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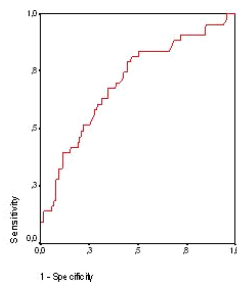
Correlation Between Brain Natriuretic Peptide and Cardiopulmonary Exercise Test Parameters in Patients With Chronic Heart Failure

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We sought to evaluate if brain natriuretic peptide (BNP) levels are associated with exercise capacity determined by cardiopulmonary exercise test (CPx) in patients (pts) suffering from CHF. One-hundred sixty-five consecutive pts with CHF (age 70; beta blockers 53%; ischemic CHF: 52%; mean ejection fraction 41%; NYHA class I: 8%; II: 68%; III: 24%) were considered. Mean BNP was 228 ± 277 pg/ml (Biosite Diagnostic, Triage BNP Test). CPx parameters were: $\dot{V}O_2$ peak ($\dot{P}VO_2$) (12.35 ± 4.48 ml/Kg/min), anaerobic threshold (AT) (9.43 ± 2.80 ml/Kg/min), ventilation and carbon dioxide production ratio ($\dot{V}E/\dot{V}CO_2$) (38.02 ± 8.27), $\dot{V}E/\dot{V}CO_2$ slope (33.82 ± 7.78).

Results: A reverse statistically significant correlation between BNP level, $\dot{P}VO_2$ ($r = -0.297$; $p < 0.0001$) and AT ($r = -0.271$; $p < 0.05$) was respectively observed. A significant correlation between BNP and abnormally high ventilatory response to exercise, expressed as $\dot{V}E/\dot{V}CO_2$ ($r = 0.345$; $p < 0.0001$) and $\dot{V}E/\dot{V}CO_2$ slope ($r = 0.432$; $p < 0.0001$) was observed. The ROC curves demonstrated BNP ≥ 97 pg/ml to be the best cut-off for determining $\dot{P}VO_2 < 14$ ml/Kg/min, with overall accuracy of 71% (sensitivity: 65%; specificity: 65%), area under the curve (AUC): 0.69. Moreover, ROC demonstrated BNP ≥ 138 pg/ml to be the best cut-off for determining $\dot{P}VO_2 < 10$ ml/Kg/min, with overall accuracy 62% (sensitivity: 67%; specificity: 64%), AUC 0.72. BNP offers an alternative tool for distinguishing pts with moderate-to-severe reduction of exercise capacity.

ROC

BNP vs $\dot{P}VO_2 < 10$ ml/Kg/min

AUROC: 0.702 (95% CI: 0.60 to 0.79)

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Increased Plasma Levels of Nt-ProANP and Nt-ProBrain Natriuretic Peptide as Markers of Cardiac Depression in Septic Patients

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Background: The family of natriuretic peptides comprises several structurally-related 22-53-amino acid peptides, such as atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), which are vasoactive peptides that have vasodilator and diuretic properties and play an important role in cardiovascular homeostasis. The salutary cardiovascular effects of natriuretic peptides suggest that ANP and BNP have a pathophysiological significance in cardiac depression in septic patients. Aim of the present study was to determine plasma levels of the stable N-terminal prohormone forms of ANP (Nt-proANP) and BNP (Nt-proBNP) in septic patients and healthy controls.

Patients and Methods: Nt-proANP and Nt-proBNP levels were measured in plasma samples from 18 septic patients at day 1 of severe sepsis and 13 healthy controls by ELISA-methods.

Results: The mean APACHE-Score of septic patients was $16.8 \pm SD = 4.0$ on day 1. Ten of the 18 septic patients died (55% = non-survivors). Significantly higher concentrations ($p = 0.006$) of Nt-proANP were measured in non-survivors ($MW = 13415$ fmol/l \pm SEM = 3640) as compared to controls ($MW = 2274$ fmol/ml \pm SEM = 1043). There was also a significant difference between Nt-proANP levels in controls and survivors ($p = 0.019$). There were no differences of Nt-proANP levels between survivors and non-survivors ($p = 0.189$). Levels of Nt-proBNP were also significantly higher in non-survivors ($MW = 3439$ fmol/l \pm SEM = 1246; $p = 0.010$) and survivors ($MW = 1009$ fmol/l \pm SEM = 263; $p = 0.001$) as compared to controls ($MW = 200$ fmol/l \pm SEM = 24). There was no significant difference between concentrations of Nt-proBNP in the non-survivor and the survivor-group.

Conclusion: Nt-proANP and Nt-proBNP levels are elevated in the early course of septic patients, possibly reflecting myocardial depression in severe sepsis.

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Endothelial Marker Big Endothelin-1 Is More Discriminant Than Brain Natriuretic Peptide to Categorize Patients With Congestive Heart Failure

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Background: Brain Natriuretic Peptide (BNP) and Big Endothelin-1 (BigET-1) are becoming central as diagnostic and prognostic neurohormonal markers to the management of patients with congestive heart failure.

Methods: The Discriminant Ratio (DR) method (Levy JC et al. Am J Physiol 276: E365-E375, 1999) was used to compare the respective performance of BNP and BigET-1 to rank patients according to heart failure severity. The DR estimates the ability of a method to discriminate subjects. It is obtained from the ratio of the underlying between-subject standard deviation (SDu) to the within-subject SD (SDw). DRs were calculated from BNP and BigET-1 duplicates, sampled on 2 consecutive days. Significance of differences in DRs was $p < 0.05$. Correlation coefficients between pairs of measurements were adjusted in order to include an estimate of the underlying correlation, since standard coefficients, due to the presence of within-subject variation, tend to underestimate the true correlation between tests through attenuation. An unbiased estimation of the linear relationship equation between methods was also derived.

Results: Plasma concentrations of BNP and BigET-1 were measured in duplicates in 31 heart failure patients (NYHA II-IV, mean EF 23%). Mean values of day 1 and day 2 (\pm SD) were 75 (52) and 77 (52) pg/mL for BNP [normal values (range): 5.4 (2.5-12.8) pg/mL], and 12.5 (7.4) and 12.0 (8.1) pg/mL for BigET-1 [normal values (range): 5.7 (4.0-7.6) pg/mL], respectively. The difference between the DRs of BNP and BigET-1 (2.73 and 4.61 respectively) was statistically significant ($p < 0.05$) in favor of a better discriminating ability for BigET-1. Unadjusted Pearson coefficient between methods was 0.70, rising up to 0.83 following adjustment for attenuation. Slope and intercept of the unbiased estimation of the linear relationship equation between measurements were 0.18 and -1.47 pg/mL, respectively.

Conclusions: According to the DR method, BigET-1 appears able to better discriminate a heart failure population than BNP. Although both markers are highly correlated in this population, BigET-1 is the choice method to categorize patients with congestive heart failure.

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Natriuretic Peptides as Predictors of Clinical Course in Patients With End-Stage Heart Failure

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Background: The optimal timing for heart transplantation (HTx) or implantation of a ventricular assist device (VAD) in patients with end-stage heart failure is a key issue.

Methods: In 86 patients with end stage heart failure requiring inotropic support and scheduled for HTx or VAD implantation blood was sampled daily. Big endothelin-1 (big ET-1) and natriuretic peptides (pro-ANP, ANP, NT-proBNP and BNP) were measured at the end of the study. Clinical and hemodynamic parameters were also evaluated daily.

The patients were divided into groups with regard to the following endpoints: Group I – immediate VAD placement due to profound cardiogenic shock on admission ($n = 10$); Group II – deterioration into cardiogenic shock after an initially stable clinical course ($n = 26$); Group III – stable clinical course allowed urgent HTx or VAD implantation ($n = 41$); Group IV – weaning from inotropic support ($n = 9$). The data are presented as median values.

Results: On admission there were no differences in clinical parameters between the