P0895 | Proinflammatory and endothelial activation profiles in hospitalized COVID-19 patients: impact of arterial hypertension and previous treatment with renin-angiotensin-aldosterone inhibitors

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Introduction

Hypertension is associated to a higher risk of severe COVID-19 disease and mortality, probably due to increased inflammation and endothelial dysfunction [1]. Additionally, there is an ongoing debate regarding the influence of prior treatment with renin-angiotensin-aldosterone (RAAS) inhibitors on COVID-19 severity and prognosis [1]. We evaluated the impact of hypertension and previous RAAS inhibitors treatment on endothelial dysfunction and proinflammatory response in hospitalized COVID-19 patients with different disease severity.

Methods

Serum endothelial activation markers [endocan, vascular cell adhesion molecule-1 (VCAM-1) and E-selectin] and proinflammatory cytokines [IL-1β, IL-6 and TNF-α] were measured in "severe" (n=27), "critical" (n=17) and "critical on veno-venous extracorporeal membrane oxygenation (VV-ECMO)" (n=17) COVID-19 patients at admission, days 3-4 and 5-8. Values were expressed as median(25th percentile;75th percentile) pg/ml (for cytokines) or ng/ml (for endothelial markers). Comorbidities and therapeutics were also analysed.

Results

"Severe" and "critical" groups had a higher proportion of hypertensives and patients on previous RAAS inhibitors treatment than "critical on VV-ECMO" group (Table 1). "Severe" patients with hypertension showed higher endocan and VCAM-1 than normotensives at days 3-4 [endocan: 6.1 (3.1;9.8) vs 2.2(2.0;5.0), $p<0.05$; VCAM-1: 5343(2825;8826) vs 2080(1453;4272), $p<0.05$] and days 5-8 [endocan: 8.6(3.7;12.1) vs 2.3(2.0;4.2), $p<0.01$; VCAM-1, ng/ml: 5799(4059;9418) vs 1789(1241;2752), $p<0.01$]. Hypertension was associated with higher VCAM-1 in "critical" patients at admission [5075(2868;6132) vs 1928(1450;3313), $p<0.05$] and at days 3-4 [4122(2786;4962) vs 2113(1512;2610), $p<0.05$] and with higher E-selectin and TNF-α in "critical on VV-ECMO" at days 5-8 [E-selectin: 43.4(38.1;63.3) vs 34.2(32.0;41.6), $p<0.05$; TNF-α: 41.9(37.7;61.6) vs 24.0 (13.9;41.1), $p<0.05$]. In contrast, hypertension was associated with lower IL-1β in "severe" patients at admission [0.4(0.3;0.9) vs 1.7(1.2;3.1), $p<0.001$] and at days 3-4 [0.8(0.4;1.0) vs 1.6(1.3;3.1), $p<0.01$], and in "critical on VV-ECMO" at days 3-4 [1.3(0.6;1.9) vs 3.8(1.2; 6.2), $p<0.05$]. A significant impact of prior RAAS inhibitors treatment was observed only in the "severe" group for endocan at days 3-4 [7.4(4.4;10.6) vs 3.1 (2.1;4.9), $p<0.05$] and days 5-8 [10.8(4.0;12.3) vs 2.7(2.1; 3.9), $p<0.05$] and for VCAM-1 at days 5-8 [6944(3568;9457) vs 2718(1441;3524), $p<0.05$].

Conclusions

Both hypertension and prior RAAS inhibitor treatment exacerbated endothelial dysfunction in severe COVID-19 patients. In critical groups, hypertension also contributed to higher endothelial activation, as well as to higher TNF-α-related inflammation in patients on VV-ECMO. Nevertheless, the lowering impact of hypertension on IL-1β deserves to be further explored.

Table 1. Hypertension and previous RAAS inhibitor treatment in COVID-19 patient groups

	"Severe" (n=27)	**"Critical"** (n=17)	**"Critical on VV-ECMO"** (n=17)	**p value**
Hypertension, n (%)	18 (67)	13 (76)	8 (47)	0.19
Previous RAAS inhibitors treatment, n (%)	15 (56)	12 (71)	4 (24)	0.02

Reference

1. Gallo G, Calvez V, Savoia C. Hypertension and COVID-19: current evidence and perspectives. High Blood Press Cardiovasc Prev. 2022;29(2):115-123.