Circulating Damage Associated Molecular Patterns (DAMPs) as prognostic markers of disease severity in ICU patients with COVID-19 ARDS

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BACKGROUND/RATIONALE

- Circulating DAMPs including High Mobility Group Box 1 (HMGB1) and Gastrin Releasing Peptide (GRP) have been implicated in the pathogenesis of ARDS in human and animal studies.

- High serum levels of these DAMPS may be associated with poor clinical outcomes in patients with COVID-19 ARDS.

METHODS

- 100 Patients with COVID-ARDS admitted to the Medical ICU of the University of Maryland Medical Center.

- Plasma and serum samples obtained from discarded, clinical blood samples.

- HMGB1 and GRP ELISA kits were used to analyze their concentrations in patients' sera at Day 1 of admission to ICU.

- Outcomes analyzed by univariate Cox model include:
  - Severity of ARDS (P/F ratio)
  - Need for mechanical ventilation,
  - Need for mechanical circulatory support (VV-ECMO).

RESULTS

	Mild ARDS (n=11)	Moderate ARDS (n=38)	Severe ARDS (n=35)	P-value	Not Intubated (n=36)	Intubated (n=64)	P-value	NO ECMO (n=89)	ECMO (n=11)	P-value
Demographics										
Age (years) mean (SD)	64.3 (11.7)	59.8 (13.7)	55.9 (14.0)	0.173	60.8 (12.5)	58.0 (13.3)	0.290	60.8 (12.1)	44.3 (11.3)	**0.00004**
BMI (kg/m^2) mean (SD)	32.9 (8.8)	32.4 (8.2)	37.8 (8.0)	**0.017**	33.4 (7.5)	35.1 (8.9)	0.360	34.1 (8.5)	38.0 (7.2)	0.150
Female	7.0 (63.6%)	14.0 (36.8%)	14.0 (40.0%)	0.274	17.0 (47.2%)	23.0 (35.9%)	0.269	38.0 (42.7%)	2.0 (18.2%)	0.117
Race				0.989			0.308			0.253
Caucasian	3.0 (27.2%)	12.0 (31.6%)	12.0 (34.3%)		8.0 (22.2%)	23.0 (35.9%)		28.0 (31.5%)	3.0 (27.2%)	
Hispanic	1.0 (9.09%)	4.0 (10.5%)	4.0 (11.4%)		4.0 (11.1%)	8.0 (12.5%)		9.0 (10.1%)	3.0 (27.3%)	
African American	7.0 (63.6%)	22.0 (57.9%)	19.0 (54.3%)		24.0 (66.7%)	33.0 (51.6%)		52.0 (58.4%)	5.0 (45.5%)	
Comorbidities										
Hypertension	7.0 (63.6%)	25.0 (65.8%)	19.0 (54.3%)	0.590	19.0 (52.8%)	38.0 (59.4%)	0.522	54.0 (60.7%)	3.0 (27.3%)	**0.035**
Hyperlipidemia	2.0 (18.2%)	15.0 (39.5%)	10.0 (28.6%)	0.346	4.0 (11.1%)	23.0 (35.9%)	**0.007**	24.0 (27.0%)	3.0 (27.3%)	0.983
Diabetes Mellitus	4.0 (36.4%)	21.0 (55.3%)	15.0 (42.9%)	0.413	10.0 (27.8%)	33.0 (51.6%)	**0.021**	39.0 (43.8%)	4.0 (36.4%)	0.637
Cardiovascular disease	5.0 (45.5%)	13.0 (34.2%)	9.0 (25.7%)	0.442	12.0 (33.3%)	21.0 (32.8%)	0.958	32.0 (36.0%)	1.0 (9.1%)	0.074
Pulmonary disease	7.0 (63.6%)	16.0 (42.1%)	12.0 (34.3%)	0.226	16.0 (44.4%)	27.0 (42.2%)	0.827	40.0 (44.9%)	3.0 (27.3%)	0.264
GRP (ng/ml) mean, (SD)	31.9 (26.6)	42.7 (39.6)	79.0 (67.6)	**0.014**	40.1 (34.6)	61.5 (59.1)	**0.063**	48.6 (41.7)	93.1 (106.5)	**0.026**
HMGB-1 (ng/ml) mean, (SD)	24.4 (12.7)	55.1 (38.5)	40.9 (24.1)	**0.021**	39.3 (26.9)	47.5 (32.1)	0.232	44.2 (30.5)	42.5 (27.8)	0.884

CONCLUSIONS

- Serum level of GRP and HMGB-1 may be associated with severity of disease in critically ill patients with COVID-19 infection.
- Future studies should identify whether HMGB1 and GRP could be potential biomarkers for severe illness and therapeutic targets in ARDS.

CONFLICT OF INTEREST

- None