

Predictive Factors for Unsuccessful Holmium: YAG Laser Lithotripsy in the Retrograde Treatment of Proximal Ureteral Stones

Proksimal Üreter Taşlarının Retrograd Tedavisinde Holmiyum: YAG Lazer Litotripsisinin Başarısızlığını Öngören Faktörler

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Introduction

Proximal ureteral stone treatment can be performed using various methods, including rigid or flexible retrograde ureteroscopy (URS), extracorporeal shock wave lithotripsy (SWL), percutaneous nephrolithotomy, or open/laparoscopic ureterolithotomy. The choice of technique depends on factors related to the stone, such as location, size, and density, as well as anatomical factors, patient comorbidities, severity and duration of pain, presence of obstruction, availability of technical equipment at the hospital, the surgeon's experience, and patient preference (1,2).

According to the 2025 European Association of Urology (EAU) Guidelines, both URS and SWL are recommended for proximal ureteral stones larger than 10 mm, while either approach may be suitable for smaller stones (3). In the context of URS, the duration of hospitalization, stone-free achievement, and time to resume normal life are all significantly reduced. The primary disadvantage of SWL is the prolonged treatment duration due to repeated applications and radiation exposure. With advancements in technology, the emergence of URS devices with finer calibrations, the development of flexible URS, and the use of lasers as lithotripters have enhanced stone-free outcomes and reduced complications (4).

Given these improvements, evaluating the determinants of procedural success remains essential. The aim of the present study was to evaluate the clinical, radiological, and procedural factors that negatively impact the success of holmium: YAG laser lithotripsy performed via semi-rigid ureteroscopy in cases of proximal ureteral stones.

Materials and Methods

This retrospective study analyzed the medical records of patients who underwent semi-rigid ureteroscopy (URS) in the management of proximal ureteral stones at the Urology Department of Adiyaman University between April 2015 and May 2025. This study received Institutional Review Board approval (Non-Interventional Clinical Research Ethics Committee, University of Adiyaman (approval number: 2021/08-11, date: October 26, 2021). All procedures were conducted in accordance with the ethical standards of the Declaration of Helsinki, and written informed consent was obtained from all patients or their legal guardians. Proximal ureteral stones were defined as calculi located between the ureteropelvic junction and the upper border of the sacroiliac joint. The following data were extracted from the patients records: age, sex, date of

surgery, routine biochemistry, complete blood count, urinalysis, urine culture, stone location, degree of hydronephrosis (grades 1 and 2 were categorized as mild, and grades 3 and 4 as severe), history of previous surgery, history of preoperative SWL, findings from direct urinary system radiography (DUSR), ultrasonography, and computed tomography (CT), including distance of the stone from the renal pelvis, stone density, stone volume, coronal and axial dimensions, and the number of stones (Figure 1), use of a stone cone, hospitalization period, operative time, and stone opacity status (opaque or non-opaque).

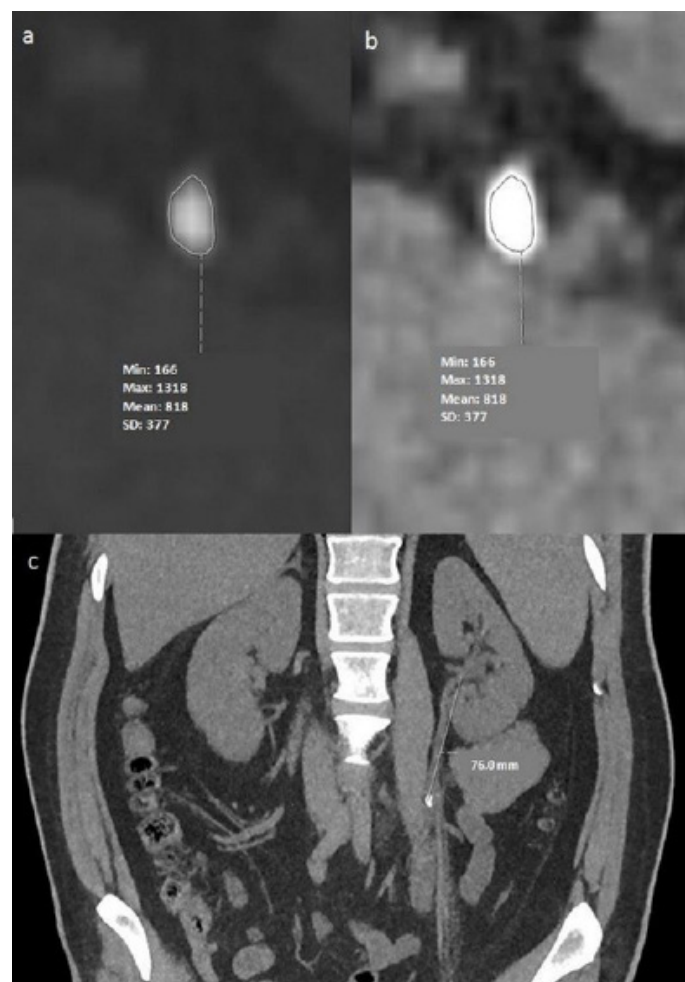


Figure 1. Measurement of the density of a patient's left proximal ureteric stone and stone distance to the renal pelvis

A total of 484 patients with proximal ureteral stones who underwent ureteroscopic lithotripsy during the study period were initially screened for eligibility. After applying the predefined exclusion criteria, 212 patients were ultimately included in the final analysis. Patients who had previously undergone ureteral stone surgery; those with a double-J (DJ)

stent; those who had a solitary kidney, bilateral ureteral stones, multiple stones in different locations, coagulation disorders, congenital anomalies, or renal failure and those who did not undergo preoperative CT, previous SWL were excluded from the study. These patients were grouped into three groups: Group 1 was composed of patients who achieved complete stone-free status. Group 2 (retropulsion, defined as proximal migration of the ureteral stone into the renal collecting system during lithotripsy due to irrigation pressure or laser-induced mechanical forces) comprised patients whose stones migrated to the kidney during fragmentation, resulting in prolonged operative time or increased laser energy requirement, with stones subsequently detected in the kidney during fluoroscopy. Group 3 consisted of patients with residual stones larger than 3 mm in the kidney after fragmentation.

Surgical Technique

The operations were performed by urology specialists with at least 10 years of experience in URS. All patients were operated on in the lithotomy position under general or regional anesthesia (spinal or epidural). To ensure patient safety, all patients underwent preoperative evaluations that included obtaining negative urine cultures prior to surgery. In cases where any patient exhibited positive urine cultures, they received appropriate antimicrobial treatment before proceeding with the surgical intervention. This approach prioritizes the health and well-being of patients undergoing surgery. After entering the bladder with an 8/9.8-Fr semi-rigid ureterorenoscope (Richard Wolf, Knittlingen, Germany), the ureter was accessed with the guidance of a guidewire. In patients for whom semi-rigid URS could not be advanced into the ureter, ureteral balloon dilation was performed to facilitate access (UroMax Ultra, Boston Scientific, USA). Stones were fragmented using a 40-W holmium: YAG laser (Dornier Med-Tech GmbH, Wessling, Germany) with a 360 µm laser fiber operating at 0.8-1.5 J and 8-12 Hz, after which large fragments were retrieved using forceps or a basket catheter. Upon completion of the procedure, the ureter was appraised endoscopically under direct visualization to assess for mucosal damage. DJ stents (4.8Fr, 28cm, Arılar, Istanbul, Turkey) were inserted in patients with high stone burden, in cases where URS remained unfeasible despite dilation, ureteral lacerations, severe edema at the stone level, or migrated stones, as well as when access to the stone was not possible. For the remaining patients, 4-5 Fr ureteral catheters were placed. Patients with macroscopic hematuria were monitored with a Foley catheter.

Postop 1. On the first postoperative day, all patients underwent DUSR to assess the position of the DJ stent and the presence of residual stones. DJ stents were removed one month postoperatively.

During the procedure, there were two different approaches for managing patients whose stones were retropulsed to the kidney. For those in whom a Flexible Ureteroscope (URS) was utilized to access the kidney, the stones were successfully fragmented with a holmium laser. In contrast, for cases where the Flexible URS was not employed to access the ureter, a double-J (DJ) stent was implanted, and a follow-up session of the procedure was scheduled to address the stone removal. Patients were classified as stone-free if no stone fragments were found during follow-up evaluations conducted via DUSR, ultrasonography, and CT scans at 1 to 3 months after surgery. Additionally, any Stone fragments ≤ 3 mm that were asymptomatic, non-obstructive, and non-infectious were considered residual fragments not clinically relevant. In this context, successful outcomes are defined as either the complete stone-free status or the presence of residual fragments that are considered clinically insignificant, specifically those smaller than 3 mm. To assess perioperative complications, the Satava classification system is utilized, while postoperative complications are assessed using the Modified Clavien-Dindo classification (5,6). Notably, complications that are classified as grade 3 or 4 under the Clavien-Dindo system, or grade 2 or 3 under the Satava system, are categorized as major complications.

Statistical Analysis

Statistical analyses were conducted using SPSS v23.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was applied to assess data normality. Normally distributed continuous variables are presented as mean $\pm$ SD, and non-normally distributed variables as median (minimum-maximum).

Comparisons between groups were made using one-way ANOVA for normally distributed data and the Kruskal-Wallis test for non-parametric data. Post-hoc analyses were performed using the Bonferroni or Tamhane T2 tests. Categorical variables were analyzed with the Pearson chi-square test. The predictive accuracy of significant variables was assessed using receiver operating characteristic (ROC) curve analysis. Statistical significance was set at $p < 0.05$.

Results

A total of 212 patients were included in the final analysis. The overall stone-free rate was 74.5% (158/212), while retropulsion

occurred in 15.1% (n=32) and residual fragments >3 mm were observed in 10.4% (n=22) of patients. The demographic and

stone-related characteristics of the study groups are summarized in Table 1.

Table 1. Analysis of categorical and numerical variables

Variable	Group 1 (n=158)	Group 2 (n=32)	Group 3 (n=22)	p (Overall)	p (1-2)	p (1-3)	p (2-3)
Sex (male/female), n (%)	104/54 (65.8/34.2)	21/11 (65.6/34.4)	15/7 (68.2/31.8)	0.975	-	-	-
Side (right/left), n (%)	74/84 (46.8/53.2)	19/13 (59.4/40.6)	11/11 (50/50)	0.431	-	-	-
Stone cone (present/absent), n (%)	16/142 (10.1/89.9)	2/30 (6.3/93.7)	5/17 (22.7/77.3)	0.136	-	-	-
Contour (smooth/lobulated), n (%)	108/50 (68.3/31.7)	22/10 (68.7/31.3)	12/10 (54.5/45.5)	0.424	-	-	-
Hydronephrosis (mild-mod/severe), n (%)	138/20 (87.3/12.7)	17/15 (53.1/46.9)	18/4 (81.8/19.2)	<0.001	<0.001	0.503	0.043
Age (years), mean $\pm$ SD	41.7 $\pm$ 16.3	42.2 $\pm$ 19.2	37.8 $\pm$ 17	0.57	-	-	-
Stone density (HU), mean $\pm$ SD	692 $\pm$ 234	916 $\pm$ 239	868 $\pm$ 191	<0.001	<0.001	0.003	1.000
Stone density (median HU)	269 (51-517)	345 (172-498)	314 (201-540)	<0.001	<0.001	0.004	0.976
Maximum density (HU), median (min-max)	1131 (343-1712)	1434 (740-1704)	1288 (1000-1879)	<0.001	<0.001	<0.001	0.928
Stone-renal pelvis distance (mm), median (min-max)	27 (6-75)	7.5 (5-36)	24 (6-48)	<0.001	<0.001	0.751	0.005
Stone volume (mm ³), median (min-max)	168 (40-1453)	459 (56-1916)	231 (54-3578)	<0.001	0.001	0.551	0.709
Coronal/Axial ratio, median (min-max)	1.29 (0.79-2.43)	1.18 (0.64-3.78)	1.33 (0.86-2.48)	0.155	-	-	-
Operative time (min), median (min-max)	40 (30-60)	40 (30-90)	40 (35-90)	0.99	-	-	-

Categorical variables were analyzed using the Pearson chi-square test. Normally distributed continuous variables were compared using one-way ANOVA. Non-normally distributed variables were analyzed using the Kruskal-Wallis test. Post-hoc pairwise comparisons were performed using Bonferroni or Tamhane T2 tests where appropriate. A p-value <0.05 was considered statistically significant.

As shown in Table 1, no statistically significant differences were observed among the groups with respect to age (p=0.57), sex distribution (p=0.975), stone laterality (p=0.431), stone contour (p=0.424), use of a stone cone (p=0.136), coronal/axial diameter ratio (p=0.155), or operative time (p=0.99).

Severe hydronephrosis (grade 3-4) was significantly more frequent in the retropulsion group (46.9%) compared to the stone-free group (12.7%) and the residual fragment group (19.2%) (overall p<0.001, Table 1). Pairwise analysis demonstrated a significant difference between Group 1 and

Group 2 (p<0.001) and between Group 2 and Group 3 (p=0.043), whereas no significant difference was found between Group 1 and Group 3 (p=0.503). The odds ratio for stone migration in patients with severe hydronephrosis was 6.1 (95% CI: 2.6-14.1; p<0.001).

Mean stone density differed significantly among the groups (overall p<0.001, Table 1), with values of 692 $\pm$ 234 HU in Group 1, 916 $\pm$ 239 HU in Group 2, and 868 $\pm$ 191 HU in Group 3. Significant differences were observed between Group 1 and Group 2 (p<0.001) and between Group 1 and Group 3 (p=0.003) (Figure 2).

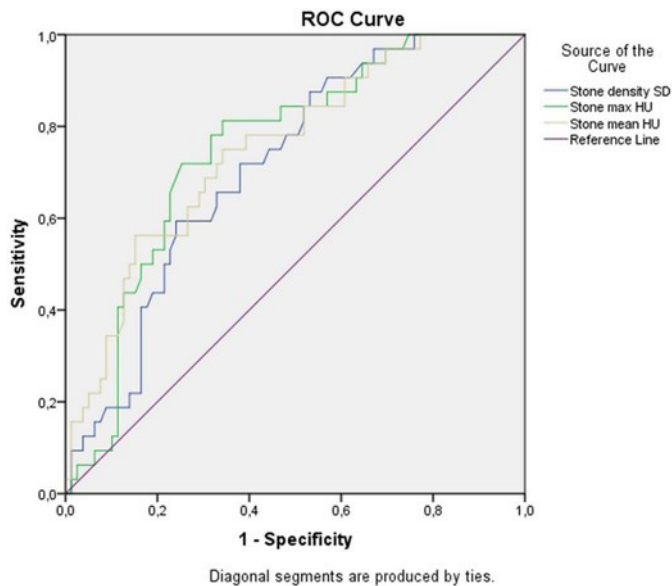


Figure 2. Receiver operating characteristic analysis for stone density

Median stone-to-renal pelvis distance was significantly shorter in Group 2 (7.5 mm) compared to Group 1 (27 mm) and Group 3 (24 mm) (overall $p < 0.001$, Table 1). Similarly, median stone volume was significantly higher in Group 2 (459 mm³) compared to Group 1 (168 mm³) ($p = 0.001$) (Figure 3).

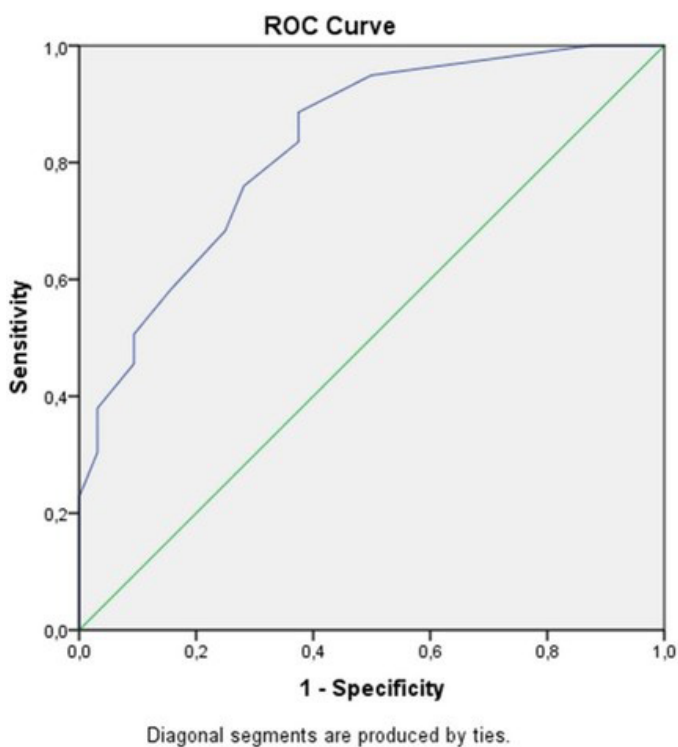


Figure 3. Receiver operating characteristic analysis for stone distance to the renal pelvis

Perioperative and postoperative complication rates are also presented in Table 1. No statistically significant differences in major postoperative complications were observed among the groups.

Discussion

The treatment of proximal ureteral stones encompasses various options ranging from invasive techniques such as open ureterolithotomy to minimally invasive methods such as SWL, retrograde or antegrade ureteroscopic lithotripsy, percutaneous nephrolithotomy, and laparoscopic ureterolithotomy (7). In recent years, the introduction of small-diameter ureterorenoscopes and laser-based lithotripters has made ureterorenoscopy a more preferred technique due to its minimal invasiveness, shorter hospital stays, and high stone-free rates achieved in a short time. Challenges in placing the ureteroscope, the pressure generated by irrigation fluid, the energy produced by laser pulses, and the increased energy applied for more effective stone fragmentation can lead to stone retropulsion or residual stones remaining in the kidney during the surgical procedure (8). This issue continues to be significant for proximal ureteral stones. Clinical studies have documented an incidence of stone migration from the proximal ureter to the kidney ranging from 28% to 60% and from the distal ureter ranging from 3% to 15%, irrespective of the type of lithotripter used (9-12).

Retrograde stone migration results in prolonged operative times, increased use of more invasive endoscopy, a higher incidence of residual stones, and the need for follow-up procedures, all of which contribute to greater morbidity and higher costs (13,14). Various methods have been utilized to avoid stone migration, including traditional gravity, optimizing the effects of reduced irrigation pressure and flow rate, and using the reverse Trendelenburg position. However, these techniques can disrupt the surgeon's comfort and reduce image quality, potentially prolonging the surgical procedure (7,15). In addition, anti retropulsion devices are critical in preventing stone migration. Equipment such as ureteral baskets, litho catch, lithovac, pass port balloons, parachutes, trapnets, accordions, stone cones, and gel-based materials has also been utilized to minimize the likelihood of stone movement during ureteroscopy (16-18).

The retrograde ureterolithotripsy technique, which employs flexible ureteroscopy and laser lithotripsy, is particularly effective in cases of retropulsion. However, the requirement for adequate ureteral dilation, the high cost of the devices, the limited number of uses per device, and the lack of availability in every center are disadvantages of this procedure (4). In our

research involving 32 patients with stone retropulsion to the kidney, we utilized holmium laser stone fragmentation for cases where we successfully achieved kidney access using flexible ureteroscopy (URS). For the remaining cases in which access could not be achieved, a double-J (DJ) stent was implanted and the procedure was postponed for a second session. In our study, we analyzed the clinical, demographic, and radiological data of patients with proximal ureteral stones who achieved complete stone-free status, as well as those with residual stones or stone migration to the kidney during stone fragmentation or irrigation pressure increases for adequate visualization. The causes of surgical failures were investigated.

In the literature, the stone-free rates for proximal ureteral stones have been reported to be approximately 85% for stones <10 mm and 75% for stones >10 mm (2). In our study, the stone-free rate was determined to be 74.5%, consistent with the literature. The retropulsion group, representing cases of surgical failure, accounted for 15.1% of all patients, while the residual stone group comprised 10.4%.

An analysis by Zhen et al. (19) involving the treatment of ureteral stones with holmium laser ureterolithotripsy found that higher grades of hydronephrosis, impacted stones, previous SWL history, and proximally located stones were associated with lower success rates. Similarly, a study by El-Nahas et al. (20) revealed that moderate-to-severe hydronephrosis significantly affected surgical failure. However, El-Hefnawy et al. (21) found no relationship between hydronephrosis grade and surgical failure. In our study, high-grade hydronephrosis and short stone-to-renal pelvis distances were found to reduce the likelihood of success. Specifically, in patients with severe hydronephrosis, the likelihood of stone migration to the kidney was 6.1 times higher. HU measures stone density and is associated with stone compactness. A study by Ofude et al. investigating predictor factors for the total energy required in holmium laser ureterolithotripsy identified significant clinical correlations between severe hydronephrosis, stone volume, mean HU, tissue edge markers, maximum stone diameter, and stone volume. Stone volume and mean HU were found to be the most important predictors of total laser energy. As stone volume and mean HU increase, the required total laser energy also increases. While this aids in easier fragmentation, it can also lead to stone migration to the kidney due to the high energy applied (8,22). Our study supports this hypothesis, as high stone volume, severe hydronephrosis, and high average HU values were observed in the retropulsion group.

The location of the stone within the ureter is crucial for surgical success. A study by Perez Castro et al. (23) noted success rates of

94.2%, 89.4%, and 84.5% for distal, middle, and proximal ureteral stones, in that order. As the stone-to-renal pelvis distance decreases, the likelihood of surgical success also decreases. Our findings suggest that reduced stone-to-renal pelvis distance and increased hydronephrosis severity lead to a higher probability of stone migration and residual stones in the kidney.

Anti retropulsion devices, such as stone cones, are used to prevent stone migration and retrieve stone fragments. However, in cases of severe hydronephrosis, when the ureteral diameter exceeds the diameter of the stone cone, the device may be ineffective in preventing stone migration to the kidney. In a study utilizing holmium: YAG laser lithotripsy, Eisner and Dretler reported a retropulsion rate of 1.5% (24). In our study, the retropulsion rate was found to be 8.7%, which we attribute to the limited use of stone cones.

For proximal ureteral stones, success rates have been reported to be 80-88% for stones under 10 mm, and 77-85% for stones over 10 mm [2]. In our study, while no significant differences were observed among the groups in terms of the coronal and axial dimensions of the stones, stone volume was significantly lower in the group that achieved complete stone-free status. This highlights the importance of stone volume, suggesting that higher volumes prolong fragmentation times with constant energy and increase the likelihood of stone migration to the kidney with levated energy and pressure.

Hematuria associated with ureteroscopy is typically self-limiting and mild. It may result from trauma during ureteroscope passage, ureteral strictures, stone fragmentation, or manipulation. In our study, no cases of significant hematuria were observed. Perioperative complications evaluated using the Satava classification and postoperative complications assessed with the Clavien classification matched the rates described in prior studies.

Study Limitations

This study has several limitations that should be deemed when interpreting the findings. First, the retrospective design inherently restricts the capability to determine causal relationships between the identified predictive factors and surgical outcomes. As data were collected from existing medical records, certain variables-such as intraoperative irrigation pressure, laser settings, and surgeon experience-could not be standardized or fully controlled, potentially influencing the results. Second, all procedures were performed using semi-rigid ureteroscopes, and the limited use of flexible ureterorenoscopy may have affected the overall success and retropulsion rates. Third, while the study's sample of 212 patients provides

important data, expanding to a larger, multicenter cohort would improve the applicability of the results to broader surgical contexts and varied patient groups.

Additionally, postoperative follow-up was based primarily on imaging and clinical data obtained from hospital records, without standardized long-term evaluation of stone recurrence or complications. The study also did not include biochemical stone analyses, which could have provided further information regarding stone composition and its potential influence on fragmentation behavior and surgical outcomes.

Future prospective, controlled studies incorporating standardized surgical protocols, detailed intraoperative assessments, and long-term follow-up are needed to confirm and further refine these findings.

Conclusion

Our study demonstrates that high-grade hydronephrosis, short stone-to-renal pelvis distance, high stone volume, and high stone density negatively affect the success of proximal ureteral stone surgery. Patients with these clinical conditions should be informed about the potential for surgical failure, and collaborative use of devices, such as flexible ureterorenoscopes, which can increase success rates, should be considered.

Ethical Approval: Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Adiyaman University (approval number: 2021/08-11, date: 26 October 2021).

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Concept: H.S., A.T.

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Analysis and interpretation: H.S., A.T., F.Ç.

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Critical revision of manuscript: H.S., A.T., B.K., C.O.

Conflict of Interest: The authors have no conflicts of interest to declare.

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