Efficacy of Hemoperfusion in Severe and Critical Cases of COVID-19

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Research Article

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Abstract

Introduction

In critically ill COVID-19 patients, uncontrolled over-production of inflammatory mediators is observed, dominantly. The excessive immune response give rise to multiple organ dysfunction. Implementing extracorporeal therapies may be useful in omitting inflammatory mediators and supporting different organ systems. We aimed to investigate the effectiveness of hemoperfusion in combination with standard therapy in critically ill COVID-19 patients.

Method

We conducted a single-center, matched control retrospective study on patients with confirmed SARS-CoV-2 infection. Patients were treated with hemoperfusion in combination with standard therapy (hemoperfusion group) or standard treatment (matched group). Hemoperfusion or hemoperfusion and CRRT (continuous renal replacement therapy) therapies were initiated in hemoperfusion group. The patients in the matched group were matched one by one with the hemoperfusion group for age, sex, the oxygen saturation (SPO2) at the admission and the frequency of using invasive mechanical ventilation during hospitalization. Two types of hemoperfusion cartridges used in this study were Jafron© (HA330) or cytosorb® 300.

Result

A total number of 128 COVID- 19 confirmed patients were enrolled in this study; 73 patients were allotted to the matched group and 55 patients received hemoperfusion. The median SPO2 at the admission in control and hemoperfusion groups was 80% and 75%, respectively (P-value=0.113). The mortality rate was significantly lower in hemoperfusion group compared to the matched group (67.3% vs. 89%; P.value=0.002). The median length of ICU stay was statistically different in studied groups (median, 12 days for hemoperfusion group vs. 8 days for the matched group; P<0.001). The median of final oxygen saturation was statistically higher and median of PaCO2 was lower in hemoperfusion group compared to the matched group.

Conclusion

Among critically ill COVID-19 patients, the use of hemoperfusion reduces the mortality rate and improves oxygen saturation and PaCO2.

Introduction

On 11th March 2020, COVID-19 was declared a global pandemic by World Health Organization (WHO). Infected cases with COVID-19 represent a wide spectrum of symptoms ranging from mild to severe forms. Although the number of infected cases with mild or no symptoms is significant, COVID-19 leads to

critical illness in some cases. Multiple organ failure can be expected among severe forms of infection with COVID-19. Therefore, extracorporeal organ support may be required (1, 2).

In some patients, excessive immune response against SARS-CoV-2 results in cytokine storm characterized by uncontrolled overproduction of pro-inflammatory cytokines (e.g., Interferon γ, interleukin (IL-) 1B, IL-6, IL-12) (3). Increased circulating levels of pro-inflammatory cytokines and chemokines are associated with endothelial dysfunction and microvascular and macrovascular thrombosis (4). Therefore, cytokine storm can result in multiple organ failure including acute respiratory distress syndrome (ARDS) and acute kidney injury (AKI). Multiple organ failure is responsible for high mortality among at least severe cases of COVID-19 (5). It has been shown that there is a positive association between mortality rate and levels of pro-and anti-inflammatory cytokines (6).

Based on the pathophysiology of COVID-19, implementing of sequential extracorporeal therapies is worthwhile in order to eliminating of extra inflammatory mediators (7). Hemoperfusion is an extracorporeal blood purification modality. Throughout hemoperfusion process, anticoagulated blood is circulated through a sorbent containing cartridge (or column) and large endogenous and exogenous molecules including targeting cytokines, endotoxin and virus particles are removed depending on the type of sorbent (for example, pure resins, polymyxin- coated resins, or heparin-coated resins)(1, 8). Hemoperfusion devices adsorb and remove both pro-inflammatory and anti-inflammatory cytokines non-selectively. Therefore, the other side of coin is excessive immunosuppression or removing anti-inflammatory mediators (7). A study by De Vriese et al. showed that levels of pro- and anti-inflammatory cytokines decreased significantly after performing continuous venovenous hemofiltration in patients with septic shock and acute kidney injury(9). However, based on a recent expert review, information regarding the fact that implementing of hemoperfusion provides beneficial effects in quenching cytokine storm products is limited and sporadic.

The Emergency Use Authorization (EUA) authority allowed FDA to grant temporary authorization for four hemoperfusion devices for treatment of severe COVID-19 with cytokine storm (10). To date, there is no effective and promising treatment, hence extracorporeal therapies can be a treatment option for improving COVID-19 outcomes and prevent organ dysfunction. We performed a matched control retrospective study to investigate the efficacy of hemoperfusion in combination with standard therapy in critically ill COVID-19 patients.

Material And Methods

Study design

We conducted a single-center, matched control retrospective study on cases with confirmed SARS-CoV-2 infection (positive reverse transcriptase polymerase-chain-reaction (RT-PCR) and/or positive computed tomography scan (CT Scan findings)). The study's participants were selected from those who hospitalized between 17 October, 2020 and 17 January,2021 at our hospital (a major referral medical center for COVID-19 outbreak). The study was approved by Medical Research Committee for Research

Ethics and signed informed consents were obtained from all patients or their legally authorized representatives. This study is registered with IRCT (Iranian registry of clinical trial), IR.SBMU.RETECH.REC.1399.582.

Patients

Inclusion Criteria for this study were 1) Adults≥18 years old 2) Oxygen saturation (SPO2) ≤ 86% or respiratory rate ≥30 3) Diffuse bilateral pulmonary opacities without effusions in chest CT scan 4) Respiratory failure not fully explained by cardiac failure or fluid overload 5) Within 1 week of a known clinical insult or new/worsening respiratory symptom and 6) Hospitalization days ≤14 from the sign and symptom onset. The manifestations were including at least one of the radiation contactless body temperature ≥37.8, cough, shortness of breath, nasal congestion/ discharge, myalgia/arthralgia, diarrhea/vomiting, headache or fatigue on admission.

Patients in the matched group also meet the same criteria defined for hemoperfusion group and were selected from the same patients within similar time period. Patients in matched group were also matched one by one with the hemoperfusion group for age, sex, the oxygen saturation (SPO2) at the admission and the frequency of using invasive mechanical ventilation during hospitalization.

Treatment

Hemoperfusion and matched groups received IFN-β1a (Recigen) (Subcutaneous injections of 44 μg (24,000 IU) on days 1, 3, 6) + remdesivir (200mg first dose then 100 mg daily dose for 5 days) + methylprednisolone pulse therapy (1000 mg for three days then 1 mg/kg twice daily) and standards of care including the necessary oxygen support, non-invasive, or invasive mechanical ventilation. In addition, hemoperfusion or hemoperfusion and CRRT (continuous renal replacement therapy) therapies were initiated in the hemoperfusion group.

Hemoperfusion treatment: The patients were administered hemoperfusion through femoral venous catheters at a blood flow rate of 250-300 mL/min. Two types of hemoperfusion cartridges used in this study were Jafron© (HA330) for 4 hours or cytosorb® 300 for 8 to 12 hours.

Hemoperfusion + CRRT: Blood was filtered and returned to the patient with replacement fluid. The modality of CRRT was pre-dilution continuous venovenous hemofiltration (CVVH). The volume of the CRRT dose was adjusted according to individual patient requirements nevertheless the CRRT dose was usually 20-25 ml/kg per hour and access was achieved through a central venous catheter placed in one of the large central veins. The cartridges were used in this method were Jafron© (HA330) for 8 hours or CytoSorb® 300 for 12-24 hours.

Based on the improvement in patient's clinical status after hemoperfusion, including being able to reduce mechanical ventilation support in the intubated patients or improve oxygen saturation in non-intubated patients, the medical team decided to perform second or third course of hemoperfusion.

Sodium heparin was used as an anticoagulant and administered as a bolus dose and continues and try to maintain activated partial thromboplastin time ratio (APTTr) ≤2. The loading dose of heparin in hemoperfusion therapy was 3000-1000 IU and the maintenance dose was between 1000 to 2000 IU per hour. The loading dose of heparin in hemoperfusion plus CRRT therapy was between 2000 to 5000 IU and the maintenance dose was between 500-1000 IU per hour (11). In patients with coagulopathy and patients treated with other anticoagulants the heparin was not used.

Outcome Measures

We studied the clinical progression of two groups during their hospital admission. The mortality rate in the late phase of admission (including the survival time), duration of hospitalization, intubation length, oxygen saturation, arterial blood gas findings, complete blood count findings and, C-Reactive Protein (CRP) have been compared between two groups.

Statistical analysis

Frequency rates and percentages were used for categorical variables, and Interquartile Ranges (IQRs) and median were used for continuous variables. For comparison the non-normal continuous variables, Mann–Whitney U test was used. Chi-Square test was used for comparing the frequency of categorical variables. Cox proportional hazard regression model and Kaplan–Meier curve (with logrank test) were also applied to calculate the Hazard rate (HR) with 95% Confidence Intervals (CIs). STATA software version 14.0 was used to perform the statistical analyses and 0.05 was considered as statistically significant level.

Results

Of all recruited patients (n = 128), 55 patients received hemoperfusion and 73 patients were allotted to the control group who were matched for age, gender, oxygen saturation and incubation rate with hemoperfusion group. Mean (SD) age of total participants was 59.6 (10.92). Distribution of male and female gender was 64.1% and 35.9%, respectively. No significant difference was observed in terms of age and gender between hemoperfusion and matched control group. Table 1 outlines demographic and baseline clinical factors in two studied groups. Although Majority of clinical factors did not reach a significant difference between two groups, hypertension rate, ischemic heart disease as the underlying conditions, PH, $PaCO_2$, lymphocyte count, platelet count and creatine phosphokinase were significantly different (Table 1).

Table 1
Characteristics of the Patients at Baseline.

Parameters	Total (n = 128)	Hemoperfusion (n = 55)	Matched (n = 73)	p-value
Characteristics				
Age (year) — mean (SD)	59.6 (10.92)	57.5 (10.9)	61.2 (11.2)	0.052
Male sex - no. (%)	82 (64.1%)	40 (72.7%)	42 (57.5%)	0.076
Underlying conditions				
Diabetes	45 (36.0%)	17 (31.5%)	28 (39.4%)	0.359
Hypertension	54 (43.9%)	17 (31.5%)	37 (53.6%)	0.014
Cerebrovascular Accident (CVA)	4 (3.3%)	2 (3.7%)	2 (2.9%)	0.803
Chronic Kidney Disease (CKD)	7 (5.7%)	1 (1.9%)	6 (8.7%)	0.134
Ischemic Heart Disease	22 (17.9%)	3 (5.6%)	19 (27.5%)	0.002
Respiratory Factors				
Oxygen Saturation (SpO2) - median (IQR)	79 (68–84)	75 (66.0-82.25)	80 (70–85)	0.113
PH - median (IQR)	7.4 (7.3–7.44)	7.4 (7.33–7.43)	7.4 (7.35–7.46)	0.031
PaCO2 - median (IQR)	38.2 (29.8–45.2)	40.3 (33.8-47.05)	36 (27.2–42)	0.020
HCO3(DISS) - median (IQR)	23.6 (21.1–27)	23.8 (21.4–27.1)	23 (20.2–26.9)	0.561
White Blood Cell count ($\times 10^{-9}$/liter) — median (IQR)	7.9 (5.5–11.0)	7.3 (5.3.-11)	7.9 (5.6–10.6)	0.868
$< 4 \times 10^{-9}$/liter — no. (%)	9 (7.5%)	4 (7.4%)	5 (7.6%)	
$4–10 \times 10^{-9}$/liter — no. (%)	72 (61.7%)	31 (57.4%)	43 (65.2%)	0.64
$> 10 \times 10^{-9}$/liter— no. (%)	37 (30.8%)	19 (35.2%)	18 (27.3%)	
Lymphocyte count ($\times 10^{-9}$/liter) — median (IQR)	9.5 (5.5–14)	10.4 (7.5–17.4)	7.3 (4.9–12)	0.001

Parameters	Total (n = 128)	Hemoperfusion (n = 55)	Matched (n = 73)	p-value
≥ 1.0 ×10^{-9}/liter — no. (%)	35 (29.2%)	21 (38.9 %)	14 (21.2%)	0.034
< 1.0 ×10^{-9}/liter — no. (%)	85 (70.8%)	33 (61.1 %)	52 (78.8%)	
Platelet count (×10^{-9}/liter) — median (IQR)	172 (125-233.5)	184 (141–238)	157 (120–231)	0.083
≥ 100 ×10^{-9}/liter — no. (%)	102 (87.2%)	50 (94.3%)	52 (81.3%)	0.035
< 100 ×10^{-9}/liter — no. (%)	15 (12.8%)	3 (5.7%)	12 (18.8%)	
Creatine phosphokinase (CPK)—median (IQR)	1.43 (0.86–2.96)	1.17 (0.73–2.66)	1.65 (1.03–3.03)	0.077
≤ 1.33 µmol/liter — no. (%)	47 (44.8%)	24 (57.1%)	23 (36.5%)	
> 1.33 µmol/liter — no. (%)	58 (55.2%)	18 (42.9%)	40 (63.5%)	0.037
Aspartate Aminotransferase (AST) (U/liter) — median (IQR)	61.5 (46.2–88)	61 (46.2–88.7)	61.5 (45.5–88)	0.966
≤ 40 U/liter — no. (%)	19 (15.8%)	9 (17.3%)	10 (14.7%)	0.699
> 40 U/liter — no. (%)	101 (84.2%)	43 (82.7%)	58 (85.3%)	
Alanine Aminotransferase (ALT) (U/liter) — median (IQR)	44.5 (28–66)	45 (28-64.2)	42 (27.7–66.7)	0.870
≤ 50 U/liter — no. (%)	73 (60.8%)	34 (65.4%)	39 (57.4%)	0.372
> 50 U/liter — no. (%)	47 (39.2%)	18 (34.6%)	29 (42.6%)	
Lactate Dehydrogenase (LDH) (U/liter) - median (IQR)	747 (516–926)	842 (556–1035)	700 (513–895)	0.089
≤ 245 U/liter — no. (%)	6 (5.5%)	4 (8.2%)	2 (3.3%)	0.262
> 245 U/liter — no. (%)	104 (94.5%)	45 (91.8%)	59 (96.7%)	
C-Reactive Protein (CRP) - median (IQR)	42 (27.3–56)	42.3 (31–56)	40.3 (22-56.4)	0.488

Parameters	Total (n = 128)	Hemoperfusion (n = 55)	Matched (n = 73)	p-value
CRP < 6 — no. (%)	3 (3.5%)	1 (2.1%)	2 (5.3%)	0.436
CRP > 6 — no. (%)	82 (96.5%)	46 (97.9%)	36 (94.7%)	
Erythrocyte Sedimentation Rate (ESR) - median (IQR)	48.5 (31.7–60.2)	48.5 (33-61.5)	47.5 (28.2–58.2)	0.383
Ferritin- median (IQR)	622 (502–774)	614 (513–656)	668 (500–809)	0.074

The total number of deaths in our study was 102 (70.9%). In the hemoperfusion group, the mortality rate was significantly lower as opposed to matched control group (67.3% vs 89%; P-value = 0.002). As outlined in Table 2, median length of ICU stay and duration of incubation were significantly higher in hemoperfusion group. Final oxygen saturation was significantly higher in hemoperfusion group whilst PaCO2 was found to be lower in the respect group compared to control group. In addition, C-reactive protein (CRP) were also different between two groups (Table 2).

Table 2
Clinical outcomes of patients in matched group and patients in Hemoperfusion group

Parameters	**Total (n = 129)**	**Hemoperfusion (n = 55)**	**Matched (n = 74)**	***p-value***
Mortality	102 (79.7%)	37 (67.3%)	65 (89%)	0.002
ICU stay — median no. of days (IQR)	10 (6–13)	12 (9–17)	8 (4.5–10.5)	< 0.001
Intubation	88 (69.3%)	35 (64.8%)	53 (72.6%)	0.347
Intubation Length — median no. of days (IQR)	6 (3–8)	8 (5.7–14)	4 (2–7)	< 0.001
Sepsis	38 (34.9%)	15 (40.5%)	23 (31.9%)	0.373
Respiratory factors				
Oxygen Saturation (SpO2) - median (IQR)	70 (60.7–80.2)	80 (73–85)	64 (60–70)	< 0.001
PH - median (IQR)	7.3 (7.2–7.4)	7.4 (7.3–7.4)	7.3 (7.2–7.4)	0.105
PaCO2 - median (IQR)	46.7 (36.2–61.2)	42.9 (33.1–50.3)	53 (39.5–65)	0.006
HCO3 - median (IQR)	23.1 (19.8–26.8)	23.4 (20.3–27)	22.3 (17.1–26)	0.207
White Blood Cell count ($\times 10^{-9}$/liter) - median (IQR)	10.9 (8.3–14.6)	12.2 (9-15.6)	10.5 (7.9–14.5)	0.382
$< 4 \times 10^{-9}$/liter — no. (%)	9 (7.3%)	5 (9.3%)	4 (5.7%)	0.47
$4–10 \times 10^{-9}$/liter — no. (%)	41 (33.1%)	15 (27.8%)	26 (37.1%)	
$> 10 \times 10^{-9}$/liter— no. (%)	74 (59.7%)	34 (63%)	40 (57.1%)	
Lymphocyte count ($\times 10^{-9}$/liter) - median (IQR)	7.7 (4.5–12.6)	5.8 (3.8–11.3)	10 (5.7–13)	0.024
$\geq 1.0 \times 10^{-9}$/liter — no. (%)	51 (42.9%)	19 (35.2%)	32 (49.2%)	0.123
$< 1.0 \times 10^{-9}$/liter — no. (%)	68 (57.1%)	35 (64.8%)	33 (50.8%)	
Platelet count ($\times 10^{-9}$/liter) - median (IQR)	182 (128–250)	170 (104–231)	196 (147–235)	0.101
$\geq 100 \times 10^{-9}$/liter — no. (%)	101 (82.1%)	41 (75.9%)	60 (87%)	0.113
$< 100 \times 10^{-9}$/liter — no. (%)	22 (17.9%)	13 (24.1%)	9 (13%)	

Parameters	Total (n = 129)	Hemoperfusion (n = 55)	Matched (n = 74)	*p-value*
C-Reactive Protein (CRP) - median (IQR)	44 (19.5–62.2)	19.9 (7.7–38.5)	59 (42.9–87.7)	< 0.001
CRP < 6 — no. (%)	12 (12.2%)	9 (22%)	3 (5.3%)	0.013
CRP > 6 — no. (%)	86 (87.8%)	32 (78%)	54 (94.7%)	

To evaluate the effect of hemoperfusion on survival of severe COVID-19 patients, long-rank test was conducted on survival time of hospitalized patients which was statistically different between two groups (median, 12 days for hemoperfusion group vs 8 days for the control group; P < 0.001) and the Kaplan–Meier curve indicated that the cumulative survival was higher for patients in hemoperfusion group compared to their matches (Fig. 1).

Of 55 patients in hemoperfusion group, the number of patients received one, two and three or four courses of hemoperfusion was 18 (32.7%), 14 (25.4%) and 23 (41.9%), respectively. Number of patients received hemoperfusion with cartridge 300 and 330 was 9 and 46, respectively. The number of deaths among patients who had cartridge 300 was 4 (44.4%) and the respect number for patients who had cartridge 330 was 14 (30.4%). No significant association was found between cartridge type and mortality rate in hemoperfusion group.

Cox regression model was employed to calculate hazard of death for patients in matched group compared to hemoperfusion group. Analyses were done in crude and adjusted models. Two significant underlying diseases (hypertension and ischemic heart disease) were not included in multivariate model since the Cochran's Mantel-Haenszel test indicated conditional independence across these two underling diseases for both hypertension (P.value = 0.646) and Ischemic Heart Disease (P.value = 0.400), but age, sex, oxygen saturation and lymphocyte count at the baseline were included as the adjusting factors. According to the analysis in crude model, the hazard rate (HR) of death in matched groups compared to hemoperfusion group was 2.54 (95% CI: 0.1.67–3.87, P < 0.001) and the adjusted HR was 2.39 (95% CI: 1.49–3.83, P < 0.001). Both crude and adjusted analyses revealed that patients who treated in matched group were at higher risk of death compared to patients who treated in hemoperfusion group.

Discussion

Hemoperfusion has been suggested as an effective treatment for COVID-19 patients in conjunction with other conventional remedies. In this study, hemoperfusion group exhibited higher O2 saturation but lower PaCO2 and CRP levels compared to matched control group. An interesting finding of this study was that lower mortality rate was observed among the patients in hemoperfusion group. Jafron® and CytoSorb® are two different manufacturers of hemoperfusion cartridges. Although they employ different methodology for preforming hemoperfusion, their cartridge efficacy has not been compared so far in a study.

Cytokine storm and intensive immune responses have been addressed as the root causes of severe form of COVID-19 infection (12). It has been observed that cytokine storm plays crucial role in exerting end-organ damage and increasing mortality rate among patients with COVID-19. Of all series of cytokines, IL-1, IL-6, IL-10, and TNF-beta are the most remarkable inflammatory factors through the cytokine storm phenomenon (13–15). Furthermore, the most critical role in cytokine storm, patients mortality and the severity of the disease have been attributed to IL-6 (16). At early stages of COVID-19, increased levels of CRP can be associated with sever pulmonary complication like acute respiratory distress syndrome (ARDS)(17). Therefore, timely clearance of cytokines and inflammatory factors can decrease patients' complications and mortality in COVID-19 infection (18).

Hemoperfusion, an extracorporeal blood purification modality, is used for circulating of patients' anticoagulated blood through a circuit that contains an absorbent filter which reduces toxic agents and inflammatory factors like inflammatory cytokines(1, 19). The absorbent system in hemoperfusion usually is a cartridge which has been loaded with absorbent ingredients including charcoal (for water-soluble materials) and resins (for lipid-soluble materials) (20). HA 330 and HA 380 cartridges are two types of hemoperfusion cartridges which are used in inflammatory conditions. These cartridges have the capability of inflammatory cytokines absorption (21). In addition, HA 280 cartridges are capable to absorb smaller particle size(22). In the current study, Jafron® (HA 330) and CytoSorb® 300 cartridges were used for the hemoperfusion. In a systematic review in 2013 by Borthwick et al., it has been suggested that hemoperfusion may has significant effects on ICU stay and mortality rate in sepsis patients (13). In addition, in the pandemic era, there are some studies which have suggested the positive effects of hemoperfusion in COVID-19 patients (23, 24). In a study by Vardanjani et al., hemoperfusion and continuous renal replacement therapies were effective in ceasing ARDS progression, decreasing patient intubation and patient's oxygen dependency in addition to their preventive effects on AKI and septic shock. Moreover, it reduced mortality and length of hospital stay(25). In the study of De Rosa et al., hemoperfusion with polymyxin in COVID-19 patients with endotoxic shock was associated with organ function recovery and hemodynamic improvement(26).

This study was in the same line with the results of previous studies. In the current study, the mortality rate was significantly lower in Hemoperfusion group compared to the matched group; furthermore, it was observed that O2 saturation may be improved significantly after performing hemoperfusion in COVID-19 patients. In this study, the median length of hospital stay was lower in matched group. However, based on Kaplan model, we could find that the cumulative survival of patients in the hemoperfusion group was associated with the median length of hospital stay.

Our study's major strength was the high sample size of hemoperfusion group. A study by Asgharpour et el. was conducted on 10 patients; whereas, the current study was conducted on 55 patients which is the highest sample size in the literature(27). In addition, considering the high costs of hemoperfusion for the patients, we could not implement this treatment option for every patient due to ethical considerations, and this may be the reason for the lack of a high-sample clinical trial in this regard.

In fact, this treatment option was used in this study as a salvage treatment option in the accompaniment of the final stage treatments. Furthermore, the hemoperfusion group and matched group in this study was not homogenous. Some patients in this study received Tocilizumab which can affect the mortality of patients(28). Moreover, patients in this study received different courses of hemoperfusion (not same in the number and length of sessions) by two different cartridges. As shown in this study, hemoperfusion by Jafron® 330 cartridge had lower mortality compared to CytoSorb® cartridge; however, it failed to reach significant difference. The results can be changed in future studies with homogeneous and higher sample sizes.

Limitation

Our data collection depended on physicians completing because our study is a respectively study. This study is not a randomized clinical trial; therefore, there are not exact inclusion and exclusion criteria. It was not possible to analyze arterial blood gas for some patients because of technical procedures and trained staff limitation. In this study two types of hemoperfusion cartridge were used due to lack of access to a certain type of hemoperfusion cartridge in various times.

Conclusion

Among critically ill COVID-19 patients, we found a significant reduction in mortality rate and improvement of oxygen saturation and pCO2 in hemoperfusion group. To evaluation of the efficacy of hemoperfusion due to some limitations in this study, randomized controlled clinical trials are needed.

Declarations

Ethics approval: The study was confirmed by the Ethics in Medical Research Committee of the Shahid Beheshti University of Medical Sciences. This study is registered with IRCT (Iranian registry of clinical trial), IR.SBMU.RETECH.REC.1399.582.

Consent for publication: Not applicable

Availability of data and materials: The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

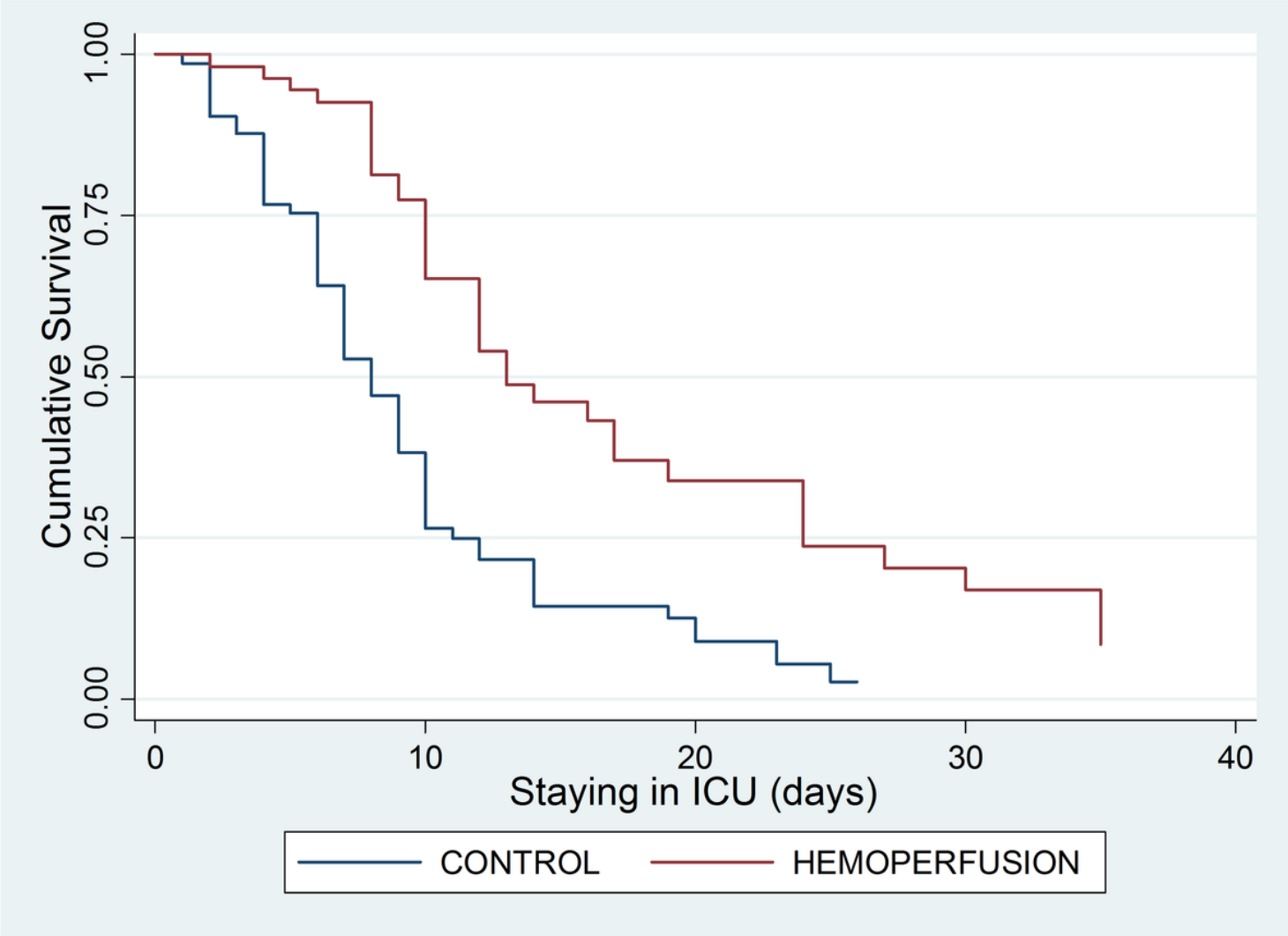

Figure 1

The Kaplan–Meier curve for cumulative survival of patients in control group vs patients in hemoperfusion group.