Anticoagulation Strategies and Filter Life in COVID-19 Patients Receiving Continuous Renal Replacement Therapy

A Single-Center Experience

Divya Shankaranarayanan,[1] Thangamani Muthukumar,[1] Tarek Barbar,[2] Aarti Bhasin,[1] Supriya Gerardine,[1] Perola Lamba,[1] Lorenz Leuprecht,[1] Sanjay P. Neupane,[1] Thalia Salinas,[1] Daniil Shimonov,[1] Elly Varma,[1] and Frank Liu[1,3]

CJASN 16: 124–126, 2021. doi: https://doi.org/10.2215/CJN.08430520

[1]Division of Nephrology and Hypertension, Weill Cornell Medicine, New York, New York
[2]Department of Medicine, Weill Cornell Medicine, New York, New York
[3]The Rogosin Institute, New York, New York

Correspondence:
Dr. Frank Liu, Rogosin Institute, 505 East 70th Street, HT-230, New York, NY 10021.
Email: fmliu@nyp.org

Because of the unprecedented increase in critically ill patients with coronavirus disease 2019 (COVID-19), capacity to provide continuous RRT (CRRT) for AKI may quickly be overwhelmed (1). Exacerbating this resource crunch is the hypercoagulability observed in COVID-19 (2,3). Frequent CRRT circuit clotting leads to blood loss and wastage of already overextended resources, and need for troubleshooting increases health care provider exposure to infected patients.

At our quaternary care academic institution, we perform CRRT using a uniform protocol in five intensive care units (ICUs). We do not use anticoagulation routinely but add it (mostly heparin) as needed. Additionally, for more than a decade, we have used regional citrate anticoagulation (RCA) as the default protocol in our surgical ICU. During the COVID-19 pandemic, our hospital added ten more ICUs. Systemic anticoagulation was available in all 16 ICUs, whereas RCA remained restricted to the surgical ICU, albeit with less frequent postfilter ionized calcium monitoring to reduce nurse exposure to infected patients.

Herein, we describe our experience with the life of 502 CRRT circuits on different anticoagulation regimens in 80 patients with RT-PCR–confirmed COVID-19 who received continuous venovenous hemodialysis (NxStage System One) between March 5 and May 8, 2020 (Figure 1A). These circuits were categorized by their anticoagulation regimen at the time of filter stoppage: heparin (systemic unfractionated or low–mol wt heparin [LMWH]), prefilter heparin, argatroban, RCA (citrate), citrate plus heparin (when patients received systemic heparin for medical indications), or no anticoagulation (none).

Circuit clotting was our analysis end point. Circuit life was the time (hours) from initiation of CRRT to clotting or censoring. Circuits that functioned beyond 72 hours were censored at 72 hours. Circuits terminated for reasons other than clotting were censored at the time of termination. We determined the association between circuit clotting and anticoagulation groups by Cox regression in Stata 16 software.

Initial anticoagulation regimens for the 80 patients were systemic heparin (n=32), prefilter heparin (n=8), citrate (n=3), argatroban (n=2), citrate plus heparin (n=1), and none (n=34). While 39 of the 80 patients received the same anticoagulation (17 systemic heparin, four prefilter, two argatroban, and 16 none) for all of their circuits, 41 patients were switched to different anticoagulation regimens for subsequent circuits on the basis of the treating nephrologist's discretion.

Of the 502 circuits, 350 (70%) received anticoagulation, and 152 (30%) did not. Among the circuits that received anticoagulation, heparin was used in 265 (76%; 191 systemic, 64 prefilter, and ten LWMH), citrate was used in 46 (13%; target postfilter ionized calcium <0.35 mmol/L), and argatroban was used in 39 (11%). Of the 46 citrate circuits, 25 (54%) received additional systemic heparin. For the purposes of this analysis, systemic heparin and LWMH were analyzed as one group.

Clotting occurred in 203 (40%) circuits. Among 350 circuits with anticoagulation, 124 (35%) clotted, and among 152 with no anticoagulation, 79 (52%) clotted. Among circuits with anticoagulation, 13 (62%) with citrate, 33 (52%) with prefilter heparin, 63 (31%) with systemic heparin, ten (26%) with argatroban, and five (19%) with citrate plus heparin clotted. Median clotting-free survival was 21 hours (interquartile range, 48–7 hours) for no anticoagulation. For anticoagulated circuits, clotting-free survival was 25 hours (interquartile range, 57–10 hours) for prefilter heparin, 40 hours (interquartile range, 63–10 hours) for citrate, 49 hours (interquartile range, >72–14 hours) for systemic heparin, >72 hours (interquartile range, >72–40 hours) for argatroban, and >72 (interquartile range, >72–43 hours) for citrate plus heparin (Figure 1B).

The hazard ratios for circuit clotting, independent of patient age and sex, were 0.92 (95% confidence interval, 0.50 to 1.68) for citrate, 0.85 (95% confidence interval, 0.56 to 1.29) for prefilter heparin, 0.59 (95% confidence interval, 0.44 to 0.80) for systemic heparin, 0.29 (95% confidence interval, 0.15 to 0.56) for argatroban, and 0.21 (95% confidence interval, 0.08 to 0.54) for citrate

A

Baseline characteristics at first CRRT	
Age (years), Median (IQR)	67 (59, 75)
Males, N (%)	57 (71)
On mechanical ventilation, N (%)	77 (96)
Requiring vasopressor, N (%)	64 (80)
Thromboembolic episode, N (%)	20 (25)
SOFA score, Median (IQR)	13 (11, 14)
Mortality, N (%)	43 (54)

B

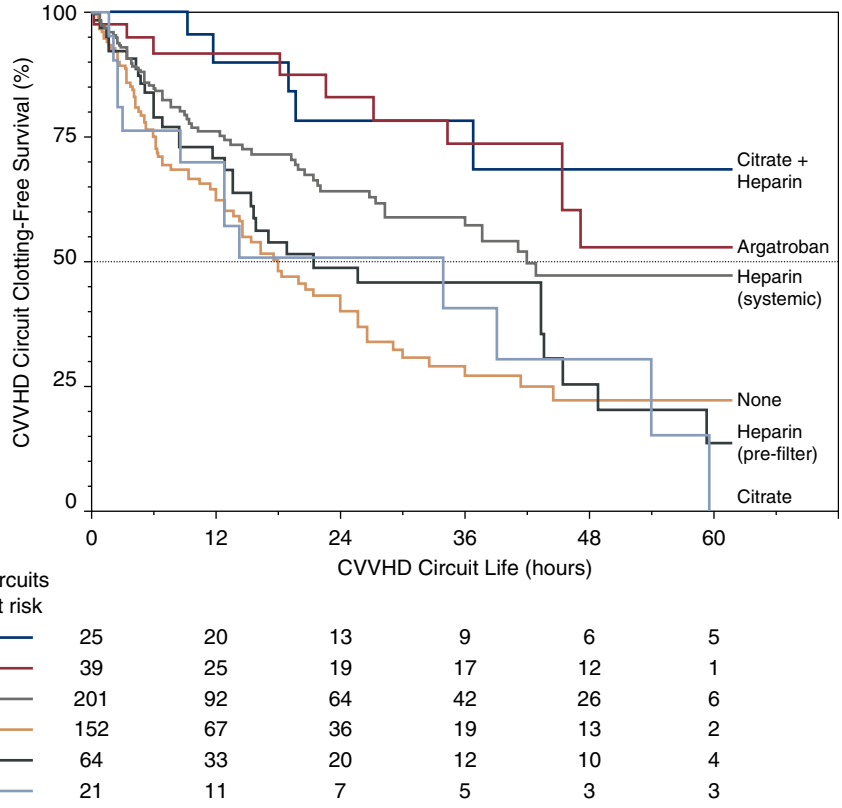

Figure 1. | **Baseline characteristics of the study population and CRRT circuit survival.** (A) Baseline characteristics at the start of continuous RRT (CRRT) and in-hospital mortality rate. (B) Kaplan–Meier estimated probability of continuous venovenous hemodialysis (CVVHD) circuit clotting-free survival on the basis of different anticoagulation regimens. IQR, interquartile range; SOFA, sequential organ failure assessment score.

plus heparin compared with no anticoagulation. Frailty analysis revealed significant patient heterogeneity, suggesting that other patient-level characteristics were associated with filter clotting.

Our findings are notable for several reasons. First, circuits with no anticoagulation performed below expectation. Data on filter patency using the NxStage system without anticoagulation are sparse; one study found 96.7% filter patency at 9 hours (4), and another documented an average filter life of 54.2 hours in a cohort in which nearly 90% of the circuits were run without anticoagulation (5). In contrast, >30% of filters in our study had clotted by 9 hours, and median filter life was only 21 hours. As such, treating teams may wish to empirically anticoagulate circuits to mitigate potential filter clotting. Second, citrate anticoagulation was not overtly effective. This contrasts with published data and our own experience over the last decade of citrate use. However, of the seven patients who were ever on citrate, four had circuit clotting on initial anticoagulation modality prior to being switched to citrate, and two had known episodes of thromboembolism during their hospital course. We speculate that aside from this possible selection bias, slightly reduced frequency of postfilter ionized calcium monitoring and other patient-level confounders may have affected citrate efficacy. Third, although argatroban and citrate plus heparin cannot be unequivocally recommended for routine use without further studies on safety and efficacy in this population, it is notable that these regimens performed extremely well, even though they were mostly used as escalation therapy in high-risk patients who had already developed thromboembolism necessitating systemic anticoagulation.

Our report is limited by the study design, sample size, and patient-level heterogeneity. Further studies to elucidate these patient-level characteristics in circuit clotting are ongoing. Nevertheless, we believe that this first report of CRRT circuit life in the highly thrombophilic cohort of patients with COVID-19 will help physicians plan resources during this public health emergency.

Disclosures

F. Liu reports receiving consulting fees from CVS/Accordant, serving on the speakers' bureau for Janssen Pharmaceutical, and receiving personal fees from Fresenius as a guest lecturer for sales staff. He also served on the clinical events committee for Outset Medical and received consulting fees from Medtronic. All remaining authors have nothing to disclose.

Funding

None.

References

1. Goldfarb DS, Benstein JA, Zhdanova O, Hammer E, Block CA, Caplin NJ, Thompson N, Charytan DM: Impending shortages of kidney replacement therapy for COVID-19 patients. *Clin J Am Soc Nephrol* 15: 880–882, 2020
2. Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, Clark C, Iba T: ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost* 18: 1023–1026, 2020
3. Sise ME, Baggett MV, Shepard JO, Stevens JS, Rhee EP: Case 17-2020: A 68-year-old man with COVID-19 and acute kidney injury. *N Engl J Med* 382: 2147–2156, 2020
4. Gashti CN, Salcedo S, Robinson V, Rodby RA: Accelerated venovenous hemofiltration: Early technical and clinical experience. *Am J Kidney Dis* 51: 804–810, 2008
5. Razavi SA, Still MD, White SJ, Buchman TG, Connor MJ Jr.: Comparison of circuit patency and exchange rates between 2 different continuous renal replacement therapy machines. *J Crit Care* 29: 272–277, 2014

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