



PROSPECTIVE COMPARATIVE STUDY ON OUTCOMES OF VENTRAL ONLAY BUCCAL MUCOSAL GRAFT URETHROPLASTY WITH OR WITHOUT FIBRIN GLUE.

Urology

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ABSTRACT

Objectives: We described the use of fibrin glue in ventral onlay Buccal Mucosal Graft Urethroplasty (BMGU) in patients of bulbar urethral stricture and compared the outcome without fibrin glue.

Methods: Sixty patients underwent bulbar urethroplasty with ventral onlay buccal mucosal graft and were included in this study. They were divided into 2 groups with 30 in each with group 1 with fibrin glue and group 2 without fibrin glue. The urethra was mobilized from the corpora cavernosa and opened along its ventral surface. The buccal mucosal graft was applied in the standard ventral onlay technique. Intraoperative evaluation included the lengths of surgery, stricture, and admission. Patients were followed up at 3 and 6 months in the outpatient department and primary outcome measures, that is, IPSS and Qmax were recorded at each follow-up along with complications if any.

Results: No significant difference was observed in mean lengths of surgery, stricture and admission, and distribution of pre-op IPSS and Qmax between the two groups. While a significant difference was observed in distribution of IPSS and Qmax between the two groups at 3 months and 6 months follow-up. Distribution of early complications was observed at 3 weeks follow-up after surgery with a peri catheter RGU in both groups. 3 patients were presented with a leak in group 1 and 4 patients in group 2. At 3 months 2 patients were showing complications while at 6 months follow-up only 1 patient was showing complications in each group.

Conclusions: The use of fibrin glue represents a slight but significant step toward the perfection of the surgical technique of bulbar urethral reconstruction.

KEYWORDS

Buccal Mucosa, Bulbar Urethra, Ventral onlay, Fibrin Glue, Urethral Stricture.

INTRODUCTION

Urethral injury is quite frequent in Urology with an occurrence rate reported to be as high as 0.6% in some vulnerable populations¹. Urethroplasty is the gold standard for urethral reconstruction, for the treatment of long primary urethral strictures and recurrent urethral stricture disease². Buccal mucosa has achieved extensive popularity as the graft of choice for urethroplasty for bulbar urethral strictures since the first report in 1996³.

This graft is easy to harvest and handle during surgery, it has a wet environment hence growth is early and the survival rate of graft is more⁴. Different techniques of BMGU have been reported, it includes lateral onlay, dorsal onlay, ventral onlay, and combined techniques, all these techniques are reported to have a success rate exceeding 90%, even though the most commonly used techniques are dorsal onlay and ventral onlay^{5,6,7,8,1}. Ventral onlay BMGU has many advantages compared to other techniques as it has easy exposure and a well-vascularized graft bed⁸. Numerous studies confirmed exceptional stricture recurrence-free survival of buccal mucosa graft urethroplasty (BMGU) for the treatment of urinary stricture disease^{9,10}. Stricture recurrences can, however, occur despite using an adequate surgical technique and substitution material may deteriorate over time^{11,12,13}. Recently, the use of fibrin sealant was suggested to decrease immediate urinary leakage following prostatectomy¹⁴ or to reduce the catheterization time following penile urethroplasty¹⁵. With better viral safety and optimized preparation procedure, fibrin glue has been used as a hemostatic, adhesive, and sealing agent in Europe and the United States. Some reports have shown that the application of fibrin glue to the repair of hypospadias can greatly decrease the incidence of fistula formation¹⁶. In addition, using fibrin glue as a transport and support matrix seeded with urothelial cells successfully created an artificial urethra¹⁷. Fibrin glue was used in cardiovascular surgery as a hemostatic agent against diffuse bleeding from friable tissue and along suture lines. In a sciatic nerve repair model, fibrin glue can evade the typical learning curve in micro neurosurgical operations¹⁸.

In this study, we used fibrin glue in ventral onlay buccal mucosal graft urethroplasty in patients of bulbar urethral stricture and compared the outcome without fibrin glue.

Study Design:

This randomized prospective comparative study was conducted at the Department of Urology and Renal Transplant, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, UP, after getting approval from the Institute Ethics Committee. Informed written

consent was obtained from the patient or a legal representative. All cases of bulbar urethral stricture were included in the study while patients not giving consent to participate in the study or undergoing dorsal onlay BMGU or patients suffering from major neuropsychiatric ailments, syndromes, or spinal pathology were excluded from the study.

Sample Size Calculations:

Effect Size (d): = 0.65

Tail = 1-tail

Alpha = 0.05 and Power = 0.80

Allocation ratio N2/N1 r = 1

Sample size group 1 = 30

Sample size group 2 = 30

Total sample size = 60

$$n \geq \left(\frac{1+r}{r} \right) \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2}{d^2} + \frac{Z_{1-\alpha/2}^2}{2(1+r)}$$

Formula:

All the 60 patients included in the study were examined and investigated by uroflowmetry, RGU+MCU, USG, and routine blood investigations. Preoperative evaluation included: (i) a detailed history including etiology of stricture; (ii) general and systemic examination (including oral examination) and IPSS; and (iii) investigations – urinalysis to rule out any active UTI, ultrasonography of kidney, KUB region with PVRU, Qmax by UFR, RGU, and MCU to record the site and length of the stricture.

All patients underwent ventral onlay BMGU by the same team of surgeons and were divided into two randomized groups on an alternate admission basis;

Group 1 Patients underwent ventral onlay BMGU with fibrin glue applied on the graft bed. Quilting of the graft to the graft bed was done in both arms.

Group 2 Patients underwent ventral onlay BMGU without fibrin glue application on the graft bed.

Follow-up of patients was done on an OPD basis 3 weeks after surgery with a peri catheter RGU followed by at 3 months; 6 months after surgery.

Surgical Techniques. A two-team approach for graft harvest and

perineal dissection was used. The perineal dissection team laid the stricture open to determine its length before the graft harvest team proceeded.

Buccal Harvest. The buccal harvest technique below was described before in 2011¹⁹. Patients were instructed to use a mouthwash containing chlorhexidine in the preoperative period. All the patients received intraoperative antibiotics (Ceftriaxone and Metronidazole) intravenously before the oral mucosa was excised. The face and cheek were prepped with 0.5% chlorhexidine and draped in the usual sterile manner with sterile linen.

Three 3-0 silk sutures are placed through the lip to provide traction. A mouth gag and a retractor were used to facilitate exposure. Using a marking pen, the graft was outlined 2.5 cm wide and as long as required. 0.5% of bupivacaine with epinephrine was injected underneath the graft for preemptive analgesia and intraoperative haemostasis. The graft was incised and dissected off of the buccinators muscle while avoiding Stensen's duct. The graft was pinned out and thinned on the back table. It was kept in saline until the time of transfer. The donor site was left unstitched as a routine practice²⁰⁻²². The donor site is packed with a gauze piece soaked in adrenaline and lignocaine. The oral pack is removed in the evening and the patient is asked to rinse his mouth with cold water and dilute mouth wash. The cavity was inspected for any bleeding and the patient was asked to start cold oral liquids in the evening. In a day or two, the patient was advised to shift to a semisolid, nonspicy diet and can consume a normal diet as soon as he can tolerate it.

Ventral Urethroplasty:

Ventral onlay BMGU was carried out by the technique described by Wessels²³. The patient was placed in a high lithotomy position, properly padded, and secured. Subsequently, the patient's perineum was prepped with 0.5% of chlorhexidine and draped in a normal sterile fashion. A 22F catheter was used to delineate the urethral contour and to determine the exact location of the distal portion of stricture; a number 15 scalpel was used to incise the urethra over the urethral catheter and the urethral stricture is opened completely. The lumen of the stricture was intubated with either an 8F-feeding tube or with a small (<8 mm) guidewire, and the stricture was incised until normal urethra was identified. Both proximal and distal urethral stumps were bougied to ensure they are wide open to 30F.

The buccal mucosa was then sewn onto the ventral defect using a running and interlocking 5/0 vicryl suture, for a good seal. An F16 silicone catheter was placed through the urethra. The tunic of the spongiosum is closed over the graft for a well-vascularized bed. The bulbospongiosus muscle was closed with a running 3-0 vicryl and the skin was closed with multiple vertical mattress stitches using 2-0 vicryl rapide.

Before skin closure, the wound is anaesthetized with 0.5% bupivacaine. Next, 2 mL of fibrin glue (Tissuocol, Baxter) was applied to the corpora cavernosa to facilitate the adhesion of the graft to its vascular bed. Four interrupted polyglactin 5-0 sutures were used to fix the graft corners. The ventral margins of the urethral edges were sutured to the graft. The urethra was rotated back to cover the graft, and the urethral ends were anastomosed together. After the anastomosis was completed, adjunctive fibrin glue was injected over the urethra.

The surgical site was first inspected at 48 hr postoperatively, and the dressing was changed at that time and on a daily basis thereafter for the duration of the hospital stay. Patients were discharged with per urethral catheter in situ. Oral antibiotic (tab levofloxacin 500 mg OD) was continued until catheter removal. Sutures were removed on the 10th postoperative day. Postoperatively at 3 weeks, a pericatheter RGU was carried out as an outdoor procedure. If no extravasations were discovered, PUC was removed, whereas PUC was kept for one more week in case of extravasations. After a successful voiding trial, patients were sent home with instructions for follow-up.

Intraoperative evaluation included the length of surgery, an approximate amount of blood loss during surgery, the caliber of the diseased urethra, length of stricture, length of harvested buccal mucosa, and length of admission. Patients were followed up at 3 and 6 months in the outpatient department, and IPSS and Qmax were recorded at each follow-up. Complications, if any, were recorded at

each follow-up visit.

Primary Outcome Measures Were:

- 1 Subjective: IPSS
 - 2 Objective: Qmax
- Secondary outcome measures were:
- 1 Intraoperative parameter
 - 2 Complications, if any.

Data were collected in the predetermined format. All the data were coded and entered into a master spreadsheet on MS Office Excel 2007.

Statistical Analysis:

The Shapiro-Wilk test is used to check the normality of the continuous variables. From table 1, we can see that none of the variables is normally distributed in both groups. For continuous variables, the Mann – Whitney U test was used to detect the difference between the two groups. The categorical data were analyzed by Fisher's exact test. The P <0.05 was considered significant. The data was analysed using SPSS (Windows, version 21.0; IBM, Armonk, NY, USA) and R – software version 4.0.3. The sample size was calculated using G*Power version 3.1.9.6.

RESULTS:

Table 1 is showing the distribution of the patients in two groups i.e. with Fibrin Glue and without Fibrin Glue. There was an equal distribution of patients among both the groups with 30 subjects in each group (50%). The mean age of Group 1 was 40.8 ± 5.647 while that of Group 2 was 41.4 ± 6.521 and there was no significant difference between the median age of both the groups with p-value = 0.514. The distribution of patients according to etiology of stricture was 40 % of the each in idiopathic and iatrogenic while 20% were of infective etiology, while the mean stricture length in group 1 was 3.547 cm and 3.457 cm in Group 2 and the difference was not significant. The mean length of surgery in group 1 is 106.33 ± 6.630 minutes and that in Group 2 is 104.80 ± 4.838 minutes and the difference between the two groups was found to be non-significant.

The length of admission was the same across both groups. The mean length of admission (in days) in Group 1 and Group 2 is 3.07 ± 0.254.

Table 2 is showing the distribution of primary clinical outcomes in both the groups at pre-op, 3 months post-surgery, and 6 months post-surgery. At pre-op the distribution of IPSS, the primary subjective outcome was observed the same across group 1 and group 2. The Mean IPSS pre-op in group 1 was 18.30 ± 2.020 and in group 2 was 19.40 ± 1.976. No significant difference was found between the two groups (p-value = 0.064). While the distribution means Qmax, the primary objective outcome in group 1 was 5.083 ± 0.901, and group 2 was 5.133 ± 0.718 and the difference was non-significant (p-value = 0.607).

At 3 months post-surgery the comparison of IPSS and Qmax values was done between Group 1 and Group 2. The Mean IPSS value in Group 1 was 5.47 ± 2.921 while in Group 2 was 6.57 ± 2.582 and this difference was found to be significant (p-value = 0.0001). The Mean Qmax value in group 1 was 19.6 ± 3.558 while in group 2 was 17.93 ± 3.581 and this difference too was found to be significant with a p-value = 0.0001.

At 6 months post-surgery IPSS and Qmax values were again compared between group 1 and group 2. The Mean IPSS value at 6 Months in group 1 was 6.03 ± 2.042 and in group 2 was 6.80 ± 1.769 while the Mean Qmax value in group 1 was 19.57 ± 3.048 while in group 2 was 18.07 ± 2.815. There is a significant difference found in the IPSS and Qmax values of patients between the two groups (p-value = 0.0001)

Table 1: Distribution Of Patients In Both The Groups

	Group 1 (With Fibrin Glue)	Group 2 (Without Fibrin Glue)	P-Value
Total Patients (%)	30 (50)	30 (50)	
Age (years) Mean ± SD	40.8 ± 5.647	41.4 ± 6.521	0.514
Etiology of Stricture (Total Number of patients)			
Idiopathic (24)	12	12	
Iatrogenic (24)	12	12	
Infective (12)	6	6	

Stricture Length(in cms) Mean± SD	3.547± 0.412	3.457±0.439	0.443
Length of Surgery(in min) Mean± SD	106.33± 6.630	104.80±4.838	0.317
Length of Admission (in days) Mean± SD	3.07± 0.254	3.07± 0.254	1

Distribution of early complications observed at 3 weeks follow-up after surgery with a peri catheter RGU in both the groups-In group 1, 3 patients were presented with leak and 27 were with no leak while in group 2, 4 patients were presented with leak and 26 were with no leak. The distribution of complications was noted at 3 months and 6 months follow-up in both the groups. At 3 months 2 patients were showing complications while at 6 months follow-up only 1 patient was showing complications in both the groups.

Table 2: Distribution Of Clinical Outcomes In Both The Groups (Mean± SD)

	Group 1 (With Fibrin Glue)	Group 2 (Without Fibrin Glue)	P-value
Pre-op			
IPS	18.30± 2.020	19.40±1.976	0.064
Qmax	5.083± 0.901	5.133± 0.718	0.607
3 months post-surgery			
IPSS	5.47 ± 2.921	6.57 ± 2.582	0.001
Qmax	19.6 ± 3.558	17.93± 3.581	0.001
6 months post-surgery			
IPSS	6.03 ± 2.042	6.80 ± 1.769	0.001
Qmax	19.57± 3.048	18.07± 2.815	0.001

CONCLUSION:

The use of fibrin glue represents a slight but significant step toward the perfection of the surgical technique of bulbar urethral reconstruction but more studies with a larger sample size and longer follow-up are required.

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