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Endo-urology

First-in-clinical Evaluation of Dual Contrast-enhanced Ultrasound-guided PCNL: A Multicenter Randomized Trial Versus Fluoroscopy

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Abstract

Background and objective: Puncture is critical in percutaneous nephrolithotomy (PCNL), influencing access failure and vascular or adjacent organ injury. This study aimed to compare the clinical efficacy and safety of dual contrast-enhanced ultrasound (D-CEUS) with fluoroscopic guidance for renal access during PCNL.

Methods: This two-center prospective trial was conducted between January 2024 and November 2024. A total of 150 patients were randomized to the D-CEUS group (n = 75) or the fluoroscopy group (n = 75). Outcomes included first-attempt puncture success rate, puncture and tract establishment time, stone-free rate, hospital stay, hemoglobin changes, and complications.

Key findings and limitations: In the intention-to-treat analysis, the first-attempt puncture success rate was higher with D-CEUS than with fluoroscopy (92% vs 80%; difference 12%, 95% confidence interval [CI] = 0.77–23%; Mantel-Haenszel odds ratio [OR] 2.87, 95% CI = 1.04–7.87; p = 0.040). The per-protocol analysis showed consistent results (95% vs 83%; difference 11%, 95% CI = 0.81–22%; Mantel-Haenszel OR 3.45, 95% CI = 1.06–11.24; p = 0.040). Median puncture time (56 vs 120 s; p < 0.001) and tract establishment time (236 vs 480 s; p < 0.001) were shorter with D-CEUS. Median hospital stay was shorter (2 vs 5 d; p < 0.001), with lower hemoglobin loss (median 7.0 vs 11.5 g/l; p = 0.023). There was no significant difference in the complication rate (8.2% vs 15%; p = 0.19). A limitation is that the open-label design may compromise the robustness of the findings.

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Conclusions and clinical implications: D-CEUS facilitates accurate and safe puncture, efficient tract establishment, and real-time confirmation of calyceal access while avoiding radiation exposure. These findings support further evaluation of D-CEUS as a radiation-free alternative to fluoroscopy for renal access during PCNL.

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ADVANCING PRACTICE

What does this study add?

Following intravenous contrast administration, the renal pyramids became more clearly delineated during the arterial phase in contrast-enhanced ultrasound mode, and this enhancement was not limited by the presence or absence of hydronephrosis. Dual contrast-enhanced ultrasound (D-CEUS) facilitates a puncture trajectory aligned with the central axis of the renal pyramid, which is associated with significantly less hemoglobin loss. D-CEUS provides real-time confirmation of needle depth within the collecting system by using intracavitary contrast injection through a coaxial puncture needle. D-CEUS integrates both intravenous and intracavitary contrast delivery through a coaxial puncture needle, eliminating the need for retrograde catheterization and thereby facilitating the safe and effective implementation of tubeless percutaneous nephrolithotomy.

Clinical Relevance

Various imaging technologies can be used for renal puncture in patients undergoing percutaneous nephrolithotomy (PCNL). In the present RCT, the authors compared dual contrast–enhanced ultrasound (D-CEUS) with fluoroscopic guidance for renal access during PCNL. The authors found that first-attempt puncture success rate was higher with D-CEUS than fluoroscopy, while median punture time and tract establishment time were shorter with D-CEUS. These results suggest that renal puncture with D-CEUS appears as a safe and efficient alternative for renal puncture in PCNL if expertise with the technology is available. Associate Editor: Malte Rieken.

Patient Summary

In this study, we evaluated a new ultrasound-based technique, dual contrast-enhanced ultrasound, to guide kidney stone surgery. Our findings show that this method can help doctors place the needle more accurately, improve safety, and reduce procedural burden compared with traditional x-ray guidance. It may become a promising alternative for guiding this procedure in the future.

1. Introduction

Percutaneous nephrolithotomy (PCNL) is widely used for large renal calculi and cases unsuitable for ureteroscopy or shock wave lithotripsy [1]. Puncture is one of the most important stages of PCNL, directly affecting the risk of access failure and injury to the vasculature and adjacent organs [2]. Renal puncture can be performed using different imaging modalities, such as fluoroscopy, ultrasound, or a combination of both, or by applying new technologies [3].

A meta-analysis demonstrated that ultrasound-guided PCNL had comparable efficacy for stone-free rate (SFR) and a favorable safety profile, with a significantly lower complication rate than fluoroscopy; it also provided radiation-free, real-time, and repeatable imaging [4]. However, the notable limitations of ultrasonography include relatively low spatial resolution and difficulty visualizing a nondilated collecting system. Moreover, in B-mode, needle visualization decreases once the needle enters the collecting system, making confirmation of successful calyceal access challenging [5].

SonoVue has been well established as a safe contrast agent that enhances microvascular and anatomic visualization in contrast-enhanced ultrasound (CEUS) [6,7]. In PCNL, intracavitary contrast injection via a retrograde ureteral catheter, known as intracavitary CEUS (IC-CEUS), improves puncture localization and stone detection even without hydronephrosis [8,9]. Dual CEUS (D-CEUS), an emerging technique that integrates parenchymal vasculature and collecting system imaging without the need for retrograde catheterization, has been reported to improve safety, access accuracy, and precise stone localization in vivo [10].

To further investigate the clinical feasibility of D-CEUS, this prospective study evaluates the efficacy and safety of D-CEUS for puncture access and tract establishment in PCNL compared with conventional fluoroscopic guidance. The null hypothesis assumed no difference in first-attempt

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puncture success rate between D-CEUS and fluoroscopic guidance.

2. Patients and methods

2.1. Study design

The open-label randomized trial was conducted from January 2024 to November 2024 at the Chinese People's Liberation Army General Hospital (Center A) and the First Affiliated Hospital of Guangzhou Medical University (Center B). A total of 166 patients consecutively underwent PCNL, of whom 150 met the eligibility criteria and were randomized in a 1:1 ratio to the D-CEUS or fluoroscopy-guided group, with stratification by center. Randomization was performed using a computer-generated permuted block sequence (block size of 4), which was placed into sequentially numbered, sealed opaque envelopes. Envelopes were opened in sequential order, and treatment allocation remained concealed until the intervention.

Inclusion criteria were as follows: (1) aged ≥18 yr; (2) renal or upper ureteral stones ≥2 cm in diameter, multiple renal calculi, or staghorn calculi, with preoperative Computed Tomography (CT) confirming the absence of parallel calyces and involvement of no more than three calyces; and (3) absence of hydronephrosis, or mild hydronephrosis which is characterized as having normal renal parenchymal thickness and echogenicity, normal renal size, dilatation of the collecting system <1.5 cm, and O- or C-shaped anechoic areas within the renal sinus. Exclusion criteria included the following: (1) urinary tract infection, (2) complex stones requiring multiple tracts or with anatomical abnormalities, (3) bilateral renal or upper ureteral stones, (4) renal malignancy, (5) severe spinal deformities precluding prone positioning, (6) obesity, defined as a percutaneous tract length exceeding 15 cm on preoperative CT, and (7) contraindications to CEUS agents. The enrollment flowchart is shown in Fig. 1.

This multicenter, randomized controlled trial was approved by the ethics committee (S-2024-208-02) and registered in the Chinese Clinical Trial Registry (ChiCTR2500101947). Written informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

2.2. Procedures

Two PCNL surgeons from two centers, each with >10 yr of experience, participated in this study. Both completed training in ten cases on standardizing the novel guidance technique. All patients at each institution were treated by the same surgeon. Procedures were performed under general anesthesia in the prone position.

2.2.1. Percutaneous puncture and tract establishment

The first technique was D-CEUS-guided PCNL. A schematic illustration of the D-CEUS-guided puncture procedure is shown in Fig. 2A–C. Conventional ultrasound (3.5–5.5 MHz, Mindray, Shenzhen, China) was used to scan the kidney along its maximal longitudinal axis. An 18G percutaneous transhepatic cholangiography (PTC)needle (Hakko, Japan) was advanced to the renal capsule with conventional ultrasound and then filled with 1:100 diluted SonoVue (Bravalent, Italy). After intravenous administration of 1.5 ml of contrast, the puncture needle was further advanced toward the tip of the renal papilla and into the target calyx in CEUS mode. Intracavitary injection of 10–20 ml of contrast through the needle confirmed calyceal entry, depth, and collecting-system anatomy.

A guidewire (BWS-035150, Cook, USA) was inserted, and the tract was initially dilated to 16F (5.3 mm); a ureteroscope was used to verify puncture depth. A balloon dilator (X-Force N30, BD, USA) was then positioned to further dilate the tract to 24F (8.0 mm), allowing placement of a working sheath for the 9.5F (3.2 mm) nephroscope.

The second technique was fluoroscopy-guided PCNL. Renal access was obtained using the bull's-eye fluoroscopy technique as described by Miller et al. [11]. After calyx selection, puncture was performed under fluoroscopy and confirmed by fluoroscopic imaging. After urine efflux from the needle was confirmed, a guidewire was inserted. Tract dilation and sheath placement followed the same steps as in the D-CEUS group.

2.2.2. Lithotripsy

After tract establishment, lithotripsy was performed using a Lumenis Pulse 120H (Ho:YAG, 550 μm, 3.0 J, 30 Hz, Lumenis, Israel). Stone fragments were cleared with a perfusion-suction system (AFP200B, Zhejiang YiGao Medical Technology Co., Ltd., China) at an irrigation flow rate of 100 ml/min. The combination of a larger working sheath and a smaller rigid nephroscope facilitated passive evacuation of fragments through the working channel without auxiliary extraction devices. Tract patency and calyceal filling were assessed with conventional ultrasound.

2.3. Definitions of outcomes and follow-up

The primary efficacy end point was first-attempt puncture success rate, defined as successful calyceal access achieved with a single needle insertion. Successful renal access was further defined as the placement of a guidewire into the renal collecting system with urine backflow.

Secondary end points were prespecified and included efficacy and safety. Efficacy end points comprised (1) *puncture time*, defined as the interval from identification of the maximal longitudinal axis to successful needle entry into the collecting system; (2) *tract establishment time*, defined as the interval from initial entry to completion of dilation; and (3) SFR, assessed postoperatively at 1–3 d and 1 mo by noncontrast CT. Residual fragments >4 mm were considered significant, and fragments ≤4 mm were deemed clinically insignificant [12]. Safety end points included (1) postoperative hospital stay; (2) change in serum hemoglobin, defined as the difference between baseline and 24-h postoperative measurements; and (3) overall complication rate, defined as the proportion of patients experiencing ≥1 complication, graded according to the Clavien-Dindo classification.

2.4. Statistical analysis

Based on pilot data and previous studies, the first-attempt success rates were estimated to be ∼90% for D-CEUS guidance and 64% for fluoroscopic guidance [13,14]. Sample size was calculated using PASS 2021 (NCSS, USA) for a two-sided z-test ($\alpha = 0.05$, power = 90%, 1:1 allocation), resulting in a minimum of 106 patients. To account for potential nontreatment, withdrawal after randomization, or crossover to an alternative stone treatment strategy, the sample size was inflated by 20%, resulting in a required sample size of 133 patients (67 per group).

Statistical analyses were performed with SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R version 4.5.2. Data were summarized as *n* (%) or mean ± standard deviation or median (interquartile range), as appropriate. The first-attempt puncture success rate was analyzed in both the intention-to-treat (ITT) and per-protocol set (PPS) populations. Owing to the multicenter design, treatment groups were compared using a center-stratified Mantel-Haenszel test, and odds ratios (ORs) for first-attempt puncture success were estimated.

Secondary end points were assessed in the PPS population; the χ^2 test or Fisher exact test was used to compare categorical outcome rates between techniques, whereas the Mann-Whitney U test was used to assess differences in continuous variables, including procedural time, postoperative hospital stay, and change in serum hemoglobin. No multiplicity adjustment was performed; therefore, secondary end point findings should be interpreted as exploratory. All statistical tests were two sided, with a significance level of 0.05.

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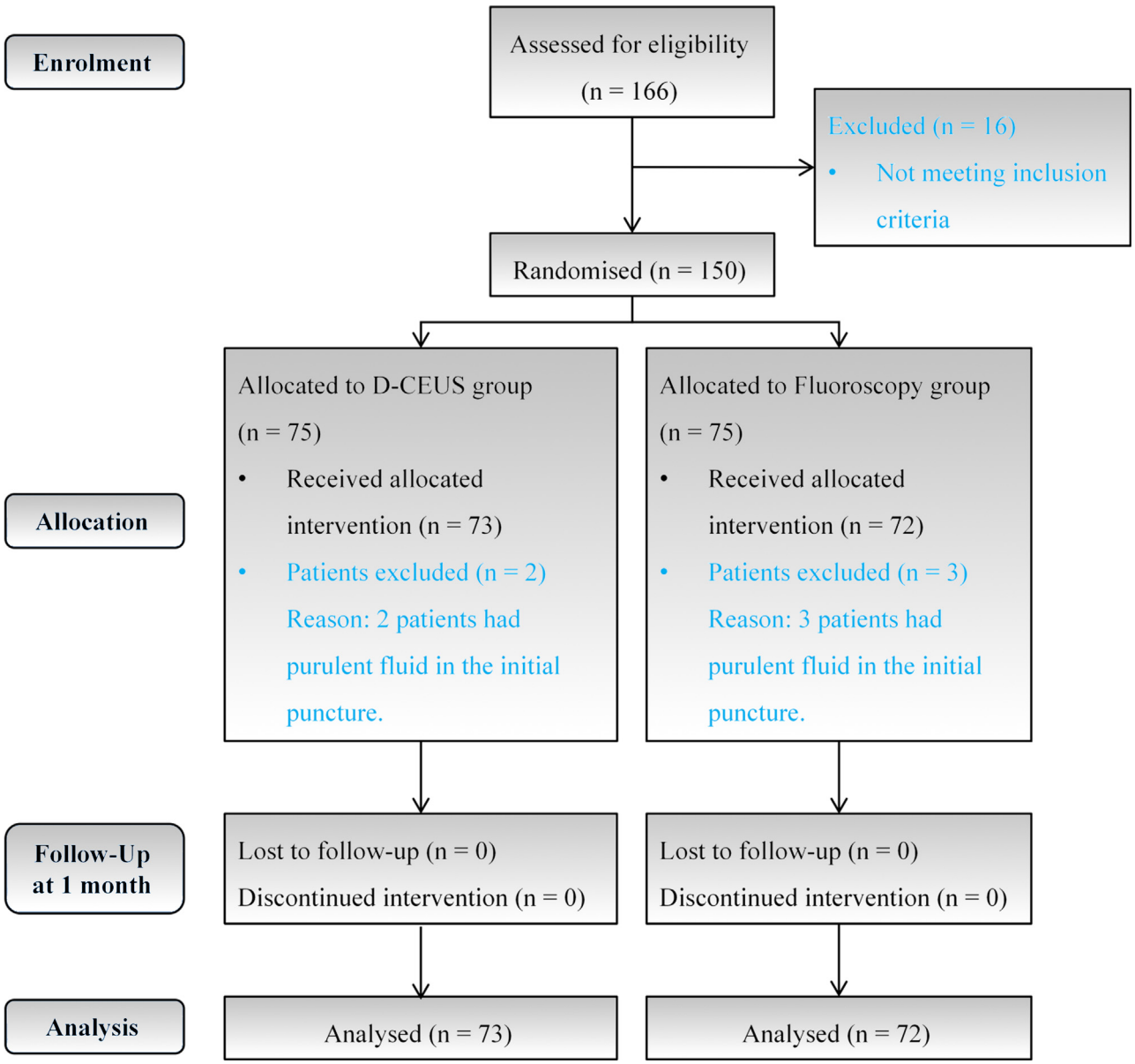


Fig. 1 – Flowchart of patient enrollment. D-CEUS = dual contrast-enhanced ultrasound technique.

Differences and 95% confidence intervals (CIs) were estimated using a score-based method for binomial proportions for categorical variables and the Hodges-Lehmann estimator with the Mann-Whitney U test for continuous variables.

3. Results

Representative images of D-CEUS-guided renal access are shown in Fig. 2. Compared with B-mode, CEUS provided clearer delineation of the renal pyramids during the arterial phase (Fig. 2D and G). The renal pyramid–associated anechoic region served as a landmark for guiding needle advancement toward the target calyx (Fig. 2E and H), which was confirmed by intracavitary contrast injection (Fig. 2F and I).

A total of 150 patients were randomized to the D-CEUS (n = 75) or fluoroscopy group (n = 75), with baseline characteristics summarized in Table 1. Five participants (two in the D-CEUS arm and three in the fluoroscopy arm) who did not undergo the procedure because of purulent fluid were classified as failures (Fig. 1). Consequently, the first-attempt puncture success rates were 92% and 80% in the D-CEUS and fluoroscopy groups, respectively, with a difference of 12% (95% CI = 0.77–23). The center-stratified Mantel-Haenszel analysis showed an OR of 2.87 (95% CI = 1.04–7.87; p = 0.040).

The PPS included 73 and 72 patients in the D-CEUS and fluoroscopy groups, respectively. All patients who underwent the procedure achieved successful access to the target calyx. The first-attempt puncture success rate was higher in the D-CEUS group (95% vs 83%), with an absolute difference of 11% (95% CI = 0.81–22%). The Mantel-Haenszel OR was 3.45 (95% CI = 1.06–11.24; p = 0.040). In addition, D-CEUS was associated with shorter puncture time (median 56 vs

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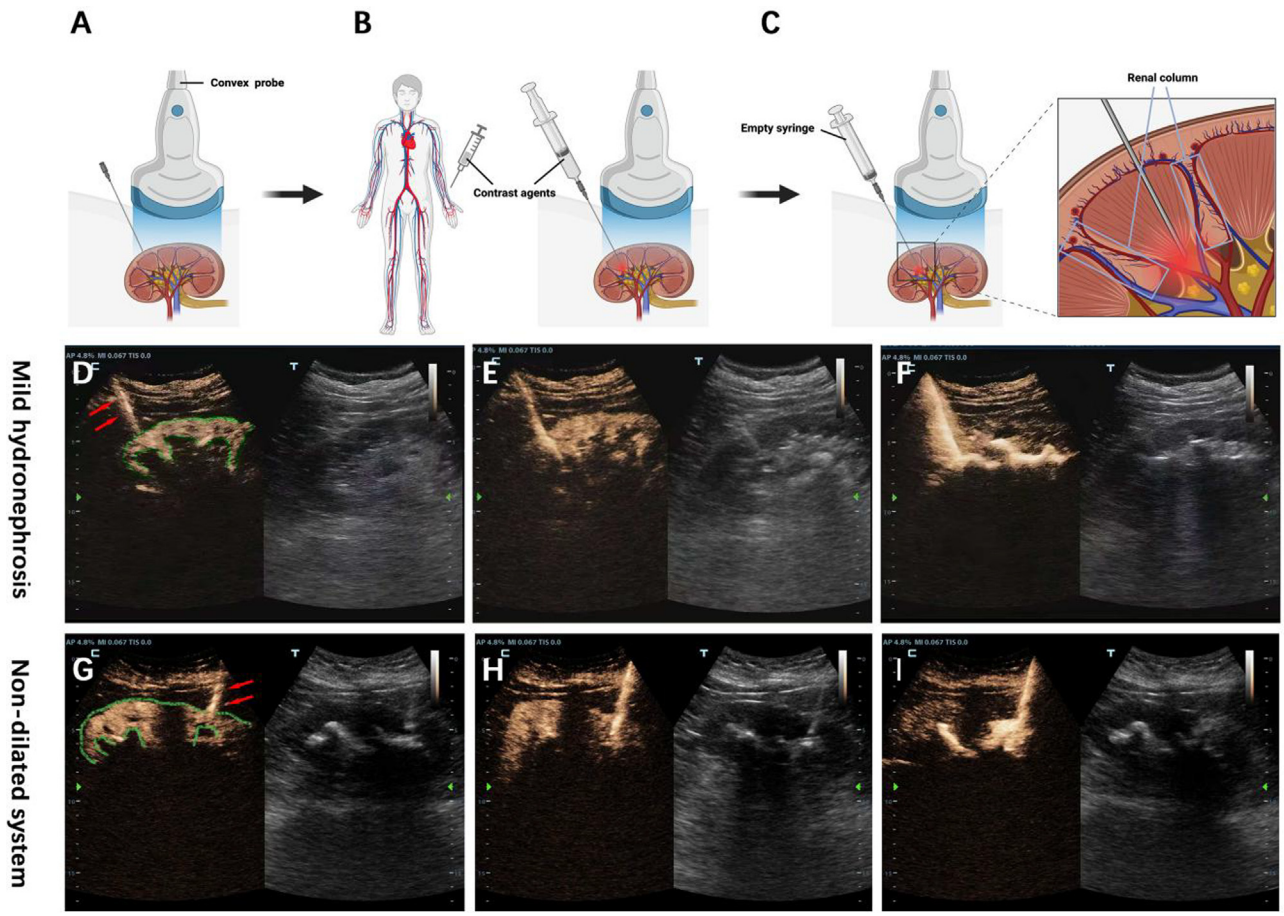


Fig. 2 – Puncture procedure under D-CEUS guidance. (A–C) Schematic illustration of the D-CEUS–guided puncture procedure, created in BioRender. Liang H. (2026) https://BioRender.com/rv1dw93. (A) Advancement of the puncture needle toward the renal capsule under conventional ultrasound, (B) needle advancement toward the renal papilla entering the target calyx after intravenous contrast administration, and (C) intracavitary CEUS following contrast injection through the needle to confirm successful puncture. (D–I) Representative D-CEUS images in patients, (D–F) with hydronephrosis, and (G–I) without hydronephrosis, shown in CEUS mode (left) and B-mode (right). (D, G) Arterial-phase enhancement, (E, H) needle puncture toward the target calyx, and (F, I) confirmation of successful puncture. The red arrows indicate the puncture needle, and the green line indicates the renal pyramid. D-CEUS = dual contrast-enhanced ultrasound; CEUS = XXX.

120 s; $p < 0.001$) and tract establishment time (median 236 vs 480 s; $p < 0.001$). There were no statistically significant differences in the postoperative SFR at 1–3 d (71% vs 75%; $p = 0.6$) or at 1 mo (85% vs 85%; $p > 0.9$). Detailed results are shown in Table 2.

Median postoperative hospital stay was shorter with D-CEUS (2 vs 5 d; $p < 0.001$), with lower median hemoglobin loss (7.0 vs 11.5 g/l; $p = 0.023$). Bleeding-related complications (including hemorrhage and perirenal/subcapsular hematoma) occurred in 1 and 2 patients (1 vs 4 events). No statistically significant difference was observed in overall complication rates (8.2% vs 15%; $p = 0.19$), which were mostly Clavien-Dindo grade I–II (8.2% vs 14%; $p = 0.3$). One grade IV case of septic shock occurred in the D-CEUS group (1.4%), whereas the fluoroscopy group had six grade III–IV events (8.3%): four grade IV cases of septic shock, one grade III hemorrhage, and one grade III pleural injury (Table 2). All complications resolved; details are shown in Table 3.

4. Discussion

This study evaluated the efficacy and safety of D-CEUS compared with fluoroscopic guidance during PCNL. D-CEUS achieved a higher first-attempt puncture success rate and shorter puncture and tract establishment times while showing a comparable safety profile to fluoroscopy.

Technically, a safe puncture path is defined as one that aligns with the central axis of the renal pyramid, corresponding to the path that minimizes injury to the interlobar artery [16]. Arterial injury has been reported in 26%, 23%, and 13% of upper, middle, and lower infundibular punctures, respectively, but in <8% of the punctures made through a calyceal fornix [17]. In D-CEUS, following intravenous contrast administration, the renal pyramid becomes more clearly delineated during the arterial phase in CEUS mode compared with B-mode. Therefore, within the arterial-phase window, simultaneous visualization of the puncture needle and the renal pyramid provides anatomical

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Table 1 – Demographic characteristics (*n* = 150)

Characteristic	D-CEUS group (*n* = 75)	Fluoroscopy group (*n* = 75)
Age (yr), mean ± SD	53 ± 12	51 ± 9
Center (center A), *n* (%)	38 (51)	38 (51)
Gender (male), *n* (%)	51 (68)	43 (57)
BMI (kg/m^2), mean ± SD	25.2 ± 3.7	23.7 ± 2.9
aCCI [15], *n* (%) [a]		
≤2	35 (47)	49 (65)
3–5	37 (49)	26 (35)
>5	3 (4.0)	0 (0)
Kidney (left), *n* (%)	44 (59)	45 (60)
Complex stone (multiple or staghorn), *n* (%)	50 (67)	57 (76)
Mild hydronephrosis, *n* (%)	50 (67)	50 (67)
Stone diameter (mm), median (IQR)	25 (20–33)	25 (21–31)
Stone density (HU), mean ± SD	856 ± 271	936 ± 289
Stone composition, *n* (%)		
Calcium oxalate	41 (55)	45 (60)
Uric acid (including suspected)	9 (12)	6 (8.0)
Calcium orthophosphate	10 (13)	9 (12)
Struvite	15 (20)	15 (20)
Puncture location, *n* (%)		
Upper calyx	15 (20)	16 (21)
Middle calyx	40 (53)	35 (47)
Lower calyx	20 (27)	24 (32)

BMI = body mass index; D-CEUS = dual contrast-enhanced ultrasound; HU = Hounsfield unit; IQR = interquartile range; SD = standard deviation; aCCI = age-adjusted Charlson comorbidity index.
[a] For each decade of age beginning at 40 yr, one point was added.

guidance for controlled needle advancement toward the target calyx. In this study, D-CEUS was associated with significantly less hemoglobin loss, although the overall incidence of bleeding was low in both groups. In addition, puncture efficiency was reflected by a higher first-attempt success rate and a significant reduction in puncture time.

Moreover, owing to the enhanced procedural guidance provided by D-CEUS, no contrast medium extravasation was observed during intracavitary contrast injection. In the D-CEUS group, intracavitary contrast injection allows direct confirmation of the needle's depth within the collecting system before tract establishment. This facilitates a more efficient tract establishment process by reducing the need for additional instrument manipulation. With fluoroscopy guidance, two primary approaches are used for percutaneous access: the bull's-eye method and the triangulation method [18]. Compared with triangulation, the bull's-eye method is associated with shorter operative and fluoroscopy times and was therefore adopted in the fluoroscopy group in this study [19]. In the bull's-eye approach, loss of resistance indicates entry into the calyx, with subsequent fluoroscopic confirmation of appropriate needle depth [20]. However, needle redirection and repeated imaging may still prolong tract establishment and increase radiation exposure, which is consistent with our finding that the fluoroscopy group exhibited a significantly longer tract establishment time than the D-CEUS group.

Conventional PCNL typically relies on retrograde catheterization to achieve artificial hydronephrosis or enable retrograde contrast injection and has been widely used to facilitate puncture in nondilated collecting systems [8,9,21]. However, retrograde catheterization may cause complications such as ureteral mucosal injury, perforation, avulsion, catheter misplacement, renal injury, and postoperative pain [22,23]. Recently, tubeless PCNL has gained increasing adoption because of its ability to shorten opera-

Table 2 – Per-protocol analysis comparing clinical outcomes between groups (*n* = 145)

Variable	D-CEUS group (*n* = 73)	Fluoroscopy group (*n* = 72)	Difference, 95% CI [a]	*p* value
First-attempt puncture success rate, *n* (%)	69 (95)	60 (83)	11% (0.81–22)	0.040 [b]
Puncture time (s), median (IQR)	56 (46–80)	120 (80–175)	−57 (−72 to −43)	<0.001
Tract establishment time (s), median (IQR)	236 (200–255)	480 (300–600)	−227 (−272 to −182)	<0.001
Immediate SFR, *n* (%)	52 (71)	54 (75)	−3.8% (−18 to 11)	0.6
1-mo SFR, *n* (%)	62 (85)	61 (85)	0.2% (−12 to 12)	>0.9
Postoperative hospital stay (d), median (IQR)	2 (2–2)	5 (3–5)	−2 (−3 to −2)	<0.001
Hemoglobin loss (g/l), median (IQR)	7.0 (2.0–13.5)	11.5 (4.0–19.0)	−3.0 (−6.0 to −0.0001)	0.023
Overall complication rate, *n* (%)	6 (8.2)	11 (15)	−7.1% (−18 to 3.7)	0.19
Bleeding-related complications, *n* (%)	1 (1.4)	2 (2.8)	−1.4% (−8.3 to 4.9)	0.6
Class of complications, *n* (%)				
Clavien I–II	6 (8.2)	10 (14)	−5.7% (−16 to 4.9)	0.3
Clavien III–IV	1 (1.4)	6 (8.3)	−7.0% (−16 to 0.50)	0.063

CI = confidence interval; D-CEUS = dual contrast-enhanced ultrasound; IQR = interquartile range; SFR = stone-free rate.
[a] Difference was calculated as D-CEUS minus fluoroscopy.
[b] The *p* value was based on a center-stratified Mantel-Haenszel test of the common odds ratio.

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Table 3 – Details of complications

Complications, *n*[a]	D-CEUS group (*n* = 73)	Fluoroscopy group (*n* = 72)
Fever	6	8
Septic shock	1	4
Hemorrhage	1	3
Perirenal/subcapsular hematoma	0	1
Pleural injury	0	1
Perirenal effusion	0	1

D-CEUS = dual contrast-enhanced ultrasound.
[a] The number of complications was calculated by summing the occurrences of each event.

tive time, reduce hospital stay, and alleviate postoperative pain and is increasingly considered as a favorable approach [24–26]. A recent study reported that a total tubeless PCNL without retrograde catheterization is feasible in nonhydronephrotic kidneys under ultrasound guidance; however, this technique is limited by the requirement for substantial puncture expertise and extensive ultrasound experience [27].

In our study, D-CEUS-guided PCNL was successfully performed in patients with or without mild hydronephrosis; no artificial hydronephrosis was required even in nondilated systems. Visualization of the renal pyramids after intravenous contrast administration was not affected by the presence of hydronephrosis. Therefore, D-CEUS may facilitate tubeless PCNL, particularly in patients without significant hydronephrosis. Technically, the key distinction between IC-CEUS and D-CEUS lies in the route of contrast administration. IC-CEUS requires retrograde catheterization for intracavitary contrast injection, whereas D-CEUS combines intravenous and intracavitary contrast delivery via a coaxial puncture needle [10]. Consequently, D-CEUS preserves the advantages of intracavitary injection for visualizing needle or catheter position, cavity morphology, and fistulous tracts [28] while additionally enabling real-time spatial visualization of the needle relative to the collecting system and eliminating the need for retrograde catheter placement and manipulation. Moreover, although a formal learning curve analysis was not performed for this novel technique, approximately ten training cases were required for an experienced surgeon, whereas more cases may be needed for novice operators.

In addition, compared with fluoroscopy, D-CEUS guidance was associated with a shorter hospital stay. Previous studies have reported that urologist-obtained percutaneous renal access is associated with reduced hospitalization duration [29]. As all procedures in this study were performed by experienced urologists, the observed difference may be partly attributable to the number of puncture attempts and the degree of bleeding, as reflected by hemoglobin loss and postoperative bloody drainage.

Despite these encouraging findings, some limitations should be acknowledged. First, because the study was open label, operator-dependent outcomes such as procedural time and postoperative hospital stay may have been influenced. Second, although randomization was stratified by center, each center had only a single operating surgeon, making it difficult to fully separate treatment effects from potential center- or surgeon-level effects. Finally, the conservative ITT approach, which classified untreated participants as *failures*, may have underestimated the true treatment effect. Moreover, per-protocol analyses of secondary outcomes could introduce selection bias and compromise the benefits of randomization, thereby reducing the robustness and generalizability of the findings.

5. Conclusions

D-CEUS is a feasible radiation-free technique for renal access during PCNL, enabling real-time visualization of the renal parenchyma and collecting system without the need for retrograde catheterization. It facilitates needle advancement along the central axis of the renal pyramid and tract establishment, with a safety profile comparable to fluoroscopy. Although D-CEUS shows promising potential for PCNL, further well-designed studies are required to validate its clinical efficacy and safety.

Author contributions: Haixing Mai, Bingding Huang, and Xu Zhang had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Shen, S. Li, Z. Li, Mai.
Acquisition of data: All authors.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: Chen, Tian.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Shen.
Obtaining funding: Zhang, Huang, Mai.
Administrative, technical, or material support: Wang, Mai.
Supervision: Zhang, Huang, Mai.

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Data sharing statement: Data generated or analyzed during the study are available from the corresponding author upon request.

Ethics statement: The study protocol and written informed consent were approved by the ethics committee of the Third Medical Center, Chinese People's Liberation Army General Hospital, with approval number S-

2024-208-02. The trial was registered in the Chinese Clinical Trial Registry (https://www.chictr.org.cn/, ChiCTR2500101947). All participants provided written informed consent in accordance with the Declaration of Helsinki.

References

[1] Preminger GM, Assimos DG, Lingeman JE, et al. Chapter 1: AUA guideline on management of staghorn calculi: diagnosis and treatment recommendations. J Urol 2005;173:1991–2000.
[2] Alken P. Percutaneous nephrolithotomy - the puncture. BJU Int 2022;129:17–24.
[3] Rassweiler J, Rassweiler MC, Klein J. New technology in ureteroscopy and percutaneous nephrolithotomy. Curr Opin Urol 2016;26:95–106.
[4] Yang YH, Wen YC, Chen KC, Chen C. Ultrasound-guided versus fluoroscopy-guided percutaneous nephrolithotomy: a systematic review and meta-analysis. World J Urol 2019;37:777–88.
[5] Li JX, Tian XQ, Niu YN, Zhang X, Kang N. [Percutaneous nephrolithotripsy with pneumatic and ultrasonic power under B-type ultrasound guidance for treatment of renal calculi in non-dilated collecting system]. Zhonghua Wai Ke Za Zhi 2006;44:386–8.
[6] Piscaglia F, Bolondi L, Italian Society for Ultrasound in Medicine and Biology (SIUMB) Study Group on Ultrasound Contrast Agents. The safety of Sonovue in abdominal applications: retrospective analysis of 23188 investigations. Ultrasound Med Biol 2006;32:1369–75.
[7] Tang C, Fang K, Guo Y, et al. Safety of sulfur hexafluoride microbubbles in sonography of abdominal and superficial organs: retrospective analysis of 30,222 cases. J Ultrasound Med 2017;36:531–8.
[8] Guo X, Zhang Z, Liu Z, et al. Assessment of the contrast-enhanced ultrasound in percutaneous nephrolithotomy for the treatment of patients with nondilated collecting system. J Endourol 2021;35:436–43.
[9] Wang L, Li KP, Yin S, Yang L, Zhu PY. Contrast-enhanced ultrasound versus conventional ultrasound-guided percutaneous nephrolithotomy in patients with a non-dilated collecting system: results of a pooled analysis of randomized controlled trials. BMC Urol 2023;23:93.
[10] Shen D, Li S, Chen H, et al. Percutaneous kidney puncture using a novel contrast-enhanced ultrasound-guided technique: first swine model in vivo experience. Eur Urol Open Sci 2025;81:13–20.
[11] Miller NL, Matlaga BR, Lingeman JE. Techniques for fluoroscopic percutaneous renal access. J Urol 2007;178:15–23.
[12] Psihramis KE, Jewett MA, Bombardier C, Caron D, Ryan M. Lithostar extracorporeal shock wave lithotripsy: the first 1,000 patients. Toronto lithotripsy associates. J Urol 1992;147:1006–9.
[13] Taguchi K, Hamamoto S, Okada A, et al. A randomized, single-blind clinical trial comparing robotic-assisted fluoroscopic-guided with ultrasound-guided renal access for percutaneous nephrolithotomy. J Urol 2022;208:684–94.
[14] Pakmanesh H, Kharazmi F, Vejdani S, Eslami N. Ultrasound-guided renal puncture followed by endoscopically guided tract dilatation vs standard fluoroscopy-guided percutaneous nephrolithotomy for non-opaque renal stones; a randomized clinical trial. Urolithiasis 2024;52:75.
[15] Koppie TM, Serio AM, Vickers AJ, et al. Age-adjusted Charlson comorbidity score is associated with treatment decisions and clinical outcomes for patients undergoing radical cystectomy for bladder cancer. Cancer 2008;112:2384–92.
[16] Sampaio FJ, Zanier JF, Aragão AH, Favorito LA. Intrarenal access: 3-dimensional anatomical study. J Urol 1992;148:1769–73.
[17] Kyriazis I, Kallidonis P, Vasilas M, Panagopoulos V, Kamal W, Liatsikos E. Challenging the wisdom of puncture at the calyceal fornix in percutaneous nephrolithotripsy: feasibility and safety study with 137 patients operated via a non-calyceal percutaneous track. World J Urol 2017;35:795–801.
[18] Tepeler A, Armağan A, Akman T, et al. Impact of percutaneous renal access technique on outcomes of percutaneous nephrolithotomy. J Endourol 2012;26:828–33.
[19] Yin A, Diab C, Andonian S, et al. Which renal access technique for PCNL is more difficult to teach using simulation? Can Urol Assoc J 2023;17:E128–33.
[20] Ko R, Soucy F, Denstedt JD, Razvi H. Percutaneous nephrolithotomy made easier: a practical guide, tips and tricks. BJU Int 2008;101:535–9.
[21] Montvilas P, Solvig J, Johansen TE. Single-centre review of radiologically guided percutaneous nephrostomy using "mixed" technique: success and complication rates. Eur J Radiol 2011;80:553–8.
[22] De Coninck V, Keller EX, Somani B, et al. Complications of ureteroscopy: a complete overview. World J Urol 2020;38:2147–66.
[23] Grosso AA, Sessa F, Campi R, et al. Intraoperative and postoperative surgical complications after ureteroscopy, retrograde intrarenal surgery, and percutaneous nephrolithotomy: a systematic review. Minerva Urol Nephrol 2021;73:309–32.
[24] Bryniarski P, Rajwa P, Życzkowski M, Taborowski P, Kaletka Z, Paradysz A. A non-inferiority study to analyze the safety of totally tubeless percutaneous nephrolithotomy. Adv Clin Exp Med 2018;27:1411–6.
[25] Yang G, Liang F, Sun X, Qin L. Safety and feasibility of tubeless PCNL without urinary catheter or retrograde intubation under paravertebral block. Int Urol Nephrol 2026;58:3447–56.
[26] Ni S, Qiyin C, Tao W, et al. Tubeless percutaneous nephrolithotomy is associated with less pain and shorter hospitalization compared with standard or small bore drainage: a meta-analysis of randomized, controlled trials. Urology 2011;77:1293–8.
[27] Fu X, Hu W, Deng W, et al. Total tubeless percutaneous nephrolithotomy without retrograde insertion of a ureteral catheter for the treatment of kidney stone patients without hydronephrosis: a randomized controlled trial. Int Urol Nephrol 2025;57:759–67.
[28] Cui XW, Ignee A, Maros T, Straub B, Wen JG, Dietrich CF. Feasibility and usefulness of intra-cavitary contrast-enhanced ultrasound in percutaneous nephrostomy. Ultrasound Med Biol 2016;42:2180–8.
[29] Speed JM, Wang Y, Leow JJ, et al. The effect of physician specialty obtaining access for percutaneous nephrolithotomy on perioperative costs and outcomes. J Endourol 2017;31:1152–6.

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