The Effect of Hemoperfusion on the Clinical Outcome of Severe and Critical COVID-19 patients admitted at the University of Santo Tomas Hospital: An Analytical Cohort Study

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Introduction: Severe sepsis is a life-threatening end organ dysfunction resulting from dysregulated host response to infection and poses a significant burden to healthcare systems worldwide. Since the advent of CoVID-19, cytokine release syndrome has also been attributed to clinical deterioration presenting as acute respiratory distress syndrome and acute kidney injury of infected individuals. Objective: To determine the clinical outcome of Severe and Critical COVID-19 patients who underwent hemoperfusion compared with patients who did not undergo hemoperfusion.

Methods: This study entailed a retrospective cohort analysis of patients aged ⩾ 18 and < 90 years old admitted at University of Santo Tomas Hospital who were diagnosed with Severe or Critical COVID-19. Subjects were grouped between those who underwent hemoperfusion (HP group) using HA 330 cartridge and those who did not undergo the procedure (non-HP). Demographic and clinical data collected for both groups included age, sex, comorbidities present, time to initiation of hemoperfusion, total hemoperfusion time, use of other medications specifically: immunomodulator and anti-viral drugs, antibiotics and steroid, length of hospital stay and in-hospital mortality. Mean arterial pressure, cardiac rate, oxygen saturation, arterial blood gas, complete blood count, oxygen requirement, inotropic score, serum creatinine, urine output, LDH, ferritin, HsCRP, Interleukin-6 values and Acute Physiology and Chronic Health Evaluation II (APACHE II) score were compared from baseline and after 4 sessions of hemoperfusion for the HP group. The clinical outcomes: length of hospital stay, in-hospital mortality and time to off high flow nasal cannula (HFNC) between two groups were also compared.

Results: A total of 98 cases were included, 49 subjects underwent hemoperfusion using HA 330 and 49 patients did not undergo hemoperfusion. Demographic data is similar between both groups. Baseline clinical data between Hemoperfusion and non-Hemoperfusion group did not show statistical difference. However, Baseline LDH, HsCRP, Ferritin, IL-6, PF ratio and APACHE II score were statistically different between two groups. There was no statistical difference between the two groups in terms of primary therapy for COVID-19 and presence of co-morbid conditions except for presence of chronic kidney disease. (Table 1)

Table 1. Demographic data of both Hemoperfusion and non-Hemoperfusion group.

	Total (n=98)	HP (n=49)	Non-HP (n=49)
	Frequency (%); Mean ± SD; Median (IQR)		
Age	58.84 ± 16.31	59.96 ± 14.78	57.71 ± 17.79
Sex*			
Male	54 (55.1)	36 (73.47)	18 (36.73)
Female	44 (44.9)	13 (26.53)	31 (63.27)
COVID-19 status*			
Severe	14 (14.29)	2 (4.08)	12 (24.49)
Critical	84 (85.71)	47 (95.92)	37 (75.51)
Weight*	73.23 ± 17.90	79.08 ± 18.17	67.37 ± 15.72
Medication			
Antibiotic	98 (100)	49 (100)	49 (100)
Antiviral	98 (100)	49 (100)	49 (100)
Steroid	96 (97.96)	49 (100)	47 (95.92)
Enoxaparin	94 (95.92)	49 (100)	45 (91.84)
Tocilizumab	41 (41.84)	25 (51.02)	16 (32.65)
Others	8 (8.16)	3 (6.12)	5 (10.20)
Comorbid conditions			
Hypertension	71 (72.45)	37 (75.51)	34 (69.39)
Diabetes mellitus	38 (38.78)	17 (34.69)	21 (42.86)
Coronary artery disease	24 (24.49)	13 (26.53)	11 (22.45)
Stroke	7 (7.14)	4 (8.16)	3 (6.12)
Obesity	4 (4.08)	3 (6.12)	1 (2.04)
Chronic kidney disease*			
None	81 (82.65)	37 (75.51)	44 (89.8)
3a	6 (6.12)	5 (10.20)	1 (2.04)
3b	4 (4.08)	4 (8.16)	0
5d	6 (6.12)	2 (4.08)	4 (8.16)
5kt	1 (1.02)	1 (2.04)	0
Other comorbidity	10 (10.20)	3 (6.12)	7 (14.29)

** p-value <0.05*

Effect on Disease Severity Length of hospital stay and time to off HFNC was shorter in the non-HP group vs the HP group, median of 13 days vs 18 days (p-value 0.003) and 107 hours vs 222 hours (p- value <0.001), respectively. There is also no significant difference in in-hospital mortality between two groups. (Table 2, Figure 1). Time to hemoperfusion and total treatment time did not show any statistical difference between expired and discharged patients who underwent the procedure (Table 3).

Table 2. Comparison of clinical outcome: length of hospital stay, time to off High flow nasal cannula, occurrence of Acute Kidney Injury, in-hospital mortality and other outcomes between Hemoperfusion and non-Hemoperfusion group.

	Total (n=98)	HP (n=49)	Non-HP (n=49)	p-value
	Frequency (%); Median (IQR)			
Occurrence of AKI	n=20	n=16	n=4	
Time to AKI from Baseline	180 (144 to 288)	216 (108 to 242)	180 (144 to 216)	0.814
Outcome of AKI (n=20)				0.538
RRT	4 (20)	4 (25)	0	
Resolved	16 (80)	12 (75)	4 (100)	
Pulmonary status				
Time to Off HFNC or int after Baseline, hours	168 (96 to 288)	222 (141 to 338)	107 (74 to 216)	<0.001
Time to extubation	216 (120 to 269)	235 (120 to 269)	156 (120 to 216)	0.344
Other outcomes				
Secondary Infection	55 (56.7)	30 (62.5)	25 (51.02)	0.307
CV event				0.030
None	76 (78.35)	33 (68.75)	43 (87.76)	
MI	12 (12.37)	7 (14.58)	5 (10.2)	
ALI	1 (1.03)	1 (2.08)	0	
Myocarditis	2 (2.06)	1 (2.080	1 (2.04)	
Pulmonary embolism	6 (6.19)	6 (12.5)	0	
Neurologic event	4 (4.12)	3 (6.25)	1 (2.04)	0.362
Length of hospital stay	15 (11 to 24)	18 (14 to 25)	13 (10 to 18)	0.003
In-hospital mortality				0.261
Expired	15 (15.31)	10 (20.41)	5 (10.2)	
Discharged	83 (84.69)	39 (79.59)	44 (89.8)	

Table 3. Influence of time to hemoperfusion and total treatment time to in-hospital mortality.

	In-hospital mortality			P-value
	Total (n=49)	Expired (n=10)	Alive (n=39)	
	Frequency (%); Median (IQR)			
Time to hemoperfusion	29 (15 to 67)	45 (12 to 72)	28 (15 to 66)	0.646
< 24 hours	19 (38.78)	3 (30)	16 (41.03)	0.904
24 to 48 hours	14 (28.57)	3 (30)	11 (28.21)	
> 48 hours	16 (32.65)	4 (40)	12 (30.77)	
Total Treatment time	12 (12 to 15)	12 (12 to 17)	12 (12 to 15)	0.669
10 to 12 hours	44 (89.8)	9 (90)	35 (89.74)	1.000
> 12 hours	5 (10.2)	1 (10)	4 (10.26)	

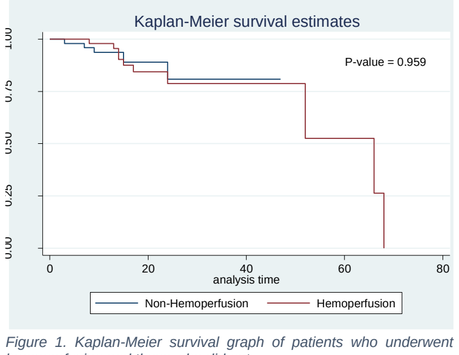

Figure 1. Kaplan-Meier survival graph of patients who underwent hemoperfusion and those who did not.

Conclusion: This retrospective study did not show survival benefit with the use of hemoperfusion. Undergoing hemoperfusion did not show a significant effect on changes in disease severity as represented by no significant difference seen in APACHE II score, PF ratio, acute kidney injury, length of hospital stay and in-hospital mortality. Hemoperfusion also has no significant effect in terms of decreasing the values of inflammatory markers LDH, ferritin, and IL-6. It did, however show a significant decrease in HsCRP values. The rise in D-dimer is attributed to disease progression and severity. Treatment related factors: time to hemoperfusion and total hemoperfusion time also did not show significant difference in in-hospital mortality. A large, multi-center, randomized clinical trial is warranted to truly determine the clinical benefit of hemoperfusion not only in severe to critical COVID-19 but also in severe sepsis and conditions that trigger systemic inflammatory response and cytokine storm.