

Soluble neprilysin and survival in critically ill patients

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Results:

Background:

Critically ill patients admitted to an intensive care unit (ICU) exhibit a high mortality rate irrespective of the initial cause of hospitalization. Neprilysin, a neutral endopeptidase degrading an array of vasoactive peptides became a drug target within the treatment of heart failure with reduced ejection fraction. The aim of this study was to analyze whether circulating levels of neprilysin at ICU admission are associated with 30-day mortality.

Methods:

In this single-center prospective observational study, 222 consecutive patients admitted to a tertiary ICU at a university hospital were included. Blood was drawn at admission and soluble neprilysin levels were measured using ELISA.

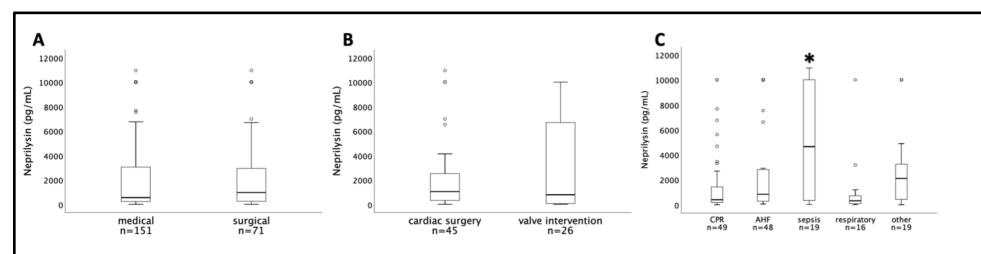


Figure 1: Soluble neprilysin levels of medical versus surgical and valve intervention patients, at time of admission to the intensive care unit (A); levels of neprilysin in patients after cardiac surgery or heart valve intervention (B); neprilysin levels in medical patients according to primary diagnosis (C); * $p < 0.05$.

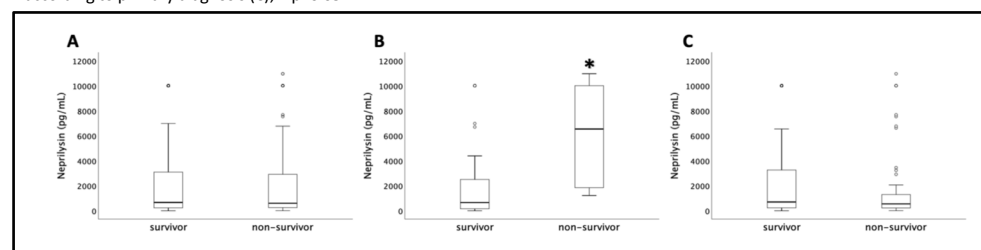


Figure 2: Serum levels of neprilysin in 30-day survivors and non-survivors in the total cohort (A), in patients that were admitted due to cardiac surgery or heart valve intervention (B) and medical patients (C); * $p < 0.05$.

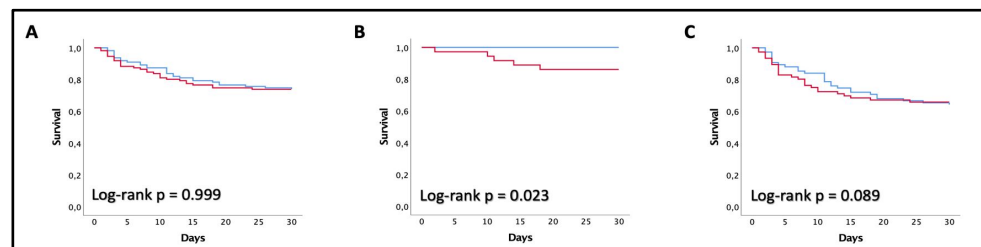


Figure 3: Survival according to neprilysin levels above (red line) or below (blue line) the median in the total cohort (A), in patients that were admitted due to cardiac surgery or heart valve intervention (B) and in medical patients (C).

In the total cohort, Soluble neprilysin levels did not differ according to survival status after 30 days as well as type of admission. However, in patients after surgery or heart valve intervention, 30-day survivors exhibited significantly lower circulating neprilysin levels as compared to those who died within 30 days (660.2, IQR: 156.4 – 2512.5 pg/ml versus 6532.6, IQR: 1840.1 – 10000.0 pg/ml; $p = 0.02$). Soluble neprilysin predicted mortality independently from age, gender, NT-proBNP, and SAPS II (hazard ratio (HR) per 1-standard deviation (SD) increase of neprilysin: 2.52, 95%CI 1.01–6.32; $p < 0.05$). Additionally, soluble neprilysin was markedly elevated in patients with sepsis and septic shock ($p < 0.05$).

Conclusion:

At the time of ICU-admission, circulating levels of neprilysin independently predicted 30-day mortality in patients following cardiac surgery or heart valve intervention, but not in critically ill medical patients. Furthermore, patients suffering from sepsis and septic shock displayed significantly increased circulating neprilysin levels.