Timed Controlled Repeated Rotation of the CAR-170-C NXSTAGE Chronic Cartridge Hemodialysis Filter: A Novel Approach to Enabling Heparin-Free Frequent Daily Home Hemodialysis

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Abstract

Heparin-free hemodialysis is often warranted in postoperative states, bleeding diathesis, and critically ill patients. Conventionally, this is achieved through normal saline flushes or regional citrate anticoagulation. An 87-year-old white man with end-stage renal disease and atrial fibrillation, who was taking warfarin and using maintenance home hemodialysis (HHD) with an NxStage machine, underwent laparoscopic appendectomy. The procedure was complicated by intra-abdominal abscess, sepsis, and tamponade from a bloody pericardial effusion. He needed emergent therapeutic pericardiocentesis. Warfarin was promptly discontinued. He was discharged home with heparin-free HHD. Prior heparin anticoagulation for HHD was an initial bolus of 4000 units of heparin. He continued to clot his extracorporeal system with resultant very high venous pressures and compromised HHD. Heparin anticoagulation was still contraindicated. Flushes with 250-500 mL normal saline, delivered in aliquots every 15-30 minutes, failed to prevent the frequent clotting. The first author, our HD Senior Technician, had astutely observed that the horizontally placed hemodialysis filter exhibited early “clot” formation at the 12-o’clock position, despite the saline flushes. Through trial and error, he discovered that rotating the horizontally placed hemodialysis filter along its long axis, 60 degrees clockwise for 15 minutes, return to the neutral position for 15 minutes, rotating the filter another 60 degrees counterclockwise for 15 minutes, with this repeated cycle of rotations “did the trick.” It promptly and consistently resolved the clotting problem. The lines stopped clotting, and he has not needed saline flushes for smooth heparin-free HHD for more than 7 months. To our knowledge, this is the first such report. Further study is justified. We have hypothesized a mechanism and have named this the “Locke-Onuigbo Maneuver.”

Generally, anticoagulation is necessary for hemodialysis (HD) lasting more than 1-2 hours, because blood contact with the extracorporeal circuit results in activation of the intrinsic coagulation pathway, leading to thrombogenesis.1-4 Nevertheless, heparin-free hemodialysis is often warranted as in postoperative states, in patients with bleeding diathesis, and in critically ill patients in the intensive care unit.5-9 Conventionally, this is achieved through normal saline flushes, or with the application of regional citrate anticoagulation.1-6-9 We recently encountered a set of converging clinical scenarios in which a male patient on home hemodialysis (HHD) using an NsStage machine had to be discharged home from hospital on heparin-free HHD; despite large-volume saline flushes, he had continued to clot his extracorporeal circuits and filters with resulting inadequate HHD. The use of heparin or warfarin was contraindicated, and the patient and the caregiver (wife) were considering stopping HHD. Indeed, there was some discussion about a
possible switch to peritoneal dialysis. Thanks to the observations of our Senior HD technician, the first author, we, the last author working closely together with the first author, found a unique solution to this problem. We have mastered a novel approach to performing sustainable, heparin-free HHD by intermittently rotating the horizontally aligned CAR-170-C NXSTAGE Chronic cartridge clockwise and counterclockwise, as described herein. The CAR-170-C NXSTAGE Chronic cartridges are single use, are gamma sterilized, include an integrated dialyzer, and are manufactured from glycerin-free polyethersulfone membranes (PUREMA H) known for biocompatibility.10 The filter comes with the dialysis lines from the manufacturer as a preattached dialyzer.10

CASE REPORT
An 87-year-old white man with end-stage renal disease and atrial fibrillation, who was also using warfarin and maintenance HHD with an NxStage machine, underwent laparoscopic appendectomy. The procedure was complicated by intra-abdominal abscess, sepsis, and tamponade from a bloody pericardial effusion. He needed emergent life-saving therapeutic pericardiocentesis in the intensive care unit. Warfarin was discontinued promptly. He was discharged home on heparin-free HHD. Before discharging the patient from the hospital, we were able to perform intermittent heparin-free hemodialysis with a Fresenius machine and Optiflux 160 NR dialyzers, with pump-delivered normal saline flushes. Extracorporeal circuits and filters started to clot, with resultant high venous pressures and compromised HHD. Heparin anticoagulation was still contraindicated. Flushes with 250-500 mL of normal saline, delivered in aliquots every 15-30 minutes, failed to prevent frequent clotting. The use of heparin or warfarin was still contraindicated, and the patient and the caregiver (wife) were considering stopping HHD. Indeed, there was some discussion about a possible switch to peritoneal dialysis. A thorough review of the literature failed to provide guidance to resolve this repeated clotting problem. Nevertheless, the first author, our HD Senior Technician, observed that the horizontally placed CAR-170-C NXSTAGE Chronic cartridge (hemodialysis filter) exhibited an early “clot” formation at the 12-o’clock position, despite repeated, large-volume, normal saline flushes (Figure 1). He noticed that blood was pooling around the site and that the first signs of clotting was appearing. Through trial and error, multiple and staggered physical manipulations and maneuvers of the HD filter, he confirmed one finding: that rotating the horizontally placed hemodialysis filter along its long axis, 60 degrees clockwise for 15 minutes, returning to the neutral position for 15 minutes, rotating the filter another 60 degrees counterclockwise for 15 minutes, and continuing these repeated cycles of to-and-fro rotations throughout the HHD
### TABLE. Transition to Heparin-free Hemodialysis in Mid-December 2019 With No More Need for Repeated Normal-Saline Flushes

| Treatment date | Treatment duration, min | Dialysate, L (processed/Rx) | UF, L | Weight, kg (post/dry-Rx) | Pre-Tx sitting BP, mm Hg | Pre-Tx standing BP, mm Hg | Post-Tx sitting BP, mm Hg | Post-Tx standing BP, mm Hg | VP at 200 BFR, mm Hg | Normal saline flushes, mL |
|----------------|-------------------------|-----------------------------|------|--------------------------|--------------------------|---------------------------|--------------------------|---------------------------|------------------------|--------------------------|
| 1/3/2020       | 108                     | 20.0 / 20.0                 | 1.3  | 76.3 / 76.0              | 109 / 55                 | 113 / 55                  | 136 / 65                 | 135 / 65                 | 76                     | —                       |
| 1/2/2020       | 108                     | 20.0 / 25.0                 | 1.3  | 76.2 / 76.0              | 135 / 57                 | 138 / 63                  | 143 / 70                 | 130 / 60                 | 52                     | —                       |
| 12/31/2019     | 108                     | 20.0 / 25.0                 | 1.3  | 77.0 / 76.0              | 141 / 60                 | 122 / 54                  | 142 / 64                 | 124 / 58                 | —                      | —                       |
| 12/30/2019     | 104                     | 20.0 / 25.0                 | 1.0  | 77.6 / 76.0              | 163 / 69                 | 136 / 67                  | 155 / 72                 | 138 / 68                 | 74                     | —                       |
| 12/27/2019     | 105                     | 20.0 / 25.0                 | 1.0  | 77.1 / 76.0              | 132 / 59                 | 119 / 46                  | 141 / 66                 | 122 / 60                 | 100                    | —                       |
| 12/26/2019     | 96                      | 18.4 / 20.0                 | 0.9  | 77.2 / 76.0              | 125 / 53                 | 124 / 53                  | 148 / 66                 | 125 / 66                 | 70                     | —                       |
| 12/24/2019     | 116                     | 20.0 / 25.0                 | 1.3  | 76.7 / 76.0              | 130 / 55                 | 134 / 60                  | 135 / 57                 | 122 / 62                 | 82                     | —                       |
| 12/23/2019     | 77                      | 14.7 / 25.0                 | 0.8  | 76.8 / 76.0              | 163 / 72                 | 131 / 51                  | 147 / 66                 | 124 / 57                 | 96                     | —                       |
| 12/20/2019     | 114                     | 18.8 / 25.0                 | 1.3  | 76.6 / 76.0              | 120 / 54                 | 128 / 54                  | 134 / 65                 | 109 / 54                 | 107                    | —                       |
| 12/19/2019     | 90                      | 16.7 / 25.0                 | 1.0  | 77.1 / 76.0              | 111 / 43                 | 111 / 51                  | 136 / 68                 | 125 / 58                 | 86                     | —                       |
| 12/17/2019     | 129                     | 20.0 / 25.0                 | 1.5  | 76.7 / 76.0              | 126 / 60                 | 123 / 60                  | 122 / 58                 | 119 / 58                 | 113                    | —                       |
| 12/16/2019     | 87                      | 16.2 / 25.0                 | 0.9  | 77.6 / 76.0              | 139 / 70                 | 121 / 61                  | 133 / 62                 | 124 / 55                 | 87                     | 450                     |
| 12/13/2019     | 76                      | 14.4 / 25.0                 | 0.8  | 75.7 / 76.0              | 134 / 58                 | 114 / 58                  | 119 / 55                 | 113 / 59                 | 75                     | 400                     |
| 12/12/2019     | 118                     | 22.1 / 30.0                 | 1.2  | 75.9 / 76.0              | 128 / 55                 | 108 / 55                  | — / —                    | 109 / 49                 | 90                     | 350                     |
| 12/11/2019     | 157                     | 29.2 / 30.0                 | 1.8  | 75.6 / 76.0              | 107 / 48                 | 100 / 49                  | 118 / 52                 | 112 / 54                 | 66                     | 400                     |
| 12/9/2019      | 163                     | 30.0 / 30.0                 | 1.6  | 76.7 / 76.0              | 137 / 58                 | 117 / 52                  | 140 / 54                 | 120 / 58                 | 99                     | 500                     |
| 12/6/2019      | 167                     | 30.0 / 30.0                 | 2.0  | 77.3 / 76.0              | 122 / 48                 | 116 / 55                  | 123 / 63                 | 118 / 55                 | 83                     | 450                     |
| 12/5/2019      | 146                     | 26.8 / 30.0                 | 1.7  | 77.8 / 80.0              | 126 / 61                 | 114 / 51                  | 134 / 65                 | 147 / 60                 | 56                     | 600                     |
| 12/3/2019      | 166                     | 29.4 / 30.0                 | 2.0  | 77.0 / 80.0              | 149 / 63                 | 133 / 61                  | 127 / 64                 | 135 / 59                 | 60                     | 600                     |
| 12/2/2019      | 197                     | 30.0 / 30.0                 | 2.4  | 78.9 / 80.0              | 123 / 62                 | 138 / 62                  | — / —                    | — / —                    | 51                     | 750                     |
| 12/1/2019      | 197                     | 29.4 / 30.0                 | 2.4  | 79.5 / 80.0              | 143 / 70                 | 133 / 56                  | 159 / 69                 | 122 / 54                 | 72                     | 750                     |
| 11/30/2019     | 196                     | 30.0 / 30.0                 | 2.4  | 79.8 / 80.0              | 152 / 66                 | 143 / 68                  | 154 / 71                 | 149 / 70                 | —                      | 750                     |

BFR = blood flow rate; BP = blood pressure; Rx = hemodialysis treatment; Tx = treatment; UF = ultrafiltration; VP = venous pressure.
session “did the trick” (Figure 1). It promptly and consistently resolved the clotting problem. The lines stopped clotting, and he has not needed saline flushes for smooth heparin-free HHD for more than 7 months (Table). The Table demonstrates the clear difference in the need for normal saline flushes since mid-December 2019, when we started this maneuver. The patient did not just have smooth heparin-free and normal-saline flush-free HHD treatments; the treatments were stable and streamlined. In November 2019 and in December 2019, because of multiple treatment interruptions owing to clotting of the extracorporeal circuits including the dialyzers, some treatment sessions lasted almost twice as long (Table). Others lasted more than 1 hour, and treatment was abandoned for that day (Table).

All through these manipulations and rotational maneuvers of the dialysis filters, the signs of early clot formation continued to be only observed around the air bubble at the 12-o’clock position (Figure 1). After each hemodialysis treatment, at rinse back, we had consistently observed that all the dialyzer fibers that exhibited increased fibrin formation (characterized by a different color from the rest of the otherwise all-white fibers) were aligned and restricted to the group of fibers around the 12-o’clock position of the filter or cartridge (Figure 1). With the repeated timed-controlled rotational maneuvers, only these 12-o’clock filter fibers showed, if at all, any of these signs of early clotting (Figure 1). We together observed that the longer the cartridge was left at the same position (without rotation), the more likely it was to clot. By rotating the filter repeatedly throughout the HHD treatment, 60 degrees back and forth clockwise and counterclockwise, around the 12-o’clock neutral position, and along the long axis of the filter, every 15 minutes, as described earlier, the NxSTAGE filter is able to run for longer periods without clotting (Figure 1). The last author and the first author have revisited these manipulations and maneuvers with the same patient at least once per month during the last 7 months, during patient visits to the home dialysis unit, with consistently reproducible results, 100% of the time.

To our knowledge, this is the first such report in the English-language literature. We have hypothesized a mechanism and have named it the “Locke-Onuigbo Maneuver.” Coincidentally and most fortuitously, the patient’s wife maintained a meticulously detailed daily diary of events with a calendar that we routinely provided to all of our patients for record keeping of HHD. She kept these daily diaries since the patient started his HHD treatments. The month of December 2019 was troublesome, and was a difficult
month with lots of notations owing to the multiple interruptions during the HHD treatments (Figure 2A). After the new rotating maneuver, the month of January 2020 “was a breeze,” as recalled recently by the patient’s wife during a visit to the home dialysis unit (Figure 2B). Both patient and wife have been highly satisfied with his heparin-free normal saline-flush-free HHD during the last 7 months.

DISCUSSION
Despite considerable technological advances in the design and functionalities of hemodialysis, there still remains space for significant improvement both in the patient outcomes and in the outcomes of circuit survival, as frequent circuit changes increase not only the nursing workload, blood loss, and economic costs, but also compromise achievement of the filtration rate goals.11 We completed a meticulous review of the literature regarding the origins and development of the art of hemodialysis dating back several decades.12 The nearest comparator to our observations and results is the description of the rotating drum dialyzers by Zbylut J. Twardoski in his 2008 treatise on the history of hemodialyzers’ designs—the Kolff rotating drum (1943).13 In another related counterpoint scenario, Ponte et al14 described, in 2007, the use of an extracorporeal membrane oxygenation (ECMO) system aided by gravitational pull through the filter of the ECMO to treat anuric postoperative acute kidney injury. The authors used “gravity dialysis” in this report, with the ECMO system hemofilter as another depurative technique.14 We therefore, after a methodical review of the foregoing historical evidences have hypothesized that our repeated rotational manipulations of the NxStage CAR-170-C Chronic cartridge created a continuing antigravity effect, thus preventing any sustained thrombogenesis in the extracorporeal system. In this way, we were able to achieve reproducible smooth, heparin-free and normal saline-flush—free HHD in our patient. Our hypothesis is that somehow, the repeated helical rotational movements every 15 minutes of the CAR-170-C NXSTAGE Chronic cartridge, created continuously along the long axis of the cartridge, provides some kind of physical defense against progressive clotting of the filter fibers. The result is therefore a sustainable maintenance of fluidity in the extracorporeal circuit to enable adequate hemodialysis to occur. Our observations with one patient demand further study for repeatability and reproducibility. Furthermore, our hypothesis calls for further study by biomedical engineers. We did not consider just having the dialyzer placed vertically, because this is not the manufacturer’s recommendation and the NxStage machine holder for the filter is only so designed. Moreover, unlike ‘standard’ dialyzer filters used with conventional hemodialysis machines like the Optiflux 160 NR filter, the CAR-170-C NxStage Chronic cartridges do not have an air trap; therefore, the visualization of the air bubble in the 12-o’clock position is possible only with the cartridge aligned in the horizontal position.

Of the various ways and means of anticoagulation available for hemodialysis—including the use of unfractionated heparin (systemic and regional), the use of low-molecular-weight heparin, saline flushing, regional citrate, prostacyclin, heparinoids, hirudoid (recombinant hirudin), protease inhibitors, and extracorporeal device modifications—the method that we have described in this case report has not been reported previously.

CONCLUSION
We have described a novel method of achieving heparin-free home hemodialysis using the NxStage machine with the CAR-170-C Chronic Cartridge Hemodialysis Filter. We have hypothesized a mechanism to explain this observation and have named this the “Locke-Onuigbo Maneuver.” If confirmed by subsequent research, we propose that a miniaturized electric motor that is programmed to mimic these repetitive, timed controlled rotations of the horizontally placed filter along the long axis of the filter could translate to a commercially successful method of performing heparin-free dialysis.

Abbreviations and Acronyms. ECMO = extracorporeal membrane oxygenation; HHD = home hemodialysis

Potential Competing Interests. The authors report no competing interests.
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REFERENCES
1. Saltisi D. Management of anticoagulation for hemodialysis. In: Nissenson AR, Fine RD, eds. Dialysis Therapy. 3rd ed. Philadelphia: Hanley and Belfus; 2002:82-86.
2. Skagerlind MSE, Stegmayr BG. An evaluation of four modes of low-dose anticoagulation during intermittent haemodialysis. Eur J Clin Pharmacol. 2018;74(3):267-274.
3. Miklaszewska M, Korohoda P, Zachwieja K, et al. Filter size not the anticoagulation method is the decisive factor in continuous renal replacement therapy circuit survival. Kidney Blood Press Res. 2017;42(2):327-337.
4. Stegmayr BG, Jonsson P, Mahmood D. A significant proportion of patients treated with citrate containing dialysate need additional anticoagulation. Int J Artif Organs. 2013;36(1):1-6.
5. Rossignol P, Dorval M, Fay R, et al. Rationale and design of the HepZero study: A prospective, multicenter, international, open, randomized, controlled clinical study with parallel groups comparing heparin-free dialysis with heparin-coated dialysis membrane (Evodial) versus standard care: Study protocol for a randomized controlled trial. Trials. 2013;14:163.
6. François K, Wissing KM, Jacobs R, Boare D, Jacobs K, Tieleman C. Avoidance of systemic anticoagulation during intermittent haemodialysis with heparin-grafted polyacrylonitrile membrane and citrate-enriched dialysate: A retrospective cohort study. BMC Nephrol. 2014;15:104.
7. Brunet V, Serre JE, Mourad G, Kouache K, Pennin V. Heparin-free renal replacement therapy for chronic hemodialyzed patients at high risk for bleeding: A comparison of on-line predilution hemodiafiltration with conventional hemodialysis. Hemodial Int. 2018;22(4):463-473.
8. Faguer S, Sant-Cricq M, Nagier MB, Labadens L, Lavaysiere L, Kamar N, Cointault O. Heparin-free prolonged intermittent hemodialysis using calcium-free citrate dialysate in critically ill patients. Crit Care Med. 2017;45(11):1887-1892.
9. Islam MS, Hassan ZA, Chalmir F, et al. Vitamin E-coated and heparin-coated dialyzer membranes for heparin-free hemodialysis: A multicenter, randomized, crossover trial. Am J Kidney Dis. 2016;68(5):752-762.
10. NxSTAGE Chronic Cartridges. Available at: https://www.nxstage.com/hcp/products/chronic-cartridges/. Accessed March 23, 2020.
11. Kleger GR, Fassler E. Can circuit lifetime be a quality indicator in continuous renal replacement therapy in the critically ill? Int J Artif Organs. 2010;33(139-146.
12. Clark WR. Hemodialyzer membranes and configurations: A historical perspective. Semin Dial. 2000;13(5):309-311.
13. Twardowski ZJ. History of hemodialyzers’ designs. Hemodial Int. 2008;12(2):173-210.
14. Ponte B, Tenorio MT, Hiller R, Candela A, Lianio F. Continuous dialysis by gravity through the filter of the extracorporeal membrane oxygenation. Nephrol Dial Transplant. 2007;22(12):3676-3677.