Randomized Comparative Study Between Buccal Mucosal and Acellular Bladder Matrix Grafts in Complex Anterior Urethral Strictures

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Purpose: Urethral strictures have been a reconstructive dilemma for many years due to the limited availability of tissue substitutes and incidence of recurrence. Buccal mucosal grafts have been a favored material in instances where penile skin is unavailable due to its durability and excellent graft survival. Recently collagen based matrices derived from the bladder have been used successfully in patients with stricture disease and hypospadias. We performed a randomized comparative study to assess the outcome of the acellular bladder matrix compared to buccal mucosa in patients with complex urethral strictures.

Materials and Methods: Human demineralized bone matrix, obtained from cadaveric donors, was processed and prepared for use as an off-the-shelf material. Thirty patients with stricture 21 to 59 years old (mean 36.2) were enrolled and assessed using a standard protocol. The stricture length ranged from 2 to 18 cm (mean 6.9), of which 11 patients had bulbar, 7 had pendulous and 12 had combined bulbopendulous strictures. Of the 30 patients 7 had received no previous intervention while the remaining 23 had undergone 1 to 7 procedures (mean 1.9). All patients were randomized and alternatively assigned to receive either buccal mucosa or demineralized bone matrix and underwent an onlay procedure.

Results: All patients except 2 who were lost during followup were followed for 18 to 36 months (mean 25). In patients with a healthy urethral bed (less than 2 prior operations) the success rate of buccal mucosa grafts (10 of 10) was similar to the bladder matrix grafts (8 of 9) in terms of patency. In patients with an unhealthy urethral bed (more than 2 prior operations) only 2 of 6 patients with a bladder matrix graft were successful, whereas all 5 patients with a buccal mucosa graft had a patent urethra. Postoperative uroflowmetry showed significant voiding improvement in both groups. Histology of the graft biopsies showed normal urethral tissue characteristics.

Conclusions: This study demonstrates that the use of acellular bladder matrix is a viable option for urethral repair. Demineralized bone matrix as an off-the-shelf biomaterial achieves the best results in patients with a healthy urethral bed, no spongiofibrosis and good urethral mucosa.

Key Words: urethra, urethral stricture, reconstructive surgical procedures

Multiple techniques have been practiced to treat anterior urethral strictures using a penile skin flap for urethral reconstruction.[1,2] However, penile skin is not always available in instances where the penile skin is insufficient or diseased, which prevents its use for reconstruction.[3] In such circumstances, surgeons have used grafts as an alternative measure for urethral repair. The graft materials that have been used include skin grafts,[4] bladder epithelium,[5] buccal mucosa,[6–9] tunica vaginalis,[10–14] small intestinal submucosa[15–17] and tissue engineered buccal mucosa[18,19] with various degrees of success. Of these, the buccal mucosa has been widely accepted as the gold standard for graft procedures in the anterior urethra due to its durability and excellent graft take.[20]

Recently an off-the-shelf matrix derived from the bladder has been introduced as an acellular matrix material for urethral repair. This biomaterial is obtained from donor bladders and prepared through a multiple step process that results in the removal of cellular components, leaving a tissue matrix consisting of collagen and elastin, growth factors and macromolecules.[21] Acellular bladder matrix has been shown to be biocompatible and is able to guide urethral tissue growth in several experimental and clinical studies involving urethral pathologies.[22–24] However, it is uncertain whether ABM could serve as a universal graft material for all urethral stricture diseases. In this study we conducted a randomized comparative study using ABM and buccal mucosal grafts to determine specific applications of urethral stricture conditions through evaluating the outcome of repair.

PATIENTS AND METHODS

Patients

Between January 2002 and January 2004, 30 male patients 21 to 59 years old (average 36.2) and fulfilling the inclusion

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criteria were enrolled in this study (see table). All patients had an anterior urethral stricture, scarce or diseased penile skin (balanitis xerotica obliterans), and a stricture length greater than that amenable for end-to-end anastomosis (2 cm or greater). These patients were candidates for an onlay procedure and not a tubularized graft.

The length of the strictures ranged from 2 to 18 cm (average 6.9 cm). A total of 11 patients had bulbar strictures, 7 had pendulous strictures and 12 had combined bulbopendulous strictures. None of the patients had a stricture extending to the distal penile or meatal segments.

A total of 19 patients had received 1 or no previous interventions, while the other 11 had received 2 to 7 interventions (average 2.7), whether endoscopic or previous trials of reconstruction by other methods. The cause of the stricture was posttraumatic in 9 patients, idiopathic in 1, previous catheterization in 8, iatrogenic in 5, infectious in 5 (after urethritis) and following failed hypospadias repair in 2.

The inert acellular bladder matrix used in the study was obtained and processed in strict compliance with state and federal guidelines in a manner described in previous publications.[23] Briefly the mucosa (urothelium/suburothelium) of the bladder was grossly removed by surgical delamination. The dissected tissue was crosssectioned, and using hematoxylin and eosin stain bladder submucosa was confirmed. The BSM was rinsed with water in a stirring flask (200 rpm) for 2 days at 4 1C, and subsequently treated with 0.03% trypsin for 1 hour followed by rinsing in 10% FBS with PBS overnight at 4 1C and finally treated with Triton X-100 (0.5%) and ammonium hydroxide (0.05%) in distilled water for 72 hours at 4 1C. The solution was changed every day. After this washing step a small piece of tissue was sampled for histology to confirm the levels of decellularization. The tissue was washed with distilled water for 2 days at 4 1C, frozen, lyophilized and sterilized using Gamma irradiation (800 Rads) for subsequent use.[21]

Patients

Pt No.—Pt Age	Etiology	No. Previous Interventions	Length (cm)	Position	Surgery Performed	Outcome
1—30	Postcatheterization	1	5–6	Pendulous	Primary end-to-end anastomosis in posterior part+ buccal mucosal graft on floor of anterior part	Success
2—42	Postcatheterization	2	16–18	Bulbopendulous	ABM patch graft in posterior part + Monsieur urethroplasty in anterior part	Success
3—28	MCA	1	3–4	Bulbar	Buccal mucosal patch graft on floor	Success
4—31	Postcatheterization	1	5–6	Bulbar	ABM patch on floor	Failed
5—59	After endoscopy for transurethral prostate resection	1	13–15	Pendulous	Russell's on bulbar part + augmentation by buccal mucosa on rest of stricture (11 cm)	Success
6—35	Penoscrotal hypospadias	2	10	Pendulous	ABM patch graft on floor of urethral plate	Failed
7—39	Blunt trauma to perineum	1	3–4	Bulbar	Russell's procedure on roof + buccal mucosa on floor	Success
8—42	Idiopathic	0	5–6	Bulbar	Russell's on roof + ABM patch graft on floor	Success
9—56	After endoscopy for bladder stone	7	5–7	Bulbopendulous	Buccal mucosa patch on roof	Success
10—36	Postinfectious (urethritis)	2	5–7	Bulbopendulous	ABM patch graft	Failed
11—41	MCA	3	5–6	Bulbar	Russell's procedure on roof + buccal mucosa on floor	Success
12—38	Postinfectious (urethritis)	3	7–8	Bulbopendulous	ABM patch graft	Failed
13—21	After hypospadiac correction	1	4–5	Pendulous	Buccal mucosal patch graft on strictured part	Success
14—27	Postcatheterization	0	7–8	Bulbopendulous	ABM patch graft	Success
15—46	Postcatheterization	2	5–6 Bulbar + 2–3 pendulous	Bulbopendulous	Russell's procedure on roof of bulbar urethra + buccal mucosal patch graft on whole urethra joining 2 strictures	Success
16—36	Postcatheterization	2	5–7	Bulbar	Russell's procedure on roof + ABM patch graft on floor	Success
17—28	Blunt trauma to perineum	1	2–3	Bulbopendulous	Buccal mucosal patch graft	Success
18—34	Postinfectious (urethritis)	0	9–10	Pendulous	ABM patch graft	Success
19—44	MCA	2	6–7	Bulbar	Russell's procedure + buccal mucosal patch graft	Success
20—29	Postcatheterization	1	5–6	Bulbar	Russell's procedure + ABM patch graft	Success
21—43	Blunt trauma to perineum	0	4	Bulbar	Roofing urethroplasty with buccal mucosal patch graft	Success
22—29	After endoscopy for bladder stone	1	6–7	Bulbopendulous	ABM patch graft	Success
23—36	After endoscopy for ureteral stones	1	5–6	Bulbar	Buccal mucosal patch graft	Success
24—35	Postinfectious (urethritis)	0	8–9	Bulbopendulous	ABM patch graft + Russell's procedure on roof	Success
25—26	MCA	1	4–5	Bulbopendulous	Russell's procedure on roof + buccal mucosal patch graft on floor	Success
26—27	Postinfectious (urethritis)	0	3–4	Pendulous	ABM patch graft	Success
27—32	Blunt trauma to perineum	1	3–4	Bulbopendulous	Buccal mucosal patch graft on roof	Success
28—38	Post catheterization	0	5–6	Bulbar	Russell's procedure on roof + ABM patch graft on floor	Success
29—35	Blunt trauma to perineum	2	6–7	Pendulous	Buccal mucosal patch graft	Success
30—36	Postinfectious (urethritis)	2	5–6	Bulbopendulous	ABM patch graft	Failed