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UROLOGY

External validation and comparison of current scoring systems in retrograde intrarenal surgery: Multi-institutional study with 949 patients

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Abstract

Objectives: To externally validate and compare Resorlu-Unsal stone score (RUSS), modified Seoul National University Renal Stone Complexity Score(S-ReSC), Ito's nomogram, and Retrograde Intra-Renal Surgery (R.I.R.S.) scoring systems for predicting capabilities of both the stone-free status and complications in a multi-institutional study.

Materials and Methods: We performed a retrospective analysis of 949 patients who underwent flexible ureterorenoscopy (f-URS) and laser lithotripsy for renal stones in two institutions between March-2015 and June-2020. The RUSS, modified S-ReSC, Ito's nomogram, and R.I.R.S. scores were calculated for each patient by the same surgeon on imaging methods. Results were compared for their predictive capability of stone-free status and complications.

Results: Of 949 patients 603 were male and 346 were female with a mean age of 47.2 $\pm$ 14.3 (range 2-84 years). Mean stone burden was 102.6 $\pm$ 42.2 (48-270 mm^2). All nomograms predicted stone-free status (Area Under Curve (AUC) were 0.689, 0.657, 0.303, and 0.690, respectively). All four scoring systems predicted complications with AUC values of 0.689, 0.646, 0.286, and 0.664 for RUSS, modified S-ReSC, Ito's nomogram, and R.I.R.S., respectively. Although all scoring systems were able to predict complications only Ito's nomogram was able to predict Clavien $\geq$2 complications.

Conclusion: All four scoring systems (RUSS, modified S-ReSC, Ito's nomogram, and R.I.R.S.) could predict stone-free status after f-URS, however, the AUC values are not satisfactory in our large patient cohort. Although these scoring systems were not developed for predicting post-operative complications, they were associated with complications in our study. However, these four scoring systems have some significant limitations. The ideal scoring system is yet to be developed.

1 | INTRODUCTION

In parallel to the minimal invasive surgery trend in urological surgery, flexible ureterorenoscopy (f-URS) and laser lithotripsy gained a significant popularity in the treatment of renal stones. Despite the technological advancements in optical and lithotripsy systems, there are still some limiting factors including stone burden and abnormal renal anatomy.[1] To standardize reporting the outcomes in scientific studies and pre-operative counseling of patients some scoring systems were developed but none of them gained popularity and were not widely used. The ideal nomogram should include all the variables that might affect the outcome, besides should be simple, accurate, and easy to apply in office conditions. The success of a f-URS can not only be evaluated with stone-free rates, but the ideal success should be stone-free rates without any complication or with acceptable complication rates. So, the ideal scoring system should predict the complications besides the stone-free rates. The first scoring system for predicting the success of f-URS was developed by Resorlu et al in 2012.[2] After than modified Seoul National University Stone Complexity score (S-ReSC),[3] a nomogram by Ito et al[4] and R.I.R.S. scoring system[5] were developed. We aimed to externally validate and compare these four scoring systems for predicting capabilities of both the stone-free status and complications in a multi-institutional study.

What's known?

- The search for a widely available and generalizable scoring system in retrograde intrarenal surgery continues.

What's new?

- In this study, we aimed to shed light on the development of the ideal scoring system by emphasizing the lack of the current scoring systems. We have also showed that these scoring systems can also predict the risk of complications.

2 | MATERIALS AND METHODS

We performed a retrospective analysis of 949 patients who underwent f-URS and laser lithotripsy for renal stones in two institutions (HSU Izmir Bozyaka Training and Research Hospital, HSU Ankara Diskapi Training and Research Hospital) between March 2015 and June 2020. Preoperative evaluation of the patients included medical history, physical examination, complete blood count, urine analysis and culture, serum biochemistry, and non-contrast computed tomography (NCCT). Cefazolin and Ceftriaxone were used for prophylaxis in the patients. Patients who had positive urine culture preoperatively and treated accordingly were continued with the same antibiotics. Stone characteristics and renal anatomical characteristics were evaluated on NCCT. Stone size was determined by measuring the longest axis at NCCT; in case of multiple stones, the sum of each stone size was calculated. Stone surface area and lower pole infindibulo-pelvic angle (IPA) were measured as defined before.[6,7] All procedures were performed by experienced surgeons by using different size and brand ureterorenoscopes (7.5F Flex –X2 (Karl Storz, Tuttlingen Germany), Olympus URF P-5 (Olympus, Tokyo, Japan), 9.5F Pusen (Zhuhai Pusen Medical Technology Co, Ltd., Zhuhai, China). Patients with missing data and/or lacking 1st month post-operative NCCT were excluded from the study. All procedures were performed under general anesthesia in the lithotomy position. A diagnostic ureteroscopy with a semi-rigid ureterorenoscope was always performed at the beginning of surgery both to dilate the ureter and pass a safety guidewire. A ureteral access sheath (9,5-11,5; 12-14 Fr) was placed according to the surgeon's preferences. The stones were fragmented by using a holmium:YAG laser. If needed some fragments were removed with tipless nitinol stone baskets. At the end of the procedure, a D-J stent was placed according to the surgeon's decision. All patients were evaluated with NCCT at 1st month for stone-free status. Residual fragments <2 mm were accepted as insignificant.

The RUSS, modified S-ReSC, Ito's nomogram, and R.I.R.S. scores were calculated for each patient by the same surgeon on imaging methods. Results were compared for their predictive capability of stone-free status and complications.

2.1 | Summary of scoring systems

2.1.1 | Resorlu-Unsal stone score (RUSS)

Stone size >20 mm, lower pole stone and IPA < 45°, stone number in different calyces >1, abnormal renal anatomy (horseshoe kidney or pelvic kidney). Each condition was given 1 point. Total score of 0-4.

2.1.2 | Modified S-ReSC

The modified S-ReSC score was assigned according to the number of sites involved in the renal pelvis (#1), superior and inferior major calyceal groups (#2-3), and anterior and posterior minor calyceal groups of the superior (#4-5), middle (#6-7), and inferior calyx (#8-9). If the stone was in the inferior sites (#3, #8-9), one additional point per site was added.

2.1.3 | Ito's nomogram

Stone volume (≤500, 500< × ≤1000, 1000< × ≤2000, >2000 mm^3), lower pole calculi, operator experience (<50, ≥50), hydronephrosis, and number of stones. A nomogram score was calculated according to these parameters (total score 0-25). High total score was predictive of a successful outcome.

2.1.4 | R.I.R.S. score

Renal stone density (≤1000, >1000), inferior pole stone (non-inferior, inferior with RIPA>30°, inferior with RIPA≤30°), renal infindibular length (≤25, >25 mm), stone burden (≤10, >10 and ≤20, >20 mm). Total score range 4-10 points. Ten points indicate the most complex situation.

2.2 | Statistical analysis

All analysis were performed by using Statistical Package for the Social Sciences (SPSS, Version 22.0; SPSS, Chicago, Ill). Patients were divided into two groups according to SF status. *T*-test and Pearson χ^2 test were used to compare variables between SF and non-SF groups. ROC curve analysis was used for prediction levels of the nomograms. Statistical significance was accepted as $P < .05$ for all analyses.

3 | RESULTS

A total of 949 who underwent f-URS and laser lithotripsy between March 2015 and June 2020 were included in the study. Of 949 patients 603 were male and 346 were female with a mean age of 47.2 ± 14.3 (range 2-84 years). Mean stone burden was 102.6 ± 42.2 (48-270 mm^2). In Table 1, the comparison of characteristics of stone-free and non-stone-free patients was shown. There were significant

TABLE 1 The comparison of characteristics of stone-free and non-stone-free groups

Variables	Stone-free group (n = 743)	Non-stone-free group (n = 206)	*P*
Age	46.3 ± 14 (2-84)	50.4 ± 15 (4-83)	**<.001**
BMI	27.2 ± 4.5 (12.4-53.3)	27.6 ± 7.1 (7.1-46.7)	.195
Gender			
Male	484 (65.1)	119 (57.8)	.052
Female	259 (34.9)	87 (42.2)	
Previous SWL history	122 (16.4)	35 (17)	.845
Previous URS or PNL history	161 (21.7)	79 (38.3)	**<.001**
Renal anatomical anomaly	28 (3.8)	14 (6.8)	.062
Laterality			
Right	358 (48.2)	98 (47.6)	.371
Left	361 (48.6)	105 (51)	
Bilateral	24 (3.2)	3 (1.5)	
Number of stone			
Single	545 (73.4)	107 (51.9)	**<.001**
Multiple	198 (26.6)	99 (48.1)	
Stone density (Hounsfield Units (HU))	1051.2 ± 221.4 (365-1651)	981.1 ± 236.6 (426-1600)	**<.001**
Maximum Stone diameter (mm)	14.3 ± 7.8 (5-70)	20.4 ± 10.8 (7-76)	**<.001**
Stone burden (mm^2)	87.9 ± 21.1 (48-150)	139.7 ± 57.4 (64-270)	**<.001**
Stone location			
Lower calix	174 (23.4)	90 (43.7)	**<.001**
Other locations	569 (76.6)	116 (56.3)	
Preoperative hydronephrosis	430 (57.9)	87 (42.2)	**<.001**
Preoperative J stent			
No	636 (85.6)	151 (73.3)	**<.001**
J stent	107 (14.4)	55 (26.7)	
Operation time	46.5 ± 19 (10-150)	58.3 ± 27.2 (10-150)	**<.001**
Access sheath usage	573 (77.1)	148 (71.8)	.117
Hospitalization time	1.3 ± 1 (1-15)	1.7 ± 1.7 (1-15)	**<.001**
Complication presence	58 (7.8)	53 (25.7)	**<.001**
Clavien complication groups			
Grade 0-1	728 (98)	194 (94.2)	**.004**
Grade 2-4	15 (2)	12 (5.8)	

Bold indicates $P < .05$.

TABLE 2 Data of the nomograms between stone-free and non-stone-free groups and prediction levels of the nomograms for stone-free status

Nomograms	All patients (n = 949)	Stone-free group (n = 743)	Non-Stone-free group (n = 206)	*P*	AUC	CI
RUSS	0.6 ± 0.8 (0-3)	0.5 ± 0.7 (0-3)	1.1 ± 0.9 (0-3)	**<.001**	0.689	0.648-0.730
Modified S-ReSC	1.6 ± 0.9 (1-8)	1.5 ± 0.8 (1-7)	2 ± 1 (1-8)	**<.001**	0.657	0.614-0.700
Ito's nomogram	19 ± 4.3 (8-25)	19.6 ± 4 (8-25)	16.7 ± 4.3 (8-25)	**<.001**	0.303	0.264-0.343
R.I.R.S.	5.8 ± 0.9 (4-9)	5.6 ± 0.8 (4-8)	6.3 ± 1.1 (4-9)	**<.001**	0.690	0.648-0.732

Note: ROC curve analysis was used for prediction levels of the nomograms. Bold indicates $P < .05$.

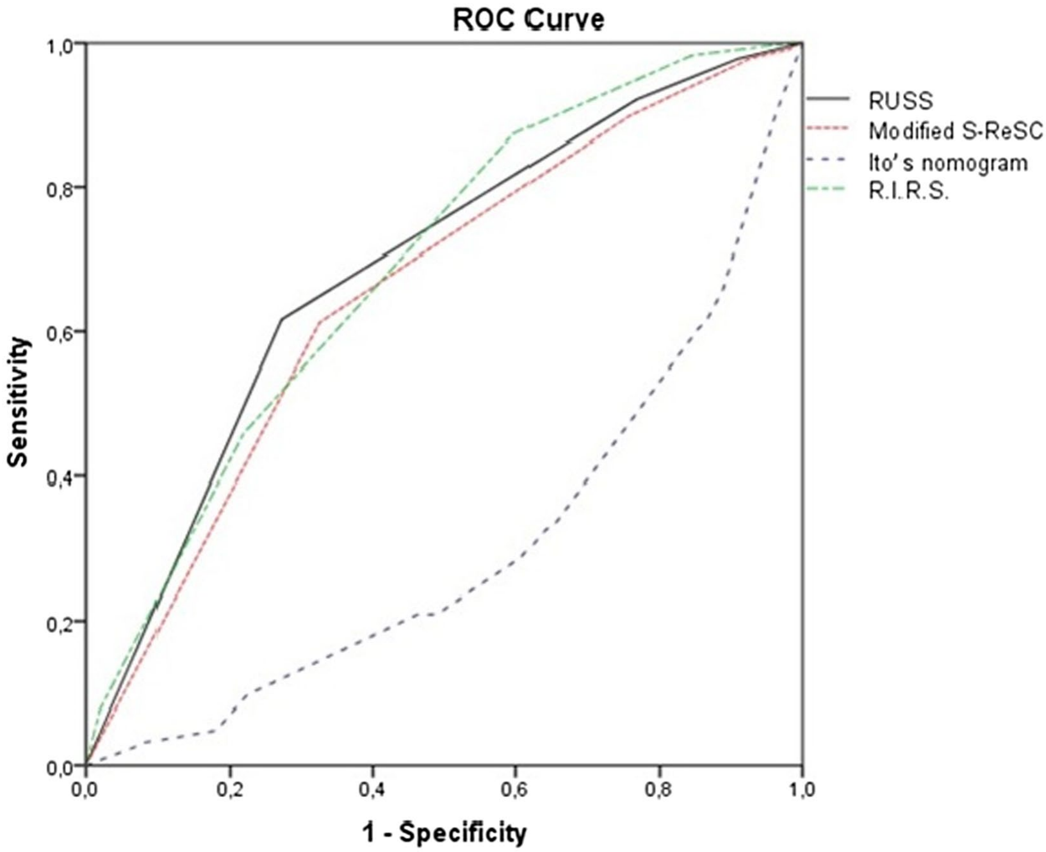

FIGURE 1 ROC curves of the nomograms for prediction of SF status

differences between two groups according to age, previous URS or percutaneous nephrolithotomy (PCNL) history, number of stone, stone density, maximum stone diameter, stone burden, lower calyx localization, preoperative hydronephrosis, preoperative J stent placement, operation time, hospitalization time, and complications. All nomograms (RUSS, modified S-ReSC, Ito's nomogram, R.I.R.S.) were predicted stone-free status (AUCs were 0.689, 0.657, 0.303, and 0.690, respectively) (Table 2). Only the Ito's nomogram's ROC curve was below the reference line, because the higher score indicates the residual stone presence in this nomogram, however, a higher score was predictive of stone-free in others (Figure 1). All scoring systems were predicted complications with AUC values of 0.689, 0.646, 0.286, and 0.664 for RUSS, modified S-ReSC, Ito's nomogram, R.I.R.S., respectively (Table 3). Although all scoring systems were able to predict complications only Ito's nomogram was able to predict Clavien ≥2 complications ($P = .016$) (Figure 2).

3.1 | Comment

Recent technical improvement including miniaturization, improved deflection, and enhanced optical quality have increased the use of flexible ureterorenoscopes in renal stones. Although f-URS is not recommended as a first-line treatment modality for renal stones <2 cm at current guidelines, a recent meta-analysis resulted in an average of 91% stone-free rate with acceptable complication rates and with an average of 1.45 procedures per patient (range 1.11-1.82).[6,8] As being more widely used, we need some scoring systems that can

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TABLE 3 Data of the nomograms between non-complicated and complicated groups and prediction levels of the nomograms for non-complication

Nomograms	Non-complicated group (n = 838)	Complicated group (n = 142)	*P*	AUC	CI
RUSS	0.5 ± 0.7 (0-3)	1.2 ± 1.1 (0-3)	**<.001**	0.689	0.632-0.746
Modified S-ReSC	1.6 ± 0.8 (1-7)	2.2 ± 1.4 (1-8)	**<.001**	0.646	0.585-0.707
Ito's nomogram	19.4 ± 4 (8-25)	15.7 ± 5 (8-25)	**<.001**	0.286	0.230-0.341
R.I.R.S.	5.7 ± 0.9 (4-8)	6.4 ± 1.1 (4-9)	**<.001**	0.664	0.608-0.720

Note: ROC curve analysis was used for prediction levels of the nomograms. Bold indicates $P < .05$.

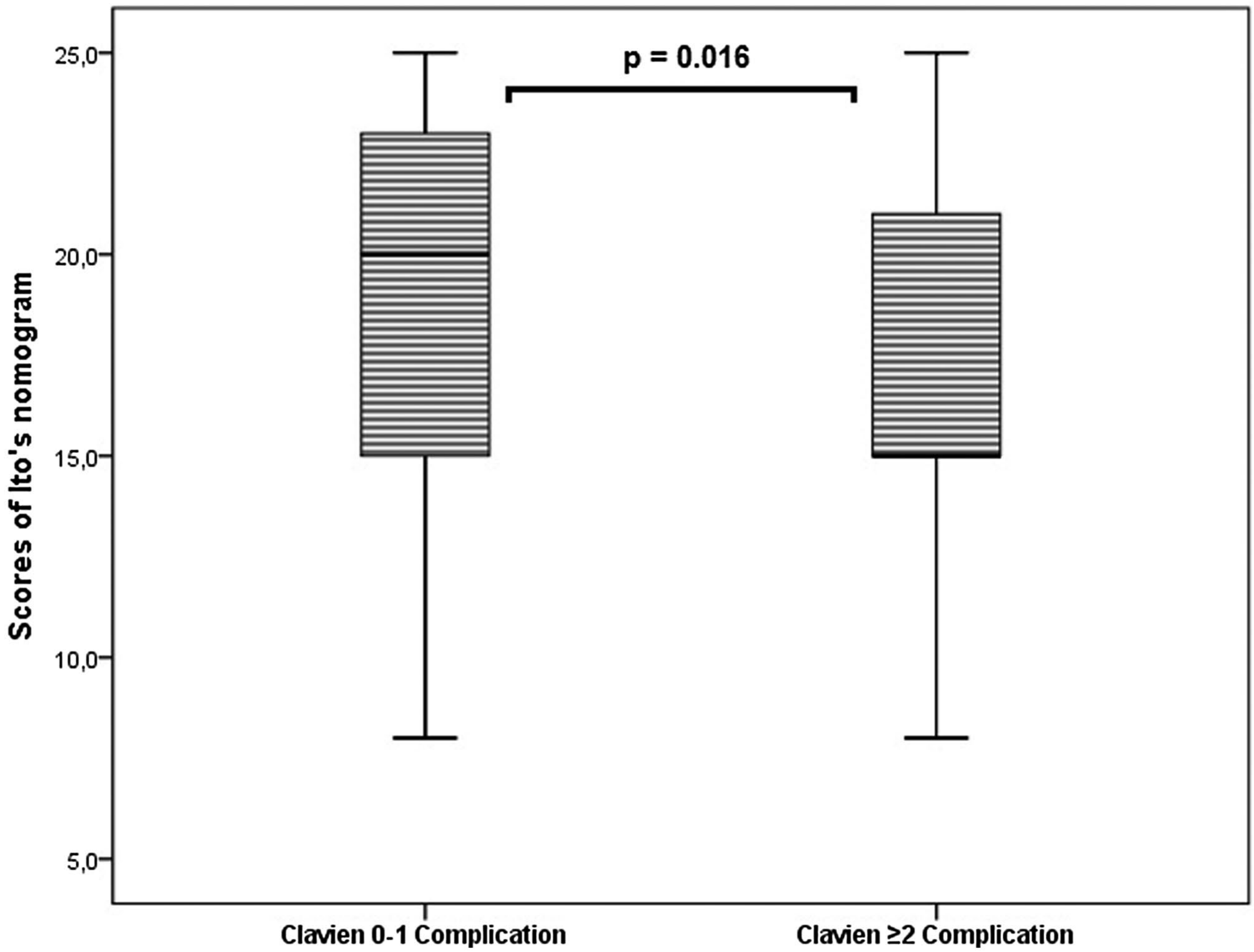

FIGURE 2 Box-plots of the prediction of Clavien ≥2 complications for Ito's nomogram

be used to predict the success and potential complications after f-URS for counseling of the patients preoperatively.

The variables that were used in these four studies were not standard. Although abnormal renal anatomy is one of the parameters of RUSS, patients with musculoskeletal and renal abnormality are directly excluded in R.I.R.S. Also, the renal anomaly was not studied in modified S-ReSC. IPA was an independent predictive factor in RUSS and R.I.R.S., however, it was not studied in modified S-ReSC and nomogram by Ito et al So, if a variable was not evaluated in a study we cannot know if it is an independent predictive factor or not.

The success was defined as stone-free status in all scoring systems. However, no standard imaging modality was used and also the timing of imaging was different between studies. And thus, there can be a significant bias between studies. In R.I.R.S stone-free status was evaluated with kidney-ureter-bladder (KUB) plane graphy at 1st month and >2mm fragments were accepted as not-stone-free, computed tomography (CT) was used whenever necessary. In the nomogram of Ito et al stone-free status was evaluated with non-contrast CT at 3rd month. In RUSS, treatment success was defined as stone-free or residual fragment ≤1 mm at 1st month non-contrast CT imaging. In modified S-ReSC stone-free was defined as no evidence of residual stone at 1st month NCCT.

The success of a procedure can be defined as to reach a targeted end-point without any complication or with acceptable complication rates. Thus, an ideal f-URS scoring system should foresee complications besides stone-free. None of the scoring systems examined the relation of complexity scores and complications. Only in R.I.R.S. authors indicated that the score is correlated with operation time and thus it can be used to predict to leave the operation for a second session and complications can be avoided. All four scoring systems were able to predict complications in the present study, but only nomogram by Ito et al could predict Clavien ≥2 complications.

Stone burden is one of the most important predictors of stone-free after f-URS as we know from previous studies.[8,9] As expected, stone burden was an independent predictor of success in all scoring systems except modified S-ReSC. This is unsurprising for modified S-ReSC, because the mean stone burden was significantly lower compared with other studies. The authors indicated that patients with high stone burden were undergone percutaneous nephrolithotomy and excluded from the study. Although modified S-ReSC can be predicted stone-free status even in our study, it can be no doubtfully said that success of f-URS for 1cm stone cannot be equivalent to 3 cm stone in the same location that both were given the same score in S-ReSC.

There are two studies comparing the current nomograms. Erbin et al compared the RUSS and modified S-ReSC and found out that RUSS, musculoskeletal deformity, and stone size were independent factors in logistic regression analysis.[10] And the AUC values were not satisfactory in terms of nomogram's predictive accuracy (0.655 and 0.596 for RUSS and modified S-ReSC, respectively). In another recent study by Richard et al RUSS, modified S-ReSC, S.T.O.N.E., and Ito's nomogram were compared.[11] The major limitation of that study was evaluation of the stone-free status that they made it via visual inspection using ureterorenoscope and fluoroscopy at the end of the procedure in the absence of clinical complications. They concluded that all scoring systems were predicted the stone-free status but none of them were predictive of complications after RIRS. Different from the former study all nomograms could predict the stone-free status and complications in our study as being the Ito's nomogram most sensitive.

In the present study, all four nomograms underwent external validation in a significantly high number of patient population. Although all nomograms were predictive of stone-free status, the AUC values were lower than that in the original study and were not satisfactory. The AUC values in the original study and in our study were 0.806 versus 0.657, 0.87 versus 0.697, and 0.904 versus 0.690 for modified S-ReSC, Ito's nomogram, and R.I.R.S., respectively. The AUC value was not calculated in RUSS.

Strengths of our study include a high number of the study group, standardized post-operative imaging at a determined time period and various cases including different anatomical abnormalities. Limitation of our study is its retrospective design.

We think that none of these four scoring systems is ideal. Because the success definition is not standard and studied variables are limited. To constitute an ideal nomogram a multi-center study examining the all known potential variables with a strict success definition in a defined time period can be planned with a high number of patients. The ideal scoring system could also be used in daily clinical practice. In clinical practice, it is hard to calculate stone burden by measuring the diameter of all calculi (especially in multiple stones) or to measure the IPA. In our opinion, a stone score should be given by radiologists in imaging reports whenever a widely used ideal nomogram can be developed.

4 | CONCLUSION

All four scoring systems (RUSS, modified S-ReSC, Ito's nomogram, and R.I.R.S.) could predict stone-free status after f-URS, however, the AUC values are not satisfactory in our large patient cohort. Although these scoring systems were not developed for predicting post-operative complications, they were associated with post-operative complications in our study. All these four scoring systems have some significant limitations. The ideal scoring system is yet to be developed.

DISCLOSURES

All authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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