Histopathological Characteristics of Buccal Mucosa Transplants in Humans after Engraftment to the Urethra: A Prospective Study

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Purpose: Histopathological changes in buccal mucosa transplants after engraftment to the urethra and exposure to urine remain nebulous. We investigated histopathological changes in buccal mucosa transplants integrated into the urethra in humans.

Materials and Methods: We prospectively evaluated 22 patients with recurrent urethral stricture after buccal mucosa urethroplasty between November 2012 and October 2013. All patients underwent repeat buccal mucosa urethroplasty performed by a single surgeon. Intraoperatively we harvested a sample of the integrated buccal mucosa transplant previously engrafted to the urethra, a sample of healthy urethra, a sample of freshly harvested buccal mucosa from the contralateral inner cheek and a sample of fibrotic tissue from the area of the current stricture. A dedicated uropathologist performed meticulous histopathological examination of all tissue samples using hematoxylin and eosin staining. Preoperative clinical data were also collected on all patients.

Results: The mean interval from previous to current buccal mucosa urethroplasty was 22.2 months (range 4.1 to 76.0). Mean stricture length at repeat urethroplasty was 52.7 mm (range 30.0 to 70.0). Histopathological characteristics of the integrated buccal mucosa transplants were completely preserved in all patients, consisting of thick sheets of stratified nonkeratinized squamous epithelium with a stratum spinosum. Transplants were not partially or entirely overgrown with urothelium.

Conclusions: Buccal mucosa transplants retain their histopathological characteristics and are not overgrown with urothelium after urethral engraftment and urine exposure in humans. These findings may explain the superiority of buccal mucosa transplants on the outcome of substitution urethroplasty compared to that of other materials.

Key Words: urethral stricture, mouth mucosa, autografts, reoperation, histology

Abbreviations and Acronyms

DVIU = direct visual internal urethrotomy

SIS = small intestinal submucosa

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Study received institutional review board approval.

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SUBSTITUTION urethroplasty is the treatment of choice for long urethral strictures.[1] Various tissues are available for substitution, including skin, tunica vaginalis and SIS.[2–5] However, outcomes of different substitution materials vary substantially and not all succeed in daily clinical practice.[6–8]

Autologous buccal mucosa transplants, which are most commonly used for substitution urethroplasty, represent an established procedure for treating primary and recurrent urethral strictures.[9] These transplants are readily available and easy to harvest.[10] Despite use in urogenital

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surgery since the early 1990s and excellent long-term success rates for urethral stricture[11,12] the natural history of buccal mucosa transplants after engraftment to the urethra is poorly understood and has been investigated almost exclusively in animal models.[13,14] The histopathological changes of buccal mucosa transplants after integration into the human urethra and urine exposure are currently unclear.

Therefore, we histopathologically investigated the natural history of buccal mucosa transplants after engraftment to the urethra in humans.

MATERIALS AND METHODS

This study received local ethics committee approval. We prospectively evaluated 22 patients with recurrent urethral stricture after buccal mucosa urethroplasty between November 2012 and October 2013. The clinical diagnosis of recurrent urethral stricture was confirmed by uroflowmetry, and combined retrograde urethrogram and voiding cystourethrogram. Urethrocystoscopy was done in select cases.

All patients underwent repeat buccal mucosa urethroplasty performed by a single surgeon (RD) using a 1-stage ventral onlay for bulbar strictures or a dorsal inlay for penile strictures as previously described in detail.[12,15] Intraoperatively we harvested a sample of the integrated buccal mucosa transplant previously engrafted to the urethra, a sample of healthy urethra, a sample of freshly harvested buccal mucosa from the contralateral inner cheek and a sample of fibrotic tissue from the area of the current stricture. All samples were immediately transferred to 4% formol solution. After cutting 4 μm sections the slides were stained with hematoxylin and eosin using a standard protocol.[16] A dedicated uropathologist (SS) subsequently performed meticulous histopathological examination of all slides at 25×, 50× and 100× magnification.

Preoperative clinical data were prospectively collected on all patients. All statistical analysis was done with SPSS® 20. For descriptive statistics we used the mean as a measure of central tendency and the range as a measure of dispersion.

RESULTS

Patient Preoperative Clinical Characteristics

The table lists patient preoperative clinical characteristics. No patient had lichen sclerosus at repeat buccal mucosa urethroplasty. The etiology of initial urethral stricture was idiopathic in 18 patients (81.8%) and traumatic transurethral catheter placement in 4 (18.2%). In 10 cases (45.5%) the interval from previous to current buccal mucosa urethroplasty was 4.1 to 11.5 months. Six patients (27.3%) had an interval of 14.0 to 23.3 months and in the remaining 6 (27.3%) the interval was 37.3 to 76.0 months.

Preoperative clinical characteristics of 22 patients with recurrent urethral stricture after buccal mucosa urethroplasty

Mean age (range)	49.4 (20—75)
Mean ml/sec preop uroflow (range):	
Max	9.2 (1—26.3)
Av	5.5 (1—16)
Mean secs micturition (range)	67.4 (20—203)
Mean ml post-void residual urine (range)	134.9 (0—500)
Mean mm urethral stricture length (range)	52.7 (30—70)
No. urethral stricture location (%):	
Bulbar	20 (91.0)
Penile	2 (9.0)
Mean No. DVIUs (range)	3.4 (0—14)
Mean No. buccal mucosa urethroplasties (range)	1.1 (1—2)
Mean mm previous buccal mucosa transplant length engrafted to urethra (range)	56 (30—100)
Mean mos previous-current buccal mucosa substitution urethroplasty (range)	22.2 (4.1—76.0)

Preoperatively buccal mucosa urethroplasty was performed once in 21 patients (95.5%) and twice in 1 (4.5%). The technique of the previous buccal mucosa substitution urethroplasty was a ventral onlay in 18 cases (81.8%) and a dorsal inlay in 4 (18.2%). The length of the previously grafted transplant was 30 to 50 mm in 8 cases (36.4%), 60 to 100 mm in 7 (31.8%) and unknown in 7 (31.8%). In 15 patients (68.2%) the previous urethroplasty was performed at our institution by dedicated, highly experienced reconstructive surgeons (RD and MF). DVIU was performed once or twice preoperatively in 10 patients (45.5%) and 3 to 14 times in 10 (45.5%). In the remaining 2 patients (9.0%) DVIU was not performed.

Histopathological Findings

Freshly harvested buccal mucosa tissue from the inner cheek showed characteristic stratified nonkeratinized squamous epithelium (part *A* of figure). In the urethral specimen characteristic urothelium was identified, consisting of typical thin layers of pseudo stratified urothelial cells and/or foci of metaplastic nonkeratinized squamous epithelium (part *B* of figure). On gross examination the integrated buccal mucosa transplant could be distinguished from the light reddish urethra by its slightly raised smooth surface and whitish-grey appearance.

The integrated buccal mucosa transplant completely preserved the histological characteristics of oral mucosa in all patients, consisting of typically thick sheets of nonkeratinized squamous epithelium with a stratum spinosum (parts *C* and *D* of figure). Thus, the epithelium of the integrated transplant could be distinguished from the adjacent pseudo stratified, thin urothelium (parts *C* and *D* of figure).

The integrated buccal mucosa transplant was not partially or entirely overgrown with urothelium and it was well demarcated from urothelium (part *D* of figure). The junction between the integrated