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Treatment outcomes of buccal mucosa graft urethroplasty in male patients with bulbar and panurethral strictures

Bulbar ve panüretral darlığı olan erkek hastalarda bukkal mukoza greft üretroplasti tedavisinin sonuçları

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ABSTRACT

***Aim*:** To present the treatment outcomes of buccal mucosal graft (BMG) urethroplasty in male patients with bulbar and panurethral strictures and also to identify the factors associated with stricture recurrence.

Methods: Male patients who underwent BMG urethroplasty for anterior urethral strictures were reviewed retrospectively. Success was defined as a voiding with >15mL/s in maximal voiding velocity. If stricture recurrence occured, cystourethrography and urethroscopy were performed. Success rate, stricture recurrence and other complications were analyzed.

Results*:* 24 male patients were identified. 12 patients underwent BMG urethroplasty for bulbar stricture and 12 patients underwent BMG urethroplasty for panurethral stricture. Success rate was 79% at a mean 18 months follow up. Success rate was 75% in patients with bulbar stricture and 83% in patients with panurethral stricture. In total, 5 patients developed stricture recurrence. No statistically significant association was found between stricture recurrence rate and stricture length. All of the recurrences were occurred in patients who underwent ≥3 previous internal urethrotomies. The number of previous internal urethrotomy procedure was significantly associated with stricture recurrence.

Conclusion: Buccal mucosa graft urethroplasty is effective in both bulbar and panurethral strictures. The number of previous internal urethrotomy procedure is significantly associated with stricture recurrence. Buccal mucosa graft urethroplasty should be offered to the patients after first internal urethrotomy failure.

Keywords*:* buccal mucosa; male; urethral stenosis

ÖZET

Amaç: Bulbar ve panüretral darlığı olan erkek hastalarda bukkal (yanak) mukozal greft (BMG) üretroplasti tedavi sonuçlarını sunmak ve ayrıca darlık nüksü ile ilişkili faktörleri belirlemek.

Yöntem: Üretra darlığı nedeniyle BMG üretroplasti uygulanan erkek hastalar geriye dönük olarak incelendi. Başarı, maksimum işeme hızında >15mL/s ile işeme olarak tanımlandı. Darlık nüksü varsa sistoüretrografi ve üretroskopi yapıldı. Başarı oranı, darlık nüksü ve diğer komplikasyonlar analiz edildi.

Bulgular: 24 erkek hasta tespit edildi. Bulbar darlık için 12 hastaya BMG üretroplasti ve panüretral darlık için 12 hastaya BMG üretroplasti uygulandı. Ortalama 18 aylık takipte başarı oranı %79 idi. Bulbar darlığı olan hastalarda başarı oranı %75, panüretral darlığı olan hastalarda ise %83 idi. Toplamda 5 hastada darlık nüksü gelişti. Darlık nüks oranı ile darlık uzunluğu arasında istatistiksel olarak anlamlı bir ilişki bulunamadı. Tüm nüksler daha önce ≥3 internal üretrotomi geçirmiş hastalarda meydana geldi. Önceki internal üretrotomi prosedürünün sayısı, darlık nüksü ile önemli ölçüde ilişkiliydi.

Sonuçlar: Bukkal mukoza greft üretroplasti hem bulbar hem de panüretral darlıklarda etkili bir tedvi yöntemidir. Önceki internal üretrotomi prosedürünün sayısı, darlık nüksü ile önemli ölçüde ilişkilidir. İlk internal üretrotomi başarısızlığından sonra hastalara bukkal mukoza greft üretroplastisi önerilmelidir.

Anahtar kelimeler*:* yanak mukozası; erkek; üretra darlığı

Introduction

Urethral stricture is narrowing of the urethral lumen resulting from epithelial tissue and corpus spongiosum fibrosis. Treatment options include endoscopic interventions and urethroplasty. Substitution urethroplasty is the treatment of choice for long primary and recurrent urethral stricture disease (Soave et al., 2019). Although several urethroplasty techniques have been described, the preferred surgical technique depends on stricture length, location, underlying pathology and surgeon experience (Al-Hakeem, Chung, Chung & Tse, 2019; Soave et al., 2019). Strictures greater than 2 cm are successfully treated with substitution urethroplasty with the use of skin flaps or tissue grafts (Levy & Elliott, 2017). Buccal mucosa graft (BMG) is the gold standard for substitution urethroplasty for the following reasons: 1-easy to access and harvest, 2-hairless, 3-durable (full-thickness graft), 4-viable in a wet environment, and 5-have thin lamina propria that facilitates neovascularization (Chapple et al., 2014; Levy & Elliott, 2017;). Several studies have confirmed that BMG urethroplasty (BMGU) provides excellent stricture recurrence-free survival for the treatment of urethral stricture (Soave et al., 2019). However, despite these successful results, recurrence of urethral stricture is a common complication (Yalçınkaya & Kartal, 2020). Some risk factors associated with stricture recurrence have been described in the current literature (Kessler et al., 2003; Wessells et al., 2017). In this study, we aimed to present the success rate and the complications of BMGU for the treatment of bulbar

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and panurethral strictures in male patients and to identify factors associated with stricture recurrence.

Methods

In this retrospective study, adult male patients who underwent BMGU for the treatment of urethral stricture between January 2017 and April 2020 in our institution were reviewed. Patients with panurethral strictures and short bulbar strictures were also evaluated separately. The success of the surgery was defined as a voiding >15mL/s in maximal voiding velocity without significant postvoid residual urine (PVR). Success rate and complications (including stricture recurrence) were analyzed.

Evaluation of the patients

Detailed history taking and physical examination was done to all patients. Urine analysis, uroflowmetry (with MMS 5000) together with PVR volume (with Bladder Scan BVI 6100) (Uroflow-PVR) and combined retrograde and voiding cystourethrography were performed to detect the location and lenght of the stricture. Oral mucosa was examined for any pathology that could be a contraindication for BMG harvesting. Mouth movements and expansion was especially noted.

Surgical procedure

Nasal intubation was preferred in order to make the oral cavity seen in a better fashion. An operation team was harvested the BMG, while another team was performing the perineal dissection. Mouth was opened with mouth retractors, lidocaine and epinephrine (1:100.000) solution was injected under the harvested inner cheek mucosa to facilitate better dissection, and BMG was harvested while protecting the opening of Stenon channel.

Exact stricture length was confirmed intraoperatively by seen the healthy urethral mucosa during dissection. BMG was harvested approximately %20 longer than stricture length measured intraoperatively. If the graft harvested from one cheek was not enough, other cheek and lingual graft was also used, respectively. After removal of the graft, defective mucosa was repaired with 4-0 vicryl suture.

One-sided dorsolateral onlay BMGU as previously described by Kulkarni et al. was performed for bulbar urethral strictures (Kulkarni, Barbagli, Sansalone & Lazzeri, 2009). Dorsal inlay BMGU with ventral sagittal urethrotomy as previously described by Asopa et al. was performed for panurethral strictures (Asopa et al., 2001). 18 Fr urethral catheter was placed through the external urethral meatus to the bladder and left for 4 weeks.

Follow up

At 4 weeks postoperatively, a peri-catheter retrograde urethrography was performed and the urethral catheter was removed if there was no extravasation. After catheter removal, free uroflow-PVR was performed. Uroflow-PVR was performed at 3, 6, and 12 months postoperatively and then annualy. After 12 months, patients were ordered to come to visit if they feel any discomfort about the urine stream. If stricture recurrence was suspected, cystourethrography and urethroscopy were performed. Stricture recurrence was treated by internal urethrotomy (IU).

Statistical analysis

Statistical analysis was done using Statistical Package for Social Sciences 25.0 software (SPSS 25.0 for MAC) (Chicago, USA) by an expert biomedical statistician. Descriptive statistics of nominal samples were expressed with numbers and/or percentiles. Descriptive statistics of scale samples were expressed as mean ± standard deviation (minimum-maximum). Shapiro-Wilk, Kurtosis, and Skewness Tests were used to assess the variables' normalization. The Mann-Whitney U Test was used to compare the independent scale parameters without normally distribution. The Student T Test was used to compare independent scale parameters with normal distribution. Chi Square Test was used to compare independent nominal parameters. Kaplan-Meier test was used to compare the recurrence free survival rate between groups. Probability of $p < 0.05$ was accepted as statistically significant.

Ethical aspect of the study

Health Sciences University Gülhane Faculty of Medicine Ethics Committee approved this study (Date: 01 July 2020; Number: 2020-289), Helsinki Declaration rules were followed and patient written informed consent was obtained (64th WMA General Assembly, Fortaleza, Brazil, October 2013).

Table 1. Clinical characteristics of 24 male patients with urethral stricture

Characteristics	Mean ± SD (range)	p value
Age, years	51.6±14.3 (29-78)	
Bulbar (n=12)	54.1±16.3 (29-78)	0.41
Panurethral (n=12)	49.1±12.2 (29-65)	
Follow up, months	18.3±11.4 (3-36)	
Bulbar (n=12)	17.4±11.8 (4-36)	0.692
Panurethral (n=12)	19.3±11.5 (3-36)	
Stricture length, cm	6.7±3.8 (2-14)	
Bulbar (n=12)	3.16±0.68 (3-5)	0.001
Panurethral (n=12)	10.25±1.76 (8-14)	
Previous surgical interventions	**n (%)**	
Urethroplasty	0	
Internal urethrotomy		
1	4 (16.6)	
2	6 (25)	
≥3	14 (58.4)	

Results

24 male patients were identified. 12 patients underwent BMGU for bulbar stricture and 12 patients underwent BMGU for panurethral stricture. Mean patient age was 51.6±14.3 (range: 29-78). Mean follow-up duration was 18.3±11.4 (range: 3-36) months. Mean stricture length was 6.7±3.8 (range: 2-14) cm. Clinical characteristics of the patients are summarized in table 1. At a mean 18.3 months follow-up, overall success rate was 79.1%.

Also, success rate was 75% for bulbar strictures with a mean follow-up of 17.4 months and 83.3% for panurethral strictures with a mean follow-up of 19.3 months (Table 2).

Stricture recurrence occurred in 5 patients (20.8%). No statistically significant association was found between stricture recurrence and stricture length (p=0.631) (Table 2). In total, 14/24 patients underwent ≥3 previous IU.

Table 2. Success rate and complications

Variable	n (%)	p value
Success rate	19 (79.1)	
Bulbar	9 (75)	0.615
Panurethral	10 (83.3)	
Complications	6 (25)	
Recurrence	5 (20.8)	
Bulbar	3 (25)	0.631
Panurethral	2 (16.6)	
Penile chordee	1 (4.2)	

All of the recurrences were occurred in patients who underwent ≥3 previous IU (table 3). No recurrence occurred in 10/24 patients who underwent ≤ 2 previous IU. The number of previous IU procedure was significantly associated with stricture recurrence (p=0,034) (table 3). All recurrences were <1 cm and treated successfully with IU. Also, one patient who underwent BMGU for bulbar stricture developed penil chordee and treated primarily without complication. Additionally, no oral complication was occurred and mouth movements returned to normal within 6 months in all patients.

Table 3. Association between previous IU number and recurrence

Variables	Previous IU number (n= 24)		
	1 and 2 IU (n=10)	≥3 IU (n=14)	p value
Recurrence, n (%)	0	5 (35.7)	0.034
Success, n (%)	10 (100)	9 (64.3)	0.021

IU: internal urethrotomy

Discussion

Surgical treatment techniques of anterior urethral strictures have been recently widened and improved with new techniques (Barbagli, 2004). BMG has been reported as a successful technique in many studies (Furr, Wisenbaugh & Gelman, 2019). When considering the complications and the surgery outcomes, BMGU technique would be used for urethral strictures with several lengths (McKibben et al., 2020).

Different techniques for grafting have been mentioned in the literature with different success and recurrence rates. Currently, buccal mucosa harvested from the inside of the cheek is most widely used as a urethral substitute, and is recognized as the best urethral substitute (Horiguchi, 2017). Patterson and Chapple (2008) reviewed the literature and they found that BMG was an effective choice in experienced hands. Success rates of dorsal onlay BMGU was 75-100% (Patterson & Chapple, 2008). Kulkarni et al. (2009) reported that their one-sided dorsolateral onlay BMGU technique had a success rate of 92%, at a mean follow-up of 22 months. Pisapati et al. (2009) stated that the ventral sagittal urethrotomy approach was easier to perform than the dorsal urethrotomy approach, and was especially useful in long anterior urethral strictures with high success rates. The authors reported 87% overall success rate in 45 patients with recurrent urethral strictures, with a mean follow-up period of 42 months. In this study, stricture length was <5 cm in 31 patients, 5.1-10 cm in 8 patients and >10 cm in 6 patients (Pisapati et al., 2009). It was reviewed the results of 318 patients treated for panurethral stricture by Kulkarni technique, which consists of single-stage, penile invagination, one-side dissection, dorsal onlay buccal graft urethroplasty (Kulkarni S, Kulkarni J, Surana & Joshi, 2017). The mean stricture length was 14 cm, and the success rate was 84.9% at a median follow-up was 59 months (Kulkarni et al., 2017). Zimmermann and Santucci (2011) stated in a literature review that BMGU demonstrated excellent short and long-term results. In our study, we performed dorsal inlay BMGU with ventral sagittal urethrotomy technique for panurethral strictures as described by Asopa et al. (2001), because we believe that it is easy to perform and also effective. For bulbar urethral strictures, we performed one-sided dorsolateral onlay BMGU as described by Kulkarni (Kulkarni et al., 2009). Similarly with the literature, overall success rate in our study was 79%. When considered according to the stricture length, our success rate was 75% for bulbar strictures with a mean follow-up of 17 months and 83% for panurethral strictures with a mean follow-up of 19 months. Consistently with the literature, both techniques that we performed had similar success rates. But our follow-up period was short. Although success rate seems higher in panurethral strictures, we found no statistically significant association between stricture length and success rate.

Pisapati et al. (2009) reported that the recurrence rate of dorsal inlay BMGU was 13%. 7 patients developed minor wound infection, and 5 patients developed fistulae in their series (Pisapati et al., 2009). Kulkarni et al. (2017) reported that the failure rate was 15.1% by Kulkarni technique for panurethral strictures. Yalcinkaya and Kartal (2020) reported for eight surgical techniques performed by single surgeon and they found that the length of the stricture and the number of previous IU procedures affected the failure. Postoperative complication rate was 10.3% for dorsolateral onlay BMGU (Yalçınkaya & Kartal, 2020). Verla, Waterloos, Spinoit, Oosterlinck and Lumen (2020) evaluated the risk factors for anterior urethroplasty failure and they found that significant extravasation at first urethrography was an independent risk factor for urethroplasty failure. The authors found no association between previous IU procedure and failure (Verla et al., 2020). Also, oral complications may be seen after BMGU. Dubey et al. (2007) reported that oral complications after BMGU were minor, short-term, and few and most of the oral complications were settled within 30 days postoperatively. Our overall complication rate was 25% and this rate was similar with the literature. Although stricture recurrence rate in our study was 25% for bulbar and 16% for panurethral strictures, we did not find statistically significant association between stricture length and recurrence rate. And also, we did not observe any oral complication during the follow up period. All 5 patients who developed stricture recurrence underwent 3 or more IU and the number of previous IU procedure was significantly associated with stricture recurrence. As a result, we stated that 3 or more previous IU procedures affected the stricture recurrence rate of BMGU, regardless of the stricture length and location. Therefore, BMGU should be offered to the patients who developed stricture recurrence after first IU.

Barbagli et al. (2019) evaluated 1242 patients with bulbar urethral stricture and found that the stricture length was an independent predictor factor for failure. Breyer et al. (2010) reviewed the results of 443 patients who underwent urethroplasty and reported that the length of urethral stricture (greater than 4 cm) is predictive of failure after urethroplasty. In our study, success rates were similar for bulbar and

panurethral strictures and no association was shown between stricture length and failure.

We found that all recurrences occurred in patients with a history of 3 or more IU. The sole indication for IU is a primary, isolated stricture shorter than 1.5 cm (Yalçınkaya & Kartal, 2020). Even in the first treatment of short strictures, the success rate of IU is no more than 50% (Yalçınkaya & Kartal, 2020; Mundy & Andrich, 2011). In addition, long-term success rate after repeated IU procedures (> 1-5) are close to 0% (Santucci & Eisenberg, 2010). Urethral strictures that have been previously treated with dilatation or IU are unlikely to be successfully treated with another endoscopic procedure (Wessells et al., 2017). Repeated endoscopic treatment negatively effects urethroplasty outcomes by increasing tissue damage and inducing inflammatory fibrotic changes (Yalçınkaya & Kartal, 2020). Kessler et al. (2003) reported that risk of urethroplasty failure is increased in patients who previously treated with urethral stent and by 2 or more IU. Similarly, Yalcinkaya and Kartal (2020) reported that the greater number of previous IU procedures are associated with greater risk for urethroplasty failure. Increased urethroplasty failure rate after repeated IU is associated with urine extravasation into the corpus spongiosum, which results in fibrosis. The characteristic feature of a stricture is replacement of the corpus spongiosum deep to the urethral epithelium by dense fibrous tissue and excessive urine extravasation results in worse fibrosis (Barbagli et al., 2019). The strictured urethra loses the relationship among smooth muscle, extracellular matrix and vascular sinusoids. In the tissue adjacent to the urethral lumen there were prominent collagen type III deposits and lower vascular density (Breyer et al., 2010). As a result, we think that urethroplasty failure in our patients who had a previous repeated IU history was due to tissue damage and increased fibrosis in the corpus spongiosum. Our recurrence rate for bulbar strictures is slightly higher than the literature. This is mainly due to the fact that patients who have had a history of 3 or more IU procedures are mostly those with bulbar urethral stricture.

Retrospective design, 2 different surgical techniques, short follow-up period, and low patient number are the main limitations of the study. But the techniques performed in this study were both proven to be effective and safe with similar results.

Conclusion

BMGU would be preferred as a safe technique with high success rates and low complication rates in both bulbar and panurethral strictures. The number of previous IU procedure is associated with stricture recurrence. To increase the success rate, BMGU should be recommended after the first IU failure in patients with short urethral strictures. For long segment and panurethral strictures, IU should be avoided and BMGU should be recommended.

Conflict of Interest

There is no conflict of interest.

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Ethics Committee Approval

Health Sciences University Gülhane Faculty of Medicine Ethics Committee approved this study (Date: 01 July 2020; Number: 2020-289).

Informed Consent

Patient written informed consent was obtained preoperatively.

Peer-review

Externally peer-reviewed.

Author Contributions

A.E.C.: Design, Conception, Manuscript, Writing
S.Y.: Literature review
T.E.: Data Collection and/or Processing
S. S.: Data Collection and/or Processing
D.N.U.: Literature review
B.T.: Literature review
M.G.: Supervision, Critical review

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