Criteria for Continuous Kidney Replacement Therapy Cessation in ICU Patients

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Keywords
Acute kidney injury · Continuous kidney replacement therapy · Continuous renal replacement therapy · Intensive care · Survey

Abstract
Introduction: In intensive care unit (ICU) patients with acute kidney injury, specific recommendations to guide the decision to cease continuous kidney replacement therapy (CKRT) are lacking. \textbf{Methods:} We performed a survey to identify criteria currently used to cease CKRT in real-life clinical practice in the Netherlands. We used an online questionnaire with multiple choice questions designed with web-based software from SurveyMonkey. \textbf{Results:} We received 169 completed questionnaires from intensivists (\(n = 126\)) and nephrologists (\(n = 43\)). Essential determinants for the cessation of CKRT were a spontaneously increasing diuresis (indicated by 92\% of the respondents), absence of fluid overload (indicated by 88\% of the respondents), and improvement in creatinine clearance (indicated by 61\% of the respondents; intensivists 56\%; nephrologists 77\%, \(p = 0.03\)). Most often mentioned cut-off values used for increase in diuresis were 0.25 and 0.5 mL/kg/h (35\% and 33\%, respectively). Actual CKRT cessation was often postponed until the filter clots or until circuit disconnection is needed because of patient transport for diagnostic or intervention procedures (indicated by 58\% of the respondents). Expected discharge from the ICU was the most frequently reported determinant to switch from CKRT to hemodialysis (indicated by 67\% of the respondents). \textbf{Conclusions:} CKRT cessation in clinical practice is mostly based on spontaneously increasing diuresis, absence of fluid overload, and improvement in creatinine clearance and is often delayed until filter clotting or disconnection of the circuit because of logistic reasons.

Introduction

Many patients admitted to the intensive care unit (ICU) develop acute kidney injury, and approximately 24\% of these patients require kidney replacement therapy (KRT) \[1\]. Continuous KRT (CKRT) is the most frequently used modality of KRT in the ICU and is preferred over intermittent hemodialysis (HD) because it is associated with fewer shifts of volumes and solutes and a favorable hemodynamic profile \[2\]. Most patients requiring
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KRT during their ICU stay have sufficient recovery of kidney function to discontinue KRT before hospital discharge [3]. The Kidney Disease Improving Global Outcomes (KDIGO) provides no specific recommendations to guide the decision to cease KRT [4]. Unnecessary prolonged KRT may expose patients to additional risks, such as catheter-related infections, thrombosis, vascular injury, bleeding, and hemodynamic instability [5]. In addition, unnecessary prolonged KRT may lead to a shortage of equipment and personnel capacity and higher costs.

A recent systematic review and meta-analysis showed that urine output was the most frequently used variable for the decision to cease KRT, although the minimum daily urine volume needed for KRT cessation is still unclear [6]. Two clinical trials, designed for other purposes than the evaluation of KRT cessation strategies, used urine output as a criterion for KRT cessation; thresholds were 1,000 mL/24 h and 2,100 mL/24 h, respectively [7, 8]. Three observational studies suggested that a rise in endogenous creatinine clearance was associated with successful KRT cessation [9–11]. However, only one study took endogenous creatinine clearance, based on urinary creatinine excretion, before KRT cessation into account [9]. In two clinical trials, again not designed for the evaluation of KRT cessation, endogenous creatinine clearance >20 mL/min was used as a ceasing criterion [8, 12]. Explicit criteria for KRT cessation are needed to avoid unnecessary prolongation of KRT.

Material and Methods

This study’s objective was to identify criteria currently used to stop CKRT in critical care daily clinical practice.

Study Design

The study was a survey based on a questionnaire designed with Web-based software from SurveyMonkey (nl.surveymonkey.com). The questionnaire had an adaptive design, meaning that specific additional questions were only asked once a specific answer was given. The questionnaire consisted of a maximum of 23 questions. The questionnaire aimed to unravel all factors that are taken into account when deciding whether or not to cease CKRT or to switch from CKRT to intermittent KRT. Additionally, the incidence of reinitiation of KRT and the actual timing of CKRT cessation were addressed. A translated version of the Dutch questionnaire is available as online supplementary Data (for all online suppl. material, see www.karger.com/doi/10.1159/000524180).

The questionnaire was pretested by eight intensivists and eight nephrologists at our hospital. In response to their feedback, specific questions were rephrased and clarified and additional answer possibilities were added.

Apart from intensivists, nephrologists are also frequently involved in decisions involving CKRT treatment in ICU patients.

Therefore, we intended to invite both intensivists and nephrologists to participate in this study. The Dutch Federation of Nephrology (Nederlandse Federatie voor Nefrologie [NfN]) and the Dutch Society of Intensive Care (Nederlandse Vereniging voor Intensieve Zorg [NVIC]) consented to the final questionnaire and sent their members an email invitation with a link to the online questionnaire on October 10, 2019, and November 11, 2019, respectively.

Participation was voluntary and anonymous, and response was possible from October 10, 2019, to January 9, 2020. After filling out the questionnaire, respondents were able to review their answers by going back and forth on the pages before final submission. Submission was only possible after answering all the necessary questions. Responses were excluded if respondents were employed in hospitals where acute KRT for ICU patients was unavailable or when they were not involved in decisions of KRT cessation.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 26.0 (Armonk, NY, USA). An overall analysis of the questionnaires was conducted as well as a comparison between intensivists and nephrologists. Respondents’ characteristics for both groups are presented as numbers (with percentages). A χ² test was performed to evaluate the differences between groups. p values <0.05 were considered statistically significant. The methodology and results are reported using the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) statement [13].

Results

Completed questionnaires were received from 221 respondents, of which 193 confirmed to be involved in the decision to cease (C)KRT in the ICU (Fig. 1). Within the prespecified respondent groups, we received 126 completed questionnaires from intensivists (18% of the total number of approximately 700 intensivists in the Netherlands) and 43 completed questionnaires from nephrologists (12% of the total number of 371 nephrologists in the Netherlands). In addition to intensivists and nephrologists, we also received completed questionnaires from renal nurse practitioners (n = 14), intensivists in training (n = 5), a nephrologist in training (n = 1), and a pediatric nephrologist (n = 1). These questionnaires were excluded from this analysis.

Respondents’ Characteristics

As shown in Table 1, 51 (30%) respondents (intensivists n = 29 [24%]; nephrologists n = 22 [51%], p = 0.003) worked (predominantly) in university medical centers. A total of 141 (85%) respondents (intensivists n = 104 [85%]; nephrologists n = 37 [86%], p = 0.47) worked in hospitals with at least 12 intensive care beds.

Available possible treatments for KRT differed between intensivists and nephrologists: 95 (75%) intensiv-
ists and 38 (88%) nephrologists reported to have access to both HD and continuous venovenous hemo(dia)filtration ($p = 0.001$). Two intensivists reported acute peritoneal dialysis as an available dialysis method in patients with acute kidney injury.

137 (81%) respondents (intensivists $n = 104$ (84%); nephrologists 33 (77%), $p = 0.40$) reported that kidney function is assessed by the course of serum creatinine (Table 2) in their hospital. Eighty-two (49%) respondents (intensivists $n = 55$ [44%]; nephrologists $n = 27$ [63%]) reported that kidney function is assessed by the course of serum creatinine (Table 2) in their hospital.

**Fig. 1.** Flow diagram of respondent selection. KRT, kidney replacement therapy; CKRT, continuous kidney replacement therapy.

**Table 1.** Respondent characteristics

| Overall ($n = 169$) | Intensivists ($n = 126$) | Nephrologists ($n = 43$) | $p$ value |
|---------------------|------------------------|-------------------------|-----------|
| University medical center, $n$ (%) | 51 (30) | 29 (24) | 22 (51) | 0.003 |
| <5 ICU beds,$^1$ | 1 (1) | 1 (1) | 0 (0) | |
| 6–8 | 15 (9) | 12 (10) | 3 (7) | |
| 9–11 | 8 (5) | 5 (4) | 3 (7) | 0.470 |
| 12–15 | 48 (29) | 38 (31) | 10 (23) | |
| 16–19 | 15 (9) | 13 (11) | 2 (5) | |
| >19 | 78 (47) | 53 (43) | 25 (58) | |
| The annual number of CKRT treatments in AKI patients,$^1$ | 10 (6) | 8 (7) | 2 (5) | |
| <10 | 34 (21) | 28 (23) | 6 (14) | 0.080 |
| 11–30 | 26 (16) | 23 (19) | 3 (7) | |
| 31–50 | 74 (45) | 51 (42) | 23 (54) | |
| >50 | 21 (13) | 12 (10) | 9 (21) | |
| Modality of renal replacement therapy, $n$ (%) | 31 (18) | 30 (24) | 1 (2) | 0.001 |
| CVVH(DF) | 1 (1) | 0 (0) | 1 (2) | |
| HD | 133 (81) | 95 (75) | 38 (88) | |
| Both HD and CVVH(DF) | 4 (2) | 1 (1) | 3 (7) | |
| Other | 1 | 1 | 1 | |

$^1$ ICU, intensive care unit; CKRT, continuous kidney replacement therapy; AKI, acute kidney injury; CVVH(DF), continuous venovenous hemo(dia)filtration, HD, hemodialysis. $^1$ Percentages are based on the respondents who specified their answers (4 intensivists did not specify the number of ICU beds and the annual number of CKRT treatments in AKI patients).
[63%], \( p = 0.03 \) reported that measured creatinine clearance is used to determine kidney function at their institution. Indicated frequencies for the use of estimated glomerular filtration rate formulas were 40% for the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (intensivists \( n = 40 \) [32%]; nephrologists \( n = 27 \) [63%]; \( p < 0.001 \)) and 34% for the Modification of Diet in Renal Disease (MDRD) equation (intensivists \( n = 54 \) [43%]; nephrologists \( n = 4 \) [9%]; \( p < 0.001 \)).

**CKRT Cessation**

A total of 156 respondents (92%; intensivists \( n = 114 \) [90%]; nephrologists \( n = 42 \) [98%], \( p \) value for difference between intensivists and nephrologists = 0.18) reported that a spontaneously increasing diuresis is considered a useful determinant for successful CKRT cessation (Table 3). Fifty-five (35%) respondents (intensivists \( n = 40 \) [35%]; nephrologists \( n = 13 \) [31%], \( p = 0.50 \)) reported to use a minimal spontaneous diuresis rate of 0.25 mL/kg/h in the decision to cease CKRT, and 52 (33%) respondents (intensivists \( n = 40 \) [35%]; intensivists \( n = 12 \) [29%], \( p = 0.44 \)) specified a minimal spontaneous diuresis rate of 0.5 mL/kg/h to decide to cease CKRT (Fig. 2). Thirty-four (22%) respondents (intensivists \( n = 18 \) [16%]; nephrologists \( n = 16 \) [38%], \( p < 0.001 \)) reported that the cut-off value depends on additional variables, such as fluid balance, creatinine clearance, and the amount of fluid withdrawn by CKRT per unit of time. Eighty-four (50%) respondents (intensivists \( n = 61 \) [48%]; nephrologists \( n = 23 \) [53%], \( p = 0.77 \)) indicated that an increase in diuresis after administration of diuretics is a useful determinant to cease CKRT; of these respondents, 35 (42%) specified a cut-off value of at least 1,000 mL/24 h after the administration of diuretics (Fig. 3).

The absence of fluid overload was reported as a determinant to cease CKRT by 148 (88%) respondents (intensivists \( n = 107 \) [85%]; \( p = 0.034 \)). The considered minimum creatinine clearance before CKRT cessation differed significantly between groups; 10 (14%) of the intensivists and 18 (55%) of the nephrologists considered a creatinine clearance of at least 10 mL/min necessary before (C)KRT can

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**Table 2. Reported frequencies of used modalities for kidney function assessment**

| Modality                        | Overall \((n = 169)\) (%) | Intensivists \((n = 126)\) (%) | Nephrologists \((n = 43)\) (%) | \( p \) value |
|---------------------------------|---------------------------|-------------------------------|-------------------------------|--------------|
| Serum creatinine, \( n \) (%)   | 137 (81)                  | 104 (83)                      | 33 (77)                       | 0.402        |
| Measured creatinine clearance, \( n \) (%) | 82 (49)                  | 55 (44)                       | 27 (63)                       | 0.030        |
| MDRD equation, \( n \) (%)      | 58 (34)                   | 54 (43)                       | 4 (9)                         | <0.001       |
| CKD-EPI equation, \( n \) (%)   | 67 (40)                   | 40 (32)                       | 27 (63)                       | <0.001       |

MDRD, modification of diet in renal disease; CKD-EPI, chronic kidney disease epidemiology collaboration.

**Table 3. Reported determinants for CKRT cessation**

| Diuresis                        | Overall \((n = 169)\) (%) | Intensivists \((n = 126)\) (%) | Nephrologists \((n = 43)\) (%) | \( p \) value |
|---------------------------------|---------------------------|-------------------------------|-------------------------------|--------------|
| Spontaneous diuresis            | 156 (92)                  | 114 (90)                      | 42 (98)                       | 0.177        |
| Diuretic induced diuresis       | 84 (50)                   | 61 (48)                       | 23 (53)                       | 0.770        |
| Absence of fluid overload, \( n \) (%) | 148 (88)               | 107 (85)                      | 41 (95)                       | 0.115        |
| Improvement in creatinine clearance, \( n \) (%) | 103 (61)          | 70 (56)                       | 33 (77)                       | 0.034        |
| NGAL, \( n \) (%)               | 3 (2)                     | 3 (2)                         | 0                             | 0.299        |
| Serum cystatin C, \( n \) (%)   | 2 (1)                     | 1 (1)                         | 1 (2)                         | 0.438        |

CKRT, continuous kidney replacement therapy, NGAL, neutrophil gelatinase-associated lipocalin.
be ceased safely \((p = 0.001)\) (Fig. 4). The biomarker neutrophil gelatinase-associated lipocalin (NGAL) was suggested as a determinant by 3 (2%) respondents (intensivists \(n = 3\)). The biomarker cystatin C was suggested as determinant by 2 respondents (1%; intensivist \(n = 1\) [1%]; nephrologists \(n = 1\) [2%], \(p = 0.44\)). We did not ask respondents if biomarkers were available for routine clinical practice in their hospitals.

Once the decision is made that CKRT treatment is no longer indicated, 91 (54%) respondents (intensivists \(n = 72\) [57%]; nephrologists \(n = 19\) [44%], \(p = 0.14\)) indicated that CKRT cessation is most often postponed until the filter clots or until circuit disconnection is needed because of patient transport for diagnostic or intervention procedures. Thirty-six (21%) respondents (intensivists \(n = 22\) [17%]; nephrologists \(n = 14\) [33%], \(p = 0.037\)) report that they immediately cease CKRT after concluding that CKRT treatment is no longer indicated. Fifty-eight (34%) respondents (intensivists \(n = 41\) [33%]; nephrologists \(n = 17\) [40%], \(p = 0.40\)) estimated that the need for reinitiation of KRT therapy within 72 h after CKRT ceasing ranges between 1 and 10% of patients (Fig. 5).

**CKRT Conversion to HD**

Table 4 shows the reasons reported by the respondents for the decision to convert CKRT to intermittent KRT. The foreseen transfer from the ICU to the ward was the most frequently reported reason (reported by 114
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In this survey among Dutch intensivists and nephrologists, an increase of spontaneous diuresis, the absence of fluid overload, and an increase in creatinine clearance were the most frequently reported determinants to cease CKRT. There was variance with regard to the urine output threshold and the minimum required creatinine clearance to cease CKRT. Compared to intensivists, nephrologists more often reported an increase in creatinine clearance as a determinant for CKRT cessation. Remarkably, most respondents indicated that CKRT was not immediately discontinued once the need for CKRT had disappeared but was continued until filter clotting or until disconnection of the circuit because of logistic reasons. The most frequently reported reason for converting CKRT to HD was an expected discharge from the ICU.

Fig. 5. Estimated need for continuous kidney replacement therapy (CKRT) re-initiation within 72 hours after cessation of CKRT. Shown values are percentages of the total number of intensivists (126) and nephrologists (43). Data on the estimated reinitiation rate was not reported by 5 intensivists.

Table 4. Reported determinants for conversion CKRT to intermittent HD

| Determinant                                      | Overall (n = 169) (%) | Intensivists (n = 126) (%) | Nephrologists (n = 43) (%) | p value |
|-------------------------------------------------|-----------------------|----------------------------|---------------------------|---------|
| (Expected) discharge of the ICU, n (%)           | 114 (67)              | 85 (68)                    | 29 (67)                   | 0.998   |
| No or little vasopressors needed, n (%)         | 98 (58)               | 73 (58)                    | 25 (58)                   | 0.981   |
| Expanding mobilization, n (%)                   | 84 (50)               | 56 (44)                    | 28 (65)                   | 0.019   |
| No recovery of diuresis, n (%)                  | 67 (40)               | 55 (44)                    | 12 (28)                   | 0.068   |
| Absence of fluid overload, n (%)                | 25 (15)               | 17 (14)                    | 8 (19)                    | 0.415   |
| Lack of CKRT machines in the ICU, n (%)         | 21 (12)               | 13 (10)                    | 8 (19)                    | 0.155   |
| A trial with regular dialysis is performed, n (%)| 19 (11)               | 13 (10)                    | 6 (14)                    | 0.515   |
| Cannot say, n (%)                               | 4 (2.4)               | 1 (0.8)                    | 3 (7.0)                   | 0.021   |

ICU, intensive care unit; CKRT, continuous kidney replacement therapy; HD, hemodialysis.

Discussion

In this survey among Dutch intensivists and nephrologists, an increase of spontaneous diuresis, the absence of fluid overload, and an increase in creatinine clearance were the most frequently reported determinants to cease CKRT. There was variance with regard to the urine output threshold and the minimum required creatinine clearance to cease CKRT. Compared to intensivists, nephrologists more often reported an increase in creatinine clearance as a determinant for CKRT cessation. Remarkably, most respondents indicated that CKRT was not immediately discontinued once the need for CKRT had disappeared but was continued until filter clotting or until disconnection of the circuit because of logistic reasons. The most frequently reported reason for converting CKRT to HD was an expected discharge from the ICU.

Our finding that urine output was considered as a useful predictor for successful CKRT cessation by many intensivists and nephrologists corresponds well with a recent systematic review which showed that urine output was the most frequently used variable for the decision to cease KRT [6]. However, this review did not identify an exact minimum-value for urine output before KRT can be ceased.

Approximately, half (49%) of the respondents indicated that they ceased CKRT when urine output increases after administration of diuretics with a most frequently applied cut-off value for diuresis of more than 1,000 mL/24 h. Notably, controversy exists whether the response to diuretics can be helpful in the KRT cessation decision. Studies investigating whether a diuretic-induced increase in urine output was associated with a lower incidence of restarting CKRT after cessation of this treatment yielded conflicting results, with 3 studies hav-
ing a positive effect [14–16], whereas in another study, there was no effect [17]. Other studies investigated the effect of diuretics to aid with the decision to cease CKRT before cessation of this treatment also yielded different conclusions; a higher diuretic response index (24 h urine output divided by furosemide dose) was associated with successful CKRT cessation in one study [10], whereas including the response to diuretics resulted in a lower predictive value of urine output in another study [18].

There is only one observational study supporting an increase in creatinine clearance as a determinant for successful CKRT cessation. In this study, a 2 h creatinine clearance of 23 mL/min before CKRT cessation had a positive predictive value of 89% (sensitivity 76%, specificity 84%) [9]. Despite the scarcity of evidence, over 61% of the respondents considered improvement of creatinine clearance a useful determinant. Still, only 49% of the respondents use measured creatinine clearance for renal function assessment.

Most respondents considered kidney injury biomarkers like cystatin C and NGAL not useful in determining the optimal moment to cease CKRT. Although a small prospective study showed that a serum cystatin C level of less than 1.85 mg/L before discontinuation was associated with successful discontinuation of CKRT (sensitivity 76% and specificity 63%) [19], the exact role of biomarkers such as NGAL and cystatin C are uncertain for the prediction of successful KRT cessation and timing of KRT cessation.

Even in the absence of a clear indication to continue CKRT, this therapy is often continued until filter clotting or until the circuit is disconnected because of patient transport for diagnostic or interventional procedures. This may expose the patient to unnecessary risks, such as catheter-related infections, thrombosis, vascular injury, bleeding, and hemodynamic instability [5]. In addition, prolonged CKRT may induce a shortage in CKRT equipment. In daily practice, physicians are reluctant to discard the hemofilter prematurely because of a presumed adverse effect on costs. This assumption is incorrect since the daily costs for CKRT replacement fluids by far exceed the costs of the hemofilter; in our hospital, for example, the daily costs for CKRT replacement fluids exceed the costs of the hemofilter by 257%.

The majority (60%) of the respondents (intensivists 60%; nephrologists 60%) estimated that the reinitiation of CKRT within 72 h occurs in less than 20% of patients. This percentage is considerably lower than estimates described in earlier studies [18, 20] and is possibly due to the longer timeframe (respectively 7 and 5 days) to define successful CKRT cessation in these studies. This difference is more likely explained by a new episode with incremental illness with a secondary deterioration of kidney function and the need for reinitiation of KRT. This could also explain the higher mortality rate reported in one study of patients needing KRT reinitiation compared to patients not needing KRT reinitiation (43% vs. 29%, respectively) [18]. There might also be a difference between the respondents’ estimation of the reinitiation rate and the actual reinitiation rate due to a recall bias.

The most often reported reasons for conversion of CKRT to intermittent KRT were (1) the foreseen transfer from the ICU to the ward (reported by 67% of the respondents), (2) (almost) absence of the need for vasopressors (reported by 58% of the respondents), and (3) expanding opportunities for mobilization (reported by 50% of the respondents). Regarding the optimal timing of CKRT initiation in the ICU, multiple randomized controlled trials have been performed [7, 8, 21, 22]. However, concerning the optimal timing of CKRT cessation, no single randomized controlled trial was performed, and only data of prospective observational and retrospective studies are available using different determinants with varying cut-off values and definitions of success [6]. Across these studies, the optimal urine production threshold to predict successful CKRT varies widely (range from 191 mL to 1,720 mL/24 h). Notably, all these studies [16, 18, 23, 24] investigated the predictive value of urine production rate before the cessation of CKRT for successful weaning. Two (other) studies investigated the urine production after the cessation of CKRT to evaluate whether the stop of CKRT was successful [10, 14]. Based on this survey’s responses, prospective studies should investigate whether a diuresis of 0.5 mL/kg/h without diuretics before CKRT cessation can predict successful CKRT weaning.

Since most respondents consider an improvement in measured creatinine clearance during CKRT treatment a useful determinant for CKRT cessation, future studies should explore the predictive value of the assessment of the endogenous creatinine clearance for successful CKRT cessation.

**Strengths and Limitations**

A strength of our study is that the majority of the respondents are health care professionals working in hospitals with large ICU’s where CKRT is performed frequently. A limitation of our study is that we reached a response rate of only 18% for intensivists and 12% for nephrologists. The lower response rate of nephrologists in this survey might in part be due to less involvement of this discipline in the ini-
tiation and cessation of CKRT. Due to the design of the study, there could also be a difference between responders’ answers and actual actions in clinical practice.

Conclusion

In clinical practice, the decision to cease CKRT is based on multiple arguments. The most reported determinants are increasing spontaneous diuresis, absence of fluid overload, and improvement of creatinine clearance. Actual cessation is often postponed until filter clotting or until disconnection of the circuit because of a transfer for diagnostic or intervention procedures outside the ICU.

Acknowledgments

We thank the NNfN and the NVIC for sending their members an email invitation with a link to the online questionnaire.

Statement of Ethics

The study was performed according to the Helsinki Declaration. Since the survey was addressed to physicians and did not involve patients, the study was exempt from approval by the Medical Ethical Committee.

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Conflict of Interest Statement

The authors declare that they have no conflict of interest.

Funding Sources

Not applicable.

Author Contributions

Meint Volbeda, Eric Keus, Jacqueline Koeze, Iwan C.C. van der Horst, and Casper F.M. Franssen contributed to the conception of the study. All the authors contributed to the design, interpretation of data, drafting, and revising of the article and provided intellectual content of critical importance. Meint Volbeda and Martha Orod performed data collection, organized the database, and performed the statistical analyses.

Data Availability Statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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Blood Purif 2023;52:32–40
DOI: 10.1159/000524180

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