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# Extracorporeal Immunomodulation Treatment and Clinical Outcomes in ICU COVID-19 Patients

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**OBJECTIVES:** To evaluate safety and clinical outcomes of extracorporeal immunomodulation treatment with a selective cytopheretic device (SCD) in COVID-19 ICU patients with multiple organ failure.

**DESIGN:** Two-center, prospective, single-arm treatment clinical trial.

**SETTING:** ICUs at two academic medical centers between September 2020 and July 2021.

**PATIENTS:** Twenty-two COVID-10 patients in the ICU with acute respiratory distress syndrome who required mechanical ventilation. Nearly all included patients in the intervention group except one had acute kidney injury requiring continuous renal replacement therapy (CRRT). Sixteen subjects meeting enrollment criteria were selected as contemporaneous controls from a concurrent prospective registry CRRT trial.

**INTERVENTION:** Treatment with an SCD integrated into a continuous renal replacement extracorporeal blood circuit for up to 10 days to provide autologous leukocyte cell processing to immunomodulate the hyperinflammatory disease state of COVID-19.

**MEASUREMENTS AND MAIN RESULTS:** SCD treatment in COVID-19 ICU patients with multiple organ failure demonstrated an acceptable safety profile with no device-related serious adverse events. Treatment of these patients resulted in the selective removal of highly activated circulating leukocytes as determined by flow cytometry. Significant reductions were observed in the elevated plasma levels of eight cytokines and biomarkers, including interleukin (IL)6, IL15, IL10, and soluble ST2, which are predictive of mortality in COVID-19 patients. Significant improvements of leukocytosis and $Po_2/Fio_2$ ratios occurred during treatment not observed in the control group. SCD-treated subjects had a reduction in 60-day mortality of 50% compared with 81% in the control cohort. The subjects who received greater than 96 hours of SCD treatment, per protocol, had a further reduction in mortality to 31% ($p < 0.012$).

**CONCLUSIONS:** Extracorporeal immunomodulation therapy with an SCD demonstrated safety without any device-related serious adverse events. As a rescue therapy in COVID-19 ICU patients progressing to multiple organ failure despite maximal pharmacologic and organ support interventions, SCD treatment resulted in improved clinical outcomes. This autologous leukocyte cell processing technology may provide a new approach in the treatment of unremitting hyperinflammation of COVID-19.

**KEY WORDS:** acute kidney injury; acute respiratory distress syndrome; COVID-19; extracorporeal therapy; immunomodulation; intensive care unit

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an enveloped RNA beta coronavirus (1, 2). Most infected individuals have no or mild-to-moderate symptoms, but a small subset may worsen clinically and require hospitalization (3). These hospitalized



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patients may progress further to acute respiratory distress syndrome (ARDS) requiring mechanical ventilation (MV) and, at times, extracorporeal membrane oxygenator (ECMO) support (4). Accumulating evidence suggests that this progression arises from "cytokine storm" defined as excessive inflammation and uncontrolled release of proinflammatory cytokines, leading to endothelial dysfunction and consequent organ failure (5–8). COVID-19 also promotes acute kidney injury (AKI) in over one-third of hospitalized patients and is an independent risk factor for death. ICU patients with COVID-19 and severe AKI requiring renal replacement therapy (RRT) have very high mortality rates (up to 82%) (9–12). New and innovative therapies are needed to reduce these extremely high mortality rates both from COVID-19 infections in the ongoing pandemic and for new COVID-19 variants currently unknown without available efficacious therapies.

The current therapeutic approach to hospitalized COVID-19 patients is the use of escalating therapy determined by the development of progressive respiratory insufficiency. This approach includes the antiviral agent, remdesivir, and immunosuppressant corticosteroids (13). Despite these interventions, some patients continue to worsen with acute respiratory insufficiency and ARDS, thereby requiring MV and/or ECMO. Similarly, those who progress to severe AKI are supported with RRT, most often requiring continuous renal replacement therapy (CRRT).

Despite these advances in pharmacologic treatments for hospitalized COVID-19 patients, hospital mortality rates continue to be unacceptably high. Additional approaches with sorbent-based extracorporeal therapies to reduce pathogen load or capture circulating blood cytokines have been evaluated with little evidence for clinical efficacy as well as, perhaps, safety concerns (14–19). Another extracorporeal therapeutic device with a fundamentally different mechanism of action is directed to immunomodulation of circulating leukocytes of the innate immune system. This approach focuses on the central effector cells responsible for excessive cytokine production rather than removing a small percentage of the systemic cytokine pool. This device is called the selective cytopheretic device (SCD) and when incorporated into an extracorporeal blood circuit preferentially binds activated circulating neutrophils and monocytes. These bound leukocytes are deactivated and returned back to the systemic circulation (20). This continuous cell processing activity results in measurable diminution of excessive inflammatory responses with improvement of solid organ dysfunction in a variety of preclinical and clinical studies, including sepsis, AKI, ischemia/reperfusion injury, intracerebral hemorrhage, cardiopulmonary bypass, chronic kidney disease, and type 2 diabetes mellitus (21–28). This approach was recently evaluated under expanded/emergency use in four ICU COVID-19 patients with cytokine storm and severe ARDS requiring ECMO, and the encouraging results in the first two cases treated were reported (29). With these encouraging results, a pilot feasibility clinical trial was undertaken to further evaluate SCD treatment in critically ill COVID-19 ICU patients with ARDS on MV and/or AKI requiring CRRT. The results are detailed in this report.

## MATERIALS AND METHODS

This clinical study was a treatment arm-only investigation at two clinical sites and was performed under a Food and Drug Administration (FDA)-approved investigational device exemption (G150179; clinicaltrials.gov NCT 04395911). Each enrolling site had local institutional review board approval (University of Michigan: 180159/181353; University of Kentucky: 59366) to undertake this clinical investigation. All participants or their Legal Authorized Representative signed informed consent before enrollment into this study. SCD cartridges were provided by the sponsor of the clinical trial (SeaStar Medical, Denver, CO).

The two medical centers were selected in this pilot feasibility study because of their involvement in CRRTnet, an ongoing prospective multicenter observational study of CRRT practices (30). This registry identified COVID-19 ICU patients on CRRT to serve as contemporaneous controls (CCs) to the SCD treatment group.

Twenty-two subjects were enrolled between September 29, 2020, and July 6, 2021. All patients were treated with the SCD integrated into a CRRT circuit (see **Supplemental Fig. 1**, http://links.lww.com/CCX/A989), utilizing a Prismaflex CRRT pump system (Baxter, Deerfield, IL). SCD formulation and treatment implementation are detailed in **Supplemental Appendix A** (http://links.lww.com/CCX/A989).

Subjects were enrolled into the study if they met all inclusion and exclusion criteria including a positive reverse transcriptase-polymerase chain reaction COVID-19 test (see **Supplemental Table 1**, http://links.lww.com/CCX/A989) and after informed consent was obtained. An inclusion criterion of intent to treat with SCD for at least 96 hours was included in the original clinical protocol due to prior clinical experience demonstrated that 72 to 96 hours of treatment was required to see clinical and laboratory improvement. For the CC group, all ICU patients from CRRTnet were identified with COVID-19 disease and selected after meeting all inclusion/exclusion criteria similar to the treated group (27). Only patients from the registry that began CRRT treatment during the study period were included into the CC group. Clinical parameters of this control group were collected beginning on the first day of CRRT. SCD treatment consisted of up to 10 days of continuous therapy with a new SCD placed in the circuit every 24 hours. The key primary end points of this evaluation were mortality at day 60 and dialysis dependency at day 60 (day 90 post hoc). Secondary end points included safety and device integrity, $Po_2/Fio_2$ (P/F) ratios, and urine output.

The incidence and severity of adverse events were documented and were reviewed by an independent Safety Review Committee (SRC).

### Immunologic Parameters

A subgroup of eight subjects were evaluated for plasma biomarkers and leukocyte cytometric analysis. These samples were obtained at baseline just prior to initiation of SCD treatment and after 1, 3, 5, 7, and 9 days of treatment just prior to SCD replacement on that day as well as 24 hours after the end of SCD treatment. On the same days of blood analysis, SCDs were evaluated with elution of bound cells from the extracapillary space, as previously described (21). See **Supplement Appendix B** and **Supplemental Table 2** (http://links.lww.com/CCX/A989) for detailed description of methods and materials for cytokine and biomarker analysis and for leukocyte cytometric analysis.

### Statistical Methods

All data are expressed as mean ± SE. Comparison of mortality rates was calculated from 2 × 2 contingency table with chi-square analysis with Yates' correction. Effects of SCD on various clinical and immunologic parameters within the treated group were evaluated with paired Student *t* test. Comparison of the WBC counts between the treated and contemporaneous nontreated groups was made with analysis of variance. Statistical significance was defined as $p < 0.05$.

## RESULTS

### Clinical Characteristics

Twenty-two subjects were enrolled in this study, 13 at site 1 and nine from site 2 during the study period from September 29, 2020, to July 6, 2021. Although the FDA-approved protocol allowed enrollment of COVID-19 patients with ARDS on MV without AKI and CRRT, only one patient was enrolled into this trial without AKI-requiring CRRT. Thus, all patients but one had AKI, and all were on CRRT and MV; nine were on ECMO support. All enrolled patients were treated with corticosteroids, either dexamethasone or hydrocortisone (31, 32 38, 39). The majority of enrolled patients also received remdesivir. Sixteen patients were included in the CC group: nine from site 1 and seven from the site 2. Sixteen of the SCD treated patients received greater than 96 hours of SCD treatment: 12 at site 1 and four at site 2. This latter subgroup is called SCD.96 cohort since the inclusion criteria required an intent to treat for at least 96 hours.

The baseline demographic and clinical characteristics were generally similar between the SCD-treated and CC groups (Table 1). The acuity of illness in both groups was near-identical with Sequential Organ Failure Assessment scores near 12; all were on MV, and most were on inotropes/vasopressors.

### Clinical End Points

Mortality rate of the SCD-treated group at 60-day postinitiation of SCD treatment was 50% (11/22) and was 31% (5/16) for the SCD.96 subgroup. The CC group had a mortality rate of 81%, which was statistically similar to the SCD-treated group ($p = 0.102$), but significantly worse than the SCD.96-treated group ($p = 0.012$), as displayed in **Figure 1**. Of note, all patients on ECMO in the CC group did not survive (4/4), while four of nine (44%) survived in the treated group. For dialysis dependency at 60 days in the SCD-treated group, 60%

**TABLE 1.**
**Clinical Characteristics of Selective Cytopheretic Device–Treated and Nontreated Control Subjects**

| Characteristic | Selective Cytopheretic Device Treated, *n* = 22 | Nontreated Control, *n* = 16 |
|---|---|---|
| Age, mean (SD) | 53 (17.7) | 56 (13.4) |
| Women, *n* (%) | 5 (22.7) | 8 (50) |
| Men, *n* (%) | 17 (77.3) | 8 (50) |
| Race, *n* (%) | | |
| Black | 3 (14) | 5(31) |
| White | 17 (77) | 11 (69) |
| Asian | 0 | 0 |
| Other or unknown | 2 (9) | 0 |
| Ethnicity, *n* (%) | | |
| Hispanic | 1 (4.5) | 0 |
| Non-Hispanic | 19 (86) | 16 (100) |
| Other | 2 (9) | 0 |
| Body weight (kg), mean (SD) | 112.4 (26.9) | 102.6 (28.5) |
| Body mass index (kg/m$^2$), mean (SD) | 36.92 (10.4) | 36.5 (12.2) |
| Comorbidities, *n* (%) | | |
| Hypertension | 13 (59) | 11 (69) |
| Chronic heart failure | 1 (4.5) | 1 (6) |
| Diabetes mellitus | 10 (45.5) | 5 (31) |
| Chronic obstructive pulmonary disease | 2 (9) | 0 |
| Asthma | 3 (14) | 0 |
| Peripheral vascular disease | 1 (4) | 0 |
| Chronic liver disease | 0 | 0 |
| Chronic kidney disease (stages 3 and 4) | 3 (14) | 2 (12.5) |
| Cancer | 2 (9) | 1 (6) |
| Sequential Organ Failure Assessment score, mean (SD) | 11.8 (3) | 12.5 (2.8) |
| Mechanical ventilation, *n* (%) | 22 (100) | 16 (100) |
| Extracorporeal membrane oxygenator, *n* (%) | 9 (40) | 4 (25) |
| Inotropes/vasopressors, *n* (%) | 20 (91) | 11 (69) |

of the survivors (6/10) had not recovered renal function, but post hoc follow-up at 90 days demonstrated that only 30% (3/10) still required dialytic support. As a secondary end point, the course of P/F ratio was monitored to assess respiratory function improvement during SCD treatment. As displayed in **Figure 2**, the P/F ratios showed continuous improvement after 4 days of SCD treatment. At days 8–10 of SCD treatment, the P/F ratios were significantly higher than the values on days 1–3 ($p < 0.004$). The CC group showed no change in P/F ratios during the 10 days of observation. This group's baseline P/F ratio was 120 ± 15 versus 125 ± 21 at 10 days.

## Safety Assessment

Fifty serious adverse events (SAEs) occurred in 18 subjects of the SCD-treated group (**Supplemental Table 3**, http://links.lww.com/CCX/A989). Of note, 22 nosocomial and opportunistic infections were reported in 12 subjects during the entire 60 day follow-up period. Sixteen of the 22 infections occurred after SCD

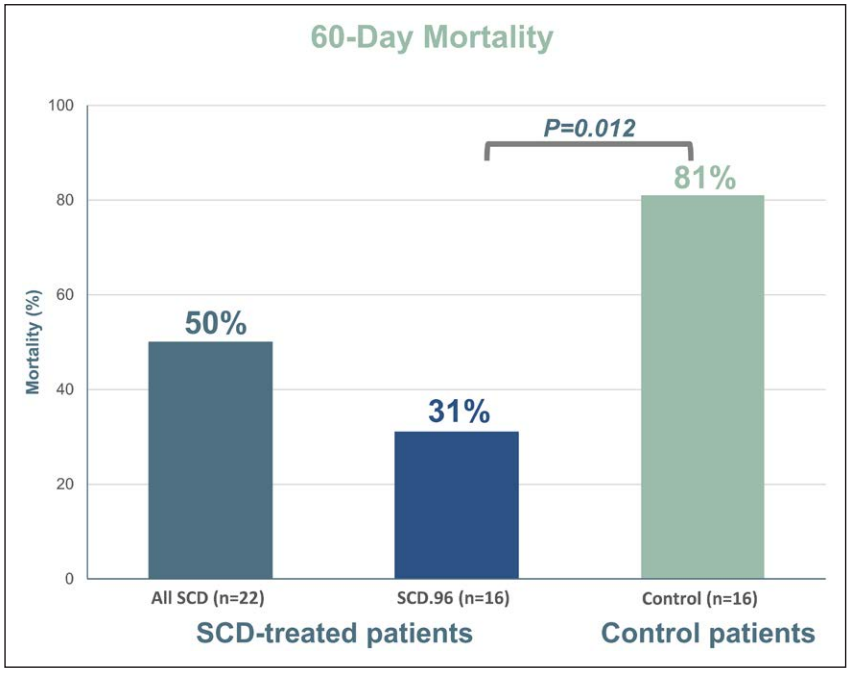


**Figure 1.** Mortality rates of various clinical trial groups; 60-d mortality rates of selective cytopheretic device (SCD) and SCD.96-treated groups, and contemporaneous control group. SCD.96 subgroup comprised subjects treated with SCD for at least 96 hr, as per protocol. *p* values were calculated from chi-square with Yates correction.

treatment. None of these SAEs were device-related as determined by the site clinical investigators and the independent SRC. No regional citrate anticoagulation-related adverse events were observed with greater than 90% of measured circuit ionized calcium (iCa) values less than 0.4 mmol/L. Systemic iCa values were within the normal ranges required by the clinical protocol. Two circuit clotting events were reported; clotting was initiated in the hemodialysis catheter in one instance and in the hemofilter in the other. No SCD clotting episodes were reported. No episodes of thrombocytopenia, neutropenia, or leukopenia were observed. In fact, the leukocytosis associated with severity of COVID-19 (33) was significantly reduced after 96 hours of SCD treatment (Fig. 2).

## Cytometric Analysis

To correlate the clinical outcomes of SCD treatment and leukocyte parameters, flow cytometry was undertaken to see changes in cell surface markers of circulating and SCD-bound neutrophils and monocytes before, during, and after SCD treatments. Demonstration of SCD removal of activated leukocytes with changes in circulating phenotypes would link the SCD effects and immunologic rebalancing of the COVID-19-dysregulated immunologic state. The elution of cells from the SCDs after treatment days 1, 3, 5, 7, and 9 demonstrated that the SCD bound on average 6.67% of the circulating pool of neutrophils and 20.8% of the circulating pool of monocytes, respectively. As detailed in **Supplement Appendix C** (http://links.lww.com/CCX/A989) and **Figure 3**, cytometric analysis demonstrated that the SCD bound the more activated circulating neutrophils and monocytes with an effect to diminish the inflammatory activity level and phenotype of circulating leukocytes as determined by the mean fluorescence intensity (MFI) of various cell surface markers.

## Soluble Immunologic Biomarkers

This next analysis was undertaken to evaluate whether SCD removal of substantive numbers of highly activated circulating leukocyte effector cells was able to diminish systemic levels of immunologic mediators associated with the ongoing hyperinflammation and poor outcomes in COVID-19 ICU patients. Recent publications have reported that elevated levels of various cytokines and biomarkers are predictive of mortality in COVID-19 patients (8, 34). The most comprehensive evaluation to date assessed 66 biomarkers from 175 COVID-19 patients and discovered that elevated blood levels of 12 biomarkers (monocyte chemoattractant protein [MCP]-1, interleukin [IL]-15, soluble ST2 [sST2], neutrophil gelatinase-associated lipocalin [NGAL], soluble TNF receptor superfamily 1A [sTNFRSF1A], ferritin, IL-6, S100 Calcium Binding Protein A9 [S100A9], matrix metalloproteinase-9, IL-2, IL-10, and soluble vascular endothelial growth factor receptor 1) were independently associated with mortality (8). Among these 12 when analyzed longitudinally, four of them, specifically sST2, sTNFRSF1A, IL-10, and IL-15, had levels that were separated without crossover between survivors and nonsurvivors throughout hospitalization. The influence of SCD treatment on the baseline elevated levels of 10 of the 12 biomarkers was evaluated during the 10-day course of SCD treatment (**Fig. 4**).

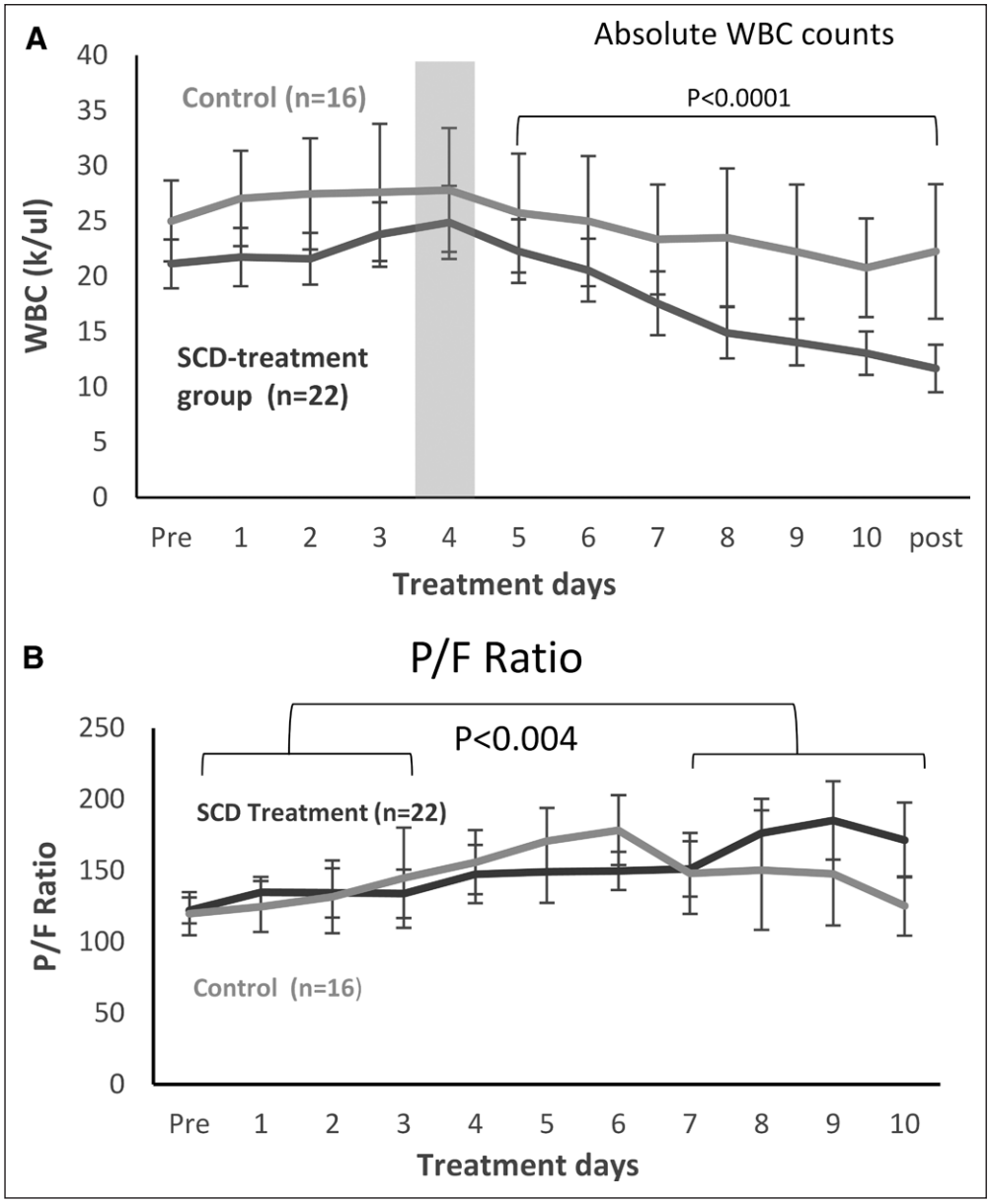


**Figure 2.** Clinical parameter improvements with selective cytopheretic device (SCD) treatment. **A**, Daily total WBCs of the SCD-treated vs control groups. SCD treatment resulted in a significant decline to normal levels over the course of 10 treatment days compared with controls, as determined by analysis of variance. **B**, Improvement of $Po_2/Fio_2$ ratios comparing the values during the first 3 d and the last 3 d of treatment during SCD treatment. No improvements were observed in the contemporaneous control group.

As demonstrated, despite being on corticosteroids, most of the measured biomarkers were elevated above normal and approached or surpassed median levels reported for severe COVID-19 patients who did not survive. Of the 10 predictive biomarkers assessed, eight of these biomarkers had significant reductions during SCD treatment except for sTNFRSF1A and S100A9. These reductions included three of the four soluble mediators (IL-15, IL-10, and sST2), which have been shown to have longitudinal and noncrossover separation of levels between survivors and nonsurvivors through the duration of their hospitalization (Fig. 3).

## DISCUSSION

COVID-19 is an infection caused by the coronavirus, SARS-CoV-2. In some patients, COVID-19 may progress to severe respiratory failure and, at times, multiple organ failure (1, 2). Similar to other severe infections, the organ injuries are due in large part to a dysregulated and excessive systemic hyperinflammatory state (5–8). Central to this process is the activation of the innate immunologic system, primarily circulating neutrophils and monocytes, interacting with tissue microvasculature with release of cytokines, critical soluble mediators of the inflammatory response. If this dysregulated hyperinflammatory state is severe and prolonged, multiple organ damage occurs due to the combination of ischemic and toxic damage emanating from the excessive and dysregulated innate immunological response to infection (35). Recognition of this process in COVID-19 has led to progress in treating this disease with pharmacologic interventions including antivirals, cytokine inhibitors, and immunosuppression with corticosteroids. Despite these improvements in this treatment regimen, some patients still progress to multiple organ failure and death. Therefore, other approaches

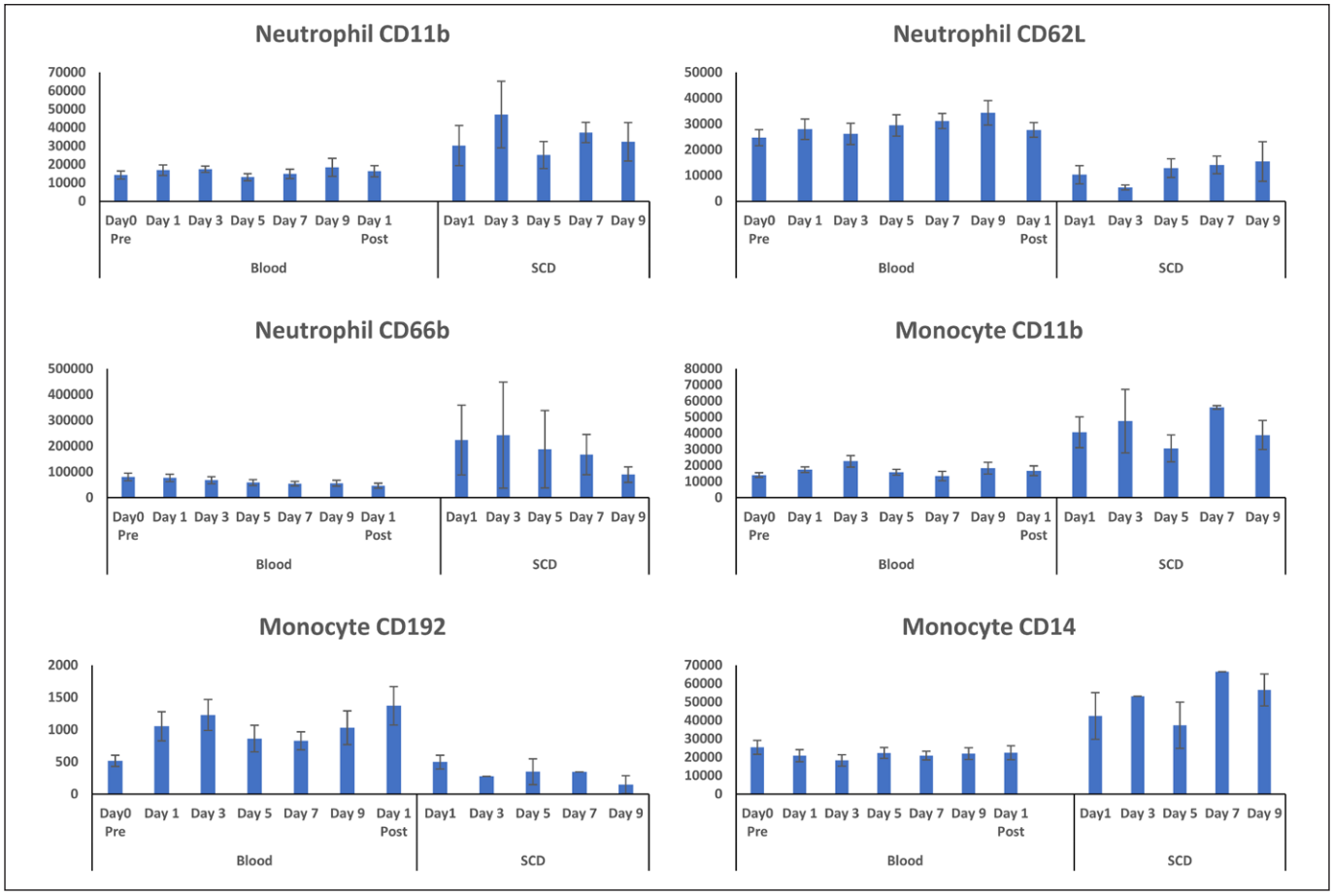


**Figure 3.** Selective cytopheretic device (SCD) treatment effects on leukocytes by cytometric analysis. Each graph displays the MFI of various cell surface markers on either circulating blood neutrophils or monocytes during the 10 d course of daily SCD treatment. Also displayed are the MFIs of the eluted neutrophils or monocytes from the SCD after treatments on days 1, 3, 5, 7, and 9. All monocyte graphs depict the MFI of the entire monocyte population.

directed to the immunologic effector cells central to this hyperinflammatory state need to be evaluated. Accordingly, extracorporeal immunomodulatory SCD treatment was assessed for safety and potential efficacy of SCD treatment in severely ill COVID-19 ICU patients with ARDS on MV and/or ECMO and AKI on CRRT.

A key objective of this clinical trial was to assess first and foremost the safety of SCD treatment in this seriously ill patient population with ARDS and severe AKI requiring both MV and CRRT.

The safety profile of SCD treatment in this study, like other SCD clinical trials, was excellent with no device-related SAEs, including nosocomial or opportunistic infections. With these important safety results, the data from the trial could be evaluated to assess the clinical outcomes associated with SCD treatment compared with a CC group. In addition, exploratory research analysis could measure changes in leukocyte phenotypes and inflammatory biomarkers during SCD treatment to provide mechanistic insight into this approach.

The results of this clinical study clearly demonstrated that SCD treatment selectively removed the more activated circulating leukocytes from COVID-19 patients and diminished the inflammatory phenotype of circulating effector cells central to maintaining the hyperinflammatory state. Flow cytometry demonstrated that the SCD bound the more activated circulating neutrophils and monocytes, as measured with well-accepted cell surface activation markers of CD11b and CD66b and CD11b and CD14, respectively (36-40). Of importance, the decline of circulating neutrophil 66b MFIs during SCD treatment suggests a significant

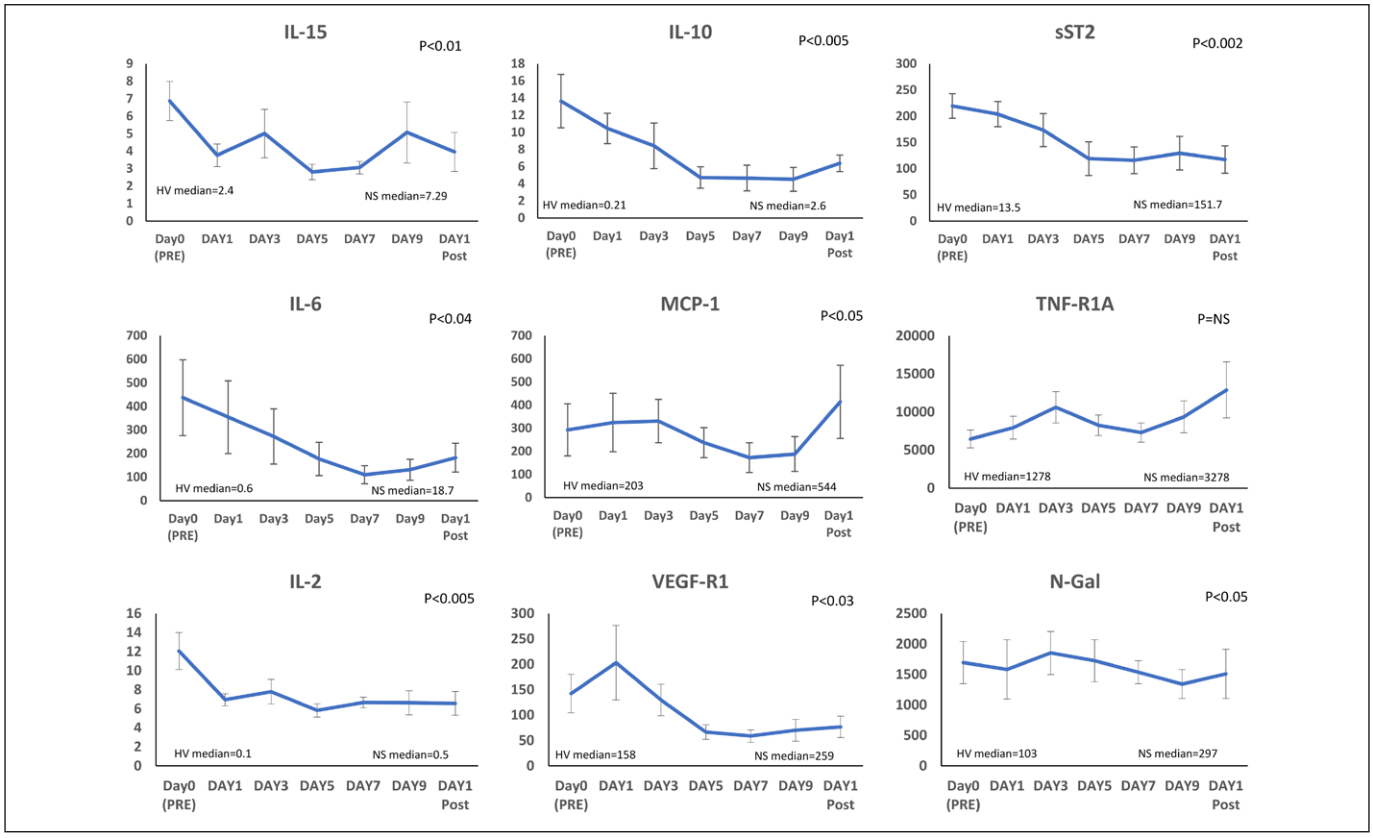


**Figure 4.** Selective cytopheretic device (SCD) treatment effects on immunologic biomarkers. Time course of various biomarkers before (Day0pre), during, and after (Day1post) SCD treatment. For each panel, the *p* value was determined by paired *t* test of Day0pre to lowest value during treatment. Healthy volunteer [HV] median and nonsurvivor [NS] median refer to the median values reported in (8). All values are in pg/mL.

reduction of a cell surface marker associated with severity of sepsis and COVID-19 (44, 45). The cell surface expression of circulating monocyte CD192 also suggests an associated SCD-related change in the monocyte pool.

The SCD removal of the highly activated circulating effector cells of the innate immunologic system resulted in declines of the elevated plasma levels of various inflammatory biomarkers and cytokines associated with poor clinical outcomes (8). Measurements of 10 of these plasma moieties predictive of mortality demonstrated that eight had significant reductions in their elevated levels during SCD treatment. The declines were seen in a spectrum of immunologic markers associated with monocyte/macrophage activation, nuclear factor kappa B [NF-kB]-dependent mediators, neutrophil activation, T cell immune response, endothelial integrity, and sepsis severity (8). These biomarker and cytokine levels in the enrolled patients were highly elevated compared with healthy normal volunteers and were elevated despite being treated with corticosteroids. The elevated levels of various cytokines observed in the SCD-treated patients occurred despite use of steroids with further progression of the disease state. The fact that SCD treatment was able to have a significant lowering of multiple cytokines and biomarkers of inflammation suggests that this interventional approach had a measurable effect on the dysregulated inflammatory state even in the presence of a powerful immunosuppressant agent. These declines may also reflect the normal course of recovery from the hyperinflammatory state promoted by COVID-19.

Improvement of this dysregulated hyperinflammatory state in these COVID-19 patients was reflected with the systemic WBC declines after 4 days of SCD treatment compared with the CC group. By the end of 10 days of treatment, WBC had returned to normal. Leukocytosis has been clearly shown to be a predictive biomarker for COVID-19 severity (33) and was able to be reduced to normal levels with SCD treatment. Improvement of damaged lung function was also observed after SCD treatment with increasing P/F

ratios after 4 days. This observation coupled with the decline in WBC after 4 days of treatment in enrolled subjects emphasizes in this severe inflammatory disease that SCD treatment takes at least 96 hours before showing clinical improvement and recovery especially with the current standard use of antivirals and corticosteroids.

Most importantly, these early signs of improvement of systemic inflammation and respiratory function in the SCD-treated group were eventually translated to improved survival outcomes in a patient cohort of severely ill COVID-19 ICU patients who had progressed despite pharmaceutical and organ support interventions. The evaluation of a CC group at both clinical trial sites demonstrated the grim prognosis of these patients who have ARDS requiring MV/ECMO and AKI requiring CRRT despite treatment with corticosteroids and/or remdesivir. The mortality rate in this control group was 81% and is similar to other publications (7–10). The SCD-treated group had a mortality rate of 50%. The SCD.96 subgroup of 16 patients had a mortality rate of 31% (11/16). Of importance, in comparison with this SCD.96-treated group, seven patients in the CC group died within 96 hours of initiating CRRT resulting in a mortality rate of 67% (6/9) as a direct comparison with the SCD.96 subset of enrolled treated subjects. For the primary end point of dialysis dependency at 60 days in the treated group, 60% (6/10) of the survivors had not recovered renal function. Post hoc follow-up at 90 days demonstrated that half of these survivors recovered renal function, so that at day 90, only 30% of the survivors (6/9) were dialysis-dependent. This rate of nonrecovery of renal function is similar to other COVID-19 reports of AKI requiring RRT but higher than what has been observed with SCD treatment of non-COVID-19 ICU patients with AKI requiring RRT and multiple organ failure (26).

The major limitation in this clinical study is that the control group was a nonrandomized CC group at each clinical site. A patient was included in the CC group only if the subject met all inclusion and exclusion criteria of the trial and was in the ICU and started CRRT during the enrollment period of the study. Clinical parameters of these patients were collected starting at the first day of CRRT. Accordingly, these control patients were in the early phase of multiple organ failure and were, therefore, reasonable comparators to the SCD-treated group despite the changes in standard practice, such as corticosteroids, and changes in infective variant of COVID-19 during this clinical study. An additional limitation is the modest data set in the control group for comparisons with the treated group. Finally, a potential bias in comparing the treated to the control groups may have arisen due to subjects who consented to the treatment may have had different preferences for duration of life support and withdrawal of care compared with the controls.

## CONCLUSIONS

Extracorporeal SCD immunomodulation treatment of COVID-19 ICU patients with multiple organ failure requiring both MV and CRRT was safe without device-related adverse events. Improvements in leukocytosis and P/F ratios in the enrolled subjects were observed within 4 days of SCD treatment initiation. The SCD was used in this trial as a last resort treatment strategy in ICU COVID-19 patients who were progressing to severe multiple organ failure despite proven pharmacological approaches and organ substitution intervention. Compared with a similar CC group not treated with SCD, the reduction in 60-day mortality was compelling. Earlier intervention may be even more effective to lower mortality rate in this group of severely ill patients. A pivotal multicenter, randomized control clinical trial is planned to assess the safety and efficacy of SCD treatment in non-COVID-19 patients with severe AKI requiring CRRT. Favorable results from this planned study would allow for a premarket approval submission to the FDA.

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