



# Insight into the early postoperative improvement of the functionality of the reconstructed urethra after distal hypospadias repair treated by the Snodgrass technique

Asmir Jonuzi<sup>1</sup>, Benjamin Kulovac<sup>2</sup>, Amira Mešić<sup>3</sup>, Una Glamoclija<sup>4</sup>, Semir Vranić<sup>5</sup>, Zlatan Zvizdic<sup>1</sup>

<sup>1</sup>Department of Pediatric Surgery, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

<sup>2</sup>Department of Urology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

<sup>3</sup>Department of Anesthesiology and Reanimation, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

<sup>4</sup>Department of Biochemistry and Clinical Analysis, University of Sarajevo Faculty of Pharmacy, Sarajevo, Bosnia and Herzegovina

<sup>5</sup>Qatar University College of Medicine, Doha, Qatar

## ABSTRACT

**Objective:** This study aimed to evaluate the functional status of the urethra using uroflowmetry before surgery, as well as three and six months postoperatively in cases of distal hypospadias.

**Material and Methods:** Thirty-nine consecutive patients who underwent surgery for distal hypospadias (hypospadias group) between 2016 and 2019 were prospectively included as part of this study. The control group consisted of 40 patients with a normal urethra who underwent surgery due to conditions other than hypospadias (phimosis, undescended testis, hernia). Uroflowmetry was performed preoperatively in these patients. Postoperative uroflowmetry was performed at three and six months following hypospadias surgery. Uroflowmetric results [maximum flow rate ( $Q_{max}$ ), average flow rate ( $Q_{ave}$ ), voided volume, void duration, flow start time, time to maximum urine flow rate, post-void residual urine, flow curve] were compared between the groups.

**Results:** The mean age for the patients with distal hypospadias was  $35.9 \pm 29.6$  months and  $40.8 \pm 26.1$  months for the control group. Pre- and postoperative  $Q_{max}$  values (three and six months after surgery) were 6.9 mL/s (0.1-15), 6.4 (0.2-14), and 7.5 (2.5-15).  $Q_{ave}$  values were preoperatively 4.0 (0.1-12.1), 3.8 (0.3-8.1), and 4.7 (1.0-11.1) mL/s three and six months after surgery, respectively. Bell-type flow was the most frequent uroflow flow curve in the preoperative hypospadias and control groups (95% and 66.6%, respectively). Postoperatively, bell-type flow remained the most common pattern, while a significant reduction in plateau-type flow was observed. Four boys (10.3%) had symptoms of obstruction.

**Conclusion:** Surgery improved urination dynamics and partial urethral obstruction of hypospadias cases that were present from the baseline. The urinary flow rates improve over time as the reconstructed neourethra regains functionality six months after the tubularized incised plate procedure.

**Keywords:** Distal hypospadias repair, uroflowmetry, urethral obstruction, functional status

## INTRODUCTION

Hypospadias are common genital birth anomalies, affecting about 1/300 boys, and the incidence may increase (1). Due to the great cosmetic and functional outcomes, tubularized incised plate (TIP) urethroplasty has gained popularity and been used extensively in distal hypopadias since Snodgrass first described it in 1994 (2). To differing degrees, complications such as fistulae and obstruction of the neourethra have been documented (2). Snodgrass stressed that in order to prevent fistulae from forming, the neourethra must be covered with well-vascularized tissue. Additionally, in order to lower the risk of meatal stenosis, the urethral plate should not be closed too far distally (3). Establishing a consistent and sufficient caliber urethra up to the meatus is essential for the functional success of hypopadias repair. Uroflowmetry, voiding cystourethrography, and direct observation of the urinary stream are the available techniques to assess the reconstructed urethra (3).

Uroflowmetry has gained importance in the postoperative follow-up of hypospadias surgery (4-7) due to its non-invasiveness, inexpensiveness, and more objective assessment than direct observation.

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### Corresponding Author

Asmir Jonuzi

E-mail: jonuziasmir@hotmail.com

ORCID ID: orcid.org/0000-0002-5637-9510

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Although the cosmetic effect is satisfactory after TIP urethroplasty, there are still controversies regarding the evaluation of the functional state of the neourethra.

Numerous studies have used uroflowmetry to investigate TIP functional outcomes using various nomograms and definitions of obstruction (3,4,8). Because of the increased flow rates and spontaneous normalization of the curves observed in the first year following surgery, the study by Holmdahl et al. (6) found that early uroflowmetry appears to be unnecessary. Even before surgery, Wolffenbuttel et al. (9) demonstrated that young boys with hypospadias were more likely to have an intermittent flow pattern and lower flow rates than boys in good health of the same age. While many boys with a maximum flow rate ( $Q_{max}$ ), in the low, normal, or obstructive range did not report obstructive symptoms, Andersson et al. (10) observed spontaneous improvement seven years following TIP repair.

Primary goal of the follow-up is early detection of obstruction, with it being before or after hypospadias repair.

This study aimed to determine chronological changes in uroflowmetry before and after distal hypospadias repair using the Snodgrass technique and determine the earliest lower time limit for establishing neourethra functionality after TIP urethroplasty.

## MATERIAL and METHODS

Forty-six consecutive patients who underwent surgery for distal hypospadias (hypospadias group) at Clinical Center University of Sarajevo, Bosnia and Herzegovina, between 2016 and 2019 were assessed for eligibility. The inclusion criteria were as follows: Patients with distal hypospadias, patients who underwent uroflowmetry investigation preoperatively, three and six months after surgery, and patients whose parents signed informed consent to participate in the study.

Patients with proximal hypospadias, megameatus intact prepuce variant, and those with a previously failed repair were excluded from the study (one boy with urethral fistula who needed reoperation was switched off, four patients refused to participate, and two patients could not be contacted in the study). The study also excluded patients with any associated neurological or urological abnormality related to the bladder, which could potentially affect flow patterns. After excluding the patients who did not meet the inclusion criteria, 39 were included in the current study. All patients received preoperative local androgen therapy (2.5% dihydrotestosterone, or DHT). Androgen therapy was applied before preoperative uroflow. The follow-up rate was 84.8%. The surgical technique was standard, and the choice of technique was driven by the physician's preference. Local dartos flaps were used to cover the urethroplasty in multiple layers. Uroflowmetry was done before surgery, three months

after surgery, and six months after surgery. Within five minutes of voiding, residual urine was measured using ultrasonography.

Urological ultrasound was performed to get specific information on pre- and post-void residual volume, bladder characteristics, upper tract status and associated malformations. Uroflowmetry was performed in the outpatient office using a rotating disk sensor. The groups were compared for uroflowmetric values:  $Q_{max}$ , average flow rate ( $Q_{ave}$ ), voided volume (VV), void duration, flow start time, time to maximum urine flow rate, and flow curve. After urination, the post-void residual urine amount was examined with ultrasonography. Compared with preoperative values, postoperative dilation was done only in patients with decreased urinary flow. The flow curve classification proposed by the International Child Continence Society was used to evaluate uroflowmetry results (11).

The  $Q_{max}$  and VV results were expressed as standard deviation (SD) and interpreted according to a Siroky nomogram.  $Q_{max}$  and VV were considered normal if they were  $>-1$  SD and obstructed if they were  $<-2$  SD (12).

## Statement of Ethics

The study complied with the ethical principles of the Declaration of Helsinki and with all International Council for Harmonization and Good Clinical Practice Guidelines. The study was approved by the local Institutional Review Board Ethical Committee of the Clinical Center University of Sarajevo (protocol code: 0302-53945/17; date of approval: 21 November 2017). Informed consent was obtained from the parents of all patients or their guardians.

## Statistical Analysis

Mean and SD with range were used to present numerical variables. Absolute numbers and percentages were used to present categorical variables. The Shapiro-Wilk test was used to test the normality of the distribution of quantitative variables. The quantitative variables compared across the follow-up using Wilcoxon's, Shapiro-Wilk, and Mann-Whitney U tests. All statistical assays were performed using the Statistical Package for the Social Sciences (SPSS) IBM Version 22.0. Statistical significance was accepted at the  $p < 0.05$  level.

## RESULTS

The average age at the first uroflowmetry of the patients in the hypospadias group was  $35.9 \pm 29.6$  months and  $40.8 \pm 26.1$  months for the control group ( $p = 0.43$ ).

Uroflowmetry was performed preoperatively, three and six months postoperatively (39 boys) (Table 1). In the 39 boys with distal hypospadias at preoperative baseline, the mean max flow rate was 6.9 mL/s (range 0-15, SD 3.3),  $Q_{ave}$  4.0 mL/s (range 0.1-12.1, SD 2.9), VV of 83.8 mL (range 10-449, SD 78.2). 22.5% of patients had  $Q_{max}$  below the  $-2$  SD. Three months post-surgery,

**Table 1.** Uroflowmetry data in patients with hypospadias (preoperatively, three and six months after surgery) and controls in the study

Variable	C: Control (n=40)	H <sub>0</sub> : Hypospadias preoperatively (n=39)	H <sub>3</sub> : Hypospadias 3 months after surgery (n=39)	H <sub>6</sub> : Hypospadias 6 months after surgery (n=39)	p-value C vs. H <sub>0</sub>	p-value C vs. H <sub>6</sub>	p-value H <sub>0</sub> vs. H <sub>3</sub>	p-value H <sub>0</sub> vs. H <sub>6</sub>	p-value H <sub>3</sub> vs. H <sub>6</sub>
VV (mL) Mean, range (SD)	108, 16-337 (67.8)	83.8, 10-449 (78.2)	112.7, 14-297 (78.1)	100.6, 14-300 (61.9)	<b>0.02</b>	0.63	<b>0.02</b>	<b>0.02</b>	0.48
Tq (s) Mean, range (SD)	24.1, 4-72 (17.8)	52.5, 4-120 (32.7)	54.3, 3-136 (35.1)	40.1, 2-120 (32.2)	<b>0.000</b>	0.06	0.45	0.18	<b>0.03</b>
T100 (s) Mean, range (SD)	13.8, 4-38 (7.9)	25.2, 5-128 (21.4)	35.5, 5-180 (36.9)	25.9, 7-120 (21.9)	<b>0.000</b>	<b>0.000</b>	<b>0.03</b>	0.93	<b>0.05</b>
Q <sub>max</sub> (mL/s) Mean, range (SD)	10.1, 4.5-17.5 (3.4)	6.9, 0.1-15 (3.3)	6.4, 0.2-14 (3.3)	7.5, 2.5-15.5 (3.4)	<b>0.000</b>	<b>0.002</b>	0.14	0.56	<b>0.02</b>
Tq <sub>max</sub> (s) Mean, range (SD)	6.8, 1-17 (3.9)	11.7, 2-128 (21.2)	22.2, 1-180 (36.8)	13.3, 1-138 (22.6)	0.64	0.16	0.12	0.19	<b>0.04</b>
Q <sub>ave</sub> (mL/s) Mean, range (SD)	8.0, 1.7-13.5 (2.9)	4.0, 0.1-12.1 (2.9)	3.8, 0.3-8.1 (1.9)	4.7, 1-11.1 (2.5)	<b>0.000</b>	<b>0.000</b>	0.61	0.17	<b>0.04</b>
PVR (mL) Mean, range (SD)	0.50, 0-10 (2.2)	4.7, 0-75 (13.5)	10.7, 0-130 (24.0)	2.6, 0-34 (7.6)	0.06	0.12	0.08	0.33	<b>0.003</b>

Only significant p-values are bolded. PVR: Post-void residual urine, Q<sub>ave</sub>: Average flow rate, Q<sub>max</sub>: Maximum flow rate, T100: Void duration, Tq: Flow start time, Tq<sub>max</sub>: Time to maximum urine flow rate, VV: Voided volume.

the average Q<sub>max</sub> was 6.4 mL/s (range 0.2-14, SD 3.3), Q<sub>ave</sub> 3.8 mL/s (range 0.3-8.1, SD 1.9), with a mean VV of 112.7 mL (range 14-297, SD 78.1). Nineteen (49%) had Q<sub>max</sub> below the -2 SD. Six months post-surgery, the average Q<sub>max</sub> was 7.5 mL/s (range 2.5-15.5, SD 3.4), Q<sub>ave</sub> 4.7 mL/s (range 1-11.1, SD 2.5), with a mean VV of 100.6 mL (range 14-300, SD 61.9). Foqur (10.3%) had Q<sub>max</sub> below the -2 SD.

The Q<sub>max</sub> values differed significantly between the hypospadias and the control groups preoperatively and six months following surgery, respectively (p<0.001 and 0.002). However, the Q<sub>max</sub> values measurement results were not significant within the hypospadias group three and six months after surgery, respectively (p=0.14 and 0.56).

There was a significant difference in the preoperative Q<sub>ave</sub> values between the hypospadias and control groups (p<0.001), as well as between the groups six months after surgery (p<0.001). No significant difference in the Q<sub>ave</sub> values was observed within the hypospadias group in two tested periods (p=0.61, 0.17, respectively).

In 39 patients with distal hypospadias, there was a significant increase in maximum flow (p=0.02) and Q<sub>ave</sub> (p=0.04) in patients with calibrated urethra 15 (38.5%); moreover, in 11 patients (28.2%) with plateau-shaped urination, the curves decreased six months postoperatively after urethral dilatation. The increased flow rate was not as evident in four patients with distal hypospadias as in other cases; they retained a plateau-shaped curve and were treated with dilatation.

The flow curve shapes (Figure 1) were noted in most cases and described as plateau-shaped in 15 (38.5%), bell-shaped in 21 cases (53.8%), and three cases (7.7%) with interrupted flow curves at the three-month follow-up. However, four plateau (10.3%) and 35 (89.7%) bell-shaped curves were noticed at the six months follow-up. No statistically significant difference was present in the appearance of the curve within the hypospadias group at the baseline and three months after surgery (p=1.0). However, we noticed a significant difference in the appearance of the curve within the hypospadias group at the baseline and six months after surgery (p=0.002). Similarly, a significant difference in the appearance of the curve between hypospadias and control groups was observed at the baseline (p=0.001). However, the difference was insignificant at the six months follow-up (p=0.41).

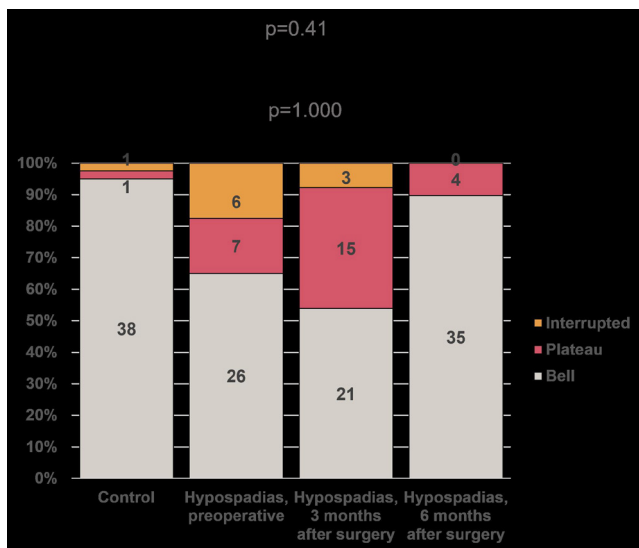


Figure 1. The flow curve shapes.

## DISCUSSION

TIP urethroplasty often obstructs flow at uroflowmetry after the surgery. However, despite that, it is still the most used technique for the surgical repair of primary hypospadias (9).

The clinical information on chronological changes in uroflowmetry before and after distal hypospadias repair from Bosnia and Herzegovina is very limited, and the present analysis is the first systematic study with a follow-up.

Uroflowmetry has become an important part of mid- and long-term follow-up following hypospadias surgery because it can identify urethral strictures even when they are asymptomatic (1,13-16). While Lorenzo and Snodgrass (13) reported flow rates in the lower part of the normal range 0.5-7 years after surgery, Marte et al. (4) reported that one-third of the boys had abnormal flow curves 1.8 years after TIP repair. The obstructed pattern has been suggested to be caused by a stiff neourethra with low compliance. Six months following surgery, our study showed spontaneous normalization of the curves and increased flow rates, which lends credence to this theory.

To avoid urethral fistulas, many surgeons advise routine urethral calibration and dilatation following TIP repair (16,17). Less than half of the patients (15 out of 39 boys) who had obstructive flow three months after surgery in this prospective study had a true obstructed urethra at calibration. Even before surgery, Wolffenbuttel et al. (9) found that young boys with hypospadias had lower flow rates and an intermittent flow pattern compared to healthy boys of the same age. These authors hypothesized that the obstructed flow we even observe after surgery may be caused by the hypospadiac urethra's already reduced compliant state, which may be caused by a partially absent or structurally abnormal surrounding spongiosal body (18,19).

Over the course of these six months, we found that one-third of the boys with extremely low flows experienced spontaneous improvements in their  $Q_{max}$  to levels within the normal range. Consistent with other reports, obstruction was strongly associated with a plateau flow curve and a low  $Q_{max}$  (20). The bell-type flow was more prevalent in our study, despite the fact that studies reporting uroflowmetry results following hypospadias surgery are more likely to have a plateau-type curve (21,22). Following surgery, the most typical uroflow curve was bell-type flow, but plateau-type flow significantly decreased. This suggests that hypospadias surgery increases urine flow and decreases urine flow duration.

A comparison of the uroflowmetry results of the hypospadias cases with the control group showed lower flow rates with residual urine in the bladder before the surgery. When they were compared again postoperatively, there was a significant difference in the flow rate and residual urine amount between the postoperative hypospadias and control groups. However, there was no difference between the postoperative and preoperative evaluation results. These results indicate that urinary dynamics in patients with hypospadias and partial urethral obstruction were already impaired preoperatively but improved following surgery. However, our study has shown that a preoperative flow assessment is equally essential. 33.4% incidence of preoperative poor flow rates is probably inherent to the anomaly.

Comparing preoperative and postoperative voiding dynamics is comparatively rare, despite the fact that similar studies have been done in the literature (7,9,22,25). Interestingly, compared to earlier studies, the patient population in this one is younger. Using an ultrasound probe to measure flow, Olsen et al. (7) examined 21 infants with hypospadias and contrasted them with an age-matched control group. They came to the conclusion that, in contrast to none in the control group, 31% of infants with hypospadias void with low  $Q_{max}$  and plateau-shaped curves. Wolffenbuttel et al. (9), using the same technique on 42 patients, found that 41% of children had a plateau pattern following surgery, compared to 6% before.

In our study as well 77.5% patients (29/40) with preoperative non-obstructive flow rates had post-operative  $Q_{max} > -1$  SD while 22.5% (9/40) with preoperative obstructive flow rates remained obstructed ( $Q_{max} < -2$  SD) even after the repair. Tuygun et al. (25) found that 25% of older children had low preoperative flow rates that normalized after TIP repair using preoperative and post-operative uroflowmetry.

Only a few studies have been made on this topic, but they all show varying rates of poor preoperative flow characteristics (7,9,23-25). All patients in our study with poor postoperative flows but good preoperative flows had clinical obstruction requiring meatal dilatation. Therefore, we suggest that such

a finding alert the surgeon to a possible correctible cause. On the other hand, obstructive flows in the postoperative follow-up were of little significance if the preoperative flows were also poor, indicating an inherent abnormality.

We also found a significant improvement in the  $Q_{\max}$  from three to 6 months postoperatively. This suggests that over time, after hypospadias surgery, the urethra improves, probably because of the resolution of edema and collagen remodeling. Several other studies have expressed a similar viewpoint (6,8,24-35).

### Study Limitations

The present study had several limitations. First, the follow-up period was short so urethral strictures after six months were not recorded and analyzed; second, the number of included patients was small; and third, the study was conducted in a single institution, limiting its generalizability. The strength of this study is that it is one of the few series reporting the results of uroflowmetry performed pre- and postoperatively in patients undergoing distal hypospadias repairs.

### CONCLUSION

The present study is the first to evaluate urethral function before and after the surgical treatment of distal forms of hypospadias in Bosnia and Herzegovina. Early uroflowmetry three months after the surgery for distal forms of hypospadias is an inadequate diagnostic method in assessing urethral function, except in the presence of clinical suspicion of urethral obstruction. In comparison, uroflowmetry six months after surgery is an adequate diagnostic method in assessing urethral function. The increase in the  $Q_{\max}$  and  $Q_{\text{ave}}$  parameters of the uroflowmetry and the normalization of the curves during the monitoring period indicate that the urethra becomes more elastic and wider over time.

The functional outcome of the neourethra, as assessed by uroflowmetry six months postoperatively, confirmed that the reconstructed neourethra achieved functional normalization following the TIP procedure. We advocate using uroflowmetry for routine postoperative follow-up after hypospadias repair as a simple, non-invasive, objective test.

### Ethics

**Ethics Committee Approval:** The study was approved by the local Institutional Review Board Ethical Committee of the Clinical Center University of Sarajevo (protocol code: 0302-53945/17; date of approval: 21 November 2017).

**Informed Consent:** Informed consent was obtained from the parents of all patients or their guardians.

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### Footnotes

#### Author Contributions

Concept - A.J., Z.Z., S.V.; Design - A.J., U.G.; Supervision - S.V., Z.Z.; Fundings - A.J., A.M., U.G.; Data Collection or Processing - A.J., U.G., A.M.; Analysis or Interpretation - A.J., Z.Z., B.K.; Literature Search - A.J., B.K.; Writing - A.J., Z.Z., B.K., S.V.

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