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Copeptin is a long term predictor of mortality and rehospitalization for decompensated heart failure - preliminary results

D. Silva; A. Magalhaes; N. Cortez-Dias; P. Carrilho-Ferreira; D. Pereira; S. Lourenco; P. Aguiar; F. Florindo; A. Nunes Diogo; D. Brito
Hospital Lisbon North, Hospital Santa Maria, Lisbon, Portugal

Background: Preliminary studies suggested that copeptin, a new neurohumoral biomarker, has prognostic value for mortality in heart failure (HF). However, its prognostic value regarding rehospitalization for decompensated HF is not well defined.
Aim: To determine the long-term prognosis value of copeptin in patients (pts) hospitalized with decompensated HF.
Methods: Prospective study of consecutive pts admitted with the diagnosis of systolic and/or diastolic decompensated HF (Framingham criteria). At admission, clinical, analytical (including the determination of NT-proBNP and copeptin levels), electrocardiographic and echocardiographic evaluation was performed. Pts were reevaluated before hospital discharge. Clinical follow-up was performed at 3 and 6 months. The primary endpoint was the occurrence of death or rehospitalization for decompensated HF. Copeptin prognostic potential was evaluated by Kaplan-Meier survival curve and Cox regression analysis.
Results: Twenty five pts, 67 ± 14 years old, 16 (64%) male were evaluated. On admission, copeptin concentration (54 ± 45 nmol/L) did not differ according to the NHYA functional class or the ejection fraction and showed no significant correlation with plasma NT-proBNP values. During hospitalization, 1 patient died and the remaining 24 have been discharged from hospital after 12 ± 9 days. Copeptin concentration decreased significantly during hospitalization to 21 ± 12 nmol/L ($p < 0.001$). During a mean follow up of 117 ± 88 days, 10 pts (40%) progressed unfavorably, 3 of whom died. Copeptin concentration on admission was an important prognostic predictor factor. The event-free survival was significantly lower in patients with higher values of copeptin (3rd tertile> 57.38 nmol / L, 125 ± 29 vs. 281 ± 32, $p=0.008$) and the risk of unfavorable outcome was 5 times higher (HR: 5.21, 95% CI 1.34-20.30, $p=0.017$). In contrast, no correlation was observed between NT-proBNP values at admission or discharge and the prognosis.
Conclusion: Copeptin is associated with a significant risk of long term mortality and rehospitalization for decompensated HF, and it may be considered a new alternative biomarker in the syndrome.

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C-reactive protein and its prognostic value on heart failure; does it hold itself?

D A. Moreira; A P. Delgado; B F. Rodrigues; C E. Correia; L M. Nunes; J. Oliveira-Santos
Hospital Sao Teotonio, Viseu, Portugal

Purpose: On hospital admission, to assess the prognostic value of C-Reactive protein (CRP) due to decompensated HF, by determining when - or if ever - patients reach combined but mutually exclusive endpoints defined by either death or hospital readmission due to HF along a 3, 6, or 12 months period after hospital release.
Methods: A prospective study commenced on April 2009 comprising 600 patients (of which 53% were women) after their admission into a Cardiology service due to HF of different etiologies. Those who were carrying a possible simultaneous infection were excluded from the sample. A subgroup of 355 patients was incorporated in the study owing to the fact that they have being given a complete clinical follow-up. Subjects were divided into 3 distinct groups, as defined by their CRP tercile (GA <0.8 mg/dl; GB ≥ 0.8 and < 2,1mg/dL; GC ≥ 2.1mg/dl). Clinical, analytical and echocardiographic parameters were then taken and compared. After hospital release, a yearly follow-up ensued encompassing all of the patients. Statistical analysis was done by means of chi-square and ANOVA tests, followed by the Pearson product-moment correlation coefficient (r) and the Kaplan-Meier log-rank survival curve test. Statistical significance was judged only if $p \leq 0,05$.
Results: The sample does not show a statistical meaningful difference concerning the patient allotment in-between groups, nor even differences related to sex distribution (males included 46.5% of GA, 42.1% of GB, and 50.9% of GC). CRP levels were inversely correlated with the systolic ($r= -0,118$, $p=0,02$) and diastolic pressure values ($r= -0,132$, $p=0,01$), as well as with the average arterial pressure figures ($r=-0,137$, $p=0,01$). CRP values were directly interrelated with BNP levels both on admission ($r=0,18$, $p<0,01$) and on hospital release ($r=0,19$, $p<0,01$), and also with the differential BNP taken amid hospital admission and release ($r=0,154$, $p=0,04$). Hospital internment times were lengthier among the higher CRP groups ($p=0.04$). There was no consequential divergence on the occurrence of complications, including the ones with infectious nature. Along the 3, 6 and 12 months endpoint clinical follow-up, statistical meaningful differences were not found between the groups; nonetheless, Kaplan-Meier curve analysis seem to show an increased tendency for those with higher CRP to reach the established endpoints.
Conclusions: Concerning the sample, it was verified that higher CRP levels do not seem to correlate with a poorer prognosis all through a 12 months period in the context of HF.

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Relation of plasma aminothiols concentration to functional state of patients with atrial fibrillation

MS. Deshko[1]; VA. Snezhitskiy[1]; AV. Naumov[1]; EM. Doroshenko[1]; OV. Panasiuk[1]; TS. Dolgoshey[2]; GA. Madekina[2]
[1]Grodno State Medical University, Grodno, Belarus; [2]Grodno Regional Cardiologic Dispensary, Grodno, Belarus

Oxidative stress is a common pathogenetic mechanism in heart failure. Aminothiols have a critical function as intracellular redox buffers and constitute furthermore an important extracellular redox system.
The purpose of research was to evaluate relation between functional state of patients with atrial fibrillation and plasma aminothiols concentration.
Patients with paroxysmal (n=37), persistent (n=28), and permanent (n=46) atrial fibrillation developed as complication of arterial hypertension and/or stable coronary heart disease, were examined (totally 86 males, 25 females, aged 50 (47-60) years). Patients were divided into three groups according to NYHA functional class as determined by 6-minute walking test: group 1 — those without heart failure (n=20); group 2 — patients with NYHA I-II (n=74); group 3 — patients with NYHA III-IV (n=17). There were no age and gender differences between groups.
Total plasma homocysteine (Hcy) and other related aminothiols — cysteine (Cys), cysteinylglycine (CysGly), and glutathione (GSH) were assessed via high performance liquid chromatography in blood plasma.
Patients underwent one-year follow-up with heart failure exacerbation as primary end point. They were receiving appropriate treatment according to rhythm or rate control strategy depending on atrial fibrillation type including ACEi and antithrombotic prophylaxis. Mann-Whitney U test, MANOVA and logistic regression were performed; data is given as median and interquartile range.
Cys (254 (190-284) umol/l) and GSH (1.79 (1.40-2.56) umol/l) were found to be significantly lower in group 3 patients comparatively to group 1 (295 (236-350) umol/l, $p=0.038$ and 3.70 (2.53-4.98), $p=0.0026$ respectively). Differences of GSH level remained significant after adjustment for age, gender, coronary heart disease and hypertension prevalence ($F=3.67$, $p=0.029$) however Cys level was determined mostly by presence of coronary heart disease ($F=6.27$, $p=0.14$) as well as heart failure effect on Cys concentration was lacking.
Heart failure progression (revealed as increase of NYHA functional class) was obtained in 14 (12.6%) of patients during estimated period of time. Baseline Cys concentration was revealed as predictor of heart failure exacerbation in atrial fibrillation independently of left ventricular ejection fraction (odds ratio 0.93, 95% confidence interval 0.85-0.99, $p=0.048$, data adjusted for age, gender, arterial hypertension and coronary heart disease prevalence).
Thus, patients with NYHA III-IV are characterized with decreased GSH concentration. Cys is an independent predictor of heart failure progression in atrial fibrillation.

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The impact of confounders on the test performance of natriuretic peptides for cardiac dysfunction in subjects aged 80 and older

B. Vaes[1]; D. Gruson[2]; G. Van Pottelbergh[1]; A. Pasquet[3]; C. Mathei[1]; W. Adriaensen[1]; N. Rezzoug[3]; JL. Vanoverschelde[3]; J. Degryse[1]; BELFRAIL study
[1]Institute of Health and Society, Brussels, Belgium; [2]Saint-Luc University Clinics, Brussels, Belgium; [3]Saint-Luc University Clinics, Department of Cardiology, Brussels, Belgium

Purpose: To study the hypothesis natriuretic peptides could be used as markers of "pan-cardiac" disease in subjects aged 80 and older and to investigate the impact of identified confounders on the test performance of natriuretic peptides for severe cardiac dysfunction.
Methods: A diagnostic cross-sectional study embedded within the BELFRAIL study (n = 567). Baseline BNP and NT-proBNP levels were measured and echocardiograms were performed at the subject's home. Severe cardiac dysfunction (CD) was defined as systolic dysfunction, valvular heart disease or isolated severe diastolic dysfunction.
Results: Aortic stenosis, LA volume, LVIDs, E/A, E' and DT, were independently related to circulating levels of natriuretic peptides. Cystatin C, BMI, β blockers, diabetes, heart frequency, usCRP, age and gender were identified as confounders. The prevalence of severe CD was 17.1% in the subjects without and 30.8% in the subjects with chronic atrial fibrillation (CAF) or pacemaker (PM). Only in subjects with CAF or PM the C statistic for severe CD improved after correcting for confounders. The negative predictive value for severe CD ranged from 85.1% to 96.8% and the positive predictive value ranged from 19.0% to 64.3% in different strata of confounders.
Conclusions: Several functional and structural echocardiographic parameters were independently related to circulating levels of natriuretic peptides. Adjusting for identified confounders did not improve the diagnostic accuracy of the natriuretic peptides for severe cardiac dysfunction, except in subjects with CAF or PM. Stratifying for individual confounders showed that different cut-off values could be used to optimise the diagnostic characteristics of natriuretic peptides.

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Impact of therapy optimisation on the level of biomarkers in patients with acute and decompensated chronic heart failure: rationale and design of the MOLITOR study

V. Tscholl[1]; E. Tahirovic[1]; TD. Trippel[1]; S. Inkrot[1]; D. Obradovic[1]; D. Matic[2]; M. Lainscak[3]; S. Apostolovic[4]; W. Haverkamp[5]; HD. Duengen[1]; Competence Network Heart Failure
[1]Charite-Campus Virchow Klinikum, Competence Network Heart Failure, Department of Cardiology, Berlin, Germany; [2]Clinical Center of Serbia, Clinic for Cardiology, Belgrade, Serbia; [3]Department of Cardiology, University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia; [4]Clinical Center, Clinic for Cardiology, Nis, Serbia; [5]Charite - Campus Virchow-Klinikum, Department of Internal Medicine-Cardiology, Berlin, Germany