Revisiting Filtration Fraction as an Index of the Risk of Hemofilter Clotting in Continuous Venovenous Hemofiltration

Parta Hatamizadeh,[1] Ashita Tolwani,[2] and Paul Palevsky[3]

CJASN 15: 1660–1662, 2020. doi: https://doi.org/10.2215/CJN.02410220

[1]Division of Nephrology, Hypertension and Renal Transplantation, University of Florida, Gainesville, Florida
[2]Division of Nephrology, University of Alabama at Birmingham, Birmingham, Alabama
[3]Renal-Electrolyte Division, University of Pittsburgh, Pittsburgh, Pennsylvania

Correspondence: Dr. Parta Hatamizadeh, Division of Nephrology, University of Florida, 1600 SW Archer Road, Room CG-98, P.O. Box 100224, Gainesville, FL 32610. Email: hatamizadehp@ufl.edu

Introduction

Hemofilter clotting is a major challenge in continuous venovenous hemofiltration (CVVH). Experts recommend keeping filtration fraction, the fraction of plasma water that is removed by ultrafiltration, below 20% or 30% to avoid clotting (1). Clotting risk is believed to markedly increase when the postfilter hematocrit (Hct) exceeds 0.4–0.5, and a filtration fraction of 30%–50% is presumably associated with an increase in the postfilter Hct to this range (2).

However, a key question is whether a single value of maximal filtration fraction is appropriate in all situations, independent of other parameters such as Hct and concentration of plasma proteins. Additionally, the role of prefilter as compared with postfilter administration of replacement fluids contributes to additional confusion and uncertainty regarding the interpretation of filtration fraction. Given the definition of filtration fraction (*FF*), when replacement fluids are administered postfilter, it is calculated as below:

$$\boldsymbol{FF} = \frac{Q_{UF-net} + Q_{RF-post}}{Q_B \times (1 - Hct)} \quad (1)$$

Where $Q_{UF\text{-}net}$ is fluid removal rate, $Q_{RF\text{-}post}$ is postfilter fluid replacement rate, and Q_B is blood flow rate.

For the calculation of filtration fraction when replacement fluid is administered prefilter, most experts propose adding the prefilter replacement fluid rate ($Q_{RF\text{-}pre}$) to both numerator and denominator, as in Equation 2 (3,4):

$$\boldsymbol{FF} = \frac{Q_{UF-net} + Q_{RF-pre}}{Q_B \times (1 - Hct) + Q_{RF-pre}} \quad (2)$$

According to Equations 1 and 2, with fixed Q_B and $Q_{UF\text{-}net}$, at any fluid replacement rate, the filtration fraction is higher in the postfilter compared with the prefilter replacement setting. Therefore, when comparing pre- and postfilter replacement settings, assuming that a lower filtration fraction is associated with a lower risk of hemofilter clotting would be consistent with these calculations because studies have shown a lower risk of clotting when using the prefilter compared with the postfilter fluid replacement setting (5,6). However, according to Equation 2, in the prefilter replacement setting, by increasing the $Q_{RF\text{-}pre}$, the calculated filtration fraction will increase, while there is no evidence to suggest that increasing the prefilter replacement rate increases the risk of hemofilter clotting.

Therefore, using filtration fraction as an index for risk stratification of hemofilter clotting has serious limitations, particularly in the prefilter replacement setting.

The Origin of Applying a Single Universal Filtration Fraction Cutoff Point to Prevent Hemofilter Clotting

The application of filtration fraction for risk stratification of hemofilter clotting and the assignment of a single cutoff point as the maximum allowable filtration fraction 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 (1,4). 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. Unlike CVVH, CAVH does not allow for control of the filtration rate because it is a function of the existing arteriovenous hydrostatic pressure gradient, oncotic pressures, and membrane and circuit specifications. Furthermore, these publications simply report the observed filtration fraction achieved in the CAVH setting, the importance of which was about attainment of convective clearance rather than hemofilter clotting. In fact, they have not reported any correlation between filtration fraction and hemofilter clotting. Therefore, these studies cannot be extrapolated to CVVH and provide no information regarding the relationship between filtration fraction and hemofilter clotting; hence, they should not have been the basis for defining a single filtration fraction value as the maximum allowable filtration fraction in CAVH.

A Better Alternative than Filtration Fraction for Determining the Risk of Hemofilter Clotting

In 1992, Jenkins *et al.* (9) showed in an experimental study that at a Hct close to 0.45, "operational

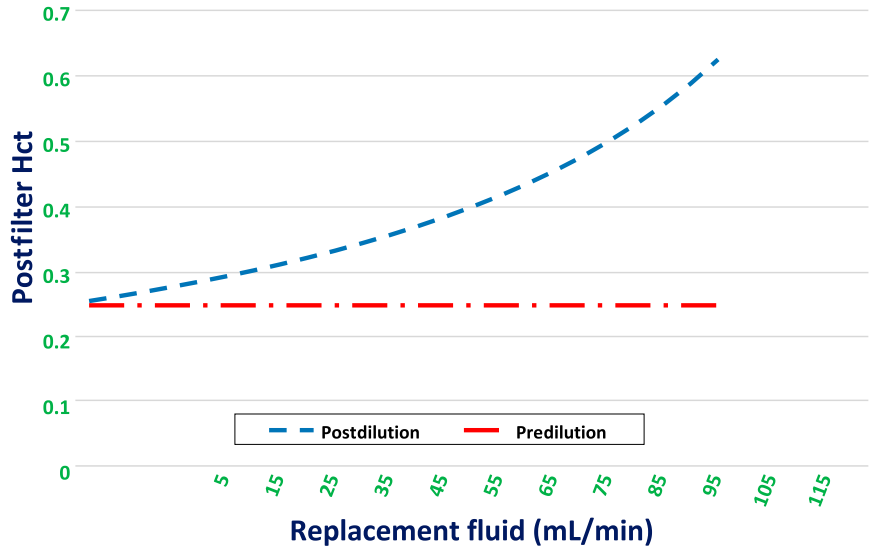

Figure 1. | Postfilter hematocrit rises exponentially by increasing postfilter replacement rate but is not affected by alterations of prefilter replacement rate. In postfilter replacement setting, with incremental increase in replacement fluid rate, the postfilter hematocrit increases exponentially; whereas in prefilter replacement setting, the postfilter hematocrit remains constant irrespective of prefilter replacement rate, provided that all other parameters remain constant. The graph shows changes in postfilter hematocrit in pre- and postfilter replacement settings in a patient with hematocrit of 0.25, blood flow rate of 200 ml/min, and no fluid removal. In practice, postfilter hematocrits >0.5 may not be achievable in most circumstances because blood will clot and the filter will stop working when the hematocrit reaches such a high level. The *x* axis represents replacement fluid rate (ml/min) and the *y* axis shows the postfilter hematocrit. Hct, hematocrit.

instability" of the hemofiltration system and impending circuit clotting occur.

Because hemoconcentration, not filtration fraction *per se*, defines the risk of hemofilter clot formation, calculating end-of-hemofilter hemoconcentration is likely to be more useful than the filtration fraction. Using Hct as a surrogate for hemoconcentration, we can calculate the filtration fraction that can lead to a certain end-of-filter Hct, depending on the patient's Hct.

According to basic mathematical concepts, we know:

$$Hct_{pre} \times Q_{pre} = Hct_{post} \times Q_{post} \quad (3)$$

Where Hct_{pre} is prefilter Hct, Q_{pre} is prefilter flow (which is Q_B), Hct_{post} is postfilter Hct, and Q_{post} is postfilter flow.

In postfilter replacement, Q_{post} can be calculated by subtracting the ultrafiltration flow from the prefilter flow which, according to Equation 1, will result in the following equation:

$$\begin{aligned} Q_{post} &= Q_B - Q_{UF-net} - Q_{RF-post} \\ &= Q_B - \left(FF \times Q_B \times \left[1 - Hct_{pre}\right]\right) \end{aligned} \quad (4)$$

By replacing Q_{post} in Equation 3, according to Equation 4, and solving it for *FF*, the following formula ensues:

$$FF = \frac{Hct_{post} - Hct_{pre}}{Hct_{post} \times \left(1 - Hct_{pre}\right)} \quad (5)$$

By plugging in the patient's Hct for Hct_{pre} and the maximum end-filter Hct threshold (Hct_{max}) for Hct_{post}, one can calculate the maximum allowable filtration fraction (FF_{max}) to avoid reaching a Hct level at which the risk of filter clotting is thought to be unacceptably high (Equation 6).

$$FF_{max} = \frac{Hct_{max} - Hct_{patient}}{Hct_{max} \times \left(1 - Hct_{patient}\right)} \quad (6)$$

Equation 6 reveals the significant effect of the patient's Hct on FF_{max}. For example, assuming Hct_{max}=0.4, the FF_{max} for a Hct of 0.35 is 19%, whereas for a Hct of 0.25, it is 50%.

For practical purposes, calculating the maximum allowable ultrafiltration rate ($Q_{UF-total}$, which is $Q_{UF-net}+Q_{RF-post}$) is useful. Using Equation 3, replacing Q_{post} with $Q_B - Q_{UF-total}$ and solving the equation for $Q_{UF-total}$ result in Equation 7:

$$Q_{UF-total} = Q_B \times \frac{Hct_{post} - Hct_{pre}}{Hct_{post}} \quad (7)$$

The maximum allowable ultrafiltration rate can then be calculated using Equation 8:

$$Q_{UF-total-max} = Q_B \times \frac{Hct_{max} - Hct_{patient}}{Hct_{max}} \quad (8)$$

Therefore, the higher the Hct and the lower the Q_B, the lower the $Q_{UF-total}$ should be set to avoid hemofilter clotting.

Equations 4–8 are applicable only in the postfilter replacement setting. For the prefilter replacement setting, in the absence of any net ultrafiltration (when $Q_{UF-total}=Q_{RF-pre}$), the same volume that has been given as the prefilter replacement fluid will be removed from it within the hemofilter, so the end-of-hemofilter Hct returns to the predilution Hct, *i.e.*, the patient's Hct. Therefore, with a fixed fluid removal rate, any increase or decrease in Q_{RF-pre} increases or decreases the convective clearance, respectively; however, it does not change end-of-hemofilter Hct

(Figure 1). Therefore, it should not affect the likelihood of filter clotting and should not be factored in calculations of FF_{max} or $Q_{UF\text{-}max}$.

Thus, for the calculation of FF_{max} and $Q_{UF\text{-}max}$ in prefilter replacement setting, the same formulas as those of the postfilter replacement setting (Equations 6 and 8, respectively) may be used with the understanding that, in the prefilter replacement setting, filtration fraction represents the filtered fraction of plasma (ignoring the prefilter fluid replacement rate) and $Q_{UF\text{-}max}$ refers to $Q_{UF\text{-}net\text{-}max}$ (maximum fluid removal rate).

Conclusion

Although end-of-filter Hct, as an index of hemoconcentration, is more relevant than filtration fraction in determination of the risk of hemofilter clotting, it still overlooks other contributing factors such as the circuit shape and design and the coagulability state of the patient.

Nevertheless, reliance on a single arbitrary maximum allowable filtration fraction, as an index for risk stratification of hemofilter clotting, lacks accuracy and validity. End-of-hemofilter Hct, which is a contributing factor to hemofilter clotting, is a more meaningful index. We propose using the above-mentioned formulas to adjust Q_{UF} to maintain the calculated end-of-hemofilter Hct below a certain number which, based on currently available data (9,10), appears to be approximately 0.4.

Although conceptually sound, these equations need to be validated in clinical studies.

Disclosures

P. Hatamizadeh has a patent titled renal replacement therapy machine. P. Palevsky reports receiving personal fees from Baxter, grants from Dascena, and grants from BioPorto, outside the submitted work. The remaining author has nothing to disclose.

Funding

None.

Acknowledgments

The content of this article does not reflect the views or opinions of the American Society of Nephrology (ASN) or *CJASN*. Responsibility for the information and views expressed herein lies entirely with the author(s).

References

1. Tolwani A: Continuous renal-replacement therapy for acute kidney injury. *N Engl J Med* 367: 2505–2514, 2012
2. Pedrini LA: On-line hemodiafiltration: Technique and efficiency. *J Nephrol* 16[Suppl 7]: S57–S63, 2003
3. MacEwen C, Watkinson P, Winearls C: Circuit life versus bleeding risk: The impact of achieved activated partial thromboplastin time versus achieved filtration fraction. *Ther Apher Dial* 19: 259–266, 2015
4. Neri M, Villa G, Garzotto F, Bagshaw S, Bellomo R, Cerda J, Ferrari F, Guggia S, Joannidis M, Kellum J, Kim JC, Mehta RL, Ricci Z, Trevisani A, Marafon S, Clark WR, Vincent JL, Ronco C; Nomenclature Standardization Initiative (NSI) alliance: Nomenclature for renal replacement therapy in acute kidney injury: Basic principles. *Crit Care* 20: 318, 2016
5. Uchino S, Fealy N, Baldwin I, Morimatsu H, Bellomo R: Predilution vs. post-dilution during continuous veno-venous hemofiltration: Impact on filter life and azotemic control. *Nephron Clin Pract* 94: c94–c98, 2003
6. van der Voort PH, Gerritsen RT, Kuiper MA, Egbers PH, Kingma WP, Boerma EC: Filter run time in CVVH: Pre- versus post-dilution and nadroparin versus regional heparin-protamine anticoagulation. *Blood Purif* 23: 175–180, 2005
7. Kramer P, Kaufhold G, Gröne HJ, Wigger W, Rieger J, Matthaei D, Stokke T, Burchardi H, Scheler F: Management of anuric intensive-care patients with arteriovenous hemofiltration. *Int J Artif Organs* 3: 225–230, 1980
8. Lauer A, Saccaggi A, Ronco C, Belledonne M, Glabman S, Bosch JP: Continuous arteriovenous hemofiltration in the critically ill patient. Clinical use and operational characteristics. *Ann Intern Med* 99: 455–460, 1983
9. Jenkins RD, James EF, Chen B, Golper TA: Operational instability in extracorporeal filtration of blood. *Blood Purif* 10: 292–308, 1992
10. Cinar Y, Demir G, Paç M, Cinar AB: Effect of hematocrit on blood pressure via hyperviscosity. *Am J Hypertens* 12: 739–743, 1999

Published online ahead of print. Publication date available at www.cjasn.org.