Patient-reported outcomes after buccal mucosal graft urethroplasty for bulbar urethral strictures: results of a prospective single-centre cohort study

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Abstract

Objectives: To describe patient-reported outcome measures (PROMs) after buccal mucosa graft (BMG) urethroplasty.

Materials and methods: We prospectively collected PROMs of patients who underwent BMG urethroplasty for bulbar urethral strictures between October 2009 and February 2017. Preoperatively and at the first, second, and third postoperative follow-up visits, patients completed five PROM questionnaires: International Prostate Symptom Score (IPSS), IPSS Quality of Life (QOL) score, Urogenital Distress Inventory Short Form score (UDI-6), International Index of Erectile Function-5 score (IIEF-5) combined with IIEF-Q9 and IIEF-Q10 for assessing ejaculatory and orgasmic functions, and International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms QOL score (ICIQ-LUTS-QOL). In addition to these questionnaires, we also evaluated the maximum flow rate, post-void residual volume and total voided volume at each follow-up visit. Buccal pain and discomfort were assessed using the visual analogue scale (VAS). Comparison of questionnaires was performed using a paired Wilcoxon rank-sum test. Treatment failure was defined as any need for urinary diversion or urethral instrumentation after surgery.

Results: A total of 97 patients met the inclusion criteria. The first postoperative follow-up visit was at a median of 2.1 months (n=97/97), and the second and third visits after a median of 7.8 (n=82/97) and 17.0 months (n=70/97), respectively. Significant improvements compared to baseline were observed in IPSS, IPSS-QOL, UDI-6, and ICIQ-LUTS-QOL scores at

the first follow-up and remained improved during the follow-up period ($p \leq 0.001$). Patients with mild to no baseline erectile dysfunction experienced a significant decline in erectile function at the first follow-up (median preoperative IIEF-5: 23.0, interquartile range [IQR]: 21.0–25.0, versus median IIEF-5 at the first follow-up: 19.5, IQR: 16.0–23.8; $p \leq 0.001$). This decline fully recovered during further follow-up (median IIEF-5 at the third follow-up: 24.0, IQR: 20.5–25.0; $p = 0.86$). No significant changes in median orgasmic and ejaculatory function were noted. The first postoperative median VAS score was 3.0 (IQR: 2.0–4.45), and a significant improvement in local pain and discomfort was observed during the follow-up (median VAS at third follow-up: 0.0, IQR: 0.0–1.0; $p \leq 0.001$). Nine patients (9/97; 9.3%) had treatment failure. Stratifying recurrence based on a difference of <10 mL/s vs. ≥ 10 mL/s between preoperative and postoperative Qmax could not demonstrate a significant difference ($p = 0.06$).

Conclusion: Significant improvements in voiding symptoms and QOL after surgery were reported. Patients with good baseline erections recovered erectile function during follow-up, although a significant decrease in erectile function was observed at the first follow-up. This study highlights the importance of PROMs in urethral reconstructive surgery, emphasising that success should not be defined only by stricture-free survival.

1. Introduction

Urethral stricture disease can have a significant negative impact on patient quality of life [1]. Treatment is tailored for each individual patient and depends on the aetiology, stricture location, length, and degree of associated spongiositis [2]. The gold standard treatment for long primary and recurrent urethral strictures is substitution urethroplasty [3]. Because of its accessibility and excellent adaptation to the urethral environment, the buccal mucosa is the most commonly used free graft in clinical practice [4].

For patients, functional outcomes and the impact on quality of life can be as important as stricture recurrence-free survival (RFS). Patient-reported outcome measures (PROMs) are therefore crucial in this field [5]. Because of increasing interest in these measures, Jackson et al. developed a validated Urethral Stricture Surgery PROM (USS-PROM) questionnaire in

2011 to evaluate functional outcomes, general health status, and patient satisfaction after urethroplasty [6-7]. This questionnaire has been widely used in clinical practice, and Verla et al. published a validated Dutch version of it in 2017 [8]. Our prospective collection started before the validation of this questionnaire, so we could not apply this instrument; however, we used several other questionnaires to assess the most notable PROMs and quality-of-life parameters after urethral reconstructive surgery.

For this study, we used these prospectively collected PROMs to evaluate the effect of buccal mucosa graft (BMG) urethroplasty for bulbar strictures on functional outcomes, patient satisfaction, erectile function, and quality of life.

2. Materials and Methods

2.1. Study design

Patients undergoing BMG urethroplasty for bulbar urethral strictures were recruited between October 2009 and February 2017 at University Hospitals Leuven. Ethical approval was obtained from the Ethics Committee Research UZ/KU Leuven (S55868), and we registered our protocol at www.clinicaltrials.gov (NCT01982136). Patients provided informed consent at diagnosis. The inclusion criterion was bulbar urethral strictures planned for BMG substitution urethroplasty. The exclusion criteria were loss to follow-up, incomplete questionnaires, and patient refusal to participate. Two experienced reconstructive urological surgeons performed all procedures (FA, SJ).

The choice of surgical technique was based on the location and length of the stricture, as well as on surgeon preference. In all patients, the buccal mucosa donor site was not closed.

The length and width of the BMG were adapted to the characteristics of the stricture.

The diagnostic work-up included urethrography, uroflowmetry, and urethroscopy. The first postoperative follow-up visit was scheduled at 2 months, the second at 8 months, and the third at 18 months. Details of complications were collected and categorised using the Clavien–Dindo classification (CDC) [9].

2.2. Outcome measures

Functional outcomes and patient satisfaction were collected through medical history, a physical examination, uroflowmetry, and collection of PROMs using validated questionnaires. The patients completed the following five PROM questionnaires preoperatively and at the first, second, and last follow-ups: International Prostate Symptom Score (IPSS) [10]; IPSS with Quality of Life score (IPSS-QOL) [10]; Urogenital Distress Inventory Short Form score (UDI-6), which was also validated for clinical research in men [11,12]; International Index of Erectile Function-5 score (IIEF-5) and IIEF-9 (question Q9) and IIEF-10 (question Q10) for assessing ejaculatory and orgasmic functions, completed only by sexually active men who engaged in masturbation or sexual intercourse [13,14]; and International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life score (ICIQ-LUTS-QOL) [15].

Uroflowmetry was performed preoperatively and at the first, second, and last follow-ups to assess the maximum flow rate (Q_{max}), post-void residual volume, and total voided volume. Pain and discomfort at the BMG donor site were assessed using a visual analogue scale (VAS) [16]. The first VAS assessment was performed postoperatively on the day of transurethral catheter removal, and the other VAS assessments were performed at all follow-up visits.

The questionnaire results and data for other variables were prospectively collected, and we excluded incomplete questionnaires from our analysis. Because clinical significance in addition to statistical significance is important in PROM studies [17], we analysed the minimal clinically important difference (MCID) for each questionnaire score (except for the UDI-6 short form because this value has not yet been investigated) and the associated impact on quality of life during follow-up.

2.3. Statistical analysis

The primary endpoint was the difference in functional outcomes between the preoperative state of patients and their state during the follow-up. The functional outcomes of interest were scores from the questionnaires (IPSS, IPSS-QOL, UDI-6, IIEF-5, and ICIQ-LUTS-QOL), ejaculatory and orgasmic functions (IIEF-Q9 and IIEF-Q10), VAS score, $Q_{\max}$, post-void residual volume, and total voided volume.

The secondary endpoint was RFS. Recurrence, or treatment failure, was defined as any need for urinary diversion, including placement of a suprapubic catheter, perineal urethrostomy, redo urethroplasty; or any need for urethral instrumentation because of postoperative recurrent bothersome obstructive voiding symptoms, such as cystoscopy, urethrography, or urethral dilatation, with confirmation of a recurrent stricture.

Analyses were performed in R (version 3.4.3) using the 'dplyr', 'survival', and 'survminer' packages. Summary statistics for continuous variables are presented as medians with interquartile ranges (IQRs), and those for categorical variables are presented as frequencies and proportions. Comparisons of questionnaires were performed using a paired Wilcoxon rank-sum test (non-parametric) in the absence of a normal distribution (F-test) and/or in the absence of equal variance (Shapiro-Wilk test). The results of all questionnaires were plotted in boxplots as the difference (Δ) between the baseline score and scores at first, second, or last follow-up. We used Kaplan–Meier plots to visualise recurrence-free survival data. To check whether variables had a significant impact on RFS, we performed a log-rank test for categorical variables and a univariate Cox proportional hazards analysis for continuous variables. If the continuous variable demonstrated a significant effect on RFS, we performed a log-rank test based on the median value of the continuous variable.

3. Results

3.1. Patient and stricture demographics

A total of 170 patients underwent BMG urethroplasty for a bulbar urethral stricture between October 2009 and February 2017. Of these, 34 patients refused to participate, 32 patients were referred from other centres, where they continued follow-up postoperatively, and 7 patients were lost to follow-up. A total of 97 patients met the inclusion criteria and

were included for analysis. All patients and stricture demographics are described in Table 1. Classically, we used the Barbagli technique for bulbar strictures maximally extending down to the penoscrotal angle in patients who did not yet undergo any urethral reconstruction. We used the Kulkarni technique for more extended strictures. The Asopa technique is mostly used in patients who already underwent any form of urethroplasty in the past and develop stricture recurrence.

In 11 patients, the catheter time was prolonged because of leakage on cysto-urethrography, which resolved in all patients at the time of the second cysto-urethrography (median time: 21 days; IQR 21.0–23.5). Two of the patients with prolonged catheter time experienced stricture recurrence during follow-up.

Table 2 provides an overview of all complications after BMG urethroplasty with the CDC grades. A total of six complications occurred in six different patients (6.2%). None of the patients were readmitted, and all reported complications occurred within the first days and weeks after surgery. No reinterventions were needed, and there was no procedure-related mortality.

3.2. Specific outcome measures

3.2.1. Voiding symptoms (IPSS and Q_{max})

The median IPSS before surgery was 18.0 (IQR: 12.0–21.5). At the first follow-up, a significant decline was observed, with a median value of 5.0 (IQR: 3.0–8.8; $p \leq 0.001$). This decline remained significant at the second ($p \leq 0.001$) and third ($p \leq 0.001$) follow-up visits, with median values of 4.0 (IQR: 2.0–7.0) and 4.0 (IQR: 1.0–6.0), respectively (Figure S1).

Median Q_{max} improved significantly at the first follow-up, with a median value of 19.0 mL/s (IQR: 13.0–25.0; median voided volume: 230.0 mL; $p \leq 0.001$) compared with the median preoperative value of 7.0 mL/s (IQR: 5.0–9.0; median voided volume: 116.0 mL). This improvement remained significant at the second (median Q_{max} : 18.9 mL/s, IQR: 11.5–24.0;

median voided volume: 223.5 mL; $p \leq 0.001$) and third (median $Q_{\max}$: 20.0, IQR: 13.0–25.0; median voided volume: 219.0 mL; $p \leq 0.001$) follow-up visits.

3.2.2. Urogenital distress and discomfort (UDI-6)

The median UDI-6 score before surgery was 33.3 (IQR: 16.7–49.9). A significant decline was observed at the first follow-up, with a median value of 5.6 (IQR: 0.0–16.7; $p \leq 0.001$). This decline remained significant at the second and third follow-up visits, with median values of 0.0 (IQR: 0.0–11.1; $p \leq 0.001$) and 0.0 (IQR: 0.0–9.0; $p \leq 0.001$), respectively (Figure S2).

3.2.3. Erectile dysfunction (IIEF-5), ejaculatory function, and orgasmic function (IIEF-Q9 and -Q10)

A total of 59 patients were sexually active before surgery and completed the IIEF-5 questionnaires. These patients were subdivided into two categories: patients with mild or no baseline erectile dysfunction (ED) (IIEF-5 score: 17–25; $n=35$) and patients with mild/moderate to severe baseline ED (IIEF-5 score: 5–16; $n=24$).

At the first follow-up, we observed a significant decline in erectile function in patients with preoperative mild or no ED (median preoperative IIEF-5: 23.0, IQR: 21.0–25.0, versus median IIEF-5 at the first follow-up: 19.5, IQR: 16.0–23.8; $p \leq 0.001$). At the second follow-up, the erectile function had recovered (median IIEF-5: 23.0, IQR: 18.5–25.0) with no significant difference compared with the preoperative value ($p=0.23$). This difference remained non-significant at the third follow-up (median IIEF-5: 24.0, IQR: 20.5–25.0; $p=0.86$) (Figure S3).

Patients with preoperative mild/moderate severe ED (median IIEF-5: 7.0, IQR: 5.0–11.5) experienced a significant improvement in erectile function at the first follow-up (median IIEF-5: 9.5, IQR: 5.3–14.8; $p=0.02$), second follow-up (median IIEF-5: 9.0, IQR: 5.0–15.0; $p=0.007$), and third follow-up (median IIEF-5: 9.5, IQR: 6.0–19.3; $p=0.002$) (Figure S4).

Ejaculatory dysfunction (EjD) was assessed with the IIEF-Q9 questionnaire, and orgasmic dysfunction was assessed using the IIEF-Q10 questionnaire. Preoperative IIEF-Q9 score

(median: 5.00, IQR: 1.3–5.0) did not differ significantly from scores at the first (median IIEF-Q9: 4.00, IQR: 2.0–5.0; $p=0.52$), second (median IIEF-Q9: 4.0, IQR: 2.0–5.0; $p=0.21$), and third (median IIEF-Q9: 4.0, IQR: 3.0–5.0; $p=0.31$) follow-up visits (Figure S5).

The median preoperative IIEF-Q10 score was 5.0 (IQR: 2.0–5.0), with no significant difference at the first follow-up (median IIEF-Q10: 4.0, IQR: 2.0–5.0; $p=1$). Further follow-up yielded no significant changes in the median preoperative score (median IIEF-Q10 at the second follow-up: 4.0, IQR: 2.0–5.0; $p=1$; and median IIEF-Q10 at the third follow-up: 4.0, IQR: 2.3–5.0; $p=0.65$) (Figure S6).

An additional analysis showed that four patients with mild or no baseline ED ($n=4/35$; 11.4%) had a significant decline in erectile function during longer follow-up ($p\leq 0.001$). These patients also experienced decreased ejaculatory and orgasmic function during follow-up. In contrast, five patients with mild/moderate to severe baseline ED ($n=5/24$; 20.8%) had a significantly improved erectile function during longer follow-up ($p\leq 0.001$), also with an improved ejaculatory and orgasmic function.

3.2.4. Quality of life (IPSS-QOL and ICIQ-LUTS-QOL)

A significant improvement in voiding quality was observed between the median preoperative IPSS-QOL score (IPSS-QOL: 5.0, IQR: 4.0–5.0) and the median score at the first follow-up (IPSS-QOL: 1.0, IQR: 0.0–2.0; $p\leq 0.001$). This improvement persisted at the second (median IPSS-QOL: 1.0, IQR: 1.0–2.0; $p\leq 0.001$) and third (median IPSS-QOL: 1.0, IQR: 0.0–2.0) follow-up visits (Figure S7).

The median ICIQ-LUTS-QOL score before surgery was 35.0 (IQR: 29.0–48.5). These values significantly decreased at the first follow-up (median ICIQ-LUTS-QOL: 25.0, IQR: 21.0–32.0; $p\leq 0.001$) and remained improved at the second (median ICIQ-LUTS-QOL: 21.0, IQR: 19.0–25.0; $p\leq 0.001$) and third (median ICIQ-LUTS-QOL: 20.0, IQR: 19.0–22.0; $p\leq 0.001$) visits (Figure S8).

3.2.5. Postoperative pain and discomfort of buccal mucosa grafting (VAS)

The first postoperative median VAS score was 3.0 (IQR: 2.0–4.45). A significant improvement in pain was observed at the first follow-up (median VAS: 1.0, IQR: 0.0–2.0; $p \leq 0.001$), which persisted at the second (median VAS: 0.8, IQR: 0.0–1.0; $p \leq 0.001$) and third (median VAS: 0.0, IQR: 0.0–1.0; $p \leq 0.001$) follow-up visits (Figure S9).

3.3. Recurrence-free survival

Nine patients (9.3%) had a treatment failure during follow-up. The 3-year RFS among all patients was 88.0% (95% CI: 80.9–95.7) (Figure 1). Surgical technique (factor) and preoperative UDI-6 score (continuous) had a significant effect on survival, whereas all other collected variables had no significant impact.

RFS was stratified based on surgical technique (Barbagli, Kulkarni, and Asopa) (Figure 2). On pairwise comparison corrected by Bonferroni, we found that patients treated with either the Barbagli or Kulkarni technique had a significantly better RFS than those treated with the Asopa technique. RFS did not differ significantly between patients treated with the Barbagli and Kulkarni techniques. The 10-month RFS by technique was 95% (95% CI: 89.7–100) with Barbagli, 100% (95% CI: 100–100) with Kulkarni, and 85.7% (95% CI: 63.3–100) with Asopa. The 20-month RFS values with the Barbagli, Kulkarni, and Asopa techniques were 91.3% (95% CI: 84.2–98.9), 100% (95% CI: 100–100), and 42.9% (95% CI: 18.2–100), respectively. The wide 95% CI of the recurrence-free survival of the Asopa technique can be explained by the low number of patients ($n=8$) and high rate of recurrences ($n=4$). However, this did not impact our analysis, as on pairwise comparison using a log rank test corrected by Bonferroni, the Barbagli and Kulkarni technique were both still significantly superior to the Asopa technique.

RFS grouped by the median preoperative UDI-6 score (33) could stratify patients significantly. Patients with an UDI-6 score of ≤ 33 and UDI-6 score of >33 had a 2-year RFS of 95.4% (95% CI: 89.4–100) and 79.0% (95% CI: 66.2–94.3), respectively. Stratifying recurrence based on a difference of <10 mL/s vs. ≥ 10 mL/s between preoperative and postoperative $Q_{\max}$ could also not demonstrate a significant difference ($p=0.06$) (Figure 3).

4. Discussion

Urethral stricture disease affects voiding function, urogenital discomfort, erectile function, and quality of life [3-5]. Here, we focused on these outcomes that are most relevant for patients and summarise our most clinically relevant findings in the context of recent studies.

4.1. Voiding symptoms and urogenital discomfort

The aims of BMG urethroplasty are to remove a stricture with associated spongiositis and reconstruct the urethra with improved diameter to resolve obstructive voiding symptoms [18]. The most pronounced obstructive symptoms in urethral stricture disease are a weak stream, dribbling, and incomplete emptying [19]. We assessed these symptoms by analysing the IPSS and Q_{max} before and after surgery.

Our statistical analysis showed a significant decline in median IPSS during the follow-up and a significant improvement in median urinary flow after surgery. However, a recent multi-institutional study by Tam et al. showed that IPSS and uroflowmetry should not be used as stand-alone tools to assess stricture recurrence [20]. A broader approach is needed because benign prostatic hyperplasia or detrusor dysfunction can also affect IPSS and uroflowmetry results. For this reason, we used several questionnaires to better assess stricture recurrence and treatment satisfaction. In addition to obstructive voiding symptoms, urethral strictures may also cause urinary incontinence and urethral and bladder pain [6]. By using the UDI-6 score, we analysed the impact of surgery on these symptoms. The median UDI-6 score decreased significantly during the follow-up, and we observed improvements in these symptoms after surgery, as well.

Significant clinical improvements also were identified along with these significant statistical differences. A 3-point improvement in IPSS score from baseline is regarded as a MCID (5 points: moderate improvement; 8 points: marked improvement) [17, 21]. In this study, the median IPSS improved by 14 points and $\geq 25\%$ from baseline at longer follow-up, indicating a clear clinical improvement. These findings can be used for patient counselling before

surgery because patients are less interested in statistical changes related to questionnaire outcomes than in potential clinical improvements after their treatment.

4.2. Erectile, ejaculatory, and orgasmic dysfunctions

Interest is growing in erectile and sexual dysfunction after surgery for urethral stricture disease [22], but outcomes in most studies are heterogeneous. Standardisation in the assessment of sexual and erectile functions after urethroplasty is clearly lacking. Vascular injury (bulbar arteries or collateral vessels between the corpus spongiosum and corpus cavernosum) or neurogenic injury (cavernous nerves in the intracavernosal space) during reconstruction can result in ED. Hard evidence is not available regarding changes in EjD after urethroplasty [20]. Some patients with urethral stricture disease have a decreased ejaculatory volume and force because of the strictured lumen, which is resolved by surgery. However, patients can also experience increased EjD after urethroplasty because of bulbospongiosus muscle dysfunction or ejaculate pooling in the augmented urethra [23]. In addition to EjD, decreased penile sensitivity and cold glans syndrome after surgery can lead to decreased orgasmic and sexual satisfaction [22, 23].

In our study, we noted a significant decline in median IIEF-5 score at the first follow-up in patients with good baseline erections. This change could be the result of pain, inflammation, and catheterisation in the first weeks after surgery [23, 24]. These patients experienced a full recovery during further follow-up. Patients with moderate to severe ED at baseline showed a significant increase in median IIEF-5 score over time, but these values remained low, without identifiable clinically relevant changes. In their recent editorial, Baumgarten et al. highlighted the fact that multiple retrospective and prospective studies have reported no long-term risk of ED after urethroplasty [26]. However, the topic remains important, especially with excision and primary anastomosis (transecting versus non-transecting) stricture repairs, but high-level data are lacking that favour one technique over another. Concerning BMG urethroplasties, dorsal or ventral grafting did not differentially affect sexual function [27], but prospective series analysing sexual function after substitution urethroplasty are lacking.

A 4-point change in the IIEF-5 score is considered a MCID after surgery [28]. Here, we identified no such changes (improvements or deteriorations) between median baseline IIEF-5 score and median IIEF-5 score at longer follow-up. This lack of change was present in both patient groups (bad and good baseline erections), so surgery had no clinical impact on erectile function.

The IIEF-Q9 and IIEF-Q10 questionnaires evaluate ejaculatory and orgasmic function, respectively. Our analysis showed that surgery had no significant impact on median ejaculatory function. This is in line with the recent literature where most studies also did not described a long-term impact of surgery on ejaculatory function. However, these studies included heterogenous, small cohort patient groups [22]. With respect to median orgasmic function, we also found no significant differences during the follow-up. However, four patients (11.8%) with good baseline erections had a persistent, significant decline in erectile, ejaculatory, and orgasmic function during follow-up. This could be due to increase psychological stress or cardiovascular comorbidities [22]. Surgery does not universally yield positive outcomes for all patients and this needs to be counselled, especially to the younger patients. On the other hand, five patients (20.8%) had a significant improvement in erectile, ejaculatory, and orgasmic function after surgery.

4.3. Quality of life

One of the primary endpoints of this study was the impact of surgery on patient quality of life. First, we evaluated the subjective voiding quality using the IPSS-QOL questionnaire. Because we noted a significant improvement in this score during the follow-up, we concluded that the patients were pleased or very pleased with their voiding function after urethroplasty. As stated above, the IPSS alone is insufficient to predict stricture recurrence, but indirectly, the IPSS-QOL also assesses urethral and bladder pain, which is quite common in urethral stricture disease.

Second, by using the ICIQ-LUTS-QOL questionnaire, we more extensively investigated the quality of life for patients and the impact of surgery on their lives. Our analysis showed a significant improvement after surgery, which remained positive during the follow-up. A recent retrospective study by Soave et al. yielded comparable results using this

questionnaire, reporting that urinary symptoms after surgery had no negative impact on quality of life [18]. Jackson et al. published a prospective study with similar outcomes, with most patients being satisfied or very satisfied after surgery [7].

A change of 0.5 points from baseline in the IPSS-QOL score and of 6 points from baseline in the ICIQ-LUTS-QOL score is considered a MCID after surgery [17, 29]. The median IPSS-QOL score improved by 4 points and the median ICIQ-LUTS-QOL score by 15 points during longer follow-up. Thus, these patients experienced both a significant clinical improvement and a significant impact on quality of life after surgery.

4.4. Pain and discomfort after buccal mucosa grafting

Buccal mucosa grafting may cause local pain and discomfort [30]. As noted, we did not close the donor site, and results are controversial with respect to closure versus non-closure. A recent review article argued that this decision should be made at the discretion of the surgeon [30, 31]. To relieve local symptoms, we applied moisturising gel and asked patients to use a chlorhexidine mouthwash daily. At each follow-up visit, we also assessed the perineal scar complaints, but not in a standardised way.

The first pain inquiry was made on the day of catheter removal. We noted that patients had serious discomfort after buccal mucosa grafting, but with a significant improvement during follow-up. A recent prospective study by Morán et al. showed that eating is mostly affected after surgery, but without significant reduction in oral quality of life [32].

A difference of 3 points on the VAS is regarded as a MCID [33]. At longer follow-up, we observed a change of 3 points, and the median VAS became 0. Thus, clinically significant pain improvement and healing of the buccal mucosa harvest site were observed during longer follow-up.

4.5. Treatment failures

Nine patients had treatment failure, all during the first year after surgery. At the longer follow-up, after 12 months, we found no new treatment failures, and no patients needed a repeat urethroplasty. These findings are similar to those of previous studies with high rates of stricture RFS [34, 35]. The procedures performed for treatment failures are listed in Table 3.

A reconstructive urologist should be familiar with various surgical techniques, but which technique is best remains to be established [36]. Barbagli et al. recently published a retrospective study analysing the success rates of different surgical techniques [37]. They concluded that each technique has a learning curve and that it is important to evaluate the surgical outcomes to achieve better quality of care. One clear consensus is that the oral mucosa is superior to skin as a substitute material for non-pedicled flaps [37]. As we noted above, we found no significant differences among patients treated with the Barbagli and Kulkarni techniques. PROMs and outcomes may vary according to level of expertise of the surgeon. This should be assessed in future trials.

Patients with a baseline UDI-6 score of >33 had a higher recurrence rate than patients with a score of ≤ 33 . This cut-off was based on statistical significance in our series but could be used as a selection criterion for patients if validated in other studies. No clear evidence with respect to this finding has been published, but patients with incontinence, pain, and discomfort at baseline should be counselled pre-surgery about an increased risk for recurrences.

4.6. Strengths and limitations

This prospective study with baseline values allowed for adequate evaluation of how surgery affected functional outcomes and patient satisfaction. The questionnaire data were added to each patient's file and recorded in our prospective database. The study did have some limitations. It was a single-centre investigation involving two surgeons, with a relatively low number of patients and relatively short follow-up. In addition, 32 patients were excluded because of a lack of follow-up, which in most cases was performed instead by the referring urologist. We did not specifically collect data on post-micturition dribbling in our study.

Furthermore, we did not use the validated USS-PROM questionnaire that Jackson et al. published in 2011 because our study began in 2009 [6]. For prospective evaluation of our patients, we used validated questionnaires (as detailed above) that are common in other clinical settings. The validated Dutch version of the USS-PROM questionnaire, published by Verla et al. in 2017, could have been beneficial because it also assesses ejaculatory and orgasmic functions and our centre is located in the Dutch-speaking part of Belgium [8].

4.7. Conclusions

As evaluated using validated questionnaires at baseline, patients with urethral stricture disease have not only bothersome voiding symptoms, pain, and discomfort but also impaired quality of life. After surgery, voiding symptoms significantly improved, with a major positive impact on quality of life. A significant decrease in erectile function was observed at the first follow-up, but this recovered during further follow-up. However, a small group of patients did experience a persistent significant decline in erectile function during longer follow-up. It is important to counsel all patients on this before surgery. Buccal mucosa grafting causes local pain and discomfort in the first weeks postoperatively, but these complaints decrease significantly over follow-up. Thus, the long-term comorbidity of buccal mucosa grafting is minimal. Our recurrence-free rates were similar to those of previous studies, and the observed postoperative complications were limited and easily treated.

In addition to the statistical difference we observed, perhaps more important were the clinically significant improvements we identified. This study highlights the importance of PROMs in urethral reconstructive surgery. Outcomes should be measured using both objective physical measurements ($Q_{\max}$, post-micturition residual volume) as well as PROMS. Furthermore, our study provides insights for surgeons to understand that the success of BMG urethroplasty cannot be defined by stricture-free survival only.

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8. Conflicts of Interest

The authors declare no conflicts of interest.

9. References

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Table 1. Patient and stricture data and follow-up visits

Median age	56.2 years	IQR: 40.8–70.0 years	
Median stricture length	3.0 cm	IQR: 2.5–5.0 cm	
Stricture location	Bulbar urethra	100%	
Stricture aetiology			
▪ Iatrogenic	42	43.3%	
▪ Idiopathic	38	39.2%	
▪ Infectious	9	9.3%	
▪ Traumatic	8	8.2%	
Subgroup iatrogenic causes			
▪ Transurethral procedures	19	45.2%	
▪ Catheterization	18	39.2%	
▪ Radical prostatectomy	3	7.1%	
▪ Radiotherapy/brachytherapy	2	4.8%	
Previous urethral stricture surgery			
▪ Dilatations/urethrotomies	78	80.4%	
▪ One dilatation/urethrotomy	8	8.3%	
▪ No previous surgery	11	11.3%	
Surgical technique			
▪ Barbagli	76	78.4%	
▪ Kulkarni	13	13.4%	
▪ Asopa	8	8.2%	
Median time to catheter removal	15.0 days	IQR: 14.0–16.7 days	
Median follow-up visits			
▪ First follow-up	2.0 months	IQR: 1.8–2.3	n=97/97
▪ Second follow-up	7.8 months	IQR: 6.2–9.1	n=82/97
▪ Third follow-up	17.0 months	IQR: 13.9–22.0	n=70/97

IQR: interquartile range.

Table 2. Postoperative complications according to the Clavien–Dindo classification

CDC type	Onset (days)	Procedure-related	No. (%)
CDC grade 1			
▪ Fever	≤30 days	No	3 (3.1%)
▪ Scrotal haematoma	≤30 days	Yes	2 (2.1%)
CDC grade 2			
▪ Bacterial epididymo-orchitis	≤30 days	Yes	1 (1%)

CDC: Clavien–Dindo classification; No.: number of patients.

Table 3. Procedures performed for treatment failures

Procedures performed for failures (n=9)	No. (%)
Urethral dilatation	3 (33.3%)
Suprapubic catheter	2 (22.2%)
Direct visual internal urethrotomy	2 (22.2%)
Revision surgery for fistula repair	2 (22.2%)

No.: number of patients

Figure 1. Recurrence-free survival after BMG urethroplasty

Figure 2. Recurrence-free survival after BMG urethroplasty stratified by surgical technique

Figure 3. Recurrence-free survival after BMG urethroplasty stratified by a difference of <10 mL/s vs. ≥ 10 mL/s between preoperative and postoperative $Q_{\max}$