Asian Journal of Urology 11 (2024) 473–479

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Original Article

Analysis of the urethral stricture score and patient-related factors as predictors of outcomes following oral mucosal graft urethroplasty

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Received 4 November 2022; accepted 21 April 2023
Available online 25 July 2023

KEYWORDS
Urethral stricture;
Urethral stricture score;
Recurrence;
Urethroplasty

Abstract *Objective:* The complexity of urethral strictures can predict outcomes following urethroplasty. The previously described urethral stricture score (U score) considered only stricture-related factors to grade the complexity of urethral strictures and to predict recurrence post urethroplasty, but not considered patient-related factors for the same. We aimed to study the correlation of both of these factors to the outcomes of oral mucosal graft urethroplasty.

Methods: We retrospectively reviewed data of 101 patients who underwent oral mucosal graft urethroplasty in our institute with a minimum follow-up of 6 months. Baseline patient characteristics and stricture-related parameters were noted. The U score was calculated for all patients which consisted of the length, location, number, and etiology of stricture. Univariate and multivariate Cox proportional hazard regression models were used to determine significant risk factors of recurrence.

Results: The mean follow-up of patients was 15 months. Recurrence was seen in 28 patients and the mean time for detection of recurrence was 8 months of follow-up. The Charlson Comorbidity Index, history of previous intervention, length of strictures, location of strictures, number of strictures, history of smoking, and etiology were independent predictors of recurrence following urethroplasty. Based on these parameters, we formulated the modified U score (MU score). The scores ranged from 0 to 6 and a score of >2 was found to be predictive of recurrence. On comparing receiver operating characteristic curves for both scores by the

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Peer review under responsibility of Tongji University.

https://doi.org/10.1016/j.ajur.2023.04.002

DeLong test, the MU score had larger area under the curve than the U score.
Conclusion: The MU scoring system is the first of its kind attempt taking into consideration both patient- and stricture-related factors to predict recurrence following oral mucosal graft urethroplasty.

1. Introduction

Management of the male urethral stricture has evolved over time with advancements in both endourological and open surgical methods [1,2]. Still, there is a recurrence rate of approximately 10% following urethroplasty [3,4]. Wiegand and Brandes [5] developed the urethral stricture score (U score) which was further modified by Eswara et al. [6] to describe the complexity of anterior urethral strictures. They classified anastomotic, augmented anastomotic, and substitution urethroplasties by grafts as low complexity and urethroplasties using flaps, combination of flaps and grafts, and double faced urethroplasties as high complexity procedures. It included the etiology, location, length, and number of urethral strictures, and ranged from 4 to 9 [6]. Alwaal et al. [7] validated the association between a higher U score and urethral stricture recurrence. In their study, they justified the need of a scoring system to predict outcome of urethroplasties as it would help in preoperative counseling and explaining prognosis to patients, requirement of alternative procedures such as perineal urethrostomy or two-stage urethroplasty in patients with high risk of recurrence, and in comparing surgical techniques and outcomes at different centers [7]. A major drawback of these scoring systems was that they did not include patient-related factors such as comorbidities, addictions, and past history of interventions. Since these factors play an important role in predicting outcomes following urethroplasty, the U score does not comprehensively reflect possibility of recurrence [4,8]. Ours was a single institutional retrospective study which aimed at identifying risk factors associated with stricture recurrence after oral mucosal graft urethroplasty for anterior urethral strictures and included attributes of both stricture- and patient-related factors to develop a modified U score (MU score).

2. Materials and methods

After obtaining approval from the Institutional Ethics Committee (AIIMS/IEC/2023/4326) and obtaining informed consents from the patients, we retrospectively analyzed prospectively maintained data of all patients who underwent oral mucosal graft urethroplasty for anterior urethral strictures from March 2018 to November 2021. Demographic details, history, and comorbidities were noted. The Charlson Comorbidity Index was calculated for all the patients. All the patients underwent retrograde urethrogram (RGU) preoperatively. The length of the stricture was calculated as the maximum distance along a tangential straight line touching the edges of the normal urethra adjoining the stricture segment either above or below on RGU. In the case of involvement of a long segment, the strictures were said to be discrete only when the intervening urethra was of normal caliber. In other words, the number of strictures was calculated as the number of segments of focal narrowing with intervening urethra of normal caliber. If there were multiple discrete narrowings in the urethra, but the intervening urethral lumen was also compromised, it was classified as a single long stricture. Along with length and number, the location of stricture was also noted as per RGU findings. Patients with follow-up of less than 6 months, those patients lost to follow-up, patients with isolated meatal or posterior urethral strictures, and those who underwent urethroplasty by other techniques (primary anastomotic, augmented anastomotic, and flap and combined urethroplasty) were excluded. All the surgeries were performed by two surgeons (Choudhary GR and Singh M). Techniques used were any one of the following—dorsal onlay, dorsal inlay, or dorsolateral onlay oral mucosal graft urethroplasty. Out of the oral grafts, either buccal, labial, or lingual mucosal graft was used. The various parameters taken into consideration are summarized in Supplementary Table 1. The U score was calculated for all patients. All the patients were managed and followed up as per the standard protocol shown in Fig. 1. Recurrence was defined as the need for instrumentation or intervention following urethroplasty at any time during the follow-up and the inability to pass less than 16 Fr cystoscope per urethrally on check cystoscopy at the follow-up. The data entry was done in the Microsoft EXCEL® (Version 16.53, Redmond, Washington DC, USA) and the final analysis was done with the use of Statistical Package for Social Sciences software (Version 25.0, IBM manufacturer, Chicago, IL, USA). For quantitative data which were not normally distributed, the Mann—Whitney test was used and normally distributed data in nature were analyzed using the independent *t*-test. Qualitative data were analyzed using the Chi-square test. If any cell had an expected value of less than 5, then the Fisher's exact test was used. The Kaplan—Meier survival analysis curve was used to assess disease-free survival. Receiver operating characteristic curve was used to assess the cut-off point, sensitivity, specificity, positive predictive value, and negative predictive value of the U score to predict recurrence. Univariate and multivariate Cox proportional hazard regression analyses were used to find out significant risk factors of recurrence.

3. Results

In our study period, 126 patients underwent urethroplasty by various techniques, out of which, 16 were lost to the

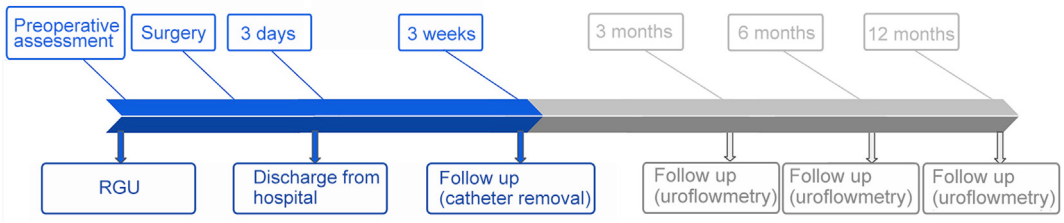

Figure 1 Management and follow-up protocol for patients undergoing urethroplasty. RGU, retrograde urethrogram

follow-up within 6 months. Two patients underwent flap urethroplasty and seven patients underwent end-to-end or augmented anastomotic urethroplasty. Owing to their low numbers and to avoid bias, the patients who underwent flap or end-to-end urethroplasty were excluded and a total of 101 patients were included in the study. The demographic details, and preoperative and postoperative characteristics of 101 patients are summarized in Table 1. Of all the patients included in the study, about 45.54% of the patients sought some sort of treatment for stricture urethra in the past. The mean length of strictures was 4.61 cm. Though the number of strictures ranged from 1 to 5, the majority of patients (71.29%) in our study had a single stricture. Twenty-eight (27.72%) patients had recurrence over a mean follow-up period of 15 (range 6–36) months. The mean duration for recurrence was 8 (range 3–24) months. The median U score was 8 in patients with recurrence. Kaplan–Meier analysis showed 73.46% disease-free survival at the end of 1 year and 59.37% at the end of 2 years (Fig. 2). Univariate analysis (Table 2) was performed to select those factors which were statistically different in groups having recurrence versus no recurrence, denoted by $p<0.05$, and then were subjected to multivariate analysis (Table 3). Although only two factors (length of stricture and history of dilatations or urethrotomies) were significant on multivariate analysis, the remaining factors which were significant on univariate analysis were independent factors predicting recurrence and have been proven to influence recurrence after urethroplasty in other studies too. Therefore, all these parameters were taken into consideration for devising the final scoring system and were scored as shown in Table 4 based on their β-coefficients. To create the weighted integer score for recurrence, individual values were calculated by dividing the β-coefficient from the regression model for each independent predictor in each group by the total β-coefficient and multiplying it by a multiplication factor. The multiplication factor was 5 if the total β-coefficient of group was less than or equal to 5 and if the β-coefficient was more than 5, then the multiplication factor was 10. Using the β-coefficient for each covariate, we created a weighted clinical decision rule by assigning a corresponding integer value for each covariate to yield the final score. Those parameters whose final value was less than 0.5 in round figures were not assigned any score. In this way, out of the various significant parameters, only the length of stricture of more than 5 cm, inflammatory etiology, presence of comorbidities, history of previous intervention, and bulbar and penile location of urethral stricture were given points. The total MU score was calculated as a sum of points given to each parameter whichever

Table 1 Distribution of demographic and clinical characteristics of patients ($n=101$).

Variable	Value
Age, year	49.42±16.11
Body mass index, kg/m^2	23.56±2.94
Length of stricture, cm	4.61±3.45
Number of strictures	1.43±0.83
Preoperative maximum flow rate, mL/s	3.87±1.59
IPSS	23.62±4.88
Etiology	
Idiopathic	54 (53.47)
Instrumentation	33 (32.67)
Traumatic	9 (8.91)
Inflammatory	5 (4.95)
Comorbidity	
Diabetes mellitus	7 (6.93)
Hypertension	22 (21.78)
Chronic kidney disease	4 (3.96)
Coronary artery disease	5 (4.95)
Deep vein thrombosis	2 (1.98)
Others	5 (4.95)
Charlson Comorbidity Index	
0	46 (45.54)
1	20 (19.80)
>1	35 (34.65)
Addictions	
Smoking	13 (12.87)
Tobacco chewing	13 (12.87)
Previous intervention	
Dilatation	27 (26.73)
Direct visual internal urethrotomy	18 (17.82)
Urethroplasty	1 (0.99)
None	55 (54.46)
Location	
Bulbar	58 (57.43)
Penile	7 (6.93)
Bulbar and penile	36 (35.64)
Type of urethroplasty	
Dorsal onlay	88 (87.13)
Dorsolateral onlay	9 (8.91)
Dorsal inlay	4 (3.96)
Oral graft used	
Buccal	87 (86.14)
Labial	3 (2.97)
Lingual	11 (10.89)

IPSS, International Prostate Symptom Score.
Note: values are presented as *n* (%) or mean+standard deviation.

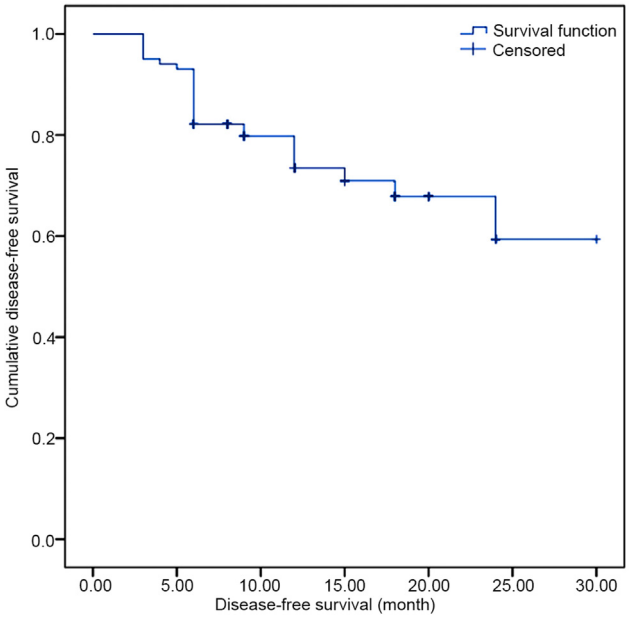

Figure 2 Kaplan–Meier survival analysis curve to assess disease-free survival.

was positive in the index patient. The scores ranged from 0 to 6, and a score of >2 was found to be predictive of recurrence. On comparison of areas under the curve (AUCs) of the MU score and U score for predicting recurrence, though the difference in the AUC on comparing receiver operator characteristic curves for both scores by the DeLong test was not statistically significant ($p=0.44$), AUC was higher for the MU score than the U score (0.95 *vs.* 0.91) (Fig. 3 and Table 5).

4. Discussion

The recurrence rate following substitution urethroplasty has been reported to be around 10%–15% in literature, but whenever encountered, is a challenge to urologists [4]. Recurrence following urethroplasty has been defined as a combination of anatomic and patient-reported outcomes, *i.e.*, the need for instrumentation in the course of follow-up of the patients, lack of improvement in symptoms of the patients, and inability to pass cystoscope of less than 16 Fr per urethrally on check cystoscopy at the follow-up [7,9,10].

In 2012, Wiegand and Brandes [5] made the first attempt to standardize the description of urethral stricture in terms

Table 2 Univariate Cox proportional hazard regression to find out significant risk factors of recurrence.

Variable	β-coefficient	Standard error	*p*-Value	HR (95% CI)
Length of stricture, cm				
≤5	Reference[a]			1.00
>5	2.15	0.41	<0.01	8.59 (3.84–19.22)
Number of stricture				
≤2	Reference[a]			1.00
>2	2.10	0.43	<0.01	8.12 (3.52–18.72)
Location of stricture				
Bulbar	Reference[a]			1.00
Penile	−11.35	448.74	0.98	0.00
Bulbar and penile	2.67	0.55	<0.01	14.37 (4.94–41.85)
Etiology				
Idiopathic	Reference[a]			1.00
Instrumentation	0.33	0.44	0.46	1.39 (0.58–3.32)
Trauma	0.91	0.59	0.12	2.47 (0.79–7.78)
Inflammatory	1.47	0.67	0.03	4.36 (1.18–16.04)
Comorbidity	1.48	0.39	<0.01	4.39 (2.02–9.54)
Smoking	1.15	0.42	<0.01	3.17 (1.39–7.21)
Tobacco chewing	−0.17	0.61	0.78	0.84 (0.25–2.80)
Previous intervention				
None	Reference[a]			1.00
Dilatations	3.92	1.03	<0.01	50.31 (6.67–379.22)
OIU	3.47	1.05	<0.01	32.24 (4.07–254.86)
Urethroplasty	4.04	1.42	<0.01	57.25 (3.56–919.88)
BMI	0.11	0.06	0.07	1.12 (0.98–1.27)
UFM	−0.04	0.12	0.74	0.95 (0.74–1.23)
IPSS	0.05	0.03	0.11	1.05 (0.98–1.13)
Type of urethroplasty				
Dorsal inlay	Reference[a]			1.00
Dorsal onlay	0.15	1.02	0.87	1.17 (0.15–8.74)
Dorsolateral	0.86	1.12	0.44	2.36 (0.26–21.45)

HR, hazard ratio; CI, confidence interval; OIU, optical internal urethrotomy; BMI, body mass index; UFM, uroflowmetry; IPSS, International Prostate Symptom Score.

[a] The sub-category has been taken as the reference for the whole category.

Table 3 Multivariate Cox proportional hazard regression to find out significant risk factors of recurrence.

Variable	β-coefficient	Standard error	*p*-Value	HR (95% CI)
Length of stricture, cm				
≤5	Reference[a]			1.00
>5	1.15	0.50	0.02	3.18 (1.18–8.58)
Number of stricture				
≤2	Reference[a]			1.00
>2	0.24	0.60	0.68	1.27 (0.39–4.16)
Location of stricture				
Bulbar	Reference[a]			1.00
Bulbar and penile	1.07	0.73	0.14	2.92 (0.68–12.41)
Etiology				
Idiopathic	Reference[a]			1.00
Instrumentation	−0.33	0.46	0.46	0.71 (0.28–1.78)
Trauma	0.09	0.81	0.90	1.10 (0.22–5.44)
Inflammatory	0.49	0.73	0.50	1.64 (0.38–6.95)
Comorbidity	0.50	0.50	0.32	1.64 (0.61–4.42)
Smoking	0.02	0.46	0.95	1.02 (0.41–2.55)
Previous intervention				
None	Reference[a]			1.00
Dilatation	3.12	1.10	<0.01	22.68 (2.58–199.24)
OIU	2.79	1.10	0.01	16.28 (1.87–141.41)
Urethroplasty	2.15	1.60	0.17	8.66 (0.37–202.01)

HR, hazard ratio; CI, confidence interval; OIU, optical internal urethrotomy.
[a] The sub-category has been taken as the reference for the whole category.

Table 4 Modified urethral scoring system for recurrence.

Variable	Score
Length of stricture (>5 cm)	1
Etiology	
Inflammatory	0.5
Charlson Comorbidity Index (>1)	0.5
Previous intervention	
Dilatation	3
OIU	2
Urethroplasty	2
Location of stricture	
Bulbar and penile	1

OIU, optical internal urethrotomy.

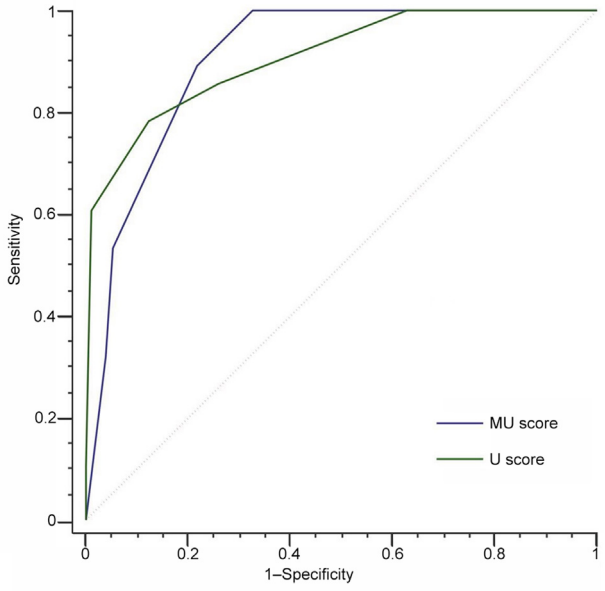

Figure 3 Comparison of area under the curve of the MU score and U score for predicting recurrence. U score, urethral stricture score; MU score, modified U score.

of complexity. Their scores consisted of the urethral stricture etiology, total number of strictures, retention (luminal obliteration *vs.* non-obliterative), and anatomic location and length. A higher score correlated with higher surgical complexity of stricture. In 2015, Eswara et al. [6] simplified it in the form of U score. In the study, they correlated increasing score with complexity of urethroplasty, but the correlation to outcome was not their intent [6]. Alwaal et al. [7] not only validated the U score to predict surgical complexity, but also showed its association with the outcome of anterior urethroplasty (incidence of recurrence) for the first time. All of these studies listed the non-inclusion of patient-related factors as their limitation [5–7]. The latest classification system for urethral strictures is the LSE system, which is a descriptive and complex system [11]. It does not give a composite numerical score like the U score [11]. Few attempts were made to describe it in points, and a recent study by Kurtzman et al. [11] validated it to be a better predictor of recurrence than the U score. Similar to other studies of the past, this study also highlighted a lack of consideration of patient-related factors as a major limitation, and thus none of these scores

Table 5 Comparison between the MU score and U score for predicting recurrence.

Parameter	MU score	U score
AUC (SE; 95% CI)	0.95 (0.02; 0.89–0.98)	0.91 (0.03; 0.83–0.96)
p-Value	<0.0001	<0.0001
Cut-off	>2	>6
Sensitivity (95% CI), %	96.43 (81.70–99.95)	78.57 (59.00–91.71)
Specificity (95% CI), %	82.19 (71.53–90.20)	87.67 (77.91–94.23)
PPV (95% CI), %	67.51 (50.90–81.44)	71.00 (52.00–85.83)
NPV (95% CI), %	98.40 (91.20–100.00)	91.40 (82.33–96.80)
Diagnostic accuracy, %	86.14	85.15

AUC, area under the curve; SE, standard error; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; U score, urethral stricture score; MU score, modified U score.

truly reflect the possibility of recurrence following urethroplasty.

Several factors have been attributed to stricture recurrence. The length of stricture is crucial in determining the outcome, with the length of >5 cm causing an increase in chances of recurrence from 6% to 14%, probably because of greater chances of ischemic contracture when larger areas are reconstructed [8]. In our study, the stricture length of >5 cm was strongly associated with recurrence ($p<0.0001$). The length was also more reliable than the number of strictures because the number may be falsely reported [5–7]. A single long stricture having a beaded appearance on retrograde urethrography may be reported as multiple short strictures or vice versa. Those patients with lichen sclerosus were grouped under inflammatory etiology. The diagnosis was made on the basis of clinical and retrograde urethrographic findings. Presence of yellowish-white patches on glans and/or saw-tooth appearance of urethra on retrograde urethrography is indicative of lichen sclerosus [9]. Biopsy is indicated only in cases where it would change course of management, which was unlikely in our patients. Therefore, biopsy was not performed [9,12]. Lichen sclerosus correlates highly with recurrence, because urethroplasty does not prevent progression of the underlying disease process [8,9,12]. Kinnaird et al. [8] conducted a multivariate analysis of 604 urethroplasties and found inflammatory etiology (lichen sclerosis) and length to be important predictors of recurrence, and they also found a recurrence rate of 75% within 6 months of surgery. Bello [13] found that the history of previous endourological interventions increased the odds of recurrence by 18-fold. Dilatations and urethrotomies can cause additional urethral injuries leading to more scarring, longer strictures, and more challenging repairs. Multiple authors have found a higher rate of recurrence in patients with obesity and comorbidities [14–18]. In our study, a higher body mass index did not correlate with higher chances of stricture recurrence. Traditionally tobacco chewing is considered to be more detrimental to the oral mucosa compared to tobacco smoking [10]. Interestingly in our study, smoking was a significant predictor of recurrence on univariate analysis but chewing tobacco was not. Combined bulbar and penile strictures fare worse compared to either penile or bulbar strictures in terms of recurrence [5] and the same has been corroborated in our study. We formulated a MU score considering all these factors, but the body mass index or history of smoking was not included in the final scoring system as the integral weighted value calculated for them was lower.

The recurrence rate post oral mucosal graft urethroplasty in our study was 27.72%. The low success rate can be attributed to late presentations, referral of more complex cases and longer strictures, and multiple interventions on these patients in low-volume centers before presenting to us for definitive management. The choice of techniques (dorsal onlay, dorsal inlay, or dorsolateral) and the choice of oral mucosal graft did not significantly influence the recurrence rate. This finding was also reported by a recent study by Barratt et al. [19]. Nearly 46% of our patients had a history of prior interventions and most of them had multiple endourological procedures before they came to us. Out of the 28 patients who had recurrence, 5 (17.86%) patients were managed by redo urethroplasty, and the rest underwent optical internal urethrotomy. On subgroup analysis, we found no significant predictors of redo urethroplasty versus endoscopic management in these patients, probably because of the low number of patients. Our study validates the previously described U score in predicting recurrence [6], but differs from it by taking into account past history of interventions and comorbidities of patients and not including number of urethral strictures in the scoring. When compared on a similar set of patients, the MU score has improved AUC on comparing receiver operator characteristic curves for both scores by the DeLong test, which is indicative of its better correlation with recurrence following urethroplasty.

Our study is limited by its retrospective nature and being a single-center study on a limited number of patients. We included only those patients who underwent oral mucosal graft substitution urethroplasty. Further validation of the MU score in the form of multi-institutional studies on large groups of patients is required.

5. Conclusion

To the best of our knowledge, this is the first attempt to develop a scoring system to predict recurrence following oral mucosal graft urethroplasty by using both patient attributes and stricture-related factors. We propose that the currently existing U score should be revised taking into account both patient- and stricture-related factors and validated on a larger cohort prospectively in order to become a more accurate predictor of outcome after

urethroplasty. The MU score can be used for prognosticating outcomes in patients with urethral strictures and comparing results of different techniques on patients with similar scores.

Author contributions

Study concept and design: Nikita Shrivastava.
Data acquisition: Nikita Shrivastava.
Data analysis: Nikita Shrivastava.
Drafting of manuscript: Nikita Shrivastava, Rahul Jena, Deepak Prakash Bhirud.
Critical revision of the manuscript: Nikita Shrivastava, Rahul Jena, Deepak Prakash Bhirud, Gautam Ram Choudhary, Mahendra Singh, Arjun Singh Sandhu.

Conflicts of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajur.2023.04.002.

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