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Management of Proximal Hypospadias with 2-Stage Repair: 20 Year Experience

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Abstract

Purpose—To describe our experience with 2-stage proximal hypospadias repair and report outcomes. To look at patient and procedure characteristics associated with surgical complications.

Materials and Methods—This was a retrospective study of patients with proximal hypospadias who underwent staged repair from January 1993–December 2012. Demographics, preoperative management, and operative technique were reviewed. Complications included glans dehiscence, fistula, meatal stenosis, non-meatal stricture, urethrocele/diverticula, and residual chordee. Cox proportional hazards model was used to evaluate the associations between the time to surgery for complications and patient- and procedure level factors.

Results—There were 134 patients. The median age at time of first stage surgery was 8.8 months. The median age at time of second stage surgery was 17.1 months and median time between surgeries was 8 months. The median follow-up was 3.8 years. Complications were seen in 71/134 (53%), the most common being fistula in 39/134 (29.1%). Reoperation was performed in 66/134 (49%) patients. Median time from urethroplasty to surgery for complication was 14.9 months. Use of preoperative testosterone decreased risk of having surgery for complication by 27% (hazard ratio (HR)=0.73 95%CI:0.55–0.98, p=0.04). In addition, patients that identified as Hispanic had an increased risk of having surgery for complications (HR=2.40 95%CI:1.28–4.53, p=0.01).

Conclusions—This study reviews the largest cohort of patients undergoing 2-stage hypospadias repair at a single institution. Complications and reoperation are close to 50% in the setting of complex genital reconstruction.

Keywords

hypospadias; urologic surgical procedures; pediatrics; complications

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Introduction

Proximal hypospadias presents a technical challenge, no matter who the surgeon and technique for repair. Surgeons have explored reconstructive techniques to correct the deformity, varying with the extent of the urethral plate maldevelopment and severity of ventral curvature. Duplay first published his technique of urethral plate tubularization in 1874, describing three stages of hypospadias repair including correction of the ventral chordee, use of the penile skin flaps to create the urethra and connection of the neourethra to the proximal meatus [1]. In 1994, Retik et al. described a 2-stage procedure: 1) correction of chordee and rotational advancement of preputial flaps ventrally and distally, thus covering the entire undersurface of the phallus from glans to the hypospadic urethral orifice, and 2) creation of a tubularized neourethra from these flaps 6–12 months later. This procedure was felt to deliver reliable functional and cosmetic outcomes.[2]

The aims of this retrospective study of Retik's 2-stage proximal hypospadias repair were 1) to report the occurrence of surgical complications, and 2) explore patient and procedure characteristics associated with surgery for complications. We wanted to use this study to identify data points that should be collected for prospective study of subsequent patients with proximal hypospadias who undergo repair.

Materials and Methods

Patient population

With IRB approval and waiver of informed consent, we reviewed institutional billing data to identify all patients at our institution who had a code for hypospadias repair on two separate dates from January 1, 1993–December 31, 2012.

Inclusion

Patients were included in our cohort if they had a planned staged hypospadias repair, confirmed if the first operative report indicated “First Stage Repair”. The meatal location had to be penoscrotal, scrotal, or perineal as indicated at time of the first surgery, to be included in our study. Patients also had to have at least one follow up visit after their final surgery.

Exclusion

Patients were excluded if any procedures were done at another institution. Patients were also excluded if the first surgery was a one-stage repair and the second surgery was correction of a complication. Patients with distal hypospadias were excluded regardless of degree of chordee.

Patient data

Patient characteristics, preoperative evaluation, operative techniques and postoperative outcomes were obtained from the medical records. Surgical complications defined by the surgeon and documented in the medical record included glans dehiscence, fistula, meatal

stenosis, non-meatal stricture, urethrocele/diverticula, and residual chordee. Time to surgery for complication was used as the outcome for our exploratory analysis. Additional urethral surgeries after definitive hypospadias repair were defined as procedures that required anesthesia in the operative room.

Data analysis

Descriptive statistics were used to characterize the cohort. Cox proportional hazards model was used to explore the association between time to surgery for complications and the potentially relevant patient- and procedure level factors in the course of follow-up. Patients who did not have surgery to correct complications were considered censored at the time of the last follow up on record. Due to some of the patients' surgeries performed by the same surgeon, the data was not entirely independent. Clustering by surgeon was used in analyses to account for the correlated nature of the data due to individual surgeon's experience/ variability. Variables that had significant univariate associations with our outcome and/or clinical relevance were included in the final multivariate model. For continuous variables, correct functional form was assessed and variables were transformed when necessary. Proportionality of hazards assumption was satisfied. To address missing information, multiple imputations using Gibbs sampling “chained reactions” were performed. Results from the analyses of imputed data were consistent with the complete-case analysis (reported). Statistical analysis was conducted using SAS v9.3 (SAS Institute Inc., Cary, NC, USA) and packages *base*, *survival* and *mice* of R statistical software. [3–5] A p-value of <0.05 was considered to be statistically significant.

Results

We identified 134 patients who met our inclusion criteria. Over the 20-year period, there were 14 surgeons involved in performing the 2-stage repair. Patient demographics and characteristics are shown in Table 1.

First Stage Characteristics

The first-stage consisted of an orthoplasty and rotation of preputial skin to the ventrum as described by Byars.[6] The median age at time of first surgery was 8.8 months [IQR 6.3–11.7]. Of the 134 patients, 50 (37%) were given testosterone prior to first surgical stage and 36 prior to the second stage. There was no change in rate of testosterone use during the study period. Dosage was not reliably available; however, 44% had topical testosterone, 46% had IM administration, and 10% were unknown. Chordee was described in the operative report after artificial erection test in 97/134 (72%) patients and 83/97 (86%) had severe chordee by subjective assessment. Maneuvers used for straightening included degloving only in 55/134 (41%), plication in 24/134 (18%), extensive ventral dissection in 21/134 (16%), and corporal grafting in 34/134 (25%). Dermal graft was used in 31 patients and tunica vaginalis graft in the remaining 3 patients. Almost all of the patients had urinary drainage for a median of 3 days [IQR 2–5].

Second-Stage characteristics

The second stage was the urethroplasty. The median age at time of second surgery was 17.1 months [IQR 14.2–20.3]. Median time between first and second stage was 8 months [IQR 6.9–9.2]. The majority of patients had a Theirsch-Duplay urethroplasty (108/134, 81%), with a modified Tubularized Incised Plate (20/134, 15%) being the second most common repair, meaning only the distal urethral plate was incised. Other procedures (bladder tube, buccal graft) were done in 6/134 (4%) patients. A urethral catheter or urethral stent was used in 126/132 (95.5%) patients. Suprapubic drainage was utilized solely in 6/132 (5%) patients and combined in 28/132 (21%) patients. Median length of drainage was 8 days [IQR 7–12] and all patients were prescribed prophylactic antibiotics until the catheter was removed. Within the first visit after surgery, 10/134 (7.5%) patients had findings that required evaluation: UTI (5), surgical site infection (4), and separation of skin incision (1). Scrotoplasty was done as a third-stage in 17/134 (12.7%) patients.

Surgical Complications

The median length of follow-up in our cohort was 3.8 years (range: 1 month–21.7 years). Surgical complications were seen in 71/134 (53%) patients. These complications are shown in Table 2. Fistula was the most common complication, seen in 39/134 (29%) patients. Reoperation was performed in 66/134 (49%) patients- 1 patient with chordee and 4 patients with glans dehiscence were not operated on in the follow up period. In those that had additional surgeries, the median number of additional procedures was 2 (range 1–18). Median time from second stage to first surgical correction of complication for all patients was 14.9 months [IQR 6.7–30.8]. In univariate analysis, there was no significant difference in risk of complications between surgeons with higher volume (>=10 or >=15) and those with lower volume (p=0.5 and p=0.2, respectively).

Predictors of complications

Using Cox proportional hazards model with clustering by surgeon, we investigated univariate associations of the time to surgery for complications with the following covariates: age at first stage, age at second stage, time between stages, race, diagnosis of DSD, prematurity, cryptorchidism, use of graft for chordee repair, meatal location, preoperative use of testosterone and type of urethroplasty. For the multivariate model, we kept those covariates that were statistically significant on univariate analysis and those that were clinically relevant and reliably collected. We included log-transformed age at first stage, log-transformed time between stages, race, use of graft for chordee and preoperative use of testosterone in our final model. The unadjusted and adjusted hazards ratio with confidence interval and p-value are reported in Table 3.

In our cohort, the use of preoperative testosterone was associated with 27% decreased risk of having surgery for a complication (HR 0.73 95%CI 0.55–0.98, p=0.04). In addition, we saw that those patients that identified as Hispanic had an increased risk (HR 2.40 95%CI 1.28–4.53, p=0.01). The use of graft for chordee repair increased the risk of having surgery for a complication by 48% and as age at time of first surgery increased by 30%, the risk increased by 12%. However, the use of graft and the age at the time of first surgery were only marginally statistically significant.

Discussion

The technique used for proximal hypospadias has evolved, but without consensus on best approach. Until the mid 20th century, most proximal hypospadias repairs were done in stages[7]. Duplay, who described his three steps for hypospadias repair, ultimately did his first successful repair in five stages.[1] A one-stage approach came into vogue in the 1960's with Horton and Devine describing their procedure using preputial graft for the neourethra.[8] The one-stage technique was improved with the advent of Duckett's description of the transverse preputial island flap for severe hypospadias in 1980.[9] In the subsequent years, surgeons revisited the staged approach, introducing modifications and citing improved cosmetic and functional outcomes [2, 10, 11]. In a recent worldwide survey of pediatric urologists, surgeons and plastic surgeons, 43.3%, 47.7%, and 76.6% will do a 2-stage repair for penoscrotal, scrotal and perineal hypospadias, respectively. In those surgeons younger than 51, these percentages were even higher, indicating a change in surgical trends toward a 2-stage repair. [12] Our institution has used Retik's 2-stage repair for the last two decades and our results are of interest because of the size of our cohort.

In our cohort of 134 patients treated with 2-stage repair for proximal hypospadias, complications were seen in just over half of the patients. The most common complication was fistula. After the final stage of hypospadias repair, 49% of our patients had an additional surgical procedure. Use of preoperative testosterone was associated with decreased risk of surgery for a complication while being Hispanic was associated with increased risk. Higher age at first surgery and use of graft for chordee were marginally significant for increasing risk of surgery for a complication in our cohort. With regard to complication rates, our findings are difficult to compare with the existing literature because of heterogeneity in cohorts and techniques. Within the one-stage repair literature, the reported complication rates range from 20–60%. These studies have a mix of meatal location and surgical technique. The largest study was from de Mattos e Silva et al of 300 patients treated with different 1-stage techniques, with complication rates of 28–61%. [13] Gershbaum et al compared 1-stage to 2-stage repair in 51 patients who had perineoscrotal hypospadias with severe chordee, treated by two surgeons. In this series, there were only 2 (18%) complications in the 2-stage group. [14] In another small series, a single surgeon reported on 22 penoscrotal hypospadias repairs, 10 of which were done in 2 stages, with a complication rate of 70%. [15] Reoperation for fistula/urethral breakdown or stenosis after 2-stage repairs was reported at 28% by Castegnetti et al. [16] The merit of preoperative testosterone has been controversial. Our study suggests an association between testosterone and reduced complications. Without randomization, however, it is not possible to know whether this association was due to the testosterone itself, or to other unmeasured confounders that may have influenced the decision to use testosterone. Concerns have been raised previously regarding the influence of testosterone on wound healing, but two recent systematic reviews of the use of testosterone were inconclusive. [13, 17–19] A recent survey of pediatric urologists showed that testosterone was still prescribed in patients with proximal hypospadias, small appearing penis, reduced glans circumference or reduced urethral plate. [20] More defined parameters for use of testosterone have been reported by others, for

example in select patients with glans measuring <14mm in diameter.[21, 22] Future prospective studies will be needed to determine the value and role of testosterone.

Our research also suggests that older age at first surgery and use of a graft for severe ventral curvature of the penis may be associated with complications. Our finding regarding age conflicts with some other reports that demonstrate that age is not associated with complications; however, patients requiring 2-stage repair were excluded from these prior analyses.[23, 24] With regard to graft use, there are few studies evaluating the use of graft and surgical complications from hypospadias repair with most looking only at residual chordee as the primary outcome.[25–27] Our study is the first to look at corporal grafting and associated complications other than chordee requiring surgery. The need for grafting could be an indicator of severity of hypospadias; alternatively, use of a graft could directly influence the tissue environment in which the neourethra is reconstructed, leading to deleterious effects on healing and higher morbidity. The finding that Hispanic ethnicity increased risk of surgery for a complication may represent a biological phenomenon or is a surrogate for an unmeasured variable that affects complications.[28] Although the complication rates and reoperation rates in this cohort were high, this is the most comprehensive reporting of complications of 2-stage proximal hypospadias repairs, which may be useful in counseling patients and families. In addition, the use of surgery for complication as an outcome is of clinical importance. In our cohort, almost all patients with complications had surgery, so this captures an important outcome. The large number of patients allowed us to look at associations between patient and surgical characteristics and risk of complications that have not been explored previously.

While our study highlighted the surgical complications, many of the functional outcomes and cosmetic issues of interest may not be evident until the patient is post pubertal. Assessment of outcomes in proximal hypospadias should include surgical complications as well as cosmetic outcomes, functional outcomes for urination and erectile function and psychological outcomes. At our institution, post pubertal evaluation was not routinely performed, but is clearly justified, as confirmed by other centers.[29, 30]

The limitations of our study are inherent in its design. This is a retrospective study that is dependent on detailed chart reviews from the past 20 years and there was missing data. Missing data was handled with multiple imputations using all the other information available on the patients. Patient characteristics, such as meatal location, were based on surgeon description; however, without standard protocols there may have been misclassification. This is one reason why we did not include this variable in the final multivariate model. There may be underreporting of complications if they did not lead to an intervention or if patients sought care with other medical providers once they completed follow up at our institution. By relying on billing data, we may have misclassified patients. We believe that we captured the appropriate patients by doing an extensive search with all CPT codes and then narrowing down our patients according to our inclusion and exclusion criteria, and confirming accuracy of the coding through extensive chart review.

Conclusion

This study reviews the largest cohort of patients with penoscrotal, scrotal and perineal hypospadias undergoing 2-stage repair at a single institution. Half of the patients experienced complications. Preoperative use of testosterone was associated with decreased complications and Hispanic ethnicity was associated with increased complications. It is our hope that this study lays the groundwork for meaningful prospective studies of severe hypospadias which may lead to a standardized approach for evaluation, treatment and follow up and, ultimately, improved outcomes.

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Table 1

Demographics and preoperative characteristics of patients undergoing 2-stage hypospadias repair. N=134*

Patient Characteristics	n (%)
Race/Ethnicity, n=134	
White	81 (60.4)
Black/African American	10 (7.5)
Asian	10 (7.5)
Hispanic	10 (7.5)
Other	7 (5.2)
Unknown	16 (11.9)
Family History of Hypospadias, n=85	
Yes	18 (21.2)
No	67 (78.8)
Prenatal Issues, n= 127	
IVF	8 (6.3)
Prematurity	48 (37.8)
None	71 (55.9)
Birth anomalies (renal, cardiac), n=127	
Yes	36 (28.3)
No	91 (71.7)
Cryptorchidism, n= 129	
Yes	30 (23.3)
Unilateral	16 (53.3)
Bilateral	14 (46.7)
No	99 (76.7)
Location of meatus, n=134	
Penoscrotal,Scrotal	114(85)
Perineal	20 (15)
Preoperative Procedures, Diagnoses, Evaluation	
Diagnosis of DSD, n=127	
Yes	19 (15)
No	108 (85)
Endocrine evaluation, n=134	
Yes	46 (34.3)
No	88 (65.7)
VCUG obtained, n=134	
Yes	42 (31.3)

Patient Characteristics	n (%)
Normal VCUG	15 (35.7)
Abnormal VCUG†	27 (64.3)
No	92 (68.7)

*missing clinical information in the chart review is indicated

†include prostatic utricle(18), VUR(15)

Table 2

Occurrence of Complications

Complications	n (%)	Underwent surgical repair, n(%)
Any surgical complication	**71/134 (53)**	**66/134 (49)**
Single complication	46/71 (65)	
2 complications	17/71 (24)	
3 complications	6/71 (8)	
4 complications	2/71 (3)	
Glans Dehiscence	19/134 (14.2)	15/19 (79)
Fistula	39/134 (29.1)	39/39 (100)
Meatal Stenosis	17/134 (12.7)	17/17 (100)
Non-meatal Stricture	16/134 (11.9)	16/16(100)
Urethrocele/Diverticula	12/134 (9)	12/12(100)
Residual Chordee	3/134 (2.2)	2/3(67)

Table 3

Cox proportional Hazards Model, Unadjusted and Adjusted HR

Characteristic	N	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
DSD					
No (reference)	115	1.00 (NA, NA)	NA		
Yes	19	0.8 (0.44, 1.48)	0.48		
Cryptorchidism					
None (reference)	99	1.00 (NA, NA)	NA		
Unilateral	16	0.79 (0.56, 1.12)	0.18		
Bilateral	14	0.66 (0.38, 1.14)	0.13		
Use of graft for chordee					
No (reference)	100	1.00 (NA, NA)	NA	1.00 (NA, NA)	NA
Yes	34	1.64 (1.06, 2.54)	0.03	1.48 (0.97, 2.24)	0.07
Age at first stage*	134	1.51 (0.95, 2.39)	0.08	1.53 (0.99, 2.37)	0.06
Age at second stage*	134	1.65 (0.79, 3.45)	0.18		
Time between stages*	134	1.16 (0.54, 2.52)	0.70	1.28 (0.56, 2.94)	0.55
Meatus Location					
Penoscrotal (Reference)	114	1.00 (NA, NA)	NA		
Perineal	20	0.79 (0.49, 1.27)	0.33		
Prematurity					
No (Reference)	69	1.00 (NA, NA)	NA		
Yes	58	0.81 (0.57, 1.16)	0.25		
Race					
White (reference)	81	1.00 (NA, NA)	NA	1.00 (NA, NA)	NA
Black	10	0.52 (0.14, 1.92)	0.33	0.49 (0.17, 1.41)	0.19
Asian	10	2.17 (1.16, 4.06)	0.02	1.65 (0.78, 3.47)	0.19
Hispanic	10	4.35 (2.04, 9.26)	<0.001	**2.40 (1.28, 4.53)**	**0.01**
Other	7	1.48 (0.73, 2.98)	0.27	1.49 (0.59, 3.77)	0.39
Preop Testosterone					
No (Reference)	68	1.00 (NA, NA)	NA	1.00 (NA, NA)	NA
Yes	66	0.87 (0.56, 1.34)	0.52	**0.73 (0.55, 0.98)**	**0.04**
Type of urethroplasty					
TIP (Reference)	20	1.00 (NA, NA)	NA		
Thiersch-Duplay	108	0.77 (0.34, 1.73)	0.52		
Other	6	1.08 (0.37, 3.15)	0.89		

*Variables were log-transformed prior to analyses