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RESEARCH

Ultrathin semirigid retrograde ureteroscopy versus antegrade flexible ureteroscopy in treating proximal ureteric stones 1–2 cm, a prospective randomized multicenter study

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Abstract
To compare the outcomes of using Ultrathin semirigid retrograde ureteroscopy and antegrade flexible ureteroscopy to treat proximal ureteric stones of sizes 1–2 cm. A prospective randomized multicenter study included patients who had proximal ureteric stones 1–2 cm, amenable for ureteroscopy and laser lithotripsy between August 2023 and February 2024. Two hundred thirty patients were divided evenly into two treatment groups. Group I included patients treated with antegrade flexible ureteroscopy and holmium laser stone fragmentation, and Group II included patients treated with retrograde ultrathin semirigid ureteroscopy. The study groups were compared in terms of patient demographics, stone access success, operation time, reoperation rates, perioperative complications, and stone-free status. Group I included 114 patients, while Group II included 111. The mean age of the patients was 33.92 ± 10.37 years, and the size of the stones was 15.88 ± 3 mm. The study groups had comparable demographics and stone characteristics. The mean operative time was significantly longer in group I than in group II (102.55 ± 72.46 min vs. 60.98 ± 14.84 min, respectively, $P < 0.001$). Most reported complications were MCCS grades I and II, with no significant difference between the study groups. The stone-free rate after four weeks was 92.1% and 81.1% for groups I and II, respectively, which increased to 94.7% and 85.6% after eight weeks ($P > 0.05$). Antegrade flexible ureteroscopy is equivalent to retrograde ultrathin semirigid ureteroscopy in treating proximal ureteric stones regarding stone-free status and procedure-related morbidity. However, the antegrade approach has a longer operative time, greater fluoroscopy exposure, and longer hospital stays.

Keywords Percutaneous renal surgery · Laser · Ureteral stones · Urolithiasis

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Abbreviations

ESWL	Extracorporeal shockwave lithotripsy
URS	Ureteroscopy
(SFR)	Stone-free rate
KSA	Kingdom of saudi arabia
F-URS	Flexible ureteroscopy
KUB	Kidney, ureter, and bladder
CTUT	Computed tomography of the urinary tract
PCS	Pelvicalyceal system
SD	Standard deviation
GW	Guidewire
VUJ	Vesicoureteric junction
PTFE	Polytetrafluoroethylene
MCCS	Modified clavien classification system
UTI	Urinary tract infections
PCNL	Percutaneous nephrolithotomy

Introduction

Proximal ureteric stones could be approached with various treatment options, including Extracorporeal shockwave lithotripsy (ESWL), retrograde ureteroscopy (URS), percutaneous antegrade URS, and in selected cases, laparoscopy or open surgery for larger stones [1]. Antegrade URS, while offering advantages over the retrograde approach, such as avoiding stone retropulsion during lithotripsy and reducing the need for auxiliary procedures, is considered a more invasive treatment option [2, 3].

Ureteroscopic lithotripsy is a well-established technique for treating urinary tract stones, owing to its high success rate and low incidence of complications. The introduction of the holmium laser has improved this procedure's efficacy [4, 5]. In recent years, URS caliber has progressively decreased to enhance success rates and lower the risk of adverse events. Nevertheless, the failure rate of ureteroscopic lithotripsy remains at around 8–10% [6–8], with a complication rate of 9–25% [9–11]. The most common cause of retrograde URS failure is an inability to pass the scope through the ureteric orifice or other segments of the ureter [6, 7]. In these instances, passive dilatation utilizing double-J ureteric stent insertion to enable completion of the procedure at a later stage or active dilatation using a balloon catheter can be employed [6–8, 12]. However, balloon dilatation may not always be successful and would increase costs, while passive ureteral dilatation via ureteric catheterization requires reoperation, raises surgical expenses, and can induce patient anxiety. Furthermore, the use of larger-diameter URSs can lead to complications, including mucosal injury (1.5%), ureteric perforation (1.7%), significant bleeding (0.1%), and ureteric avulsion (0.1%) [10]· In contrast, smaller-caliber URSs are associated with a lower incidence of such events [13–15].

Antegrade URS boasts a superior stone-free rate (SFR) while eliminating the risk of stone retropulsion. However, it comes with certain disadvantages, such as renal puncture that may lead to complications, heightened exposure to radiation, a longer operative time, and extended hospital stays [16].

This study compared the outcomes of using Ultrathin semirigid retrograde URS and antegrade flexible URS to treat proximal ureteric stones of 1–2 cm in size.

Patients and methods

A prospective randomized multicenter study was conducted to evaluate the effectiveness and safety of using Ultrathin semirigid retrograde URS compared to antegrade flexible URS in patients with solitary proximal ureteric stones (between the ureteropelvic junction and the upper border of the sacrum) of 1–2 cm in size. The study included patients admitted to the Department of Urology at Benha University, Al-Azhar University Hospitals, Egypt, and Najran Armed Forces Hospital, Saudi Arabia, for treatment from August 2023 to February 2024. The institutional review board approved the author's study. All participating patients provided informed consent before undergoing the surgical intervention.

We utilized G-power software to calculate the required sample size for our study. Specifically, we assumed a 0.5 effect size, 95% statistical power, and 5% type I error. Two hundred thirty patients were divided evenly into two treatment groups using the closed envelope method.

After the exclusion of patients with bilateral stone disease, pregnancy, coagulopathy, and UTI (urinary tract infection), Group I included 115 patients who were treated with antegrade flexible ureteroscopy (F-URS) and holmium laser stone fragmentation, and Group II included 115 patients who treated by retrograde ultrathin semirigid URS with the same method of stone fragmentation.

All patients underwent a thorough assessment, which included a detailed medical history, routine preoperative laboratory investigations, KUB x-rays (kidney, ureter, and bladder), and KUB ultrasounds. A non-enhanced computed tomography of the urinary tract (CTUT) confirmed the diagnosis of stone disease.

Surgical procedure

Three senior urologists operated on all surgical procedures. Antegrade F-URS was performed under general anesthesia. All patients were placed in the lithotomy position, and a 5 Fr ureteric catheter with an open tip was inserted to inject dye and opacify the pelvicalyceal system. Subsequently, patients were positioned prone, and an upper or middle calyceal puncture was made under fluoroscopic guidance. After that, a hydrophilic guidewire was introduced through the needle into the pelvicalyceal system (PCS). Teflon dilators were utilized to dilate the tract to 14 Fr. Then, an Amplatz sheath size 16 was inserted. The 7.5 F flexible ureteroscope (Karl Storz, Tuttlingen, Germany) was introduced through the Amplatz sheath to access the stone, which was then fragmented using a 30 W holmium: YAG laser and 200-µm fiber. The energy was applied at 0.8–1.5 J/pulse settings, 8–14 Hz frequency, and long pulse duration. After the procedure, an antegrade double-j stent (6 F, 26 cm, Percuflex; Boston Scientific) was inserted in all cases. Finally, a tube size 14 Fr was introduced into the Amplatz sheath to the renal pelvis level, guided by fluoroscopy, following which the Amplatz sheath was removed.

In Group II, the retrograde URS procedure was performed under general anesthesia. All patients were positioned in the classic dorsal lithotomy position. Guided by fluoroscopy, a guidewire (GW, Sensor polytetrafluoroethylene (PTFE)-nitinol guidewire with a hydrophilic tip; Boston Scientific, Marlborough, MA, USA) was inserted up to the kidney, with or without vesico-ureteric junction (VUJ) dilatation by balloon or Teflon dilators as appropriate. The ultrathin URS (6/7.5 Fr, with an instrumental channel for 4 Fr or 2 × 2.4 Fr, Richard Wolf, Knittlinigen, Germany) was inserted through the ureter over the GW. If there were difficulties in passing the guidewire beyond the stone at initial attempts due to stone impaction, laser fragmentation was done at the beginning to create a space for passing a safety guidewire, and then dusting the rest of the stone was carried out. Stone fragmentation was performed using the same laser device and settings as in Group I. A double-j stent (6 F, 26 cm, Percuflex; Boston Scientific) was routinely placed at the end of the procedure.

Outcome and follow-up

During surgical procedures, the status of stones was evaluated using fluoroscopy. After four and eight weeks, a plain KUB was performed for cases with radiopaque stones. For cases with radiolucent stones, a non-contrast CT scan of the abdomen and pelvis was conducted before removing the ureteric stent.

We defined the stone-free rate (SFR) as residual fragments less than two mm. Reoperation was described as a need for a second procedure for stone clearance.

The primary endpoint was the single-procedure stone-free rate (SFR) four weeks after surgery. The secondary endpoints were operative time, fluoroscopy time, lithotripsy time, hospital stay, postoperative complications, and SFR at eight weeks.

The study groups were compared regarding patient demographics, stone access success, operation time, reoperation rates, peri-operative complications according to the modified Clavien classification system (MCCS) [17], and the stone-free status at 4 and 8 weeks.

Statistical analysis

The Statistical Package for Social Science (SPSS) software, version 29 (SPSS Inc., Chicago, IL, USA), was employed for data analysis. Mean and standard deviation were used to represent numeric variables, while frequency and percentage were used for categorical variables. Association testing between two nominal variables was conducted using the Chi-square test. In contrast, the significance between the means of continuous variables for different groups was defined using the student's t-test. A P-value less than 0.05 was established as significant.

Results

Group I included 114 patients who underwent antegrade F-URS, while Group II included 111 patients who underwent retrograde Ultrathin semirigid URS (Fig. 1). The mean age of the study patients was 33.92 ± 10.37 years, and the size of the stones was 15.88 ± 3 mm. The stones were radio-opaque in 128 (56.9%) cases and were located on the right side in 124 (55.1%) cases.

The study groups had comparable demographics and stone characteristics, as depicted in Table 1. The mean operative time was significantly longer in Group I than in Group II (102.55 ± 72.46 min vs. 60.98 ± 14.84 min, respectively, $P < 0.001$). Similarly, fluoroscopy time was longer in group I with a significant P-value (Table 2).

One patient in Group I had puncture failure, and the procedure was aborted. This patient underwent retrograde double-J stent insertion and later ESWL. In Group II, advancement failed due to stone migration in two cases and guidewire insertion failure in two cases, which were converted to antegrade F-URS.

Postoperative hemoglobin levels decreased more in Group I than in Group II (0.71 ± 0.38 gm/dl vs. 0.1 ± 0.14 gm/dl, respectively, $P < 0.001$).

Although preoperative serum creatinine was comparable between the study groups, postoperative mean serum creatinine was slightly higher in Group II (1.33 vs. 1.13 mg/dl for Group II and Group I, respectively, $P < 0.001$) (Table 2). However, this difference was not clinically significant as serum creatinine levels normalized within the first postoperative week.

The mean pain visual analog score was higher in Group I than in Group II (4.31 ± 2.9 vs. 3.39 ± 2.7, respectively,

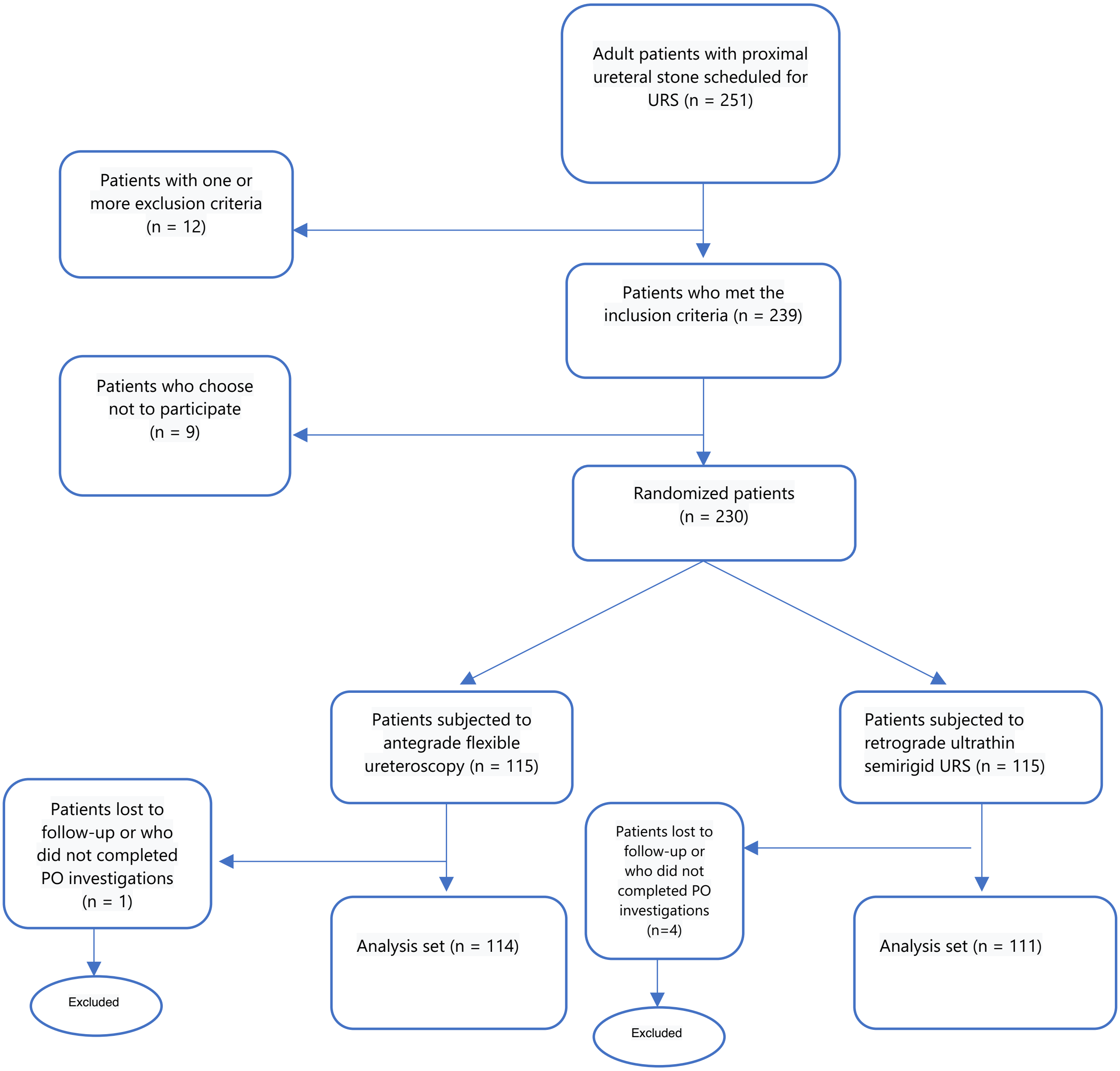

Fig. 1 Flow chart of our study population

(P = 0.008). Similarly, the hospital stay was longer in Group I than in Group II (3.89 ± 0.69 days vs. 2.57 ± 0.74 days, respectively, P = 0.004).

The two groups had no statistically significant differences in overall, intraoperative, or postoperative complications. Most reported complications were MCCS grades I and II and were managed conservatively. We reported a postoperative fever in 7 cases (6.1%) in Group I compared to 6 cases (5.4%) in Group II (P = 0.2). Similarly, postoperative UTI was documented in 3.5% of patients in Group I compared to 2.7% in Group II (P = 0.14). Hospital readmission was required for 17 cases (7.6%), with seven patients admitted due to urinary tract infections (UTI), three patients with fever and loin pain, and seven patients admitted due to hematuria with statistically insignificant differences between the study groups, as depicted in Table 3.

The stone-free rate after four weeks was 92.1% and 81.1% for groups I and II, respectively, which increased to 94.7% and 85.6% after eight weeks, but the difference was not statistically significant (Table 2).

Table 1 Comparison between Patient demographics and Stones criteria among the study groups

Parameters	Total (n = 225)	Group I (n = 114)	Group II (n = 111)	P-value
Age/years, mean ± SD	33.92 ± 10.37	35.68 ± 10.18	32.12 ± 10.3	0.88
Gender, N (%)				
Male	137 (60.9%)	68 (59.6%)	69 (62.2%)	
Female	88 (39.1%)	46 (40.4%)	42 (37.8%)	0.69
BMI, mean ± SD	25.17 ± 3.16	25.28 ± 3.35	25.1 ± 2.95	0.11
Side of stone, N (%)				
Right	124 (55.1%)	70 (61.4%)	54 (48.6%)	0.06
Left	101 (44.9%)	44 (38.6%)	57 (51.4%)	
Stone size (mm), mean ± SD	15.88 ± 3	15.84 ± 3	15.91 ± 2.95	0.51
Stone density (HU), mean ± SD	865.1 ± 330.36	868.77 ± 333.17	861.32 ± 328.91	0.58
Stone x-ray appearance, N (%)				
Radiopaque	128 (56.9%)	72 (63.2%)	56 (50.5%)	
Radiolucent	97 (43.1%)	42 (36.8%)	55 (49.5%)	0.06

Chi-square test and independent sample t-test were used

SD standard deviation, *BMI* Body mass index, *HU* Hounsfield unit

Table 2 Comparison between Intraoperative and postoperative parameters and stone-free rate among the study group

Parameters	Group I (n = 114)	Group II (n=111)	**p-value**
Operative time (min), mean±SD	102.55±72.46	60.98±14.84	< 0.001
Fluoroscopy time (seconds), mean±SD	212.33±43.84	14.2±2.85	< 0.001
Hemoglobin drop, mean±SD	0.71±0.38	0.1±0.14	< 0.001
Preoperative serum creatinine (mg/dl), mean±SD	1.08±0.14	1.09±0.17	0.65
Postoperative serum creatinine (mg/dl), mean±SD	1.13±0.22	1.33±0.31	< 0.001
Pain visual analogue score, mean±SD	4.31±2.9	3.39±2.7	0.008
Hospitalization time (days), mean±SD	3.89 ± 0.69	2.57 ± 0.74	0.004
SFR at follow-up week 4, N (%)	105 (92.1%)	90 (81.1%)	0.15
SFR at follow-up week 8, N (%)	108 (94.7%)	95(85.6%)	0.12

Chi-square test, and student's t-test was applied

Table 3 Comparison between the study groups regarding perioperative complications and hospital readmissions

Parameters	Total (n = 225)	Group I (n = 114)	Group II (n = 111)	P-value
Overall complications, N (%)	55 (24.4%)	27 (23.68%)	28 (25.2%)	0.79
Intraoperative complications, N (%)	35 (15.6%)	16(14%)	19 (17.1%)	0.52
Postoperative complications, N (%)	20 (8.9%)	11 (9.6%)	9 (8.1%)	0.69
MCCS grading of complications, N (%)				
Grade I				
Perforation	8 (3.6%)	3 (2.6%)	5 (4.5%)	0.45
Hematuria	27 (12%)	13 (11.4%)	14 (12.6%)	0.94
Fever	13 (5.8%)	7 (6.1%)	6 (5.4%)	0.2
Grade II UTI	7 (3.1%)	4 (3.5%)	3(2.7%)	0.14
Readmission (within 8 weeks), N (%)	17 (7.6%)	9 (7.9%)	8 (7.2%)	0.84

Chi-square test was used

MCCS modified clavien classification system

Discussion

Retrograde and antegrade ureteroscopic lithotripsy approaches are well-established and effective options for treating proximal ureteric stones; however, each technique has some drawbacks [18].

Retrograde URS has been associated with a lower stone-free rate and possible stone retropulsion with subsequent ancillary procedures. Moreover, Patients who experience prolonged operative time are at higher risk for developing urosepsis. In contrast, mini-percutaneous antegrade ureteroscopy has a higher radiation exposure, longer operative time, prolonged postoperative hospital stays, and more risk of significant hemorrhage compared to retrograde URS [19].

Our study revealed that the antegrade F-URS approach in treating proximal ureteric stone resulted in a higher stone-free rate, reaching 94.7%, compared to 85.6% through the retrograde Ultrathin semirigid URS. Despite the apparent disparity, the difference did not achieve statistical significance.

In the literature, stone-free rates vary between both techniques; they ranged between 80 and 97.7% after antegrade mini perc and between 60 and 85% following retrograde URS. Different surgical experiences and study populations could explain the disparities in outcomes [20].

In the current study, it was observed that the duration of the surgical procedure was considerably greater in antegrade F-URS compared to retrograde URS, with a mean (SD) of 102.5 (72.4) and 60.9 (14.8) min, respectively. The additional time incurred was due to the increased duration for attaining percutaneous renal access, which involved the puncture site, dilatation, and stone retrieval. Previous studies have supported the longer duration of the antegrade approach, with Moufid et al. reporting a higher operative time in the antegrade URS group compared to the retrograde URS group at a mean (SD) of 66.5 (±21.7) vs 52.1 (±17.3) min ($P = 0.013$) [19]. Similar results were found in the study conducted by Li et al., who reported a mean (SD) operative time for the percutaneous nephrolithotomy group at 108.7 (+/19.3) vs 63.5 (±16.3) min for the F-URS group ($P < 0.05$) [21].

The present study reports a statistically significant increase in mean serum creatinine levels from 1.09 to 1.33 umol/l in the early postoperative period following the retrograde URS procedure. However, it should be noted that this difference was clinically insignificant as it normalized within the first postoperative week. The rise in serum creatinine levels post-URS could be attributed to high intrarenal pressure during surgery, which leads to tubular interstitial inflammation, macrophage proliferation, and cytokine production, ultimately leading to tubular cell apoptosis [22–24].

In our study, no major complications occurred, while minor complications were reported and managed conservatively. The overall incidence of complications for the entire study was 24.4%. Ureteric perforation was higher in retrograde URS than in the antegrade F-URS group, 4.5–2.6%, respectively. The two techniques had no statistically significant differences regarding other minor complications.

Other studies showed an overall low and similar rate of complications in both techniques. Li et al. reported comparable complication rates in both groups, with an increased incidence of ureteric perforation and stenosis in the retrograde URS group and an increased incidence of hematuria and need for blood transfusion in the percutaneous nephrolithotomy (PCNL) group [21]. Sun et al. reported bleeding in one patient (2.3%) for the antegrade approach and ureteric injury in one patient (2.3%) for the retrograde approach, with no statistical difference [25].

Our research represents the first prospective randomized multicenter study comparing antegrade flexible ureteroscopy and ultrathin semirigid retrograde ureteroscopy in treating proximal ureteric stones. Our results indicate that antegrade flexible urethroscopy is comparable to retrograde ureteroscopy regarding perioperative complications and stone-free rates. However, the former has longer operative time, higher exposure to radiation, and longer hospital stays.

Limitations of the study

The study was conducted prospectively across multiple centers; however, certain limitations were acknowledged. These limitations included small sample size, heterogeneity in clinical practice and performing surgeons, and the fact that CT-KUB was not performed in all cases for post-operative SFRs assessment. Nonetheless, intraoperative fluoroscopy and confirmation of complete stone clearance during ureteroscopy were supplementary tools.

Conclusions

Our study findings indicate that antegrade flexible ureteroscopy and retrograde ultrathin semirigid ureteroscopy represent safe and effective treatment options for proximal ureteric stones. The antegrade approach demonstrates a higher stone-free rate. However, this difference does not achieve statistical significance, albeit with longer operative durations, increased fluoroscopy exposure, and prolonged hospitalization periods.

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Authors' contributions All listed authors have made substantial contributions to conception and design, methodology, acquisition of data, or analysis, review, and interpretation of data. And all authors read and approved the final article and confirmed that all methods were carried out in accordance with relevant guidelines and regulation.All authors reviewed the manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest None of the contributing authors have any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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