Performance evaluation of different filtration fraction during daytime continuous renal replacement therapy

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Research Article

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Abstract

Objective

To investigate the effects of different filtration fractions (FFs) during daytime continuous venovenous hemodiafiltration (CVVHDF) post-dilution.

Methods

From April to December 2021, forty patients who received CVVHDF in the Second Affiliated Hospital of Nanchang University were randomly assigned to the low FF group (FF: 20–25%) or the high FF group (FF: 25–30%) and then compared with each other. The lifespan of the extracorporeal circuit and other performance metrics were compared between the two groups.

Results

During treatment, there was no statistically significant difference in arterial pressure between the two groups at 2 hours, 6 hours and the end of treatment compared with that at 1 hour of treatment ($P = 0.30, 0.27, 0.87$). There was no statistically significant difference between the venous pressure at 2 hours, 6 hours and the end of treatment compared with that at 1 hour of treatment ($P = 0.55, 0.53, 0.53$), and there was also no statistically significant difference in transmembrane pressure ($P = 0.55, 0.63, 0.53$). There was no statistically significant difference in the clotted filter or the extracorporeal circulation circuit at the end of CRRT between the two groups ($P = 0.95, 0.31$). There were statistically significant differences in the clearance efficiency of serum creatinine ($P = 0.04$).

Conclusion

For patients with daytime CRRT, CVVHDF treatment with FFs $< 25\%$ compared with FFs of $25–30\%$ has no statistically significant difference in the risk of coagulation during cardiopulmonary bypass, while the efficacy seems to be significantly different. This study aims to provide supportive data for the criteria for defining FF in clinical practice.

1. Introduction

Continuous renal replacement therapy (CRRT) or continuous blood purification (CBP) refers to blood purification treatment that can continuously and slowly remove water and solutes for 24 hours or nearly 24 hours a day. CRRT in the broadest sense is intended to last longer than 24 hours. However, daytime CRRT is also popular, and the treatment time is generally 10–14 h/day. At present, domestic and foreign experts believe that only the use of CRRT machines for more than 8 hours can be considered CRRT. During the course of treatment, the ideal time is not as long as possible; it needs to be determined
according to the "demand". The length of time needed for treatment time to meet treatment needs (volume balance and solute removal) and maximize safety is the best length of time. This is especially true for patients who require CRRT in nephrology, usually those with hemodynamic instability, volume overload, and difficult to correct cardiac insufficiency on conventional hemodialysis. These patients are often conscious and cannot tolerate treatment for 24 hours or more; therefore, daytime CRRT is relatively more suitable for them.

In the process of CRRT, maintaining the patency of the circuit (avoiding systemic coagulation) is a crucial part of achieving the desired treatment goals. Among them, the coagulation of the filter and the supporting extracorporeal circulation pipeline is the main reason for unplanned discharge, and its incidence rate is as high as 67.6–74.6% [1, 2]. High FF (> 25%) is often associated with poor filter performance and increased risk of coagulation due to hemoconcentration-related effects. To minimize the procoagulant effects of hemoconcentration, it is recommended to keep the FF as low as possible; a value below 25% is generally recommended in postdilution mode [3]. ADQI guidelines require that the filtration fraction be less than 25% during CRRT [4]. The application of the FF > 25% for risk stratification of hemofilter clotting and the assignment of a single cutoff point as the maximum allowable FF in all clinical scenarios has been endorsed by many authors without providing strong evidence apart from referring to prior publications, which themselves have not provided any compelling evidence [5, 6]. It appears that these anecdotes originate from some publications from the early 1980s, where their observed filtration fraction in continuous arteriovenous hemofiltration (CAVH) was mainly between 20% and 30% [7, 8]. However, those publications report experience with CAVH, and not CVVH, which is the modality that is currently used. For patients undergoing daytime CRRT, the treatment time is relatively short, and it is debatable whether an FF higher than 25% actually increases the risk of filter clotting during treatment. If a 25–30% FF does not increase the risk of filter coagulation during daytime CRRT, what is the increased risk of filter clotting when the FF is greater than that during daytime CRRT? Based on the appeal question, this study intends to compare the choice of two different FFs (20–25% vs. 25–30%), which are used in the daytime CRRT of CVVHDF commonly used in our center to explore the effect of different FFs on solute clearance and the in vitro influence of the service life of the circulating line filter. This study is expected to provide a reference for formulating more detailed and individualized FFs in clinical practice in the future.

2. Methods

2.1. Ethics committee statement

This study was approved by the Regional Ethics Committee of the Second Affiliated Hospital of Nanchang University, and the approval number was No. [2021] 045. All included patients or authorized family members signed an informed consent form. The design of the study fully took the safety and fairness principle into account. The research did not harm the subjects and protected their privacy rights. There were no conflicts of interest in this research.
2.2. Patients

Patients who underwent daytime CRRT in the Department of Nephrology in the Second Affiliated Hospital of Nanchang University, Jiangxi Province, China, from April to December 2021 were prospectively enrolled. The enrollment criteria were as follows: (1) patients treated with continuous venovenous hemodiafiltration (CVVHDF) post-dilution; (2) unfractionated heparin anticoagulation; and (3) signed informed consent. The exclusion criteria were as follows: (1) machine failure during treatment; (2) automatic discharge; and (3) those who reached the therapeutic effect and terminated the treatment early according to the doctor’s advice.

2.3. Treatment protocol

A head-to-head randomized controlled study was conducted. The adjustment of machine operation and machine monitoring indices during treatment was completed by blood purification specialist nurses. During treatment, patients were randomly assigned a filter score of 20–25% (low FF group) or 25–30% (high FF group). We designed one group (n = 20) to enroll those standard-compliant patients who received low FFs and the other group (n = 20) to enroll those standard-compliant patients who received high FFs. All patients were treated with the Aquarius CRRT machine and HF1200 (1.25 m² membrane area) and extracorporeal circulation line. Specific methods included: (1) For vascular access, an internal jugular vein or femoral vein indwelling double lumen catheter was used. (2) The preflushing method involved preflushing the extracorporeal circulation pipeline with 2000 ml of normal saline. (3) The Hemofiltration Replacement Fluid produced by Chengdu Qingshan LiKang Pharmaceutical Co. Ltd. was used (the replacement solution formula was Na⁺: 113 mmol/L, Cl⁻: 118 mmol/L, Ca²⁺: 1.60 mmol/L, Mg²⁺: 0.979 mmol/L, glucose: 10.6 mmol/L). At the same time, 10% potassium chloride injection and 5% sodium bicarbonate injection were pumped according to the arterial blood gas monitoring results of the patients as instructed. (4) The anticoagulant method involved heparin. Two liters of isotonic saline containing 10000 U/L heparin was prepared through the filter, and then heparin was given at a dose of 1 U/kg/h to 20 U/kg/h. Activated partial thromboplastin time (APTT) values of patients were monitored from 60 to 80 s. (5) As for treatment methods, CVVHDF was used for all patients, blood flow was 200 ml/min, replacement fluid was 1.2–1.5 L/h, and dialysate was 1.5 L/h.

2.4. Outcomes

We predefined potential baseline indices, including sex, age, serum creatinine, urea, blood potassium and blood gas levels, which were measured before and after treatment at both low and high filtration levels.

Nursing observation indicators included arterial pressure, venous pressure and transmembrane pressure, which were recorded during loading, hourly and before unloading. Regarding the use time of the supporting extracorporeal circulation pipeline, the filter in the Aquarius machine had to be replaced when the cross-membrane pressure of CRRT reached 300 mmHg or the filter pressure value reached 200 mmHg. The extracorporeal circulation line and filter were replaced strictly as needed, and the service time
of the supporting extracorporeal circulation line was recorded. Coagulation levels in filter and extracorporeal circulation lines were assessed and recorded at the end of treatment.

The primary outcomes were as follows: (1) the difference in arterial pressure between the two groups at a treatment time of 2 hours, 6 hours and at the end of treatment compared with 1 hour of treatment; (2) the difference between the venous pressure at 2 hours, 6 hours and the end of treatment compared with 1 hour of treatment; and (3) the difference between the transmembrane pressure at 2 hours, 6 hours and the end of treatment compared with 1 hour of treatment.

The secondary outcomes were as follows: (1) the coagulation grading of the filter and the extracorporeal circulation line at the end of the treatment; and (2) the change in serum creatinine, urea, potassium concentration and pH values before and after the treatment.

### 2.5. Statistical analysis

Normally distributed variables are presented as the mean ± standard deviation (SD) and were compared using an independent or paired *t* test as appropriate. Nonparametric continuous variables are presented as medians with interquartile ranges (IQRs, 25th and 75th percentiles) and were compared using nonparametric tests as appropriate. Categorical variables were summarized using proportions and compared using the Pearson chi-square test. Repeated measures data were analyzed by the longitudinal data analysis method. Statistical analysis was performed with SPSS (version 23.0). Differences were considered statistically significant for a 2-sided *P* < 0.05.

### 3. Results

#### 3.1. Study Participants

A flow chart of the patient selection process is shown in Fig. 1. Forty-four patients who met the inclusion criteria were randomized to the high FF group or the low FF group during CRRT. Of these, 40 patients completed the study. A total of 20 patients received high FF (25–30%), and 20 patients with a similar risk profile with regard to progression received low FF (20–25%). Two low FF group patients, however, dropped out because of missing important data. There was one censored patient among the standard–compliant patients who received high FF who withdrew informed consent, and one was missing important data.

At baseline, patient characteristics were similar between the two groups, and there were 31 males (77.5%) and 9 females (22.5%). The average age was 63.25 ± 16.03 years. Thirty-one patients were diagnosed with hypertensive heart disease and renal disease, heart failure and renal failure. Five patients were diagnosed with acute renal injury, and four patients were diagnosed with chronic renal failure with severe pneumonia. The baseline serum creatinine, urea, potassium concentration and pH values were 21.75 (15.78, 30.43) mmol/L, 650.15 (509.55, 834.8) µmol/L, 4.08 (3.74, 4.93) mmol/L, and 7.38 (7.34, 7.40) mmol/L, respectively, before treatment. The following parameters were compared between the two
groups: sex, age, FF, serum creatinine, urea, potassium concentration and pH value before treatment, venous pressure, arterial pressure, and transmembrane pressure at 1 hour during CRRT. The results showed that there was no significant difference in the above parameters between the two groups (Table 1).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low FF (n = 20)</th>
<th>High FF (n = 20)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical characteristics at biopsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>15(75)</td>
<td>16(80)</td>
<td>0.71</td>
</tr>
<tr>
<td>Asian</td>
<td>20</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>Age (y)</td>
<td>65.15 ± 2.73</td>
<td>61.35 ± 4.38</td>
<td>0.47</td>
</tr>
<tr>
<td>FF (%)</td>
<td>23.86 ± 0.95</td>
<td>27.57 ± 1.03</td>
<td>0.001</td>
</tr>
<tr>
<td>AP at 1 hour (mmHg)</td>
<td>64.35 ± 19.03</td>
<td>69.25 ± 18.60</td>
<td>0.42</td>
</tr>
<tr>
<td>VP at 1 hour (mmHg)</td>
<td>64.60 ± 16.21</td>
<td>64.10 ± 19.96</td>
<td>0.93</td>
</tr>
<tr>
<td>TMP at 1 hour (mmHg)</td>
<td>67.15 ± 16.83</td>
<td>74.10 ± 23.16</td>
<td>0.28</td>
</tr>
<tr>
<td>Serum creatinine (mmol/L)</td>
<td>633.83(435.07, 740.61)</td>
<td>790.26(622.74, 1231.51)</td>
<td>0.08</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>19.27(15.54, 29.04)</td>
<td>24.69(16.99, 31.55)</td>
<td>0.52</td>
</tr>
<tr>
<td>Potassium concentration (mmol/L)</td>
<td>4.30(3.51, 5.067)</td>
<td>4.08(3.92, 4.59)</td>
<td>0.99</td>
</tr>
<tr>
<td>pH value</td>
<td>7.38(7.36, 7.41)</td>
<td>7.39(7.33, 7.40)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

3.2. Comparison of the pressure values

In this study, all patients received daytime treatment for 10–12 hours, and all patients successfully completed the treatment without the need to change the filters. In this study, the arterial pressure, venous pressure and transmembrane pressure of patients were collected and ordered at 1 hour, 2 hours, 6 hours and the end of treatment. During CRRT, there was no statistically significant difference in arterial pressure between the two groups in the treatment of 2 hours, 6 hours and at the end of treatment compared with 1 hour of treatment (P = 0.30, 0.27, 0.87). There was no statistically significant difference between the venous pressure at 2 hours, 6 hours and the end of treatment compared with 1 hour of treatment (P = 0.55, 0.53, 0.53), and there was also no statistically significant difference in transmembrane pressure (P = 0.55, 0.63, 0.53) (Table 2).
Table 2

Primary end point on the basis of the available patients at the end of the study phase. Note: values for continuous variables, as mean ± standard deviation; Abbreviations: FF, filtration fraction; AP, Arterial pressure; VP, venous pressure; TMP, transmembrane pressure; H, hour.

<table>
<thead>
<tr>
<th>End Point</th>
<th>Low FF (n = 20)</th>
<th>High FF (n = 20)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>The changes in AP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2h vs 1h</td>
<td>-2.70 ± 13.68</td>
<td>1.65 ± 12.63</td>
<td>0.30</td>
</tr>
<tr>
<td>6h vs 1h</td>
<td>0.15 ± 11.88</td>
<td>3.80 ± 8.38</td>
<td>0.27</td>
</tr>
<tr>
<td>End of treatment vs 1h</td>
<td>5.95 ± 18.12</td>
<td>5.15 ± 10.83</td>
<td>0.87</td>
</tr>
<tr>
<td><strong>The changes in VP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2h vs 1h</td>
<td>-2.40 ± 3.30</td>
<td>1.05 ± 20.01</td>
<td>0.54</td>
</tr>
<tr>
<td>6h vs 1h</td>
<td>-3.90 ± 11.73</td>
<td>-2.80 ± 17.11</td>
<td>0.81</td>
</tr>
<tr>
<td>End of treatment vs 1h</td>
<td>-1.00 ± 16.70</td>
<td>-2.75 ± 15.74</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>The changes in TMP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2h vs 1h</td>
<td>-0.85 ± 16.24</td>
<td>1.80 ± 10.76</td>
<td>0.55</td>
</tr>
<tr>
<td>6h vs 1h</td>
<td>11.75 ± 21.60</td>
<td>16.35 ± 36.05</td>
<td>0.63</td>
</tr>
<tr>
<td>End of treatment vs 1h</td>
<td>12.40 ± 21.54</td>
<td>17.70 ± 30.43</td>
<td>0.53</td>
</tr>
</tbody>
</table>

3.3. Comparison of the filter clotting

Grade II clotting was found in the filters of 3 patients, and grade III clotting was not found in any patients at the end of CRRT in the low FF group. Grade II clotting was found in the filters of 3 patients, and grade II clotting was found in the filters of 1 patient at the end of CRRT in the high FF group. There were no patients who had grade III clotting at the end of CRRT in the low or high FF groups. There was no statistically significant difference between the two groups (P > 0.05), as shown in Table 3.

Table 3

Secondary end point on the basis of the available patients at the end of the study phase. Note: Values for categorical variables were given as count (percentage); Abbreviations: FF, filtration fraction.

<table>
<thead>
<tr>
<th>End Point</th>
<th>Low FF (n = 20)</th>
<th>High FF (n = 20)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade Dialyzer coagulation</td>
<td>3(15)</td>
<td>3(15)</td>
<td>0.95</td>
</tr>
<tr>
<td>Grade Dialyzer coagulation</td>
<td>0(0)</td>
<td>1(5)</td>
<td>0.31</td>
</tr>
</tbody>
</table>
3.4. Effectiveness

Comparisons of the clinical outcomes between the two groups are shown in Table 4. The serum creatinine levels of the patients in the low FF group decreased by 228.31 (139.29, 340.05) µmol/L, and the serum creatinine levels of the patients in the high FF group decreased by 430.30 (364.72, 662.36) µmol/L after CRRT. There were statistically significant differences in the clearance efficiency of serum creatinine (P = 0.04). There were no statistically significant differences in the clearance efficiency of urea (P = 0.64), the changes in potassium concentration (P = 0.39) or the pH value (P = 0.96) between the two groups.

<table>
<thead>
<tr>
<th>Efficacy evaluation. Note: values for continuous variables, as mean ± standard deviation or median [IQR]. Abbreviations: FF, filtration fraction.</th>
<th>Low FF (n = 20)</th>
<th>High FF (n = 20)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine (µmol/L)</td>
<td>228.31 (139.29, 340.05)</td>
<td>430.30 (364.72, 662.36)</td>
<td>0.04</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>7.87 (3.48, 14.16)</td>
<td>9.28 (5.98, 13.63)</td>
<td>0.64</td>
</tr>
<tr>
<td>Potassium concentration (mmol/L)</td>
<td>0.31 (-0.12, 0.78)</td>
<td>-0.02 (-0.23, 0.26)</td>
<td>0.39</td>
</tr>
<tr>
<td>pH value</td>
<td>-0.04 (-0.05, -0.02)</td>
<td>-0.04 (-0.05, -0.01)</td>
<td>0.96</td>
</tr>
</tbody>
</table>

4. Discussion

In CRRT, coagulation of the filter and extracorporeal circulation line, which are important indicators of nursing quality evaluations [9], are factors of concern. Coagulation of the filter and extracorporeal circulation line was influenced by many factors, including anticoagulation mode, function of vascular access, formulation of treatment prescription and nursing operation during CRRT. The selection of FF is an important factor affecting the life of the extracorporeal circulation pipeline when prescription setting. An FF of less than 25% is widely used in clinical practice, both as recommended by the ADQI guidelines and as widely accepted by clinicians. However, there are not enough clinical studies to support this use. This study focused on daytime CRRT. Due to the relatively short treatment time, the treatment dose per unit time needed to be higher, especially when using citric acid anticoagulation, and the net ultrafiltration rate of patients was also higher; therefore, the FF was often more than 25%. However, it is worth considering whether an FF of more than 25% is truly associated with a higher risk of coagulation for shorter daytime CRRT. This study confirmed that an FF of 25–30% was not associated with a higher risk of coagulation during 10–12 hours of daytime therapy compared to an FF of 20–25%.

Guirao et al. [10] found that during CRRT, the venous extracorporeal circulation line pressure of the bedside hemofiltration machine was negatively correlated with the service time of supporting pipes and filters. Ejaz et al. [11] suggested that the reduced mean filter lifespan was related to abnormal blood flow (hemodialysis catheter dysfunction). However, in clinical work, it is difficult to timely monitor and deal
with outliers of blood flow, and the time of daytime CRRT is relatively fixed, so it is difficult to determine the filter lifespan of the first filter. Therefore, in this study, the specialist nurse recorded and classified hourly venous, arterial and transmembrane pressure levels, as well as coagulation levels of filters and extracorporeal circulation lines after CRRT. The results showed that there was no statistical significance in the difference in pressure at 2 hours, 6 hours and at the end of each monitoring point compared with 1 hour between the two groups. There was no significant difference in the coagulation level of the filter and extracorporeal circulation line after CRRT between the two groups. In this study, all patients were treated with CVVHDF, the postdilution method, and heparin, which was used for anticoagulation, excluding the influence of other factors on blood coagulation in the extracorporeal circulation pipeline.

A total of 40 patients were enrolled in this study, all of whom required CRRT in the Department of Nephrology. These patients had hemodynamic instability, volume overload, and difficult to correct cardiac insufficiency on ordinary hemodialysis. These patients often have difficulty tolerating treatment for 24 hours or more, so daytime CRRT is relatively suitable for them. For the treatment of patients in a relatively short time, FF should have a good treatment effect and meet the needs of patients in regard to volume control; however, 25% was sometimes difficult to achieve. This study confirmed that in 10 to 12 hours of daytime CRRT, 25–30% compared with 20–25% of the FF will not lead to a higher risk of clotting. On the basis of the same hematocrit, clinicians can choose a higher volume of replacement fluid and ultrafiltration when prescribing treatment. In this way, it not only ensures the smooth progress of CRRT but also reduces the negative impact of replacing the extracorporeal circulation pipeline during the patient's treatment and ensures patient satisfaction and an efficient use of nursing staff. It can also produce therapeutic effects in patients.

Cen Zhongran et al. showed that in CVVHDF, small molecule substances such as creatinine and urea can be removed by diffusion and convection, while both predilution and postdilution can effectively remove small molecule substances [12]. In this study, it was found that there were statistically significant differences in serum creatinine clearance efficiency between the two groups. The clearance efficiency of the high FF group was higher than that of the low FF group, which might be because the replacement fluid amount of the high FF group was higher than that of the low FF group. There were no statistically significant differences in the clearance efficiency of urea or the changes in potassium concentration and pH value between the two groups.

The limitation of this study is mainly due to the small sample size. Only the influence of FF on CRRT for 10–12 hours was studied. Compared with an FF < 25%, an FF of 25–30% does not seem to increase the risk of coagulation in CBP, but this is only applicable in treatments of short duration. Further studies are needed to explore the effects of different FFs on the risk of coagulation and the lifespan of CBP.

In 8–12 hours of daytime CRRT, an FF between 25–30% does not increase the risk of clotting in the extracorporeal circulation line compared with an FF between 20–25% and can more effectively remove small molecules such as serum creatinine to improve the treatment's effects, providing evidential support for a more detailed definition of FF standards in clinical practice.
Declarations

Ethics and consent to participate

This study was approved by the Regional Ethics Committee of the Second Affiliated Hospital of Nanchang University, and the approval number was No. [2021] 045. All included patients or authorized family members signed an informed consent form. The design of the study fully took the safety and fairness principle into account. The research did not harm the subjects and protected their privacy rights. All methods were carried out according to relevant guidelines and regulations.

Consent for publication

NA.

Author contributions

Li Wang performed the data collection, reviewed articles, and wrote the manuscript. Jinjing Huang, Fan Li and Siyue Huang completed the data analysis and provided the second views during the manuscript preparation. Chengyun Xu and Gaosi Xu revised the manuscript.

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Competing interests

There is not any conflict of interest to report here.

Availability of data and material

The datasets generated and/or analysed during the current study are not publicly available due ethical concerns but are available from the corresponding author on reasonable request.

References


Figures
Figure 1

Flow diagram for inclusion of participants.