Femoral Access and Delivery of Continuous Renal Replacement Therapy Dose

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Key Words

Dialysis · Continuous renal replacement therapy · Catheters · Femoral vein · Intensive care

Abstract

Aims: The study aims to describe the use of dialysis catheters in critically ill patients treated with continuous renal replacement therapy (CRRT) and to study the impact of femoral versus non-femoral access on CRRT dose. **Methods:** Statistical analysis and predictive modelling of data from the Randomized Evaluation of Normal vs. Augmented Level renal replacement therapy trial. **Results:** The femoral vein was the first access site in 937 (67%) of 1,399 patients. These patients had higher Acute Physiology and Chronic Health Evaluation and Sequential Organ Failure Assessment scores ($p = 0.009$) and lower pH ($p < 0.001$) but similar mortality to patients with non-femoral access (44 vs. 45%; $p = 0.63$). Lower body weight was independently associated with femoral access placement (OR 0.97, 95% CI 0.96–0.98). Femoral access was associated with a 1.03% lower CRRT dose ($p = 0.05$), but a 4.20% higher dose was achieved with 13.5 Fr catheters ($p =$

0.03). **Conclusions:** Femoral access was preferred in lighter and sicker patients. Catheter gauge had greater impact than catheter site in CRRT dose delivery.

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Introduction

The ability to maintain patient homeostasis of water, waste products, electrolytes and acid-base during continuous renal replacement therapy (CRRT) is dependent on CRRT circuit patency over time [1]. The quality of vascular access influences the ability to achieve adequate and reliable blood flow through the circuit, a major determinant of circuit life span. Catheter dysfunction requiring

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catheter replacement and/or causing circuit failure occurs in approximately 10% of patients treated with CRRT [2, 3]. Such circuit failures induce interruptions in treatment, which decrease the delivered CRRT dose and uremic control [4]. Moreover, they significantly increase nursing workload and treatment costs [5]. Thus, both choice of optimal insertion site and catheter characteristics are important to delivering optimal therapy.

There is uncertainty regarding the optimal site of catheter insertion for CRRT in critically ill patients. Femoral vein catheterization may be faster and easier than jugular vein catheterization [6] but may impede mobilization [7]. Thus, recent guidelines favor the right jugular vein in preference to femoral veins [8]. These recommendations are, however, not supported by robust evidence. Furthermore, the impact of catheter brand, gauge and length on the delivery of CRRT has only been investigated in small studies and no robust evidence exists to guide choice of catheter.

The Randomized Evaluation of Normal vs. Augmented Level of Replacement Therapy (RENAL) study collected detailed information on dialysis catheter characteristics, site of catheter insertion and circuit anticoagulation during CRRT and therefore offers a unique opportunity to explore the relationship between these factors and delivered CRRT dose [9–11]. Accordingly, we aimed to describe the use of temporary dialysis catheters in intensive care unit (ICU) patients treated with CRRT. In particular, we sought to identify factors associated with choosing the femoral vein as first site of catheter insertion and to explore the association of first insertion site (femoral vs. non-femoral) and different catheter characteristics with delivered CRRT dose during the first full day of treatment.

Materials and Methods

Study Protocol

The RENAL study was a prospective, multicenter, randomized, controlled trial comparing a higher (40 ml/kg/h) versus a lower (25 ml/kg/h) CRRT dose in 1,508 critically ill patients. The Human Research Ethics Committees of the University of Sydney and of all participating institutions approved the study. Written informed consent was obtained from patients or next of kin. Adult patients (≥ 18 years) with severe AKI requiring acute RRT were included if they met at least one of the following criteria: oliguria (urine output < 100 ml during ≥ 6 h not responding to fluid resuscitation), hyperkalemia (serum potassium > 6.5 mmol/l), severe acidosis (pH < 7.2), a serum urea level > 25 mmol/l, a serum creatinine level > 300 μ mol/l or the presence of clinically significant organ edema. Patients with previous RRT during the same hospitalization or those with end-stage renal failure requiring chronic dialysis were excluded. A detailed study protocol is found in the appendix of the orig-

inal study [11]. The primary end point was 90-day mortality. Secondary end points included RRT-free days, mechanical ventilation-free days, ICU-free days and hospital-free days at 90-day follow-up.

The site of dialysis catheter insertion, catheter choice and mode of circuit anticoagulation were determined by the treating physician. For the purpose of the present study, the delivered CRRT dose (as a percentage of prescribed dose) during the first complete 24-hour day was recorded.

Statistical Analysis

Data was analyzed by using SAS software version 9.1. Continuous variables were expressed as mean (SD) and categorical variables as numbers (%). The Student *t* test or the Mann–Whitney test was used to compare continuous variables. The χ^2 test or the Fisher's exact test was used to compare categorical variables. Multivariate logistic regression analysis was used to study the association of having the femoral vein as first site of catheter insertion. Baseline variables were considered and were included in the multivariate model if they were statistically significant at *p* value < 0.20 in the univariate analysis. The association between using a femoral catheter (vs. a non-femoral catheter) and CRRT dose during the first complete 24 h was assessed by multivariate linear regression analysis. The following potential confounders were considered: treatment group, baseline characteristics, illness severity, catheter gauge, catheter length, catheter brand, CRRT machine and anticoagulation mode. Covariates were included in the multivariate model if they were statistically significant at *p* value < 0.20 in the univariate analysis. In the final analyses, a 2-sided *p* value < 0.05 was considered statistically significant.

Results

First Site of Catheter Insertion

Of the 1,508 randomized patients in the RENAL trial, data on first dialysis catheter insertion site was available for 1,399 (93%) patients. In 937 (67%) of these 1,399 patients the femoral vein was chosen as the first site of dialysis catheter insertion (fig. 1). The right femoral vein was preferred over the left. Jugular access was used in 351 (25%) patients and subclavian access was chosen in 111 (8%) patients.

Factors Associated with Femoral Vein Catheterization

Demographics, admission diagnosis, time from ICU admission to randomization, treatment group, baseline biochemistry and outcomes for patients with femoral and non-femoral vein as first site of dialysis catheter insertion are detailed in table 1. Patients receiving femoral access weighed on an average 3.8 kg less than patients receiving a non-femoral access ($p < 0.001$; table 1) and had higher Acute Physiology and Chronic Health Evaluation (APACHE) III scores, cardiovascular Sequential Organ Failure Assessment scores, hemoglobin levels and chlo-

Table 1. Characteristics of patients according to first site of catheter insertion

Characteristic	Femoral (n = 937)	Non-femoral (n = 462)	p values
Age, years	64.3±15.2	65.0±14.2	0.5
Male sex	593 (63.3)	307 (66.5)	0.3
APACHE III score	103.5 (25.7)	100.1 (25.4)	0.02
Time from ICU admission to randomization, h	46.1±105	62.5±145	0.02
Randomized to high CRRT intensity	456 (48.7)	236 (51.1)	0.40
Estimated glomerular filtration rate, ml/min	57.5±31.1	54.7±30.6	0.2
Body weight, kg	79.5±12.5	83.3±13.4	<0.001
Mechanical ventilation	681 (72.7)	356 (77.1)	0.08
Severe sepsis at baseline	473 (50.5)	213 (46.1)	0.1
Non-operative admission diagnosis	695 (74.2)	303 (65.6)	0.6
Operative admission diagnosis	242 (25.8)	159 (34.4)	0.6
Severe acidemia (pH <7.2)	361 (38.5)	132 (28.6)	<0.001
Severe organ edema	421 (44.9)	200 (43.3)	0.6
Cardiovascular SOFA score	2.9 (1.5)	2.7 (1.6)	0.009
INR, %	1.8±1.0	1.7±1.0	0.06
APTT, s	45.8±23.9	46.3±25.3	0.7
Hemoglobin, g/l	100.7±20.1	97.8±18.8	0.008
Platelet count, ×10 ⁹ /l	183.6±131	184.3±133	0.9
Sodium, mmol/l	137.3±6.5	138.3±6.7	0.01
Chloride, mmol/l	105.0±7.4	104.1±8.0	0.05
CRRT dose during the first complete 24 h, ml/kg/h	27.5±8.2	26.2±8.3	0.01
Delivered/prescribed CRRT dose during the first complete 24 h, %	85.4±17.4	81.9±19.8	0.002
Duration first catheter/total CRRT time, %	96.6±54.9	94.5±84.2	0.58
Death in ICU	328 (35.0)	151 (32.7)	0.4
Death at day 90	410 (43.8)	208 (45.1)	0.6

Variables are given as mean ± SD or as numbers (percentage). APTT = Activated partial thromboplastin time; INR = international normalized ratio.

ride levels. CRRT was initiated 46.5 h after ICU admission in patients with femoral access and after 62.5 h in patients with non-femoral access ($p = 0.02$). The first femoral access was used during 96.6% of the total CRRT time and the first non-femoral access was used during 94.5% of the total CRRT time ($p = 0.58$; table 1). Overall, 410 (44%) patients with a femoral dialysis catheter as first access had died at 90 days after randomization compared with 208 (45%) non-femoral access patients (table 1).

Several factors were associated with a greater likelihood of the use of a femoral vein as the first site of catheter insertion on univariate logistic regression analysis. On multivariate logistic regression analysis, however, only body weight (OR 0.97 for each kg increase, 95% CI 0.96–0.98), sodium levels (OR 0.93 for each mmol increase, 95% CI 0.90–0.96) and chloride levels (OR 1.08 for each mmol increase, 95% CI 1.05–1.11) were independently associated with choosing the femoral vein as the first site of access (table 2).

Fig. 1. Site of first temporary dialysis catheter insertion in the RENAL trial (n = 1,399).

Table 2. Univariate and multivariate logistic regression analysis of femoral vein as first site of catheter insertion

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p values	OR (95% CI)	p values ^a
Body weight, kg	0.977 (0.97–0.99)	<0.001	0.972 (0.96–0.98)	<0.001
Sodium, mmol/l	0.979 (0.96–1.00)	0.01	0.928 (0.90–0.96)	<0.001
Chloride, mmol/l	1.015 (1.00–1.03)	0.05	1.078 (1.05–1.11)	<0.001

^a Adjusted for baseline characteristics with $p < 0.20$ in the univariate analyses. Only variables with $p < 0.05$ in the multivariate analysis are shown.

Fig. 2. Length (a), gauge (b) and brand (c) of dialysis catheter as well as circuit anticoagulation (d) during CRRT in the RENAL trial according to first site of catheter insertion.

Catheter Characteristics and Circuit Anticoagulation

Longer catheters were generally used for femoral access, whereas shorter catheters tended to be inserted in non-femoral sites (fig. 2a). A 13.5-Fr catheter was most commonly chosen for both femoral (68%) and non-femoral ac-

cess (59%; fig. 2b). Longer and greater gauge Niagara (Bard, Murray Hill, N.J., USA) catheters were mainly used in the femoral (62%) and non-femoral (53%) group (fig. 2c).

Information on circuit anticoagulation was available for 1,271 (91%) patients. Heparin was used in 487 (58%)

Table 3. Multivariate linear regression showing the association with delivered CRRT dose (as % of prescribed dose) during the first complete 24-hour period

Variable	Coefficient, $\pm$ SE	p values ^a
Femoral catheter (vs. non-femoral)	-1.03 ± 0.53	0.05
13.5 French catheter (vs. other gauges)	4.20 ± 1.90	0.03
20- or 24-cm catheter (vs. other lengths)	1.88 ± 1.68	0.3
Randomized to higher CRRT intensity	-26.32 ± 1.27	<0.001

^a Adjusted for age, sex, APACHE III score, body weight, oliguria, hyperkalemia, acidemia, oedema, urea, creatinine, catheter brand, CRRT machine use and mode of circuit anticoagulation.

of 846 of patients in the femoral group and 269 (63%) of 425 patients in the non-femoral group. CRRT was delivered without circuit anticoagulation in a high proportion of patients with femoral (41%) and non-femoral (36%) catheters ($p = 0.50$; fig. 2d).

Factors Associated with Delivered CRRT Dose during the First 24 h

A total of 456 (48.7%) patients with a femoral access were randomized to high intensity therapy (40 ml/kg/h) compared to 236 (51.1%) patients with a non-femoral catheter ($p = 0.40$). On an average, CRRT intensity during the first complete 24 h was 27.5 ml/kg/h in the femoral group and 26.2 ml/kg/h in the non-femoral group ($p = 0.01$). On an average, 85.4 and 81.9% of the prescribed dose ($p = 0.002$), respectively, was achieved during this period (table 1). On multivariate linear regression, adjusting for baseline characteristics, treatment group, catheter characteristics, CRRT machine and mode of circuit anticoagulation, the use of a femoral catheter was associated with a 1.03% lower CRRT dose ($p = 0.05$) during the first 24 h than when a non-femoral catheter was used (table 3). In contrast, a 4.20% higher CRRT dose was achieved with 13.5 Fr gauge catheters than with other catheter gauges ($p = 0.03$). Finally, being randomized to higher intensity CRRT was independently associated with a 26.32% lower CRRT dose than being allocated to lower intensity CRRT.

Discussion

Key Findings

We analyzed the use of temporary dialysis catheters, the choice of insertion site, the catheter gauge and their impact on CRRT dose in critically ill patients enrolled in the RENAL trial. We found that the femoral vein was used as the first site of dialysis catheter insertion in two thirds

of patients and was preferentially chosen in patients with lower body weight and in sicker patients. Using a femoral vein for vascular access had limited impact on the delivered early CRRT dose during the first 24 h. In contrast, catheter gauge was a more important determinant of delivered CRRT dose during this time frame.

Relationship to Previous Studies

Previous studies investigating the impact of vascular access site on delivered RRT dose have reported inconsistent results. Hryszko et al. [12] found an independent 5-fold higher risk of catheter dysfunction, defined as inability to maintain blood flow of at least 150 ml/h, with femoral as compared to internal jugular catheters. In that study, however, 75% of patients were fully mobile, and treatment was with intermittent hemodialysis. Liangos et al. [13] explored dialysis performance during >400 intermittent hemodialysis sessions in 81 patients with acute renal failure. Use of a femoral access, as compared to a non-femoral access, was independently associated with lower urea reduction ratio with intermittent hemodialysis. Of note, however, the femoral catheters used in this study were short, measuring only 16.5 or 19.5 cm. To optimize blood flow and CRRT dose and to avoid recirculation, it is important that the catheter tip is placed in a large vein (external iliac and close of inferior vena cava) or in the right atrium [5, 14, 15]. Therefore, it is recommended that 24-cm catheters be used in the femoral position, and that 15–20 cm catheters be used for right jugular cannulations [16]. In 11 of the 12 centers involved in the French Cathedia study, 16-cm catheters were used in the jugular and 25-cm catheters in the femoral position [17]. Similarly, 24-cm catheters were frequently used for femoral (48%) and 15- to 16-cm catheters were frequently used for jugular or subclavian access (50%) in the RENAL study patients.

The Cathedia study showed a higher rate of catheter-related infections with a femoral access in patients with

body mass index $>28.4 \text{ kg/m}^2$ [17]. Furthermore, the increased catheter-related infections risk in heavier patients ($>90 \text{ kg}$) with femoral dialysis catheters was recently confirmed in an observational study involving 458 patients [18]. It is therefore not surprising that RENAL study patients receiving right or left femoral catheterization [19] had a lower body weight than patients receiving non-femoral catheterization.

Implications of Study Findings

Our study suggests that clinicians perceive the femoral vein to be a useful potential first choice when rapid and safe access is needed and in patients with a multilumen central venous catheter in the right jugular vein [6]. Our results reflect this preference with sicker patients (more severe acidemia, higher APACHE III and cardiovascular Sequential Organ Failure Assessment score and faster initiation of CRRT after ICU admission) being more likely to have their first CRRT catheter inserted in the femoral vein. This, in turn, may reflect the fact that a central venous catheter is often inserted before a temporary dialysis catheter in hemodynamically unstable patients. Under such circumstances, the femoral route may be the only available option. Finally, we found that a femoral vein is preferred in patients with lower body weight. Although we did not assess body habitus, this finding may reflect the fact that femoral vein cannulation may be technically difficult and is therefore avoided in obese patients. In the univariate comparison, the delivered CRRT dose (as a percentage of the prescribed dose) was 3.5% higher through a femoral access than through a non-femoral access (table 1). A femoral access was, however, associated with 1.03% lower CRRT delivery in the multivariate linear regression analysis. The fact that a higher proportion of patients with femoral access were cannulated with large-gauge 13.5 Fr catheters as compared to patients with non-femoral access (67.5 vs. 59.2%, $p = 0.009$) likely explains the reversed result in the multivariate adjusted analysis. In fact, after adjusting for several potentially important confounders of the relationship between access site and dose, larger catheter gauge (13.5 Fr) was independently associated with delivery of a higher (4.2%) CRRT dose whereas the ability to achieve the prescribed dose was, as could be expected, impaired in patients allocated to higher intensity CRRT. These findings need to be interpreted in the light of the original RENAL trial results. In the RENAL trial, the high-intensity group received a 50% higher CRRT dose than the low-intensity group. Despite this difference in dose, 90-day mortality was similar in both

the groups. Our results therefore suggest that insertion of 13.5 Fr gauge CRRT catheters in the femoral vein of very sick critically ill patients have no clinically important negative impact on early CRRT delivery. This is an important finding since femoral catheter insertion is a safer and easier approach for less experienced, junior doctors than cannulation of internal jugular or subclavian veins.

Strengths and Limitations

This study has important strengths. All study data, including highly detailed information on catheter characteristics, insertion site and CRRT dose were prospectively collected. In addition, the large study size enabled adjustment for numerous factors such as patient characteristics, catheter features and mode of anticoagulation, which may potentially affect CRRT delivery. With such adjustments, important practical observations emerged, which can be used to inform clinical practice.

This study has limitations. Choice of catheter insertion site and gauge were not randomized. However, our study provides the largest description of CRRT catheter characteristics, gauge and site of insertion to date and detailed information to adjust for many key early confounders. No information on catheter tip placement was available. However, since longer catheters were used in the femoral position and since non-femoral catheters were mainly inserted in the right jugular vein, it is likely that most of the catheters were positioned correctly. Our study does not provide information on the impact of insertion site or gauge on CRRT delivery beyond the first complete 24 h. This was, however, our intention since determinants of CRRT dose unrelated to access, such as interruptions for investigations, operations and mortality would create a strong competing risk-related confounding effect, given that femoral catheters were inserted in sicker patients. By restricting the analysis to the first complete 24 h of CRRT, we aimed to diminish the impact of such confounders.

Conclusions

The femoral vein was used as the first site of dialysis catheter insertion in most patients within the RENAL trial, especially in lighter and sicker patients. Although such use of a femoral access was significantly associated with lower CRRT dose, the impact on dose was limited. However, using a larger gauge catheter was independently as-

sociated with the ability to deliver a higher CRRT dose during the first 24 h. This information provides clinically relevant information to assist clinicians in their choice of preferred access site and catheter gauge for the delivery of CRRT in critically ill patients.

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Contributions

Research idea and study design: R.B., A.C., M.G.; data analysis/interpretation: J.M., R.B., S.L.; statistical analysis: S.L.; supervision and mentorship: R.B.; drafting of manuscript: J.M., K.M.K., R.B. Each author contributed important intellectual content during manuscript revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. R.B. and M.G. take responsibility that this study has been reported honestly, accurately and transparently; that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

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