern the patient's sexual activity, the frequency and age of initiation of sexual intercourse.

Urological evaluation

Once the on-line questionnaires were completed on the Google platform, the patients were contacted for a urological evaluation.

The urological evaluation consisted in:

- reconstruction of the urological history;
- clinical inspection of the urological system;
- uroflowmetry;
- HOPE questionnaire by a resident and a fully trained urologist compiled independently.

Hypospadias Objective Penile Evaluation (HOPE)

The Hypospadias Objective Penile Evaluation (HOPE) score is the first scoring system that fulfills the criteria of a valid measurement tool: objectivity, reliability and validity. These favorable properties support its use as an objective outcome measure of the cosmetic result after hypospadias surgery (44). The HOPE-score incorporates all relevant surgically correctable items in hypospadias and uses important elements of objectivity. The HOPE-score can help to identify aspects of the operative procedure that need critical attention, enabling surgeons to adopt techniques associated with optimal cosmetic outcomes.

1. Position meatus: assess the position of the meatus?
See HOPE-score reference pictures

- Position 1 (10 points)
- Position 2 (8 points)
- Position 3 (5 points)
- Position 4 (3 points)
- Position 5 (1 point)

2. Shape meatus: what is the shape of the meatus?
See HOPE-score reference pictures

- Normal (10 points)
- Slightly abnormal (7 points)
- Moderately abnormal (4 points)
- Severely abnormal (1 point)

3. Shape glans: what is the shape of the glans?
See HOPE-score reference pictures

- Normal (10 points)
- Slightly abnormal (7 points)
- Moderately abnormal (4 points)
- Severely abnormal (1 point)

4. Shape Skin: what is the shape of the penile skin?
See HOPE-score reference pictures

- Normal (10 points)
- Slightly abnormal (7 points)
- Moderately abnormal (4 points)
- Severely abnormal (1 points)

5.1 Torsion: is there a torsion of the penis?
See HOPE-score reference pictures

- 0–30° (10 points)
- 30–50° (7 points)
- 50–70° (4 points)
- >70° (1 points)

5.2 Curvature in penile erection: is there a curvature of the penis in erection?
See HOPE-score reference

- No erection observed (5.2 does not account for the HOPE-score)
- 0–30° (10 points)
- 30–50° (7 points)
- 50–70° (4 points)
- >70° (1 point)

Hypospadias Objective Penile Evaluation (HOPE)-score = mean number of points question 1–5.

Fig.30 *The HOPE assessment form.*

2.3 Outcomes

The primary aim of the project was to determine the overall complication rate, in a long follow-up, in men who underwent a urethroplasty in the paediatric age for hypospadias repairs.

The secondary aim of the study was to determine the long term functional, cosmetic results and the psychological impact of urethroplasty for hypospadias repair in the adult patients.

Postoperative complications

Postoperative complications were defined as events occurred after surgery. We considered in this category the most common reported in literature: dehiscence, urethral fistula or stenosis.

Definition of complications

Dehiscence and fistulas were clinically assessed by inspection.

Stenosis at any level of the urethra was suspected in case of micturition problems prolonged over time, pathologic uroflowmetry (in continent children), recurrent urinary infections, and confirmed by under sedation urethroscopy.

2.4 Variables

Different parameters were collected and classified into demographic (date of birth and age at first surgery, ethnicity, geographical area of birth, sexual orientation, marital status, educational and employment status), pre-operative (external urethral meatus site), intra-operative (type of surgery and additional procedure), post-operative characteristics (number of complications, type of complication, number and type of procedure needed to correct complication, date of the last urological evaluation), questionnaires data and score, data collected during the urological evaluation (uroflow parameters).

2.5 Statistical analysis

All of the collected data were included in the descriptive analysis, whereas some variables were excluded for the statistical analysis, due to the fact that they were not related to the outcomes of the study. Data of the included patient were presented as categorical data (nominal, divided in binomial or multinomial or ordinal) and as ratio data. Variables were described and reported in tables (summarised in categories, numbers, percentage). A mean, with its standard deviation, was

calculated when data followed a normal distribution whereas a median, with its range (minimum, maximum), was determined when they were non-normal distributed. Parametric statistical tests will chosen for data with a normal distribution and non-parametric tests will performed for data not normally distributed. Descriptive statistics will focus on frequencies and proportions for categorical variables. The statistical significance of differences in medians and proportions will tested with the Kruskal-Wallis and chi-square tests. All statistical tests were two-sided with a significance level set at $p < 0.05$. Data from the univariate analysis.

Statistical Software

Data were analysed using IBM® SPSS® Statistics Base version 25.0 (SPSS Inc., Chicago, IL, USA). It is a statistical analysis software that delivers the core capabilities to lead an analytical process. With this platform, it is possible to access, manage and analyse virtually any kind of structured or unstructured data, including survey and web data, and information in corporate databases.

3. RESULTS

This paper reports preliminary data of the ongoing study.

Nine hundred forty-two patients were identified from paper or electronic medical records and from retrospective or prospective database.

Excluding the patients of whom there was not an updated telephone number; 359 patients met the inclusion criteria. 77 patients (21%) completed the psychological and sexuological tests, 94 (26%) questionnaires about penile perception and only 52 (15%) the urological evaluation.

3.1 Population characteristics

Population characteristics and pre-operative variables are summarized in Table 1.

Population characteristics and pre-operative variables	77 (%)
Median Age at the enrollment (years)	21 (18-35)
Ethnicity: - Caucasian - Not Caucasian	65 (84) 12 (16)
Geographical area of birth: - North Italy - Center Italy - South Italy - Foreign country	69 (89) 3 (4) 3 (4) 2 (3)
Sexual orientation: - Heterosexual - Unknown - Mostly heterosexual	74 (96) 2 (3) 1 (1)
Marital status - Single	57 (74)
Educational qualification - Primary - Secondary - University - PhD	30 (39) 37 (48) 9 (12) 1 (1)
Employment status - Student - Student + Worker - Worker - Unemployed - Volunteer	48 (62) 1 (1) 20 (26) 7 (9) 1 (1)
Hypospadias at birth: - Distal - Midshaft - Proximal - Unknown	36 (46) 12 (16) 16 (21) 13 (17)

Table.1 Population characteristics and pre-operative variables.

3.2 Intra-operative characteristics

Intra-operative characteristics are summarized in Table 2.

Intra-operative variables	77 (%)
Median age at surgery (years)	4 (1-14)
Urethroplasty	
- MAGPI	5 (7)
- TIP	18 (24)
- ONLAY	9 (12)
- Two stage repair (Bracka)	16 (21)
- INLAY	1 (1)
- Others	7 (9)
- Unknown	20 (26)

Table.2 Intra-operative characteristics.

3.3 Post-operative characteristics

Post-operative characteristics are summarized in table 3.

Post-operative variables	77 (%)
Date of the last urological evaluation	14 (2-24)
Complications:	23 (30)
- Fistula	6 (8)
- Stenosis	4 (6)
- Ventral dehiscence	7 (9)
- Recurrent ventral curvature	2 (2)
- Skin defects	4 (5)
Complications (Clavien-Dindo)	23 (30)
- Doesn't require intervention	0 (0)
- Office non-therapeutic intervention	0 (0)
- Minor day surgery	10 (13)
- Major surgical procedure	12 (15)
- Emergency surgical intervention	1 (1)
Surgery for complications*:	36 (47)
- Redo urethroplasty:	11 (15)
- ONLAY	5 (7)
- Two stage repair (Bracka)	6 (8)
- Redo Corporoplasty	2 (2)
- Fistula repairs	6 (8)
- Skin repairs	4 (5)
- Sovrapubic Catheter	2 (2)

Table.3 Post-operative characteristics.

* For some complication was required multiple surgery.

3.4 Results of the questionnaires about quality of life

Preliminary results of the questionnaires about quality of life are summarized in table 4-8.

Short Form Health Survey 36 (SF-36)

Definitive results from the Short Form Health Survey 36 (SF-36) are under evaluation by the psycho-sexologist. To have a complete assessment of the population we need to be correlate questionnaire results with a psychological interview that are still ongoing.

Of the 36-item of the SF-36, data reported in Table 4 could outline a preliminary picture of the general health status of the study population.

The higher score in the most questions outline a perception of low disability and a good general health perceptions of themselves.

Short Form Health Survey 36 (SF-36)	77 (%)
In general, would you say your health is:	
- Excellent	21 (27)
- Very good	36 (47)
- Good	15 (20)
- Fair	5 (6)
- Poor	0 (0)
11) How TRUE or FALSE is each of the following statements for you?	
a. I seem to get sick a little easier than other people:	
- Definitely true	0 (0)
- Mostly true	7 (9)
- Don't know	8 (10)
- Mostly false	16 (21)
- Definitely false	46 (60)
b. I am as healthy as anybody I know:	
- Definitely true	28 (36)
- Mostly true	18 (23)
- Don't know	21 (27)
- Mostly false	7 (9)
- Definitely false	3 (4)
c. I expect my health to get worse:	
- Definitely true	1 (1)
- Mostly true	10 (13)
- Don't know	16 (21)
- Mostly false	16 (21)
- Definitely false	34 (44)
d. My health is excellent:	
- Definitely true	36 (47)
- Mostly true	30 (39)
- Don't know	7 (9)
- Mostly false	4 (5)
- Definitely false	0 (0)

Table.4 Data from SF-36

Beck's Depression Inventory (BDI-II)

The BDI-II as indicator of the severity of depression, (it is not as a diagnostic tool), shown minimal depression in 3 patients (4%) and moderate depression in 3 patients (4%). Severe depression was described in only one patient. (Table 5)

Beck's Depression Inventory (BDI-II)	77 (%)
Level of Depression	
- No depression	70 (91)
- Mild	3 (4)
- Moderate	3 (4)
- Severe	1 (1)

Table.5 Data from BDI-II

State Trait Anxiety Inventory Form Y (STAI-Y1 e STAI-Y2)

Both STAI-Y1 and STAI-Y2, used to diagnose anxiety, outline in one third of patients a mild state of anxiety. (Table 6)

State Trait Anxiety Inventory Form Y (STAI-Y1/Y2)	77 (%)
Total Score Y1 (median)	38 (23-60)
Level of Anxiety Y1 - No Anxiety - Mild - Moderate - Severe	50 (65) 22 (29) 4 (5) 1 (1)
Total Score Y2 (median)	36 (20-69)
Level of Anxiety Y2 - No Anxiety - Mild - Moderate - Severe	45 (59) 24 (31) 4 (5) 4 (5)

Table.6 Data from STAY-Y1/Y2

Symptom Checklist-90-R (SCL-90-R)

Definitive results from the Symptom Checklist-90-R (SCL-90-R) are under evaluation by the psycho-sexologist. To have a complete assessment of the population we need to be correlate questionnaire results with a psychological interview that are still ongoing.

SCL-90 investigates aspects such as somatization, obsessive-compulsive, interpersonal sensivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, sleeping problems. Preliminary data are reported in Table 7.

Symptom Checklist-90-R (SCL-90-R)	77 (%)
Somatization	
- Normal	67 (87)
- Pathological	10 (13)
Obsessive-Compulsive	
- Normal	53 (69)
- Pathological	24 (31)
Interpersonal sensitivity	
- Normal	60 (78)
- Pathological	17 (22)
Depression	
- Normal	61 (79)
- Pathological	16 (21)
Anxiety	
- Normal	71 (92)
- Pathological	6 (8)
Hostility	
- Normal	64 (83)
- Pathological	13 (17)
Phobic anxiety	
- Normal	74 (96)
- Pathological	3 (4)
Paranoid ideation	
- Normal	47 (61)
- Pathological	30 (39)
Psychoticism	
- Normal	64 (83)
- Pathological	13 (17)
Sleeping problems	
- Normal	45 (58)
- Pathological	32 (42)

Table.7 Data from SCL-90-R

Multi Attitude Suicide Tendency Scale (MAST).

The Multi-Attitude Suicide Tendency Scale (MAST) designed to assess suicidal tendencies has four types of attitudes: attraction to life, repulsion by life, attraction to death, and repulsion by death. The higher median score outline a low attitude to suicide. Only 7 patients (9%) seems to show a pathological tendency to suicide but this data must be refuted by a psychological evaluation. (Table 8)

Multi Attitude Suicide Tendency Scale (MAST).	77 (%)
Attraction to life	3,86 (2-5)
Repulsion by life	2,14 (1-4)
Attraction to death	2,43 (1-4)
Repulsion by death	2,44 (1-5)
Suicide Tendency	
- No	70 (91)
- Yes	7 (9)

Table.8 Data from MAST

3.5 Results of the questionnaires about sexual activities

Results of the questionnaires about sexual activities are summarized in Table 9-11.

The International Index of Erectile Function (IIEF-15)

The questionnaire was administered to all 77 patients but the data shown in the table 9 are only of the 26 (44%) sexual active patients. Of these 26 patients, 85% have not erectile dysfunction whereas 12 have a mild and only one patients a severe erectile dysfunction.

The other areas investigated also demonstrated a high median score except the organic function were the score is lower. (Table 9)

The International Index of Erectile Function (IIEF-15)*	77 (%)
Sexual activity	26 (44)
Erectile function	
- No dysfunction	22 (85)*
- Mild	3 (12)*
- Moderate	0 (0)*
- Severe	1 (3)*
Orgasmic function	
- Positive	13 (50)*
Sexual desire	
- Positive	23 (88)*
Intercourse satisfaction	
- Positive	24 (92)*
Overall satisfaction	
- Positive	20 (77)*

Table.9 Data from IIEF-15; Test was completed by all the 77 patients but (66%) have no sexual activity. *data about the 26 patients with sexual activities

Multidimensional Sexuality Questionnaire (MSQ)

The Multidimensional Sexuality Questionnaire (MSQ) designed to measure psychological tendencies associated with sexual relationships. Definitive results from the MSQ about the study population is under evaluation by the psycho-sexologist. To have a complete view of the population the MSQ need to be correlate with a psychological interview that are still ongoing.

Some dimension investigate with the questionnaire is highlighted in the table 10. Preliminary data seems to show a low anxiety to approach sexual aspects.

Multidimensional Sexuality Questionnaire (MSQ)	77 (%)
I feel anxious when I think about the sexual aspects of my life - Not at all characteristic of me - Slightly characteristic of me - Somewhat characteristic of me - Moderately characteristic of me - Very characteristic of me	 8 (10) 12 (16) 16 (21) 28 (36) 13 (17)
I am afraid of becoming sexually involved with another person - Not at all characteristic of me - Slightly characteristic of me - Somewhat characteristic of me - Moderately characteristic of me - Very characteristic of me	 33 (43) 22 (29) 17 (22) 5 (6) 0 (0)
I am depressed about the sexual aspects of my life. - Not at all characteristic of me - Slightly characteristic of me - Somewhat characteristic of me - Moderately characteristic of me - Very characteristic of me	 30 (39) 21 (27) 14 (18) 10 (13) 2 (3)
I worry about the sexual aspects of my life. - Not at all characteristic of me - Slightly characteristic of me - Somewhat characteristic of me - Moderately characteristic of me - Very characteristic of me	 25 (32) 26 (34) 12 (16) 10 (13) 4 (5)
The sexual aspects of my life are personally gratifying to me. - Not at all characteristic of me - Slightly characteristic of me - Somewhat characteristic of me - Moderately characteristic of me - Very characteristic of me	 15 (19) 21 (28) 14 (18) 18 (23) 9 (12)
I have a fear of sexual relationships. - Not at all characteristic of me - Slightly characteristic of me - Somewhat characteristic of me - Moderately characteristic of me - Very characteristic of me	 33 (43) 23 (30) 14 (18) 7 (9) 0 (0)

Table.10 Data from *MSQ*

Male Sexual Health Questionnaire (MSHQ)

Definitive results from the Male Sexual Health Questionnaire (MSHQ) are under evaluation by the psycho-sexologist. To have a complete assessment of the population we need to be correlate questionnaire results with a psychological

interview that are still ongoing. From the preliminary data reported in table 11 a high number of these young patients (14%) need a medications to achieve an erection. This data is reported indirectly in the second question of the table 11 where 2 patients are not able to get an erection without using drugs six (8%) ha this problem in less than half of the time and 4 (5%) in about half of the time. Anejaculation is reported by 5 patient. More than half of the subjects after all are satisfied by the quality of their sexual life.

Male Sexual Health Questionnaire (MSHQ)	77 (%)
Have you ever taken any medications to achieve an erection in the last month? - Yes	11 (14)
If you are able to get an erection, without using drugs, how often are you able to stay hard as long as you want to? - None of the time - Less than half of the time - About half of the time - Most of the time - All of the time	2 (3) 6 (8) 4 (5) 14 (18) 51 (66)
Are you able to ejaculate when having sexual activity with your partner? - None of the time - Less than half of the time - About half of the time - Most of the time - All of the time	5 (6) 1 (2) 2 (3) 18 (23) 51 (66)
How satisfied are you with the quality of the sex life you have with your main partner? - None of the time - Less than half of the time - About half of the time - Most of the time - All of the time - Missing	9 (12) 11 (14) 15 (19) 6 (8) 8 (10) 28 (37)
How often did you have sexual intercourse? - Never - 1-3 time for month - 4-6 time for month - More than one in a week - Every day	8 (10) 6 (8) 5 (6) 27 (35) 31 (41)
When was the last time you have sexual intercourse? - 1-3 months ago - From more than a year up to 2 years - More than two years ago - Missing	16 (21) 1 (1) 9 (12) 51 (66)
In the last month how often have you felt the desire to have a sexual intercourse? - Never - Rarely - Sometimes - A lot of time - Always	10 (13) 5 (6) 25 (33) 29 (38) 8 (10)

Table.11 Data from *MSHQ*

3.6 Results of the questionnaires about penile perception

Results of the questionnaires about quality penile perception are summarized in table 12-14.

Hypospadias Objective Scoring Evaluation (HOSE)

The Hypospadias Objective Scoring Evaluation (HOSE) incorporates the evaluation of meatal location and shape, urinary stream, straightness of erection, presence and complexity of urethral fistula. Meatal location was distal glans in 23 (45%), proximal glans 23 (45%), coronal 5 (9%) or penile shaft 1 (1%). Meatal shape was vertical in 32 (62%) or circular 20 (29%). Urinary stream, was described as a single stream in 27 (53%) or spray in 25 (47%). Penis was straight in 35 (67%), with mild angulation in 14 (28%), moderate angulation in 2 (4%), and severe angulation in 1 (1%). Finally, any fistula was documented in 47 (93%) and a sub-coronal in 3 (5%), proximal in 2 (2%) and multiple/complex in 0. (Table 12)

Hypospadias Objective Scoring Evaluation (HOSE)	52
Meatal location	
- Distal glandular	23 (45)
- Proximal glandular	23 (45)
- Coronal	5 (9)
- Penile shaft	1 (1)
Meatal shape	
- Vertical	32 (61)
- Circular	20 (39)
Urinary stream	
- Single stream	27 (53)
- Spray	25 (47)
Straightness of erection	
- Straight	35 (67)
- Mild angulation (<10°)	14 (28)
- Moderate angulation (< 10° but >45°)	2 (4)
- Severe angulation (>45°)	1 (1)
Urethral fistula	
- None	47 (93)
- Single – sub-coronal or more distal	3 (5)
- Single – proximal	2 (2)
- Multiple or complex	0 (0)

Table.12 Data from HOSE

The Pediatric Penile Perception Score (PPPS)

In the Pediatric Penile Perception Score (PPPS) Patient express their satisfaction for the meatus, glans, shaft skin and general appearance.

About the meatus position, shape of glans and general appearance of the penis almost all the 52 patients are satisfied or very satisfied. (Table 13)

The Pediatric Penile Perception Score (PPPS)	52
Position and shape of the urethral opening - Very dissatisfied - Dissatisfied - Satisfied - Very satisfied	1 (1) 4 (8) 37 (72) 10 (19)
Shape of the glans - Very dissatisfied - Dissatisfied - Satisfied - Very satisfied	2 (3) 4 (7) 32 (62) 14 (28)
Shape of penile skin - Very dissatisfied - Dissatisfied - Satisfied - Very satisfied	2 (3) 11 (21) 30 (59) 9 (17)
General appearance of penis - Very dissatisfied - Dissatisfied - Satisfied - Very satisfied	1 (1) 7 (14) 34 (66) 10 (19)

Table.13 Data from PPPS

Satisfaction In Genital Hypospadias Treatment (S.I.G.H.T.)

More than half patients present high grade of satisfaction with the aesthetic result of the surgery, the appearance of the penis, the functionality of their penis. Lower but still with an high grade of satisfaction was satisfaction about the penis size. Only one patients considered his penis not normal and 2 (2%) fill themselves limited in masculinity and in sexuality. Two had fear to be teased because of their penis and 4 (8%) to show the penis in public.

Median age of the first intercourse was 17 (16-22). (Table 14)

Satisfaction In Genital Hypospadias Treatment (S.I.G.H.T.)	52
Satisfied with the aesthetic result - Complete disagree - Mostly disagree - Not known - Mostly agree - Complete agree	0 (0) 2 (3) 7 (13) 27 (53) 16 (31)
Satisfied with the penis appearance - Complete disagree - Mostly disagree - Not known - Mostly agree - Complete agree	0 (0) 6 (12) 5 (11) 30 (55) 11 (22)
Satisfied with the penis function - Complete disagree - Mostly disagree - Not known - Mostly agree - Complete agree	0 (0) 2 (3) 10 (19) 25 (48) 15 (30)
Satisfied with the penis size - Complete disagree - Mostly disagree - Not known - Mostly agree - Complete agree	2 (4) 9 (16) 11 (21) 23 (44) 7 (15)
Penis considered normal - Complete disagree - Mostly disagree - Not known - Mostly agree - Complete agree	1 (1) 5 (10) 9 (18) 26 (49) 11 (22)
Feel limited in masculinity - Complete agree - Mostly agree - Not known - Mostly disagree - Complete disagree	2 (2) 4 (7) 8 (15) 22 (42) 16 (34)
Hide to show penis in public (locker room....) - Complete agree - Mostly agree - Not known - Mostly disagree - Complete disagree	4 (8) 11 (22) 8 (16) 16 (29) 13 (25)
Fear to be teased because of penis - Complete agree - Mostly agree	2 (2) 6 (13)

- Not known - Mostly disagree - Complete disagree	10 (20) 20 (38) 14 (27)
Feel restricted in sexuality - Complete agree - Mostly agree - Not known - Mostly disagree - Complete disagree	2 (2) 4 (8) 7 (14) 22 (43) 17 (33)
Sexual activity	22 (43)
Median age of the first intercourse	17 (16-22)

Table.14 Data from SIGHT

3.7 Results from urological evaluation

Hypospadias Objective Penile Evaluation (HOPE)

Median HOPE score was not significantly different between score awarded by a full trained paediatric urology (Senior) and score given by a resident in urology after his/her training in paediatric urology (Junior) (p=0.543). (Table 15)

Hypospadias Objective Penile Evaluation (HOPE)	Senior	Junior	p-value
Median HOPE	41 (24-50)	41 (21-50)	0,543

Table.15 Data from HOPE

Uroflowmetry

Uroflowmetry parameters are summarized in table 16.

No. of patients	52
Uroflowmetry Vol (mL) Qmax (mL/sec) Qave (mL/sec)	225 (130-620) 17,9 (9,2-26,2) 8,95 (4,5-17,6)
Uroflowmetry curve shapes evaluated by F.I. Tower >1.253 Bell $\geq 0.659 \leq 1.253$ Plateaus <0.659	0 (0) 17 (33) 35 (67)

Table.16 Data from Uroflowmetry. F.I.= flow index (56)

During the urological evaluation in 5 (3%) patients were highlighted a complication arising from urethroplasty and unknown to the patients.

In 4 patients a stenosis was suspected by a uroflowmetry and by the urinary voiding history. The diagnosis of stenosis were confirmed by a urethrocytography in 3 and a re-urethroplasty was performed in all these patients. One patient is waiting for urethrocytography to confirm the stenosis.

A fistula was detected in one patient but he doesn't require any surgical repair.

4. DISCUSSION AND CONCLUSIONS

The general principle for hypospadias repair consists in the tubularization of ventral urethral plate, bringing the meatus all the way to the tip of the glans, depending on the presence of associated ventral penile curvature. Such accomplishment can be achieved with a single or staged procedure. Following the surgical correction of hypospadias in childhood, patients are followed up, usually until puberty. Although in literature, there are numerous studies, that evaluate outcomes of the urethroplasty, only few of them that have large sample size, long term follow-up and very few take into account the patient satisfaction.

We identified 942 patient to be enrolled in the project and 359 met the inclusion criteria. In this preliminary manuscript we report less than one third of the potential subject which is, obviously, not the large case series that the study expects to obtain.

The COVID-19 pandemic slowed down for nearly two years the selection and above all the possibility to evaluating the selected subject. As in many Italian hospitals the outpatient clinics were closed and then limited only to patients with non-chronic pathologies for many months. Another major impediment to the regular execution of the study was bureaucracy and the low priority for the ethics committee to approve the present study protocol.

We analyzed our preliminary data, and compared our results to those reported in literature.

Primary outcome and functional outcome

After a median follow-up of 21 years (18-35), we found an overall complication rate of 30%: 7 patient (9%) reported ventral dehiscence, 4 patients (6%) presented meatal/neourethral stenosis, 6 patients (8%) developed a urethrocutaneous fistula, 2 (2%) a recurrent ventral curvature and 4 (5%) skin defects. In addition to these complications reported by the patients, during the urological evaluation, should be take into account the five complication diagnosed at the urological evaluation.

Thus, recalculating the overall complication rate, it is 36% with a higher rate of stenosis 8 (10%) and fistula 7 (9%). The recorded complication rate seems to be higher than those reported in literature. However, our follow-up is longer than the others reported in literature and most of the experienced complications were meatal/neourethral stenosis. (36) (57) Excluding the new case of fistula which had been known to the patient for years, as far as we know, stenosis are the later complication occurring after urethroplasty and a shorter follow-up could not perfectly capture the complete postoperative picture. Indeed, our study could offer some interesting insights regarding this kind of surgery specifically related to late complications. In the final manuscript we will perform a statistical analysis of the data based on the type of hypospadias, the type of urethroplasty and the related complications. From the final data obtained we expect to find many more complications in the proximal hypospadias and in patients undergoing multiple surgery for complications than in the proximal one.

These results will consistent with the literature and the fact that the longer the urethral tract need to be reconstructed, the higher the chance that at a certain place graft take can go wrong with failure as a consequence. (36) (38) (57) (37) (58)

In addition to the complication rate, we also evaluated the functional outcome performing uroflowmetry, which is an established, simple and non-invasive investigation that is used to evaluate lower urinary tract dysfunction in an outpatient setting. Unfortunately the literature is sparse on urinary function after long-term follow-up for hypospadias surgery. On uroflowmetry the maximal urinary flow rate is widely accepted as a useful parameter for assessing an individual's voiding function. Qmax is largely dependent on the volume voided and, thus, nomograms have been developed to establish expected flow rates especially in pediatric populations (59) (58) (58).

After hypospadias surgery the flow shape on uroflowmetry was observed by Hammouda (60), Kaya (61) and Anwar (62) et al, who found that bell-shaped curves were present in 94%, 82% and 80% of voids. Furthermore, these studies showed that there was a higher proportion of plateau-shaped curves compared to the normal population. Evaluation of the literature on medium-term follow-up yielded conflicting results. Malyon (59), Marte (63), Hammouda (60) and Anwar (62) et al demonstrated that after medium-term follow-up of these boys, Qmax was lower compared to that in the normal pediatric nomograms. However, In the hypospadias cohort there was no significant association with LUTS and poor urinary flow. The significance of a plateau flow pattern is not known, because there are no reports of the long-term follow-up of asymptomatic patients with obstructive flows.

These considerations are echoed by the results of this study: median Qmax was 17,9 (9,2-26,2) ml/sec; median Qaverage was 8,95 ml/sec(4,5-17,6); median voided volume was 225 (130-620). A significant post-voiding residual was found in none of the patients. Uroflowmetry curve shape was evaluated by the F.I. an was Tower in 0 patient, bell in 17 (33%) and Plateau 35 (67%).

Quality of life questionnaires

Our study tried to detect quality of life and satisfaction from aesthetic and functional point of view, making use of internationally validated questionnaires and some single questions asked through a Google form, which was sent by mail or asked during the urological evaluation.

Starting from the analysis of the quality of life questionnaires, at the moment the data are partial, we found higher score in a lot of questions, This outline a perception of a good general health status of our patients.

Conducting a literature search it was not possible to identify, for many questionnaires, articles reporting data on patients treated for hypospadias. Normally, especially in urology, these tests are used in populations undergoing surgery for oncological reasons. These data do not allow us to compare our results with those of oncological patients.

Another important factor that could influence the comparison between the data of the present study and those of the literature is that part of the questionnaires were completed during the COVID-19 pandemic.

Analyzing the SF-36 questionnaire, twenty-one (27%) defined their health excellent, 36 (47%) very good and 15 (20%) good. Only five. (6%) defined their status of health as “fair” none poor.

The BDI-II that should outline case and grade of depression, (not as a diagnostic tool), confirms a good overall state of mental health with a minimal depression in 3 patients (4%) and moderate depression in 3 patients (4%). Severe depression in described in only one patient.

A mild grade of anxiety was outlined in one third of patients with both STAI-Y1 and STAI-Y2. Delfino et al in a recent systematic review and meta-analysis of over 2 millions of people during the COVID-19 pandemic included 194 studies with a prevalence of anxiety of 35.1 % (63). Therefore, if we compare the state of anxiety reported by Delfino et al with our population, it turns out to be comparable with STAI-Y1 (35%) and slightly lower with STAI-Y2 (41%).

The SCL-90 with its multiple fields of investigation underline in the mayor percentage of the population a normal condition without pathological condition.

These data need to be correlate to the other questionnaires and with a psychological investigation.

The MAST with four types of attitudes: attraction to life, repulsion by life, attraction to death, and repulsion by death had higher median score in attitudes outline and low attitude to suicide. Only 7 patients (9%) seems to show a pathological tendency to suicide but this data are only indicative of a possible discomfort which must be confirmed by a specialist in the phycological field.

Sexual activities questionnaires

The prevalence of erectile dysfunction (ED) is mainly studied in older males, whereas we measured prevalence of ED in young males after penile surgery.

Rosen et al. developed and validated the International Index of Erectile Dysfunction (IIEF-15), which was subsequently translated and validated in many countries (52).

Rynja et al determined the prevalence of ED (using the IIEF) in a young, healthy male population (64). The population selected by Rynja has a median age and range of 21,8 (17-35) years, similar to ours 21 (18-35) years.

Of 137 patients enrolled in the Rynja's study 81% reported to have an intimate relationship whereas in our study group the percentage is much lower (26%).

ED appeared to be present in 33.6% of subject in Rynjas cohort whereas in ours is much lower (15%) with mild grade in 3 patients (12%) and in one severe (3%).

We also decided to explore the psychological aspect of the sexual relationships because we believe in a multidisciplinary treatment, in which medical treatment should be combined with a psychological approach, if a subject shown a sexual disease (65). There is increasing evidence that psychological treatments of sexual disease can improve medical treatments, the patient's adherence to treatment, and the quality of the sexual relationship.

Dewitte and al consider depression and anxiety as important psychological factors. Excessive levels of anxiety may strengthen the focus on erectile failure and performance demand, which are core elements in the pathogenesis of ED (65).

Vedovo et al that study sexual function during social restrictions for COVID-19 pandemic in Italy showed that men who had spent the lockdown period alone or

with friends or relatives other than partner reported higher IIEF-15 scores than participants quarantined with their partner and/or children (66).

Preliminary data about MSQ questionnaire seems to show a low anxiety to approach sexual aspects and an overall normal sexuality in our population.

In our apparent male sexual health population, MSHQ questionnaire, outline that more than half of the subjects are satisfied by the quality of their sexual life but there was an high number of young patients (14%) that need a medications to achieve an erection. Two patients are not able to get an erection without using drugs, six (8%) had this problem in less than half of the time and 4 (5%) in about half of the time. Anejaculation is reported by 5 patient.

The psychological and sexual impact of COVID-19 restrictions and the consequent concerns due to the changes in daily habits and interpersonal relationships have revealed above all a reduction in the frequency of sexual intercourses and an expansion of the sexual repertoire by incorporating new activities such as sexting, new sexual positions, and sharing sexual fantasies (67).

Vedovo et al that investigated the longitudinal changes in sexual function during social restrictions for COVID-19 pandemic in Italy used the BDI-II, the SF-36 and IIEF-15. The questionnaires were administered to 2692 participant (1104 men) at three time points over the pandemic period. In men, good levels of physical health at the beginning of the pandemic were found to be the only predictor of sexual function improvement as the lockdown period continued. At the end of social restrictions Vedovo et al observed an overall improvement of sexual function in both genders. This result was quite predictable, as these men, with the end of the restrictions, were able to meet their sexual partners again with a positive impact on their sexual satisfaction. Being young and having good mental and physical health during the lockdown period were found to be predictive factors of improved male sexual function 1 month after the end of restrictions. Even in this measurement, for men, physical health appears to impact sexuality (66).

Penile Perception questionnaires

Starting from the analysis of the cosmetic results (SIGHT questionnaire), the satisfaction with the appearance of the penis, detected in our patients, was about 77% and the subjects who believe that their penis is normal was 71%, that is in line with the literature. Rynja et al, in their systematic review, on long term result in post-pubertal men after hypospadias repair in childhood, described a satisfaction rate, with the appearance of their penis, in more than 70% cases (68).

Regarding penis size satisfaction, it was 59% of cases apparently lower if compared with the result of the other aspects assessed by the questionnaire, but consistent with literature. Indeed, a large 2006 study by Lever et al (25,594 men, without any specification of any pathologies or penile correction surgery) found that 45% wanted a bigger penis size (69).

About patient satisfaction with the sexual function of their penis 78% was satisfied or very satisfied, approaching data found in literature, we found a similar percentage (about 80%) as reported by Rynja et al (68).

Not less important was the proportion of patients who complained of the need to hide their penis on public occasions (30%) and with fear of being laughed because of the appearance of their penis (15%), data are consistent with study from the group of Padua (70).

The HOSE questionnaire investigates the aspect of the penis reported by the patient as objectively as possible, the position of the external urethral meatus was distal in 95% of cases, and the shape is reported as vertical in 61% of cases, again in line with what has also been seen in other studies (71).

The patients also declared to perceive their penis as straight with complete absence of curvature in 67% of cases, and with a slight curvature in less than 10° and therefore not to be considered clinically significant in 28% of cases. Approximately 5% of patients report a moderate or severe residual curvature, in line with has been seen in the literature, as reported by Braga et al (72). However, the misleading factor of relying only on what patients and parents report in assessing the degree of residual penile curvature must be kept in mind.

The patients who declared themselves satisfied from the point of view of their urinary function were 53%, this is consistent with the literature where 40% of patients complain with micturition (41).

Finally, the absence of urethrocutaneous fistulas was reported by most of the patients (93%). Therefore, the subjects with residual fistulas, are in line with the incidence of this complication in the literature (57).

Limitations and bias

This study has some limitations. The first and most important limitation of this study is that it is a manuscript containing preliminary data from an ongoing study. The data analysis is therefore incomplete and can only give a partial idea of the population. Furthermore to complete the data analysis, there is also a lack of an evaluation by a psychologist who interprets and correlates the raw data of the questionnaires with each other. The psychologist's assessment is obviously a long process that cannot be concluded in a short period of time and the restrictions of the pandemic period delayed this process by more than a year.

Must be taken into account that we were not able to send the questionnaires to 12 patients because of their parents had never informed their sons about the urethral surgery.

Another major limitation of the study is the lacks of a control group. This problem could be solved by comparing the data obtained with the healthy population or with a similar population (surgeries in the genital area in the same age group) as we did in this manuscript for some data already available.

The risk of selection bias, as in any retrospective study, may be characterized by failing to enroll all patients in the selected population. To mitigate this bias, in addition to cross-referencing data from the personal archives of the surgeons involved, reference will be made to data from previous studies and to the operating room records of the centers involved.

A further risk of selection bias may arise from the difficulty of finding the patients telephone contacts who were treated many many years ago. To mitigate this bias, in addition to referring to telephone contacts on the reports, they will be searched,

in order to find updated contact details, in the online databases of the respective structures.

Furthermore, the risk of selection bias, as in any study based on the administration of questionnaires, may be due to the fact that patients in a state of well-being are less motivated than those with problems or dissatisfaction with the aesthetic result to answer to the questionnaires and to attend the follow-up clinic visit. To mitigate this bias, the subjects eligible for enrollment will be motivated to carry out both a medical and a psychological consultation on a date and time more suitable for them, motivating them to participate in a clinical study that is fundamental for improving the outcomes of patients with the same problems as them.

Conclusions

The overall complication rate seems to be slightly higher than those reported in literature. This could be due to the long follow-up reported in the study, unique in the literature.

Preliminary data show a low anxiety to approach sexual aspects and more than half of the subjects are satisfied by the quality of their sexual life.

Our study highlighted a good satisfaction rate for the cosmetic result, in more than half patients, consistent with the data reported in the literature.

We also conclude that uroflowmetry remains a useful tool in screening and prevent complication in a long term follow-up after hypospadias surgery.

5. BIBLIOGRAPHY

1. Van der Zanden LFM, van Rooij I a. LM, Feitz WFJ, Franke B, Knoers NV a. M, Roeleveld N. Aetiology of hypospadias: a systematic review of genes and environment. *Hum Reprod Update*. 2012 Jun;18(3):260–83.
2. Nordenvall AS, Frisén L, Nordenström A, Lichtenstein P, Nordenskjöld A. Population based nationwide study of hypospadias in Sweden, 1973 to 2009: incidence and risk factors. *J Urol*. 2014 Mar;191(3):783–9.
3. Steven L, Cherian A, Yankovic F, Mathur A, Kulkarni M, Cuckow P. Current practice in paediatric hypospadias surgery; a specialist survey. *J Pediatr Urol*. 2013 Dec;9(6 Pt B):1126–30.
4. Nerli R, Santhoshi P, Guntaka A, Patil S, Hiremath M. Modified Koyanagi's procedure for proximal hypospadias: our experience. *Int J Urol Off J Jpn Urol Assoc*. 2010 Mar;17(3):294–6.
5. Arnaud A, Harper L, Aulagne MB, Michel JL, Maurel A, Dobremez E, et al. Choosing a technique for severe hypospadias. *Afr J Paediatr Surg AJPS*. 2011 Dec;8(3):286–90.
6. Smith null. The history of hypospadias. *Pediatr Surg Int*. 1997 Mar 21;12(2/3):81–5.
7. Canon S, Mosley B, Chipollini J, Purifoy JA, Hobbs C. Epidemiological assessment of hypospadias by degree of severity. *J Urol*. 2012 Dec;188(6):2362–6.
8. Loane M, Dolk H, Kelly A, Teljeur C, Greenlees R, Densem J, et al. Paper 4: EUROCAT statistical monitoring: identification and investigation of ten year trends of congenital anomalies in Europe. *Birt Defects Res A Clin Mol Teratol*. 2011 Mar;91 Suppl 1:S31-43.
9. Fredell L, Kockum I, Hansson E, Holmner S, Lundquist L, Läckgren G, et al. Heredity of hypospadias and the significance of low birth weight. *J Urol*. 2002 Mar;167(3):1423–7.
10. Stoll C, Alembik Y, Roth MP, Dott B. Genetic and environmental factors in hypospadias. *J Med Genet*. 1990 Sep;27(9):559–63.
11. Akre O, Boyd HA, Ahlgren M, Wilbrand K, Westergaard T, Hjalgrim H, et al. Maternal and gestational risk factors for hypospadias. *Environ Health Perspect*. 2008 Aug;116(8):1071–6.

12. Källén B, Finnström O, Lindam A, Nilsson E, Nygren KG, Otterblad PO. Congenital malformations in infants born after in vitro fertilization in Sweden. *Birt Defects Res A Clin Mol Teratol*. 2010 Mar;88(3):137–43.
13. 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.
14. Huhtaniemi I, Alevizaki M. Gonadotrophin resistance. *Best Pract Res Clin Endocrinol Metab*. 2006 Dec;20(4):561–76.
15. McDaniel TV, Martin PA, Struger J, Sherry J, Marvin CH, McMaster ME, et al. Potential endocrine disruption of sexual development in free ranging male northern leopard frogs (*Rana pipiens*) and green frogs (*Rana clamitans*) from areas of intensive row crop agriculture. *Aquat Toxicol Amst Neth*. 2008 Jul 30;88(4):230–42.
16. Rey R, Josso N, Racine C. Sexual Differentiation. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dhatariya K, et al., editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000 [cited 2022 Nov 17]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK279001/>
17. Rey RA, Grinspon RP. Normal male sexual differentiation and aetiology of disorders of sex development. *Best Pract Res Clin Endocrinol Metab*. 2011 Apr;25(2):221–38.
18. Wedell A, Ritzén M, Nordenskjöld A. [Boy or girl? Molecular mechanisms in sex differentiation]. *Lakartidningen*. 2000 Feb 2;97(5):449–57.
19. Holcomb III M. *Ashcraft's pediatric surgery*. 5th ed: Saunders Elsevier; 2010.
20. *Langman's Medical Embryology (Twelfth Edition)* by Sadler, T.W.: Very Good Soft cover (2012) | BMV Bookstores [Internet]. [cited 2022 Nov 17]. Available from: <https://www.abebooks.com/9781451113426/Langmans-Medical-Embryology-Twelfth-Edition-1451113420/plp>
21. Yiee JH, Baskin LS. Penile embryology and anatomy. *ScientificWorldJournal*. 2010 Jun 29;10:1174–9.
22. Blaschko SD, Cunha GR, Baskin LS. Molecular mechanisms of external genitalia development. *Differ Res Biol Divers*. 2012 Oct;84(3):261–8.

23. Hughes IA, Houk C, Ahmed SF, Lee PA, Lawson Wilkins Pediatric Endocrine Society/European Society for Paediatric Endocrinology Consensus Group. Consensus statement on management of intersex disorders. *J Pediatr Urol.* 2006 Jun;2(3):148–62.
24. Massanyi EZ, Dicarlo HN, Migeon CJ, Gearhart JP. Review and management of 46,XY disorders of sex development. *J Pediatr Urol.* 2013 Jun;9(3):368–79.
25. Campbell Walsh Wein Urology - 9780323546423 [Internet]. US Elsevier Health. [cited 2022 Nov 17].
26. Dwyer ME, Salgado CJ, Lightner DJ. Normal penile, scrotal, and perineal anatomy with reconstructive considerations. *Semin Plast Surg.* 2011 Aug;25(3):179–88.
27. Rios LTM, Araujo Júnior E, Nardoza LMM, Rolo LC, Hatanaka AR, Moron AF, et al. Prenatal diagnosis of penoscrotal hypospadias in third trimester by two- and three-dimensional ultrasonography: a case report. *Case Rep Urol.* 2012;2012:142814.
28. Giannantoni A. Hypospadias classification and repair: the riddle of the sphinx. *Eur Urol.* 2011 Dec;60(6):1190–1; discussion 1191-1192.
29. Baskin LS, Ebbers MB. Hypospadias: anatomy, etiology, and technique. *J Pediatr Surg.* 2006 Mar;41(3):463–72.
30. Snodgrass W, Macedo A, Hoebeke P, Mouriquand PDE. Hypospadias dilemmas: a round table. *J Pediatr Urol.* 2011 Apr;7(2):145–57.
31. Manzoni G, Bracka A, Palminteri E, Marrocco G. Hypospadias surgery: when, what and by whom? *BJU Int.* 2004 Nov;94(8):1188–95.
32. Weber DM, Schonbucher VB, Gobet R, Gerber A, Landolt MA. Is there an ideal age for hypospadias repair? A pilot study. *J Pediatr Urol.* 2009 Oct;5(5):345–50.
33. Ververidis M, Dickson AP, Gough DCS. An objective assessment of the results of hypospadias surgery. *BJU Int.* 2005 Jul;96(1):135–9.
34. Adams J, Bracka A. Reconstructive surgery for hypospadias: A systematic review of long-term patient satisfaction with cosmetic outcomes. *Indian J Urol IJU J Urol Soc India.* 2016 Jun;32(2):93–102.

35. Subramaniam R, Spinoit AF, Hoebeke P. Hypospadias repair: an overview of the actual techniques. *Semin Plast Surg.* 2011 Aug;25(3):206–12.
36. Springer A. Assessment of outcome in hypospadias surgery - a review. *Front Pediatr.* 2014;2:2.
37. Mouriquand PD, Persad R, Sharma S. Hypospadias repair: current principles and procedures. *Br J Urol.* 1995 Dec;76 Suppl 3:9–22.
38. Örtqvist L, Fossum M, Andersson M, Nordenström A, Frisén L, Holmdahl G, et al. Long-term followup of men born with hypospadias: urological and cosmetic results. *J Urol.* 2015 Mar;193(3):975–81.
39. Moriya K, Kakizaki H, Tanaka H, Furuno T, Higashiyama H, Sano H, et al. Long-term cosmetic and sexual outcome of hypospadias surgery: norm related study in adolescence. *J Urol.* 2006 Oct;176(4 Pt 2):1889–92; discussion 1892-1893.
40. Jiao C, Wu R, Xu X, Yu Q. Long-term outcome of penile appearance and sexual function after hypospadias repairs: situation and relation. *Int Urol Nephrol.* 2011 Mar;43(1):47–54.
41. Rynja SP, de Kort LMO, de Jong TPVM. Urinary, sexual, and cosmetic results after puberty in hypospadias repair: current results and trends. *Curr Opin Urol.* 2012 Nov;22(6):453–6.
42. Schwöbel MG, Sacher P, Stauffer UG. [Denis-Browne corrective surgery of hypospadias: long-term results]. *Z Kinderchir Organ Dtsch Schweiz Osterreichischen Ges Kinderchir Surg Infancy Child.* 1987 Jun;42(3):157–60.
43. Holland AJA, Smith GHH, Ross FI, Cass DT. Hose: An Objective Scoring System for Evaluating the Results of Hypospadias Surgery: Scoring of Hypospadias Surgery. *BJU Int.* 2001 Aug;88(3):255–8.
44. Van der Toorn F, de Jong TPVM, de Gier RPE, Callewaert PRH, van der Horst EHJR, Steffens MG, et al. Introducing the HOPE (Hypospadias Objective Penile Evaluation)-score: A validation study of an objective scoring system for evaluating cosmetic appearance in hypospadias patients. *J Pediatr Urol.* 2013 Dec;9(6):1006–16.
45. Weber DM, Schönbacher VB, Landolt MA, Gobet R. The Pediatric Penile Perception Score: An Instrument for Patient Self-Assessment and Surgeon Evaluation After Hypospadias Repair. *J Urol.* 2008 Sep;180(3):1080–4.

46. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection.txt.
47. Beck Depression Inventories II .txt.
48. State-Trait Anxiety Inventory (STAI).txt.
49. Psychometric properties of the Italian version of the SCL-90-R.txt.
50. Validation of the Multi-Attitude Suicide Tendency scale in adolescent samples.txt.
51. IIEF.txt.
52. Rosen RC, Cappelleri JC, Gendrano N. The International Index of Erectile Function (IIEF): a state-of-the-science review. *Int J Impot Res.* 2002 Aug;14(4):226–44.
53. The multidimensional sexuality questionnaire: An objective self-report measure of psychological tendencies associated with human sexuality. :29.
54. MSHQ.txt.
55. SIGHT.txt.
56. Franco I, Franco J, Lee YS, Choi EK, Han SW. Can a quantitative means be used to predict flow patterns: Agreement between visual inspection vs. flow index derived flow patterns. *J Pediatr Urol.* 2016 Aug;12(4):218.e1-8.
57. Castagnetti M, El-Ghoneimi A. Surgical management of primary severe hypospadias in children: systematic 20-year review. *J Urol.* 2010 Oct;184(4):1469–74.
58. González R, Ludwikowski BM. Importance of urinary flow studies after hypospadias repair: a systematic review. *Int J Urol Off J Jpn Urol Assoc.* 2011 Nov;18(11):757–61.
59. Malyon AD, Boorman JG, Bowley N. Urinary flow rates in hypospadias. *Br J Plast Surg.* 1997 Oct;50(7):530–5.
60. Hammouda HM, El-Ghoneimi A, Bagli DJ, McLorie GA, Khoury AE. Tubularized incised plate repair: functional outcome after intermediate followup. *J Urol.* 2003 Jan;169(1):331–3; discussion 333.
61. Kaya C, Kucuk E, Ilktac A, Ozturk M, Karaman MI. Value of urinary flow patterns in the follow-up of children who underwent Snodgrass operation. *Urol Int.* 2007;78(3):245–8.

62. Anwar A, Kurokawa Y, Takahashi M, Yamamoto Y, Kanayama HO, Kagawa S. Functional evaluation of one-stage urethroplasty with parametarial foreskin flaps repair of hypospadias using uroflowmetry. *Int J Urol Off J Jpn Urol Assoc.* 2003 Jun;10(6):297–301.
63. Marte A, Di Iorio G, De Pasquale M, Cotrufo AM, Di Meglio D. Functional evaluation of tubularized-incised plate repair of midshaft-proximal hypospadias using uroflowmetry. *BJU Int.* 2001 Apr;87(6):540–3.
64. Rynja S, Bosch R, Kok E, Wouters G, de Kort L. IIEF-15: unsuitable for assessing erectile function of young men? *J Sex Med.* 2010 Aug;7(8):2825–30.
65. Dewitte M, Bettocchi C, Carvalho J, Corona G, Flink I, Limoncin E, et al. A Psychosocial Approach to Erectile Dysfunction: Position Statements from the European Society of Sexual Medicine (ESSM). *Sex Med.* 2021 Dec;9(6):100434.
66. Vedovo F, Capogrosso P, Di Blas L, Cai T, Arcaniolo D, Privitera S, et al. Longitudinal Impact of Social Restrictions on Sexual Health in the Italian Population. *J Sex Med.* 2022 Jun;19(6):923–32.
67. Weybright EH, Palen LA, Caldwell LL, Wegner L, Jacobs JJ, Smith E. Profiles of Adolescent Leisure Motivation and Substance Use in the HealthWise South Africa Research Trial: A Person-Centered Approach. *Leis Sci.* 2020;42(5–6):482–501.
68. Rynja SP, de Jong TPVM, Bosch JLHR, de Kort LMO. Functional, cosmetic and psychosexual results in adult men who underwent hypospadias correction in childhood. *J Pediatr Urol.* 2011 Oct;7(5):504–15.
69. Lever J, Frederick DA, Peplau LA. Does size matter? Men’s and women’s views on penis size across the lifespan. *Psychol Men Masculinity.* 2006 Jul;7(3):129–43.
70. Ludovica D, Bianco M, Pelizzari A, Mandato F, Esposito C, Castagnetti M. Self-reported outcomes after the onset of puberty in patients undergoing primary distal hypospadias repair by the tubularized incised plate technique combined with preputial reconstruction vs. circumcision: A norm related study. *J Pediatr Surg.* 2021 Aug;56(8):1411–6.
71. Thiry S, Saussez T, Dormeus S, Tombal B, Wese FX, Feyaerts A. Long-Term Functional, Cosmetic and Sexual Outcomes of Hypospadias Correction

Performed in Childhood. *Urol Int.* 2015;95(2):137–41.

72. Braga LHP, Lorenzo AJ, Bägli DJ, Dave S, Eeg K, Farhat WA, et al. Ventral penile lengthening versus dorsal plication for severe ventral curvature in children with proximal hypospadias. *J Urol.* 2008 Oct;180(4 Suppl):1743–7; discussion 1747-1748.

*“Se questa scienza che grandi vantaggi porterà all’uomo,
non servirà all’uomo per comprendere se stesso,
finirà per rigirarsi contro l’uomo.”*

Giordano Bruno,
(Nola, 1548 – Roma, 17 febbraio 1600)