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Critical Care

RESEARCH **Open Access**

A randomized controlled trial of catheters with different tips and lengths for patients requiring continuous renal replacement therapy in intensive care unit

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Abstract

Background The tip design and length of catheter impact catheter function. Two types of catheters with different tips, side-hole catheters and step-tip catheters, are commonly used during continuous renal replacement therapy (CRRT). However, there is insufficient evidence comparing their efficacy and safety in CRRT. In addition, whether the insertion of a longer catheter could enhance catheter function remains poorly studied and controversial.

Methods In this open-label, three-arm, randomized trial, critically ill patients receiving CRRT were randomized to three groups. Group A received 20 cm side-hole catheters (GDHK-1120), group B received 20 cm step-tip catheters (GDHK-1320) and group C received 25 cm step-tip catheters (GDHK-1325). The primary outcomes were the incidence of catheter dysfunction and catheter survival time.

Results A total of 351 patients were enrolled, with 116 in group A, 117 in group B, and 118 in group C. The incidence of catheter dysfunction in group A (35.7%, 51/143) was significantly higher than that in group B (17.7%, 22/124) ($P=0.001$). However, there was no difference between group B and group C (15.6%, 23/147) ($P=0.744$). The catheter survival time was comparable between group A (5.5 days, IQR 2.5–9.3) and group B (5.0 days, IQR 3.0–10.0) ($P=0.626$). In contrast, group C (6.4 days, IQR 3.9–12.0) demonstrated a significantly longer catheter survival time compared to group B ($P=0.019$). Cox regression analysis identified BMI (HR 1.052, 95% CI 1.003–1.103, $P=0.036$) as an independent risk factor for catheter dysfunction. Results were not consistent across BMI tertiles, with similar results observed only in patients with a lower BMI (BMI < 24.2) (chi-square 13.65, $P=0.001$). There was also a trend that patients in group C have a longer filter lifespan (36.5 h, IQR 16.9–68.1, $P=0.001$) and a lower incidence of catheter-related thrombosis (10.40 per 1000 catheter-days, 95% CI 5.93, 17.83, $P=0.019$). Other secondary outcomes were not significantly different among groups.

Conclusions Step-tip catheters may be preferable for CRRT, particularly for patients in the lower BMI tercile. Longer femoral vein catheterization demonstrated enhanced benefits in CRRT, especially among obese patients. Further high-quality, multicenter RCTs are essential to strengthen the evidence guiding catheter selection during CRRT.

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Keywords Continuous renal replacement therapy, Side-hole catheter, Step-tip catheter, Catheter dysfunction, Catheter survival time

Introduction

Continuous renal replacement therapy (CRRT) has become a widely established treatment modality for critically ill patients with acute kidney injury [1]. The tip design and length of catheter are crucial factors that significantly impact catheter function and the entire CRRT circuit efficacy [2]. Despite numerous studies have investigated catheter designs to optimize functionality, most have been limited to in vitro experiments or observational studies, and predominantly focusing on long-term hemodialysis catheters [3, 4]. Consequently, the efficacy and safety of these catheters in CRRT remains controversial.

Side-hole and step-tip catheters are commonly employed during CRRT. Side-hole catheters feature holes at the distal tip that reduce shear rate and enhance blood flow, thereby minimizing blood recirculation. Step-tip catheter adopts a staggered tip design, with the venous tip extending several centimeters (typically 2.5 cm) beyond the arterial tip, which is also believed to reduce blood recirculation [5]. The presence of side holes in the catheter may potentially increase the risks of thrombosis and catheter-related infection. However, it should be noted that these findings are primarily derived from observational studies involving long-term hemodialysis catheters used in chronic hemodialysis, rather than from high-quality randomized controlled trials (RCTs) specific to CRRT [6–8]. Moreover, an observational study by Fealy et al. [9] compared CRRT treatment with Niagara (13.5-Fr, 24 cm, step-tip catheter) and Medcomp (13.5-Fr, 24 cm, symmetrical side-hole catheter) catheters and found no disparity in filter lifespan. Although the limited sample size substantially constrains the generalizability of its findings. Therefore, there is pressing need for robust evidence to conclusively determine the comparative efficacy and safety of side-hole versus step-tip catheters during CRRT.

The length of catheter is of paramount importance in maintaining adequate blood flow and minimizing blood recirculation. However, there is currently no established consensus or standardized guidelines regarding the appropriate catheter length for femoral vein catheterization. While deeper insertion of longer catheters into the femoral vein positions the tip within a larger vessel diameter, conclusive evidence demonstrating improved catheter functionality with deeper insertion remains lacking. Furthermore, according to Poiseuille's law, blood flow through the catheter decreases proportionally with increasing catheter length [10]. Essentially, there is insufficient evidence and recommendations to establish the optimal catheter length and its impact on performance.

Therefore, we designed a RCT in a prospective, open-label, three-arm, parallel-group design. The objective of this study is to evaluate whether using a catheter with step-tip design could improve catheter function compared to a side-hole catheter. Additionally, the study aims to investigate whether the insertion of a longer catheter could minimize the occurrence of catheter dysfunction and enhance catheter survival time.

Methods

Study design and participants

We conducted an open-label, three-arm, parallel-group RCT at West China Hospital of Sichuan University in China. This study had received ethical approval from the biomedical research ethics committee of West China Hospital of Sichuan University (2023. 1221), and was registered with the Chinese Clinical Trial Registration Center (ChiCTR2300075107). Critically ill adult patients who intended to have a support with CRRT and were expected to receive a full intensive care treatment for at least 3 days were included in this trial. And patients with coagulopathy or received systemic anticoagulation therapy, or have contraindications of femoral vein catheterization were excluded. Details of the study protocol, including the inclusion and exclusion criteria, have been peer-reviewed and published [11].

Randomization, intervention, catheter insertion and care procedures, and sample size

Intensive care unit (ICU) patients requiring CRRT were included in this trial. Patients were randomly allocated into three groups at a 1:1:1 ratio, determined by a central computer-generated randomized sequence. Group A received side-hole catheters (11Fr, 200 mm; GDHK-1120, Baxter International Inc., Deerfield, Illinois), group B received step-tip catheters (13Fr, 200 mm; GDHK-1320, Baxter International Inc., Deerfield, Illinois) and group C received step-tip catheters (13Fr, 250 mm; GDHK-1325, Baxter International Inc., Deerfield, Illinois).

The processes of intervention, determination of sample size, as well as the catheter insertion and care procedures, have been previously described in detail [11]. Briefly, an estimated sample of 378 participants receiving CRRT would be recruited. A standardized seven-step strategy for catheterization was performed by physicians with extensive experience in catheterization [12]. All patients were treated with continuous veno-venous hemodiafiltration (CVVHDF) with the following initial prescriptions: post-dilution, blood flow (regional citrate anticoagulation: 150 mL/min; low- molecular- weight heparin anticoagulation or without anticoagulants: 200 mL/min), and a treatment dose at 25 to 35 mL/kg/h.

Outcomes

The incidence of catheter dysfunction and catheter survival time were coprimary outcomes of this study. Catheter dysfunction was defined when the following conditions occur during CRRT: inability to maintain an adequate blood flow, or continuous arterial pressure < -200 mm Hg, or continuous venous pressure > 200 mm Hg, or frequent pressure alarm (> 3 times/hour), or inability to aspirate blood freely [13–15]. Filter lifespan, all-cause mortality, length of stay, duration of CRRT and adverse events were secondary outcomes.

Intradialytic hypotension (IDH) is a frequent adverse event during CRRT. Recently, a new definition of IDH specific to CRRT has been proposed, defining it as a "new/sudden decrease in SBP > 40 mm Hg, a MAP of < 60 mm Hg, or SBP < 90 mm Hg; initiation or increased dosing of vasoactive drugs, or the need for intravenous fluid boluses within the first hour of CRRT" [16, 17]. And this definition was adopted for this study.

Catheter associated bloodstream infection (CRBSI) was defined as the isolation of the same pathogenic microorganism with identical antimicrobial susceptibility from both the catheter tip culture and at least one peripheral blood culture within 48 h following catheter insertion [18].

Statistical analysis

Statistical analyses were performed with SPSS 22.0 (IBM, USA). Kaplan–Meier curves and log-rank test were performed to compare the time to catheter dysfunction among groups. Univariate analysis was performed to assess the impact of patient characteristics (age, BMI and SOFA score), laboratory data at CRRT initiation and anticoagulants on the incidence of catheter dysfunction. Subsequently, a Cox regression model was employed to identify risk factors associated with catheter dysfunction. Given that platelet count, anticoagulants, and coagulation parameters during CRRT may influence catheter patency and potentially contribute to catheter dysfunction, these variables were included in the multivariate Cox regression analysis along with factors showing $P < 0.1$ in the univariate analysis. The detail of statistical analyses was included in our published protocol [11].

Results

Baseline characteristics

Between November 01, 2023, and September 30, 2024, a total of 397 critically ill patients requiring CRRT were assessed for eligibility. After excluding 19 patients based on inclusion and exclusion criteria, 378 patients were randomly assigned to three groups. 27 patients were ultimately excluded due to various reasons: receiving at least two types of catheters (n = 12), an actual ICU stay of less than 3 days (n = 12), and consent could not ultimately be obtained for any reason (n = 3). Consequently, 351 patients were included in the study: 116 patients in group A, 117 patients in group, and 118 patients in group C. The flowchart of this RCT is illustrated in Fig. 1.

The baseline characteristics of the three groups are summarized in Table 1. No significant differences were observed among the three groups of patients in terms of age, gender, BMI, height, illness severity, comorbidities, laboratory data at CRRT initiation and time from ICU admission to CRRT initiation ($P > 0.05$). The vascular access for CRRT was mainly the right femoral vein (> 60%), and regional citrate anticoagulation (RCA) was the predominant anticoagulant (> 50%). AKI is the primary indication for CRRT, but no statistically significant difference was observed among the three groups.

Primary outcomes

The results of primary outcomes were presented in Table 2. A total of 143 catheters were used in group A, 124 catheters in group B, and 147 catheters in group C. The incidence of catheter dysfunction in group A (35.7%, 51/143) was significantly higher than that in group B (17.7%, 22/124) ($P = 0.001$). However, no significant difference was observed in the incidence of catheter dysfunction between group B and group C (15.6%, 23/147) ($P = 0.744$). Similar trends were observed when analyzing the incidence of catheter dysfunction for the first catheter per patient, as well as within 3 days or 7 days. Consistent results were also demonstrated by the Kaplan–Meier curve and log-rank test for the time to catheter dysfunction (Fig. 2 and Fig. 3).

Catheter survival time was defined as the duration from insertion to removal for any reason (catheter dysfunction, achievement of treatment goals, death, or suspicion of catheter infection). Although the catheter survival time in group A (5.5 days, IQR 2.5–9.3) was comparable to that in group B (5.0 days, IQR 3.0–10.0) ($P = 0.626$), catheters in group C exhibited the longest catheter survival time (6.4 days, IQR 3.9–12.0) ($P = 0.019$).

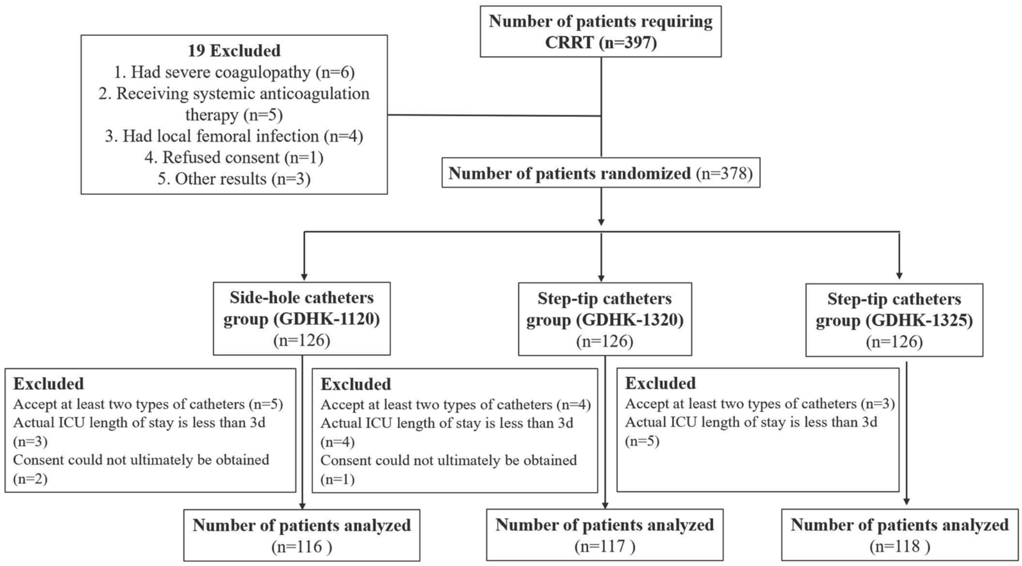

Fig. 1 Flowchart of participants. CRRT, continuous renal replacement therapy; ICU, intensive care unit

However, no statistically significant differences ($P > 0.05$) were observed in catheter survival time among groups when analyzing the first catheter per patient or catheters with dysfunction.

Univariate analysis revealed that catheter type, BMI, and hematocrit might influence the incidence of catheter dysfunction ($P < 0.05$) (Supplementary material: Table S1). Furthermore, Cox regression analysis identified catheter type and BMI (HR 1.052, 95% CI 1.003–1.103, $P = 0.036$) as two independent risk factors for catheter dysfunction (Supplementary material: Table S2). Consequently, we performed a subgroup analysis based on BMI (cutoffs according to the population tercile), with the results presented in Supplementary material: Figure S1–S3. Specifically, similar results could be observed only in patients with a lower BMI (BMI < 24.2). However, in patients with highest BMI (BMI > 28.4), no significant difference was found in the incidence of catheter dysfunction between group A and group B (Chi-square 0.33, $P = 0.567$), although the incidence in group C remained the lowest. As for patients with middle BMI (BMI 24.2–28.4), the incidence of catheter dysfunction was comparable across the three groups (Chi-square 4.62, $P = 0.099$).

Filter lifespan

Average filter lifespan among groups were detailed in Supplementary material: Table S3. During CRRT, a total of 478 filters were used in group A, 434 filters in group B, and 526 filters in group C. The difference in the number of filters used per patient was not statistically significant ($P = 0.124$). When analyzing all filters, the average filter lifespan in group C was 10.7 h longer than that in group A, and 8.5 h longer than that in group B [36.5 h (IQR 16.9–68.1) versus 25.8 h (IQR 13.4–57.9) versus 28.0 h (IQR 17.0–60.0), $P = 0.001$], whereas the average filter lifespan between group A and group B was comparable ($P = 0.194$). For the first filter used per patient, the average filter lifespan was similar across groups [24.0 h (IQR 15.0–57.9) versus 32.5 h (IQR 21.5–55.0) versus 29.5 h (IQR 16.3–59.0), $P = 0.252$].

Filters clotting is a critical factor influencing filter lifespan. The proportion of clotted filters in group B (32.3%, 140/434) was higher than that in group A (28.9%, 138/478) and group C (30.4%, 160/526), but the difference was not statistically significant ($P = 0.543$). And the number of filters clotted per patient was equivalent (1, IQR 0–2, $P = 0.859$). Although not statistically significant, the filter lifespan in group C remained the longest based on the analysis of filters with clots [24.7 h (IQR 14.0–41.6) versus 29.5 h (IQR 18.0–46.0) versus 30.2 h (IQR 16.6–51.5), $P = 0.072$].

Length of stay and all-cause mortality

The ICU length of stay showed a statistically variance among the groups ($P = 0.016$) (Supplementary material: Table S4). Specifically, patients in group C exhibited a median ICU length of stay of 14.0 days (IQR 7.8–24.5), which was 4 days longer than that of group B (10.0 days, IQR 5.3–16.0) ($P = 0.014$). However, no significant difference was detected between group A (13.3 days, IQR 6.1–21.8) and group B ($P = 0.168$). The hospital length of stay was also the longest in group C, although this

Table 1 Characteristics of the study patients

Characteristics	Side-hole catheters (GDHK-1120) (Group A) (n = 116)	Step-tip catheters (GDHK-1320) (Group B) (n = 117)	Step-tip catheters (GDHK-1325) (Group C) (n = 118)	*P* value
Demographics				
Age (y) (SD)	57.9(18.7)	56.4(17.5)	58.5(17.4)	0.640
Male	82(70.7)	72(61.5)	84(71.2)	0.206
Height (cm) (SD)	165.5(7.3)	164.6(8.7)	166.8(7.1)	0.135
Body mass index (IQR)	23.0(20.2–26.7)	23.2(21.2–26.8)	23.1(21.0–26.0)	0.849
Illness severity at admission to the ICU				
SOFA score (SD)	11.4 (3.0)	11.5 (3.1)	11.5 (3.0)	0.325
Mechanical ventilation	111(95.7)	104(88.9)	112(94.9)	0.088
Invasive	106	101	103	
Non-invasive	5	3	9	
Comorbidities, No. (%)				
Diabetes	40(34.5)	32(27.4)	30(25.4)	0.273
Chronic kidney disease (eGFR < 60 mL/min/1.73 m^2)	47(40.5)	42(35.9)	44(37.3)	0.764
Cardiovascular disease	71(61.2)	65(55.6)	73(61.9)	0.568
Hypertension	48	40	46	
Heart failure	23	21	19	
Valvular heart disease	7	9	11	
Aortic dissection	8	7	6	
Cerebrovascular disease	14(12.1)	10(8.5)	9(7.6)	0.442
Gastrointestinal hemorrhage	15(12.9)	16(13.7)	14(11.9)	0.921
Liver cirrhosis	7(6.0)	10(8.5)	7(5.9)	0.724
Pancreatitis	11(9.5)	8(6.8)	13(11.0)	0.525
Malignancy	5(4.3)	8(6.8)	10(8.5)	0.453
Laboratory data at CRRT initiation				
Serum creatinine, μmol/L (IQR)	369(215–553)	319(220–418)	361(210–545)	0.123
BUN, mmol/L (IQR)	24.4(17.0–36.8)	21.4(13.5–33.2)	23.8(16.4–33.1)	0.145
Hemoglobin, g/L (IQR)	85.0(69.5–99.0)	80.3(71.1–99.1)	83.6(74.0–94.2)	0.682
Hematocrit (SD)	27.5(7.4)	27.5(6.2)	27.8(5.9)	0.874
Platelets, 10^9/L (IQR)	108(67–159)	92(61–148)	108(70–175)	0.181
PT, sec (IQR)	14.4(12.7–17.0)	14.5(12.3–20.3)	14.1(12.8–17.1)	0.629
APTT, sec (IQR)	36.2(31.4–43.4)	35.0(30.2–42.2)	33.7(30.1–39.4)	0.063
INR (SD)	1.46(0.49)	1.57(0.66)	1.33(0.30)	0.055
Ph (SD)	7.300(0.094)	7.319(0.088)	7.319(0.073)	0.186
Bicarbonate, mmol/L (SD)	21.5(5.0)	22.1(4.9)	21.8(4.1)	0.616
Total calcium, mmol/L) (SD)	0.924(0.159)	0.968(0.119)	0.950(0.128)	0.058
Ionized calcium, mmol/L) (SD)	2.01(0.27)	2.08(0.23)	2.07(0.23)	0.139
Ionized calcium/total calcium (SD)	0.46(0.06)	0.47(0.05)	0.46(0.05)	0.283
Vascular access, n (%)				
Left femoral vein	46(39.7)	44(37.6)	39(33.1)	0.569
Right femoral vein	70(60.3)	73(62.4)	79(66.9)	0.569
Anticoagulants				
RCA	66(56.9)	60(51.3)	74(62.7)	0.214
LMWH	16(13.8)	11(9.4)	12(10.2)	0.519
No anticoagulant	31(26.7)	41(35.0)	27(22.9)	0.104
Others	3(2.6)	5(4.3)	5(4.2)	0.825
Indication for CRRT, No./total No. patients (%)				
Acute kidney injury	68(58.6)	60(51.3)	56(47.5)	0.226
Sepsis/Septic shock	17(14.7)	21(17.9)	22(18.6)	0.719

Table 1 (continued)

Characteristics	Side-hole catheters (GDHK-1120) (Group A) (n = 116)	Step-tip catheters (GDHK-1320) (Group B) (n = 117)	Step-tip catheters (GDHK-1325) (Group C) (n = 118)	*P* value
Severe electrolyte abnormalities	22(19.0)	21(17.9)	27(22.9)	0.617
Liver failure	4(3.4)	6(5.1)	4(3.4)	0.790
other	5(4.3)	9(7.8)	9(7.6)	0.506
Time from ICU admission to CRRT initiation, d (IQR)	0.8(0.4–2.2)	0.9(0.4–2.0)	1.0(0.4–3.0)	0.728

SD, standard deviation; IQR, interquartile range; SOFA, sequential organ failure assessment; CRRT, continuous renal replacement therapy; BUN, blood urea nitrogen; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio; RCA, regional citrate anticoagulation; LMWH, low molecular weight heparin; ICU, intensive care unit

Table 2 The results of primary outcomes

Catheter follow-up	Side-hole catheters (GDHK-1120) (Group A) (n = 143)	Step-tip catheters (GDHK-1320) (Group B) (n = 124)	Step-tip catheters (GDHK-1325) (Group C) (n = 147)	*P* value
Incidence of catheter dysfunction (%)				
All*	51 (35.7)	22 (17.7)	23 (15.6)	**< 0.001**
First catheter per patient**	42 (36.2)	20 (17.1)	15 (12.7)	**< 0.001**
No. of catheter duration				
≤ 3 days***	12 (8.4)	3 (2.4)	4 (2.7)	**0.027**
≤ 7 days****	26 (18.2)	14 (11.3)	11 (7.5)	**0.019**
Catheter survival time, d (IQR)				
All#	5.5 (2.5–9.3)	5.0 (3.0–10.0)	6.4 (3.9–12.0)	**0.019**
First catheter per patient	5.9 (2.5–10.0)	5.0 (3.0–9.9)	6.1 (3.8–11.4)	0.145
Catheters with catheter dysfunction	7.0 (3.5–12.0)	5.8 (4.4–11.4)	7.2 (3.5–11.4)	0.940
No. of catheters each patient received				
One	95 (81.9)	110 (94.0)	97 (82.2)	
Two	15 (12.9)	7 (6.0)	15 (12.7)	
Three	6 (5.2)	0 (0.0)	4 (3.4)	
More than three	0 (0.0)	0 (0.0)	2 (1.7)	
Reason for catheter ablation				
Catheter dysfunction$	30 (21.0)	14 (11.3)	15 (10.2)	**0.017**
Achievement of treatment goal	39 (27.3)	40 (32.3)	52 (35.4)	0.327
Treatment abandonment	38 (26.6)	39 (31.5)	45 (30.6)	0.637
Death	23 (16.1)	21 (16.8)	20 (13.6)	0.737
Suspicion of catheter infection	9 (6.3)	7 (5.7)	10 (6.8)	0.967
Unknown or not inserted	4 (2.7)	3 (2.4)	5 (3.4)	0.935

Bold "*P*-values" represent significant differences ($P < 0.05$)

IQR, interquartile range

*Incidence of catheter dysfunction (all): GDHK-1120 versus GDHK-1320, $P = 0.001$; GDHK-1320 versus GDHK-1325, $P = 0.744$

**Incidence of catheter dysfunction (First catheter): GDHK-1120 versus GDHK-1320, $P = 0.013$; GDHK-1320 versus GDHK-1325, $P = 0.203$

***Incidence of catheter dysfunction (≤ 3 days): GDHK-1120 versus GDHK-1320, $P = 0.035$; GDHK-1320 versus GDHK-1325, $P = 0.876$

****Incidence of catheter dysfunction (≤ 7 days): GDHK-1120 versus GDHK-1320, $P = 0.125$; GDHK-1320 versus GDHK-1325, $P = 0.299$

Catheter survival time (all): GDHK-1120 versus GDHK-1320, $P = 0.626$; GDHK-1320 versus GDHK-1325, $P = 0.038$

$ Reason for catheter ablation (catheter dysfunction): GDHK-1120 versus GDHK-1320, $P = 0.046$; GDHK-1320 versus GDHK-1325, $P = 0.845$

difference did not reach statistical significance [23.0d (IQR 14.0–34.0) versus 20.0d (IQR 10.3–33.5) versus 19.0d (IQR 10.0–30.0), $P = 0.051$].

Regarding ICU mortality ($P = 0.273$), hospital mortality ($P = 0.415$), 28-day mortality ($P = 0.207$), and 60-day mortality ($P = 0.231$), no significant differences were observed among groups.

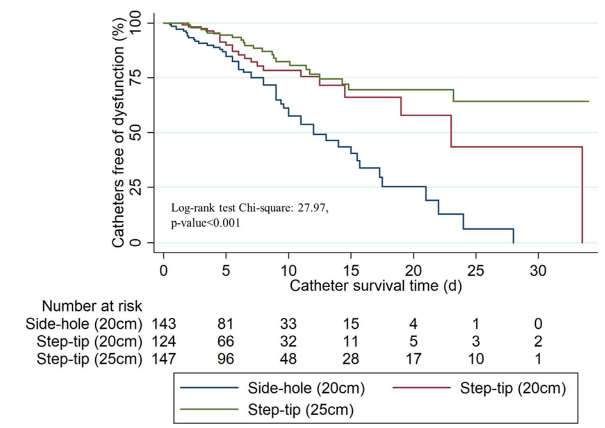

Fig. 2 Kaplan–Meier curves and log-rank test for time to catheter dysfunction of all catheters. Group A (side-hole, 20 cm, GDHK1120) versus Group B (step-tip, 20 cm, GDHK1320): Log-rank test: chi-square 10.85, $P=0.001$; Group A (side-hole, 20 cm, GDHK1120) versus Group C (step-tip, 25 cm, GDHK1325): Log-rank test: chi-square 24.66, $P<0.001$; Group B (step-tip, 20 cm, GDHK1320) versus Group C (step-tip, 25 cm, GDHK1325): Log-rank test: chi-square 1.71, $P=0.191$

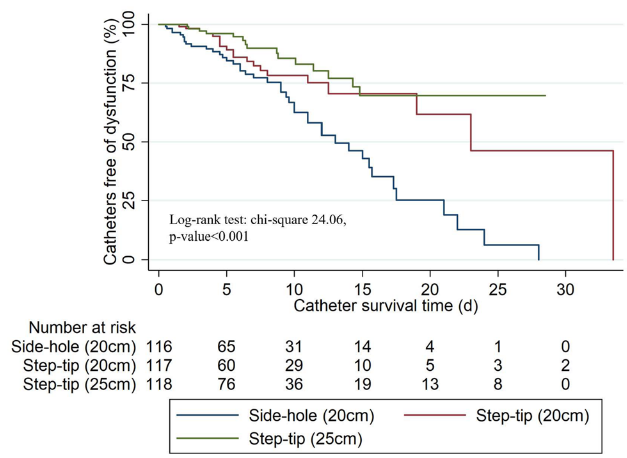

Fig. 3 Kaplan–Meier curves and log-rank test for time to catheter dysfunction of first catheter per patient. Group A (side-hole, 20 cm, GDHK1120) versus Group B (step-tip, 20 cm, GDHK1320): Log-rank test: chi-square 9.37, $P=0.002$; Group A (side-hole, 20 cm, GDHK1120) versus Group C (step-tip, 25 cm, GDHK1325): Log-rank test: chi-square 21.40, $P<0.001$; Group B (step-tip, 20 cm, GDHK1320) versus Group C (step-tip, 25 cm, GDHK1325): Log-rank test: chi-square 1.91, $P=0.167$

Adverse events

The incidence of IDH was 27.6% (32/116) in group A, 21.4% (25/117) in group B, and 19.5% (23/118) in group C, with no statistically significant difference ($P=0.306$). Incidence of CRBSI was also similar among groups [incidence per 1000 catheter-days, 3.06, (95% CI 0.79–9.70) versus 3.33, (95% CI 0.86–10.55) versus 2.97, (95% CI 0.95–8.14), $P>0.999$]. However, compared to group B and group C, patients in group A had a significantly higher incidence of catheter-related thrombosis (CRT) [incidence per 1000 catheter-days, 25.48, 95% CI 16.91–37.95 versus 13.31, 95% CI 7.23–23.82 versus 10.40, 95% CI 5.93–17.83, $P=0.019$]. The incidence of adverse events among groups were detailed in Supplementary material: Table S5.

Discussion

Key findings

In this open-label, parallel-group RCT, we demonstrated that step-tip catheters may represent a superior alternative to side-hole catheters for CRRT. The use of step-tip catheters for CRRT was associated with a reduced incidence of catheter dysfunction and CRT, without increasing the risk of IDH and CRBSI. Furthermore, our findings indicated that a deeper femoral vein catheterization improved catheter survival time and prolonged filter lifespan. Notably, multivariate Cox regression analysis identified BMI as an independent risk factor for catheter dysfunction. Subgroup analysis based on BMI revealed that only among patients within lower BMI tercile (BMI < 24.2), femoral catheterization with step-tip catheters exhibited a lower incidence of catheter dysfunction. In the middle BMI tercile (BMI 24.2–28.4), the incidence of catheter dysfunction was comparable across the three groups. And for patients with higher BMI tercile (BMI 24.2–28.4), femoral catheterization with longer step-tip catheters was preferable.

Comparison with previous studies

Previous relevant studies were summarized in Supplementary material: Table S6. Several in vitro fluid dynamics assessments and animal experiments indicated that side-holes may increase the risk of CRT and CRBSI [6, 7, 19, 20]. However, side holes may provide benefits in aspirating acute thrombus and reducing maximum velocity and shear stress [21, 22]. Currently, the majority of studies investigating the effects of side-hole catheters on dialysis have focused on maintenance hemodialysis, with notable lack of high-quality RCTs. Three observational trials conducted by Tal et al. consistently reported a decreased incidence of CRT and CRBSI with the non-side-hole cuffed catheters [8, 23, 24]. However, these studies were limited by the absence of control groups and small sample sizes (all < 100 participants). There remains insufficient evidence comparing the efficacy and safety of side-hole and step-tip catheters for CRRT in critically ill patients. To date, only one observational study by Fealy et al. [9] involving

46 participants, had compared circuit lifespan between Niagara (step-tip catheter) and Medcomp (side-hole catheter) catheters during CRRT.

The optimal length of catheter for CRRT remains uncertain and controversial. The KDOQI guideline recommend that the tip of temporary catheters should be positioned within the superior vena cava. However, intriguingly, the same guideline suggested that the tip of tunneled long-term catheters be placed within the right atrium [13]. In light of this discrepancy, Morgan et al. designed an RCT, demonstrating that longer dialysis catheters positioned in the right atrial improved filter lifespan during CRRT, without increasing the risk of atrial arrhythmias [25]. The femoral vein serves as a common vascular access site for CRRT, especially for critically ill patients. Nevertheless, the ideal length for femoral vein catheters is still unclear, and there is insufficient evidence to determine whether deeper insertion results in better catheter function.

In this study, we employed a randomized controlled design to assess the safety and efficacy of side-hole and step-tip catheters during CRRT. Furthermore, we examined the potential benefits of a deeper femoral vein catheterization in CRRT. Our study incorporated a substantial sample size, enabling comprehensive assessment of catheter performance and patient outcomes across side-hole catheters and two distinct step-tip catheters during CRRT. These findings contribute to the future developments in CRRT catheter design and establish an evidence-based foundation for catheter selection in CRRT therapy.

Clinical implications and future studies

The design of catheter tip is a crucial factor affecting catheter function. Although the diameters of the side-hole catheters and step-tip catheters used in this study were not consistent, they are both fell within the recommended range of 11-14Fr in the guidelines. Moreover, several studies have also suggested that the catheter diameter size does not necessarily affect the lifespan of extracorporeal circulation and the survival rate of patients [26–29]. Additionally, a larger diameter may be associated with an increased risk of venous thrombosis on the catheter's external surface [4]. In the future, if feasible, measuring the ratio of catheter diameter to vein size would better account for the influence of catheter size on catheter function. Compared to side-hole catheters, step-tip catheters may represent a superior option to ensure safe and effective CRRT. BMI was identified as an independent risk factor for catheter dysfunction, and the use of step-tip catheters was associated with a lower incidence of catheter dysfunction, but only in patients with lower BMI tercile (BMI < 24.2). Therefore, in future CRRT treatment, the selection of a step-tip catheter may be preferable to a side-hole catheter, especially for low BMI tercile (BMI < 24.2) patients. However, it is noteworthy that the step-tip catheters we currently used in this trial typically have a venous end that extends 2.5 cm beyond the arterial end. The optimal distance between the arterial and venous ends for improved catheter function remains undefined and warrants further investigation.

Currently, there is still controversy over the optimal length of catheter during CRRT, with one existing trial focusing on internal jugular vein catheterization. A significant challenge in accurately determining catheter tip location arises from the impracticality of performing post-procedural X-ray examinations for all critically ill patients. Given that the body proportions are generally symmetrical in most individuals and considering the minimal differences in baseline height among the three patient groups, it can be reasonably inferred that longer catheters result in deeper catheter tip placement. Our findings indicated that deeper femoral vein catheterization yielded superior catheter function, particularly in patients with higher BMI tercile (BMI > 28.4). Therefore, a deeper femoral vein catheterization may emerge as a crucial consideration for future CRRT, potentially offering greater benefits to obese patients.

Although the KDIGO clinical practice guideline (2012) recommended the right internal jugular vein as the first-choice access site [30], this trial exclusively used femoral access for the following reasons. Firstly, several high-quality studies and a meta-analysis have demonstrated that jugular vein catheterization did not significantly outperform femoral site placement in critically ill patients requiring RRT [15, 28, 31, 32]. Secondly, in most China hospitals, femoral vein catheterization is the predominant approach for CRRT, as central venous catheters (CVCs) are typically placed in the internal jugular vein. Further studies involving both femoral and internal jugular vein catheterization are urgently needed to explore the influence of catheter length on catheter performance more comprehensively.

Strengths and limitations

To the best of our knowledge, this study represents the first RCT to compare the efficacy and safety of step-tip with side-hole catheters, while simultaneously evaluating the impact of the length of femoral vein catheter on catheter function during CRRT. Utilizing an open-label, three-arm design, this trial meticulously analyzed a spectrum of outcomes including the incidence of catheter dysfunction, catheter survival time, filter lifespan, all-cause mortality, length of stay, and adverse events, to comprehensively assess the efficacy and safety of step-tip with side-hole catheters. To mitigate the potential influence of BMI on catheter function, we performed a subgroup analysis to further contrast the catheter function between step-tip with side-hole catheters. We are optimistic that this trial will contribute valuable insights to the development of catheter selection and design for CRRT in critically ill patients.

Despite strengths, this trial has several limitations. Firstly, blinding of participants and treating clinicians was not applicable due to the nature of intervention. Despite our meticulous design of randomization, allocation, outcome assessment, data collection, and analysis methodologies, there remained a potential for residual bias. Secondly, our trial was conducted at a single hospital in southwest China, and the results would need cautious interpretation concerning region and ethnicity. Additional high-quality multicenter RCTs are essential to strengthen the evidence on the choice of catheters during CRRT. Thirdly, our study did not incorporate a cost-effectiveness analysis, which represents a critical consideration for both clinical decision-making and healthcare resource allocation. It remains to be determined whether the magnitude of the gain in catheter survival time and filter lifespan could sufficiently offset the additional cost of longer CRRT duration and ICU stay. Finally, the observed catheter dysfunction rate was significantly higher than the expected rate. Since no prior relevant studies exist, the expected rate was derived from data related to long-term hemodialysis. However, the observed rate in this study pertained the population undergoing CRRT. Given that CRRT is a more complex treatment modality and typically involves critically ill patients, we consider that the discrepancy between the observed and expected rates is reasonable and justified.

Conclusions

Compared to the side-hole catheters, step-tip catheters may be preferable for CRRT, especially for patients with low BMI tercile, as they exhibited a lower incidence of catheter dysfunction without an increase in the risk of adverse events. A deeper femoral vein catheterization demonstrated enhanced benefits in CRRT, particularly in obese patients. Further high-quality, multicenter RCTs are essential to reinforce the evidence guiding catheter choice during CRRT.

Abbreviations

CRRT	Continuous renal replacement therapy
RCTs	Randomized controlled trial
ICU	Intensive care unit
IDH	Intradialytic hypotension
MHD	Maintenance hemodialysis
KDOQI	National Kidney Foundation Kidney Disease Outcomes Quality Initiative
SBP	Systolic blood pressure
MAP	Mean arterial pressure
CRBSI	Catheter associated bloodstream infection
RCA	Regional citrate anticoagulation
CRT	Catheter-related thrombosis
SD	Standard deviation
IQR	Interquartile range
SOFA	Sequential organ failure assessment
BUN	Blood urea nitrogen
PT	Prothrombin time
APTT	Activated partial thromboplastin time
INR	International normalized ratio
LMWH	Low molecular weight heparin

Supplementary Information

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Supplementary material 1

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Author contributions

LZ, as the corresponding author of this paper, was mainly responsible for program design and modification. ZFZ wrote the first draft. ZFZ, CL, PYL, YYY and FW contributed to data acquisition. ZFZ, CL, QX and LJ contributed to data analysis and interpretation. PF and LZ contributed to revision and acquisition of funding. And supervision was provided by PF and LZ. All of the authors have carefully examined this manuscript and agreed with the ideas presented in the article.

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Availability of data and materials

The data generated during and/or analyzed during the study will be shared upon request by the corresponding author for research purposes.

Declarations

Ethics approval and consent to participate

This study had received ethical approval from the biomedical research ethics committee of West China Hospital of Sichuan University (2023.1221), and was registered with the Chinese Clinical Trial Registration Center (ChiCTR2300075107). Only patients with completed written informed consents were included in this study.

Consent for publication

All authors have agreed to the publication of this manuscript.

Competing interests

The authors declare that they have no competing interests.

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Publisher's Note

QUESTIONNAIRE
R7(26)
A randomized controlled trial of catheters with different tips and lengths for patients requiring continuous renal replacement therapy in intensive care unit

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- There is only **ONE** correct answer for each question.

Introduction

Question 1: What best describes the role of CRRT in critically ill patients with acute kidney injury**?**

A: An experimental therapy used only in research settings
B: A widely established treatment modality in critically ill patients with acute kidney injury
C: A treatment limited to stable outpatients with chronic kidney disease
D: A modality largely replaced by peritoneal dialysis in intensive care units
E: A contraindicated therapy in acute kidney injury

Question 2: The current evidence comparing side-hole and step-tip catheters in CRRT is mainly derived from in vitro experiments and observational studies focused on long-term haemodialysis catheters rather than high-quality randomized controlled trials in CRRT.

A: TRUE
B: FALSE

Question 3: What is the proposed advantage of the step-tip catheter design during CRRT?

A: Increased catheter rigidity to prevent kinking
B: Reduced blood recirculation due to staggered arterial and venous tip positioning
C: Lower thrombosis risk due to the absence of side holes
D: Higher blood flow by increasing catheter diameter

Question 4: Which factor is critical for maintaining adequate blood flow and minimizing blood recirculation during CRRT?

A: Catheter length
B: Filter membrane type
C: Dialysate temperature
D: Anticoagulation strategy

Question 5: What was the primary objective of this prospective, open-label, three-arm randomised controlled trial?

A: To compare CRRT with intermittent dialysis
B: To assess whether step-tip design and longer catheter length improve catheter function
C: To evaluate anticoagulation strategies in CRRT
D: To compare infection rates by access site

Methods

Question 6: How were ICU patients requiring CRRT allocated to the three catheter groups in this trial?

A: By physician preference
B: By ward availability
C: By a central computer-generated 1:1:1 randomised sequence
D: By alternating assignment

Question 7: Which CRRT modality and initial prescription were used for all patients in this study?

A: CVVHD with pre-dilution at 20 mL/kg/h
B: CVVHDF with post-dilution and a dose of 25–35 mL/kg/h
C: Intermittent haemodialysis at fixed flow rates
D: CVVH with pre-dilution and dose of 40 mL/kg/h

Question 8: How was CRBSI defined in this study?

A: Positive catheter tip culture alone
B: Same organism with matching susceptibility from catheter tip and peripheral blood within 48 hours of insertion
C: Any positive blood culture within 48 hours
D: Clinical sepsis after catheter insertion without cultures

Results

Question 9: Which group had the longest catheter survival time?

A: Group A: side-hole catheters (200mm)
B: Group B: step-tip catheters (200mm)
C: Group C: step-tip catheters (250 mm)
D: All groups were equal

Question 10: In a CRRT study comparing filter lifespan among three groups (A, B, and C), the average lifespan of all filters in Group C was ______ hours.

- **A:** 28.0
- **B:** 36.5
- **C:** 25.8
- **D:** 32.5

Question 11: Which adverse event was significantly more common in group A compared to groups B and C?

- **A:** Intradialytic hypotension (IDH)
- **B:** Catheter-related bloodstream infection (CRBSI)
- **C:** Catheter-related thrombosis (CRT)
- **D:** None of the above

Discussion

Question 12: What factor was identified as an independent risk for catheter dysfunction during CRRT?

- **A:** Catheter diameter > 14Fr
- **B:** BMI
- **C:** Use of step-tip catheters
- **D:** Catheter venous end length

Question 13: Which approach was used exclusively in this trial for CRRT catheter placement?

- **A:** Right internal jugular vein
- **B:** Left internal jugular vein
- **C:** Femoral vein
- **D:** Subclavian vein

Question 14: Which limitation most accurately applies to this trial?

- **A:** Blinding of participants and treating clinicians was not feasible due to the nature of the intervention
- **B:** The trial lacked randomisation and allocation concealment
- **C:** Outcome assessment and data collection were not systematically performed
- **D:** No efforts were made to reduce bias in the study design

Conclusion

Question 15: Which option best describes the role of femoral vein catheterization in CRRT?

- **A:** Deeper femoral vein catheterization provides no benefit regardless of patient body habitus.
- **B:** Deeper femoral vein catheterization may enhance CRRT outcomes, particularly in obese patients.
- **C:** Femoral vein depth is only relevant in patients with low BMI.
- **D:** Catheter depth increases the risk of adverse events in all CRRT patients.

THE END

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ANSWER SHEET

R7(26)

A randomized controlled trial of catheters with different tips and lengths for patients requiring continuous renal replacement therapy in intensive care unit

A

*Time spent on activity		hour				min					
	A	B	C	D	E		A	B	C	D	E
1						9					
2						10					
3						11					
4						12					
5						13					
6						14					
7						15					
8											

How relevant was the content of this activity to your scope of practice?			
Not at all	Somewhat	Mostly	Extremely

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