PROGNOSTIC VALUE OF MILD-REGIONAL PROADRENOMEDULLIN IN PATIENTS WITH CRITICAL COVID-19 DISEASE: NEW CONFIRMS FROM A PROSPECTIVE SINGLE CENTRE COHORT STUDY

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BACKGROUND

Mid-Regional pro-Adrenomedullin (MR-proADM) is an inflammatory endothelial biomarker that improves the prognostic assessment of patients with sepsis, septic shock and organ failure. Recent studies suggest that MR-proADM may offer considerable value for predicting the risk of developing critical illness, disease progression and prognosis in patients with COVID-19.

OBJECTIVE

To compare the effectiveness of MR-proADM with respect to standard biomarkers in predicting mortality in COVID-19-patients.

TABLE 1A. Clinical characteristics of the patients

	Overall (N=64)	Survivors (N=46)	Non Survivors (N=18)	P-value
Sex				
Males	48 (75%)	34 (70.8%)	14 (29.2%)	1.000
Females	16 (25%)	12 (75%)	4 (24%)	
Smoke				
Yes	9 (14.1%)	4 (44.4%)	5 (55.6%)	0.099
No	53 (82.8%)	41 (77.4%)	12 (22.6%)	
Heart disease				
Yes	5 (7.8%)	4 (80%)	1 (20%)	1.000
No	59 (92.2%)	42 (71.2%)	17 (28.8%)	
Chronic Pulmonary Disease				
Yes	11 (17.2%)	6 (54.4%)	5 (45.5%)	0.267
No	53 (82.8%)	40 (75.5%)	13 (24.5%)	
Diabetes Mellitus				
Yes	14 (21.9%)	9 (64.3%)	5 (35.7%)	0.512
No	50 (78.1%)	37 (74%)	13 (26%)	
Chronic Kidney disease				
Yes	4 (6.3%)	1 (25%)	3 (75%)	0.064
No	60 (93.8%)	45 (75%)	15 (25%)	
Arterial Hypertension				
Yes	35 (54.7%)	24 (68.6%)	11 (31.4%)	0.585
No	29 (45.3%)	22 (75.9%)	7 (24.1%)	
Autoimmune Disease				
Yes	3 (4.7%)	3 (100%)	0 (0%)	0.553
No	61 (95.3%)	43 (70.5%)	18 (29.5%)	
Age (mean ± SD)	65±10	64.5±10	67±8	0.309
BMI (mean ± SD)	28.8±4.78	28.67±5.16	29.20±3.76	0.464

TABLE 1B. Predictive values

	Overall (N=64)	Survivors (N=46)	Non Survivors (N=18)	P-value
Severity scores at presentation				
SOFA	4.9±2.67	4.58±2.64	5.78±2.62	0.078
MuLBSTA	13.0±3.67	11.87±3.08	15.94±3.47	**<0.001**
SAPSII	28.3±10.1	26.63±10.06	33.00±8.94	**0.014**
Biomarkers at presentation				
CRP	99.2±73.3	88.10±69.64	131.74±76.61	**0.027**
PCT	0.34±0.52	0.33±0.56	0.35±0.44	0.143
D-Dimer	4749.4±10983	4319.23±11968.508	5947.86±7854.3	0.167
LDH	494.7±223.4	458.33±194.35	587.67±268.81	0.048
NT-pro-BNP	1842.3±5702.4	1437.41±5422.06	2879.63±6434.64	0.965
Biomarkers at 3 days from presentation				
CRP	107.8±78.7	119.50±86.66	90.25±73.33	0.610
PCT	0.21±0.26	0.19±0.26	0.28±0.26	0.164
D-Dimer	3574.2±9285.04	3976.43±10760.87	2448.00±1971.32	0.218
LDH	408.8±167.0	390.00±163.11	461.47±172.12	0.938
NT-pro-BNP	566.2±702.9	534.41±634.26	656.54±893.77	0.123
Biomarkers at 7 days from presentation				
CRP	83.0±97.04	44.51±66.51	166.65±101.87	**<0.001**
PCT	0.85±3.38	0.15±0.15	2,31±5.74	**<0.001**
D-Dimer	3630.4±5500.6	4126.57±6510.33	2545.00±1718.23	0.471
LDH	401.3±163.9	391.78±174.80	422.75±139.18	0.280
NT-pro-BNP	862.04±1367.2	515.27±705.59	1624.93±2056.68	0.161
MR-proADM				
	Overall (N=64)	**Survivors (N=46)**	**Non Survivors (N=18)**	**P-value**
MR-proADM at admission	1.15±0.69	1.02±0.61	1.58±0.76	**0.004**
MR-proADM 3 days	1.09±0.65	0.89±0.34	1.68±0.96	**0.003**
MR-proADM 7-days	1.71±2.31	0.92±0.55	3.19±3.44	**<0.001**

Table 1 A, Table 1 B: Predictive values, submitted data. BMI = body mass index, LDH = lactate dehydrogenase, CRP = C-reactive protein, PCT = procalcitonin, MR-proADM = mid-regional proadrenomedullin

RESULTS

64 COVID-19-patients were enrolled (SOFA 4, IQR 3-7; SAPS II 26, IQR 22-35; MuLBSTA 13, IQR 11-15).

The mean age was 65 years (SD 10) and 75% of patients were male.

Population characteristics are shown in Table 1A.

Within 48 hours of admission, MR-proADM and C-Reactive Protein were both significantly higher in non-survivors: 1.58±0.76 nmol/L versus 1.02±0.61 nmol/L (p = 0.004) and 131.74±76.61 mmol/L versus 88.10±69.64 mmol/L (p =0.027), respectively (Table 1B).

Non-surviving patients also had both a higher SAPSII score (33.0 [26-39] versus 27 [13-33]) (p = 0.014) and MuLBSTA score (16 [15-19] versus 12 [11-15]) (p < 0.001).

After 3 and 7 days, MR-proADM was significantly different between survivors and non-survivors (T3 p=0.003; T7 p<0.001) (Figure 1)

METHODS

Between January and July 2021, all adult patients hospitalized for SARS-CoV-2 pneumonia in the Intensive Care Unit and Sub-intensive Care Unit of "Michele e Pietro Ferrero", Verduno (CN), Italy, were enrolled. Inflammatory traditional biomarkers and MR-proADM were assessed at admission and on days 3 and 7. Univariate analysis and logistic regression analysis were performed to assess statistical significance. This work is part of a multicenter ongoing project.

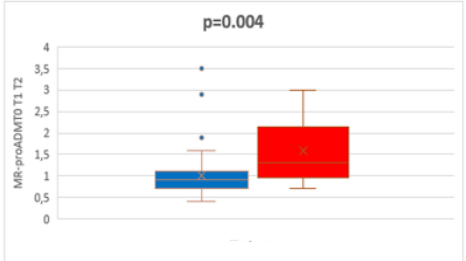

Figure 1A. MR-proADM at admission. Blue: survivors; Red: non-survivors

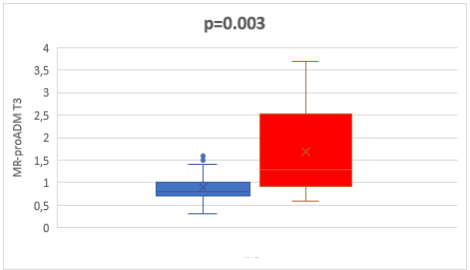

Figure 1B. MR-proADM at day 3. Blue: survivors; Red: non-survivors

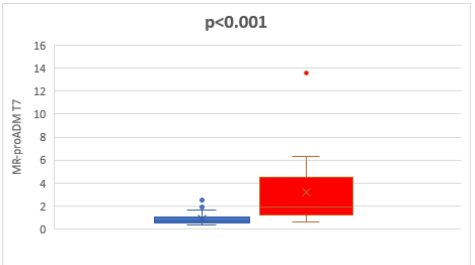

Figure 1C. MR-proADM at day 7. Blue: survivors; Red: non-survivors

CONCLUSIONS

This study highlights the prognostic potential of MR-proADM, measured at arrival, after 3 days and after 7 days, in predicting mortality in critical COVID-19-patients. MR-proADM represents the best biomarker to stratify mortality risk, but did not provide additional prognostic discrimination over MuLBSTA and SAPSII scores.