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Being born small for gestational age (SGA) might be associated with a higher reoperation rate in proximal hypospadias

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Extended Summary

Purpose

Being born small for gestational age (SGA) is associated with a higher frequency and more severe forms of hypospadias as well as with potential developmental differences. This study aims to characterize operative outcomes in SGA boys compared to boys born with normal weight and length for gestational age (appropriate/large for gestational age, AGA/LGA).

Methods

Demographic data, hypospadias characteristics, associated pathologies and operative outcomes of boys who underwent hypospadias repair at a single center (10/2012-10/2019) were evaluated. Boys were categorized into SGA and non-SGA, which were then compared using unpaired t-tests and chi square tests. To examine the effect of SGA on reoperative risk, a logistic regression model was applied integrating surgical technique, meatal localization and complex hypospadias (narrow glans/plate, curvature, micropenis, bilateral cryptorchidism).

Results

SGA boys accounted for 13.7% (n=80) of the total cohort (n=584) and 33% of all proximal hypospadias (n=99, SGA vs. non-SGA 41.3% vs. 13%, p<0.001). After a mean follow-up of 18.6 months the reoperation rate for all hypospadias was 17.9% (n=105). In distal hypospadias there was no difference in reoperation rate between SGA and AGA/LGA boys (p=0.548, multivariate regression model). For each meatal localization in proximal hypospadias SGA was a significant, independent factor predicting higher reoperation rates (p=0.019, OR 3.21) in a logistic regression model. **Figure.**

Discussion

Hypospadias surgery carries a substantial risk for unplanned reinterventions. Apart from meatal localization, there are only a few factors (urethral plate quality, glandular diameter, curvature) reported in literature to be associated with reoperative risk. Intrauterine growth retardation associated with SGA might lead to not only a higher probability of proximal hypospadias but also contribute to a higher risk for complications mediated by developmental differences. Whether these findings could help to tailor surgical strategies or

adjuvant measures, as for example the application of preoperative hormonal stimulation remains to be determined in future studies.

This study is limited by being a single-center series with limited follow-up resulting in some complications probably not yet detected – however, in the same extent in both groups.

Conclusion

Based on this study, 33% of all proximal hypospadias cases occur in boys born SGA. While the reoperation rate in boys with distal hypospadias was not influenced by SGA status, SGA proved to be an independent predictor of a higher risk of reoperation in those with proximal hypospadias. After validation of these findings in other centers, this could be integrated into counseling and risk-stratification.

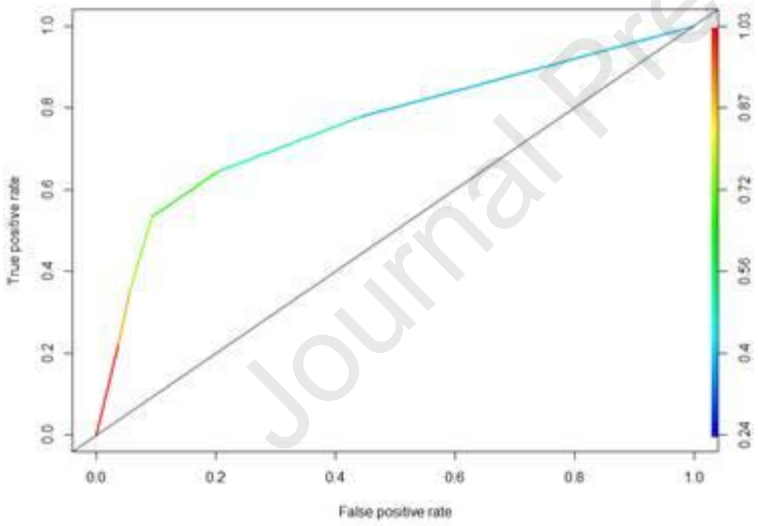

Figure ROC curve for the influence of SGA on the reoperation rate of proximal hypospadias in a multivariate analysis controlling for meatal localization, complex hypospadias, surgical technique and androgen pretreatment

Key words: hypospadias, small for gestational age, postoperative complications;

Introduction

Hypospadias is one of the most common congenital malformations in boys, affecting 0.3-0.8% of all male live births with a mean incidence of 168/10000 in Europe[1]. Matching the timeframe for urethral development, its etiological events take place during early embryogenesis, between gestational week (GW) 7-24[2]. Potential causative factors include genetic alterations as well as environmental factors which, most likely as a result of gene-environment interactions, leading to the development of the hypospadias phenotype[3]. Besides these factors, also low birthweight or premature birth are associated with a higher hypospadias incidence[4]. Birthweight or length below -2SD (standard deviations) compared with the norm for a given gestational age is referred to as small for gestational age (SGA)[5]. Boys born SGA have been described as having a higher risk of developing hypospadias, and more proximal forms compared with boys with normal weight and length for gestational age [6–9]. Furthermore, the intrauterine growth retardation associated with being SGA is linked to developmental differences leading to genetic alterations as well as physiological changes [10-12]. This might ultimately affect wound healing and thus impact complication rates after surgery.

Whilst previous studies have demonstrated an epidemiological link between hypospadias and SGA, this study takes a detailed look at SGA in a hypospadias cohort with an emphasis on reoperation risk.

We hypothesized that SGA might be associated with a higher risk for complications and reoperations independently of other potential predisposing factors.

Patients and Methods

After approval of the study protocol by the local ethics committee (EK Nr 1046/2020) data were assessed retrospectively including all boys who underwent hypospadias surgery at a single department for pediatric urology between 10/2012 and 10/2019 (n=820). Following exclusion of documentation errors (n=43) and patients with incomplete or equivocal data on gestational age at birth (term), birth length or birth weight (n=181) as well as those with known syndromes (n=7) or differences in sex differentiation with known chromosomal abnormalities (XY/X0, XXY - DSD, n=6), 584 patients remained for further analysis. DSD patients had been diagnosed by a multidisciplinary panel based on genetic tests including karyotyping, hormone assays and/or histology (e.g. streak gonads, ovotestis). **Figure 1.**

Descriptive parameters like age at surgery, term, weight and length at birth as well as weight and length at admission for hypospadias surgery and duration of follow-up were recorded.

Table 1.

The SD (standard deviation) quotients to classify patients into appropriate for gestational age (AGA, >-2SD and <+2SD for weight and length for gestational age), small for gestational age (SGA, <-2SD for weight and / or length at term) and large for gestational age (LGA, >+2SD for weight and / or length at term) were calculated.

The length of follow-up was defined as the duration from surgery to the last documented exam by one of the staff members associated with the department. All families were invited to report back and schedule a visit in case of concerns about the success of the operation or suspicion of an obvious complication.

In addition, pregnancy related complications, detailed characteristics of the hypospadias including grade of curvature, width of the urethral plate and quality of the urethra (dysplastic urethra without corpus spongiosum proximal to the meatus) as well as associated anomalies were collated.

Furthermore, any kind of postoperative complication was assessed. Complications other than minor cosmetic alterations prompting an indication for a re-intervention formed the main endpoint of this analysis.

To take account of the many associated anomalies and additional features of the hypospadias potentially influencing complication risks, the category “complex hypospadias” was defined as patients integrating at least two features of the following: glans diameter <14mm[13], narrow urethral plate <8mm[14], ventral deviation (>30°) requiring surgical correction or urethral plate dissection, associated micropenis (defined as penile length below -2SD) or bilateral cryptorchidism.

Except glans diameter, which was measured in the outpatients department to eventually indicate a preoperative androgen treatment, all above mentioned parameters including meatal localization were recorded during surgery using a standardized protocol including photographic documentation.

Dihydrotestosterone (DHT) Gel (Laboratoire Besins International, Montrouge, FR) containing 2.5% DHT is recommended as per institutional standard over 6 weeks and stopped 4 weeks prior to surgery for all patients with a narrow glans (<14mm, measured by use of a caliper), with significant curvature (>30) and all proximal forms (proximal penile, scrotal and perineal)[15]. However, as per parental preference and individualized decision making as well as adverse events (pain in few cases) it was not applied in all of the above-mentioned cases. Ultimately, it was applied in 13.1% of all distal hypospadias and 57.6% of all proximal cases. **Table 1.**

The surgical technique (foreskin resection with or without meatal advancement, MAGPI – meatal advancement and glanduloplasty, TIP – tubularized incised plate urethroplasty, Mathieu, staged repair, Duckett Onlay) used was at the discretion of the operating surgeon. While patients with a distal meatal localization (coronar, distal penile and many proximal penile cases) underwent mostly TIP urethroplasties, scrotal and perineal hypospadias and those with curvature >30-45° and shortened, dysplastic urethra underwent staged procedures as per institutional consensus[16].

All proximal hypospadias surgeries were performed by 5 different FEAPU (Fellow of the European Board of Pediatric Urology) trained urologists with at least 2 years in practice and at least 200 hypospadias surgeries performed before. Distal hypospadias were partly performed by fellows in training for FEAPU with assistance of an experienced surgeon.

Data were extracted from the local hospital information system (SAP SE, Walldorf, BW, Germany) and entered into a Microsoft (Redmond, WA, USA) Excel® sheet. Patients were pseudonymized by use of hospital track numbers for further processing of data.

Statistical analysis was performed using descriptive statistical methods, parametric (t-test) and non-parametric tests (Chi square test) for comparison of subgroups using SPSS Version 27 (IBM Corporation, Armonk, NY). To examine the effect of SGA on reoperation risk, a logistic regression model with logit link function was applied, integrating SGA vs. AGA/LGA, meatal localization and the presence of complex hypospadias using R-Statistics (www.r-project.org) version 4.0, function glm.

Results

Meatal localization and detailed features of the hypospadias, surgical technique

In this cohort, 79.1% (n=462) were born AGA, 7.2% (n=42) LGA and 13.7% (n=80) SGA. Proximal hypospadias was present in 41.3% of SGA boys and 13.2% of AGA/LGA boys (p<0.001). Of all boys with proximal hypospadias included (n=99), 33% (n=33) were born SGA. **Table 1.** SGA boys were more likely to have a narrow urethral plate (18.8% SGA vs. 8.2% AGA/LGA, p<0.001) but there was no significant difference as to the occurrence of ventral curvature >30° (23.8% SGA vs. 16.2% AGA/LGA, p=0.087). Complex hypospadias (as defined above) were present in 19.6% (n=115) of all patients (32.5%, n=26 of all patients born SGA (n=80) vs. 17.6%, n=89 patients born AGA/LGA (n=462), p=0.002). Boys with an SD Score of weight or length of less than 3 (severely SGA, n=32) did not have an even higher risk of proximal hypospadias compared to those with SGA SD score between -2 and -3 (n=40, p=1). A total of 7 different surgical techniques have been used. **Table 2.** In proximal hypospadias, the type of technique chosen was determined by meatal localization rather than SGA/AGA/LGA status. **Table 3.**

Associated anomalies, Medication, Nutritional status

Cryptorchidism, defined as a non-scrotal or non-palpable testis at age ≥12 months was significantly more common in boys born SGA and found in 12.5% (SGA) vs. 5.1% (AGA/LGA), p<0.001 unilaterally and in 8.8% (SGA) vs. 3.7% (AGA/LGA), p<0.001 bilaterally. After correction for term (considering only boys born after GW 37), there was no statistically significant difference present comparing SGA to AGA/LGA. Considering the occurrence of associated micropenis or scrotum bipartitum (corrected for meatal localization) we could not find any significant difference. There was no significant other medication used in patients included into this study (except nutritional supplements, vitamin D). Nutritional screening was without pathological findings.

Birthweight alone as surrogate for SGA

Among boys born >2500g (n=492), 3.5% (n=17) had a birth weight or length of less than -2 SD and were classified as SGA. Whereas in those born <2500g (n=92), 31.5% (n=29) had a birth weight and length of more than -2SD and were classified as AGA/LGA. 17 SGA boys (21.2% of all SGA boys) would not be diagnosed using only birthweight as criterion, whereas

in 29 AGA boys (5.6% of all AGA/LGA boys) a wrong assumption would be made in the opposite direction.

Pregnancy related problems in hypospadias patients

Placental insufficiency / intrauterine growth restriction (10.6% vs. 2.1%. p<0.001), multiple pregnancies (6.3% vs. 3.2%, p<0.001), as well as the occurrence of (pre)eclampsia, HELLP syndrome or gestational hypertension (8.8% vs. 2.8%, p0.001) were reported at a significantly higher prevalence in boys born SGA. In this cohort only a small number of boys (n=3, 0.5%) were conceived using artificial reproduction techniques or in vitro fertilization (1 / 1.25% SGA vs. 2 / 0.4% AGA).

Weight and length at time of surgery

Whilst there was no significant difference of mean age at surgery corrected for term between the groups (20.3 months AGA vs. 20.4 months SGA, p=0.493), weight and length at admission for surgery were still lower in SGA boys (12.1kg AGA vs. 10.4kg SGA p=0.032 and 83.5cm AGA vs. 78.6cm SGA p=0.018).

Correlation of SGA with complications and reoperations

Post-operative complications of any kind occurred in 122 patients (20.9%) during follow-up, including minor problems as for instance cosmetic dissatisfaction or a narrow appearing meatus without a functional effect. Reoperation was indicated due to significant complications excluding minor cosmetic alterations in 105 boys (17.9%), with 98 (16.8% total) having undergone further surgery until the end of the study period. Complications included dehsiscence (n=24, 4.1%), fistula (n=74, 12.7%), urethral diverticula (n=2, 0.3%), meatal stenosis (11 (1.9%) and recurrent curvature (n=3, 0.5%). **Table 4.**

In boys born SGA the overall risk for complications was higher compared to those born AGA or LGA (37.5% SGA vs. 14.8% AGA/LGA, p<0.001). In a univariate analysis comparing distal vs. proximal hypospadias in boys born SGA vs. AGA/LGA, a similar complication risk was found for distal hypospadias (14.9% vs. 12.1%, p=0.639). However, boys born SGA with proximal hypospadias had a higher risk compared to those born AGA/LGA for each meatal localization (proximal penile 36.3 vs. 25.7%, penoscrotal 47.3 vs. 80%, scrotal/perineal 71.4 vs. 83.3%). While this difference was not significant in a univariate analysis, it proved significant

(p=0.019, OR 3.21) in a stepwise multivariate logistic regression analysis including meatal localization, surgical technique and associated features of the hypospadias (narrow urethral plate, ventral curvature). The presence of complex hypospadias (defined as patients integrating at least two features of: glans diameter <14mm, narrow urethral plate, significant ventral deviation, associated micropenis or bilateral cryptorchidism, p=0.81) as well as androgen pretreatment had no significant effect in this model (p=0.9). In addition, a bootrapping analysis (n=7) was performed as a second mathemathical method to emulate larger group sizes, confirming further an independent and significant influence of SGA on reoperation likelihood. **Figure 2A+B. Table 5.**

Discussion

Our findings from this study demonstrate that boys born SGA represent a third of all proximal hypospadias. Furthermore, we identified being born SGA as an independent predictor of a significantly higher reoperation rate in boys with proximal hypospadias.

Considering only birth weight to identify children prone to developmental abnormalities would likely lead to unclear and inexact definitions of patients, and impaired subsequent conclusions[17]. The exact definition of SGA is – despite its extensive implications – still elusive, definitions used in literature range from <10th centile to <3rd centile[18]. For the purpose of this study, in order to define a high-risk population, SGA is defined as weight or length <-2SD (i.e. including only 2.3% of children)[5]. In this cohort, 21.2% of all SGA boys would be not diagnosed using only birthweight <2500g as criterion, whereas 5.6 % of all AGA/LGA boys born <2500g would be incorrectly classified/diagnosed as SGA following this single criterion only. This underlines the importance of using SD scores to adjust for gestational age instead of birthweight only.

The association between being born SGA and the occurrence of hypospadias has been well established: The largest report to date clearly demonstrated an association between SGA and the incidence of hypospadias with a hazard ratio (HR) up to 12x in boys born at 32 weeks, and with weight below the 20th centile[7]. Also, being born SGA has been shown to be associated to a higher prevalence of proximal hypospadias[8]. In this cohort, SGA was

significantly associated with proximal hypospadias, boys born SGA are making up for 33% of all proximal hypospadias.

Prenatal findings suggestive of intrauterine growth retardation (IUGR) or placental insufficiency have been described earlier in association with hypospadias, correlating to the severity of IUGR[19]. The postulated cause of this association is the impaired placental function, also illustrated by the fact that the incidence of hypospadias is higher in monochorionic twins and by studies linking otherwise unexplained cases of DSD and hypospadias to IUGR[20-22]. IUGR might be a transient phenomenon in many pregnancies: although IUGR may lead to a diagnosis of SGA, an infant may be born SGA without diagnosed IUGR, or vice versa. The effect of IUGR concerning hypospadias incidence is most likely relevant during genital development in weeks 8-14 of gestation[23]. In this study, more severe forms of SGA (<-3SD) were not associated with a higher likelihood of proximal hypospadias compared to <-2SD.

Another relevant factor influencing the occurrence of hypospadias is the use of assisted reproduction techniques (ART) [24]. This could act as a potential confounder, but was not found to be relevant to our cohort, with only 3/584 (0.5%) boys having been conceived using ART.

The SGA children were still significantly shorter and lighter at the time of surgery, at a mean age of 20.4 months corrected for term. As a putative catch-up growth should not be evaluated until the second year of life[25] this finding is of somewhat limited significance. Nevertheless, these boys need to be closely monitored during childhood for early referral to the pediatric endocrinology department to determine the need for growth hormone therapy.

The main factor described in literature, appearing to influence further, unplanned interventions in hypospadias is the location of the meatus[26]. However, a generally accepted and universally used system to classify hypospadias severity or even meatal localization is not available. Glans diameter was shown to affect the rate of urethroplasty complications in a single center series independently, as well as a urethral plate width <8mm[13, 14]. Used as single variables in a step-wise multivariate regression model, these

277 factors showed no influence on complication rate in this series. Therefore we decided to
278 group factors in to “complex hypospadias”, however, also boys with two or more of the risk
279 factors above showed no significantly higher risk for reoperation. Thereby, we could exclude
280 a confounding influence of these factors to the findings related to SGA.
281
282 Intrauterine growth restriction and SGA have been liked with several congenital anomalies,
283 increased morbidity in the neonatal period, neurodevelopmental issues and a higher risk of
284 metabolic syndrome and obesity as well as a higher risk of infections[27, 10, 11]. This theory,
285 similar to the thrifty gene hypothesis, may underline the observed postnatal effects,
286 potentially also influencing surgical complication rates[12]. There are reports about higher
287 complications rates in children born pre-term undergoing neonatal heart surgery [28;29].
288 Clearly, these results cannot uncritically be transferred to hypospadias patients undergoing
289 surgery much later in life with different complications in question. Nevertheless, these
290 reports point at a potential role of gestational age in the genesis of complications.
291 Considering non syndromatc hypospadias patients, it has been shown very recently, that
292 SGA is associated with adverse outcomes concerning semen parameters and a higher
293 likelihood for oligo-/azoospermia [30]. Yet not elucidated effects of prenatal impairment of
294 the development of penile tissues might contribute to impaired wound healing and thus
295 complications in hypospadias patients born SGA[31]. The genetic and molecular mechanisms
296 involved in the embryopathogenesis of hypospadias are increasingly well understood [3].
297 However, it remains unclear, how IUGR or placental insufficiency influences these pathways
298 and subsequently could contribute to the formation of hypospadias. Epigenetic mechanisms
299 resulting in altered gene expression are well explored in the context of IUGR concerning the
300 increased risk of later Diabetes Mellitus Type 2[32]. Similar effects might be present on
301 genes involved in the development of hypospadias and in wound healing, explaining our
302 findings.
303
304 Androgen pretreatment is discussed controversially in literature: besides data showing lower
305 complications rates with local as well as systemic application, there are studies showing no
306 clear benefit as well as experimental data pointing at additional complications due to local
307 inflammation [33-35]. In patients born SGA, androgen pretreatment was hypothesized to be
308 a potentially important factor for less complications, putatively based on a embryological

lack of AR stimulation. However, in this study, we could not find an influence of DHT pretreatment on the reoperation rate in our multivariate model. However, without a prospective, randomized approach, the question of how androgen pretreatment might influence the difference in reoperation rate between SGA and non-SGA born boys cannot be answered.

Providing adequate information to parents, including a detailed explanation of potential complications and their likelihood is essential in shaping expectations, and enabling families to make informed and responsible decisions. This might impact the late outcome, including the notion of decisional regret[36; 37]. SGA is readily leviable during history taking and should be taken into consideration. Whether the findings of the present study could help to tailor surgical strategies or adjuvant measures, as for example the application of preoperative hormonal stimulation remains to be determined in future studies.

We feel that the highly critical approach to classifying complications and having an indication for reoperation as the end-point of the study, are a strength of this analysis.
Limitations of this study include that the data stem from only one center, furthermore, the numbers of patients, especially in the subgroup of proximal hypospadias is relatively small (n=33). Despite the critical approach to the statistical analysis with clear results favoring a role of SGA as an independent risk factor for reoperation likelihood in proximal hypospadias, these results will have to be confirmed by larger, multicentric series. The true rate of complications can only be comprehensively documented with a longer observation period [38]. Therefore, we cannot exclude that some complications might (yet) have gone unnoticed Despite including a high number of patients and showing a clear difference in reoperation rate, our findings must be validated in further studies, as this is a single center series.

Conclusion

In this single center series SGA was found to be a independent risk factor for post-operative complications, and for further unplanned reoperations in boys with proximal hypospadias who comprised 33% of all cases of proximal hypospadias included into this study. After these results have been corroborated in larger, multi-centric studies, we believe that SGA status

should be discussed with parents during the provision of informed consent and be included in future studies analyzing complication risks and surgical outcomes in proximal hypospadias.

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Legends

Figure (Extended Summary) ROC curve for the influence of SGA on the reoperation rate of proximal hypospadias in a multivariate analysis controlling for meatal localization, complex hypospadias, surgical technique and androgen pretreatment

Figure 1 Inclusion of patients

Figure 2A ROC curve for the influence of SGA on the reoperation rate of proximal hypospadias in a multivariate analysis controlling for meatal localization, complex hypospadias, surgical technique and androgen pretreatment

Figure 2B Risk for reoperation (%, y) dependent on AGA+LGA / SGA (x): **reoperation risk is higher in boys born SGA in each meatal localization classified as proximal hypospadias**

Table 1 Patient characteristics, duration of follow-up and use of androgen pretreatment

Table 2 Surgical techniques used

Table 3 Surgical techniques used in boys with proximal hypospadias stratified for SGA/AGA/LGA

Table 4 Detailed types of complications and indications for reinterventions

Table 5 Predictors for reoperation based on the multivariate model using the logit function y = logit(p) = log(p/(1-p)); Pr(>|z|) … p-value concerning the effect estimate; z-value … number of standard errors by which the observed value is above or below the reference value;

	all patients (n=584)	**SGA (n=80)**	**AGA (n=462)**	**LGA (n=42)**	**p (SGA vs. AGA/LGA)***
age at surgery (mean) [months]	20.71	21.1	20.82	18.6	0.418
age at surgery corrected for term (40 GW + x weeks, mean) [months]	20.2	20.4	20.3	18.3	0.493
term (mean) [weeks]	38.2	36.6	38.5	38.6	**0.001**
birthweight (mean) [g]	3098.2	2007.3	3210.2	3943.3	**<0.001**
length at birth (mean) [cm]	49.5	42.4	50.1	54.9	**<0.001**
SD score weight (mean)	-0.48	-2.4	-0.34	1.3	**<0.001**
SD Score length (mean)	-0.08	-2.76	0.09	2.64	**<0.001**
weight at admission to surgery (mean) [kg]	11.9	10.4	12.1	12.1	**0.032**
length at admission to surgery (mean) [cm]	82.8	78.6	83.5	83.5	**0.018**
duration since surgery (months) [mean]	50.9	51.2	51.5	43.6	
duration surgery – last visit (months) [mean]	18.6	21.8	18.8	10.7	
duration surgery – last visit (months) proximal hypospadias [median]	23.1	24.9	19.1	19.0	
androgen pretreatment (DHT gel, applied locally)	117 (20%)	28 (35%)	85 (18.4%)	4 (9%)	
hypospadias sine hypospadias / orthotopic	61 (10.4%)	4 (5%)	51 (11%)	6 (14.3%)	
glandular	122 (20.9%)	8 (10%)	103 (22.3%)	11 (26.2%)	
coronal	221 (37.8%)	25 (31.3%)	185 (40%)	11 (26.2%)	
distal penile	81 (13.9%)	10 (12.5%)	62 (13.4%)	9 (21.4%)	
distal hypospadias	**485 (83.1%)**	**47 (58.7%)**	**401 (86.8%)**	**37 (88.1%)**	**p=<0.001**
Androgen pretreatment in distal hypospadias	64 (13.1%)	9 (19.1%)	52 (12.9%)	2 (5.4%)	
proximal penile	51 (8.7%)	11 (13.8%)	35 (7.6%)	5 (11.9%)	
penoscrotal	29 (5%)	10 (12.5%)	19 (4.1%)	0	

scrotal / perineal	19 (3.3%)	12 (15%)	7 (1.5%)	0
proximal hypospadias	**99 (16.9%)**	**33 (41.3%)**	**61 (13.2%)**	**5 (11.9%)**
Androgen pretreatment in proximal hypospadias	57 (57.6%)	19 (57.6%)	35 (57.3%)	2 (40%)
Patients included and to be considered DSD according to the Chicago consensus	**59 (10.1%)**	**16 (20%)**	**38 (8.2%)**	**5 (11.9%)**
Undescended testes and not severe hypospadias	47 (8%)	8 (10%)	34 (7.4%)	5 (11.9%)
Micropenis	5 (0.8%)	3 (3.8%)	2 (0.4%)	0
Perineal Hypospadias	7 (1.2%)	5 (6.3%)	2 (0.4%)	0

* t-test / Levene test

Table 1 Patient characteristics, duration of follow-up and use of androgen pretreatment

	all patients (n=584)	SGA (n=80)	AGA (n=462)	LGA (n=42)
TIP / Thiersch	322 (55.1%)	260 (56.3%)	39 (48.8%)	23 (54.8%)
MAGPI	151 (25.8%)	124 (26.8%)	12 (15%)	15 (35.7%)
staged repair	33 (5.7%)	13 (2.8%)	19 (23.8%)	1 (2.4%)
foreskin resection, skin reconstruction +/- curvature correction w/o urethral intervention	61 (10.4%)	53 (11.5%)	5 (6.3%)	3 (7.1%)
Duckett onlay	11 (1.9%)	7 (1.5%)	4 (5%)	0
MEMO	3 (0.4%)	3 (0.5%)	0	0
Mathieu	3 (0.5%)	2 (0.4%)	1 (1.3%)	0
other (e.g. lateral based flap)	5 (0.9%)	5 (1.1%)	0	0

	proximal penile SGA/AGA/LGA	penoscrotal SGA/AGA/LGA	scrotal/perineal SGA/AGA/LGA
TIP / Thiersch	8/31/4	3/9/0	0/0/0
staged repair	3/2/0	5/7/0	11/5/0
Duckett onlay	0/2/1	2/4/0	1/2/0

	all patients (n=584)	AGA (n=462)	SGA (n=80)	LGA (n=42)	p (AGA + LGA vs. SGA)*
patients who underwent a reintervention [n, %]	98 (16.8%)	66 (14.3%)	26 (32.2%)	6 (14.3%)	**<0.001**
patients having any kind of suboptimal result [n, %]	120 (20.5%)	78 (16.8%)	32 (40%)	10 (23.8%)	**<0.001**
Reintervention indicated because of relevant complication [n, %]	**105/584 (17.9%)**	**68/462 (14.7%)**	**30/80 (37.5%)**	**7/42 (16.7%)**	**<0.001**
dehiscence, recurrent hypospadias	24 (4.1%)	16 (3.5%)	7 (8.8%)	1 (2.4%)	
fistula	74 (12.7%)	47 (10.2%)	21 (26.3%)	6 (14.3%)	
urethral diverticulum	2 (0.3%)	2 (0.4%)	0	0	
meatal stenosis*	11 (1.9%)	6 (1.3%)	2 (2.5%)	3 (7.1%)	
recurrent curvature	3 (0.5%)	1 (0.2%)	2 (2.5%)	0	
others (major spraying, torsion)	6 (1.1%)	3 (0.2%)	3 (1.25%)	0	

*mostly relative, not urodynamically relevant and therefore without reoperation indication

	Estimate	Std. Error	z value	Pr(>|z|)
AGA/LGA, distal hypospadias, non-complex (reference category)	-1.9989	0.1528	-13.082	< 2e-16
SGA	0.2345	0.4354	0.539	0.5902
proximal hypospadias	1.2609	0.3090	4.081	**4.49e-05**
complex hypospadias	0.1084	0.2855	0.380	0.7041
SGA as independent factor in proximal hypospadias (corrected for interaction)	1.2811	0.6334	2.022	**0.0431**
Multivariate Model for each proximal meatal localization				
SGA0SGA	0.6255	0.3077	2.033	**0.04205**
penoscrotal	1.7473	0.4051	4.313	**1.61e-05**
proximal penil	1.0092	0.3409	2.960	**0.00307**
scrotal	3.3426	0.6591	5.071	**3.95e-07**