



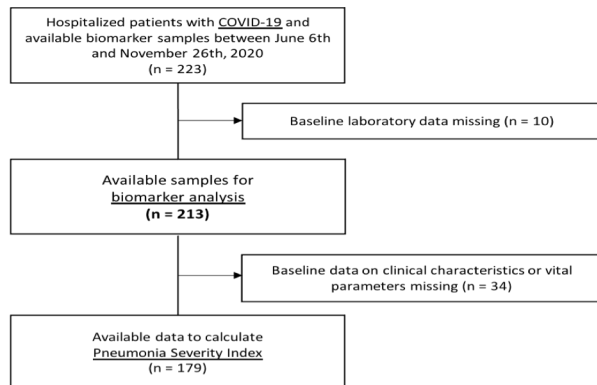
Christoph C. Kaufmann, Amro Ahmed, Mona Kassem, Matthias K. Freynhofer, Bernhard Jäger, Gabriele Aicher, Susanne Equiluz-Bruck, Alexander O. Spiel, Georg-Christian Funk, Michael Gschwantler, Peter Fasching, Johann Wojta, Kurt Huber

Background

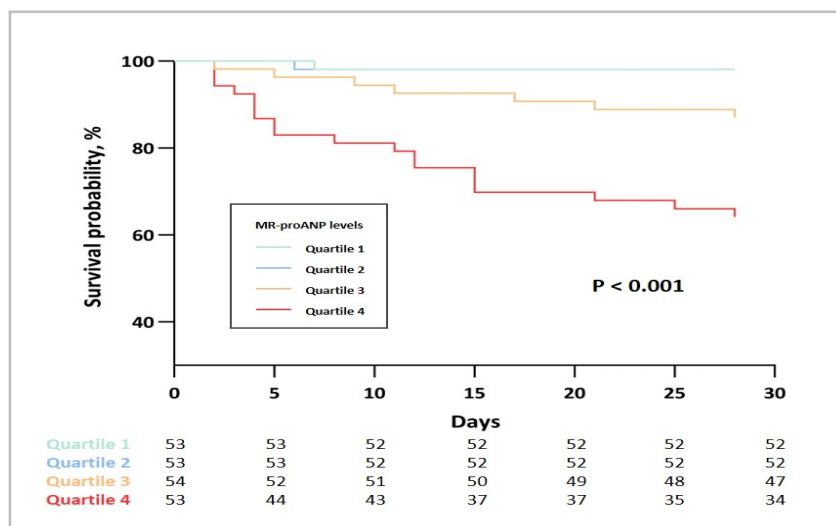
- Atrial natriuretic peptide is primarily expressed in the right atrium following atrial distension and exerts several physiological effects, including natriuresis, diuresis and vasodilation.
- Mid-regional pro atrial natriuretic peptide (MR-proANP) is a strong prognostic marker in several inflammatory, respiratory and cardiovascular conditions, but has not been studied in COVID-19 yet.

Methods

- This prospective, observational study of patients with COVID-19 infection was conducted from June 6th to November 26th, 2020, in different wards of a tertiary hospital.
- MR-proANP on admission was collected and tested for its association with disease severity and 28-day mortality.



Biomarkers	Survivors n = 185	Non-survivors n = 28	Unadjusted P-value	Area under the receiver operating curve (95% CI)	Adjusted P-value	
					Model 1	Model 2
Neutrophile to lymphocyte ratio	4.4 (2.8 – 8.0)	10.0 (7.1 – 13.1)	<0.001	0.754 (0.655 – 0.852)	0.011	0.151
Creatinine, mg/dL	1.0 (0.8 – 1.2)	1.4 (1.0 – 1.8)	<0.001	0.731 (0.615 – 0.847)	0.017	0.216
Blood urea nitrogen, mg/dL	15 (12 – 21)	31 (20 – 45)	<0.001	0.779 (0.686 – 0.873)	0.018	0.860
Lactate dehydrogenase, U/L	279 (225 – 370)	322 (230 – 516)	0.004	0.601 (0.468 – 0.734)	0.001	0.060
High sensitive troponin I, ng/L	11 (6 – 23)	62 (23 – 217)	<0.001	0.847 (0.778 – 0.917)	<0.001	<0.001
N-terminal pro-B-type natriuretic peptide, ng/L	177 (58 – 736)	1706 (600 – 7136)	<0.001	0.811 (0.728 – 0.895)	0.050	0.057
Mid-regional pro atrial natriuretic peptide, pmol/L	75 (43 – 153)	307 (161 – 532)	<0.001	0.832 (0.753 – 0.912)	0.005	0.016



Results

- A total of 213 eligible patients with COVID-19 were included in the final analyses of whom 13.2% (n = 28) died within 28-days.
- Median levels of MR-proANP at admission were significantly higher in non-survivors (307 pmol/L IQR, [161 – 532] vs 75 pmol/L [IQR, 43 – 153], P < 0.001) compared to survivors.
- Pneumonia severity index, as a marker of disease severity, was significantly associated with higher concentrations of MR-proANP with levels ranging from 53.3 pmol/L (IQR, 33.1 – 75.8) in PSI class I/II to 336.9 pmol/L (IQR, 183.6 – 562.3) in PSI class V.
- The area under the ROC-curve for MR-proANP predicting 28-day mortality was 0.832 (95% CI 0.753 – 0.912, P < 0.001). An optimal cut-off point of 160 pmol/L yielded a sensitivity of 82.1% and a specificity of 76.2%.
- MR-proANP was a significant predictor of 28-day mortality independent of clinical confounders, co-morbidities and established prognostic markers of COVID-19 (HR 2.77, 95% CI 1.21 – 6.37; P = 0.016).

Conclusion

- In hospitalized patients with COVID-19, we observed that higher admission levels of MR-proANP levels were significantly and independently associated with 28-day mortality and disease severity.
- Increased levels of MR-proANP should prompt further work-up, including a thorough assessment of fluid status, to gain an early guess of an unfavorable course of disease and enable early countermeasures.