

or COPD in picking up newly diagnosed CHF is approximately 20%. This group of patients presents a substantial therapeutic opportunity for the initiation and chronic administration of ACEI and BB therapy as well as other CHF management strategies.

1013-76

Influence of Creatinine on Plasma Concentrations and the Prognostic Value of N-Terminal Pro-BNP in Severe Chronic Heart Failure: Data From a Substudy of the COPERNICUS Trial

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Background: The impact of creatinine levels on plasma concentrations as well as the prognostic value of N-terminal proBNP (proBNP) was evaluated in patients with symptoms of congestive heart failure (CHF) at rest or on minimal exertion.

Methods: Plasma concentrations of proBNP, were measured using a newly developed sandwich ELISA in a subgroup of 1048 patients of the European part of the COPERNICUS study.

Results: ProBNP baseline values, mean \pm SD, were 741 \pm 1016 pmol/L in patients with elevated (\geq 125 U/L) creatinine, compared to 403 \pm 481 pmol/L in patients with normal (<125U/L) creatinine (p=0.0001, Wilcoxon 2-sample test). A significant positive correlation (r= 0.35, p=0.0001, Pearson Correlation Coefficient) was detected between proBNP and creatinine. By multivariate Cox regression, NT-proBNP but not creatinine was a powerful independent indicator of subsequent cardiac events. A statistical significant creatinine-proBNP interaction could be detected (p=0.02 for the primary endpoint), indicating that the prognostic value of proBNP for survival is not constant over the range of creatinine. Risk ratios for proBNP levels below vs. above median are indicated in the table according to quartiles of baseline creatinine.

Conclusions: In patients with advanced CHF treated within the COPERNICUS study, proBNP plasma concentrations are related to creatinine both at baseline and during treatment. In addition, baseline creatinine levels seem to influence the prognostic value of proBNP concentrations.

Risk Ratios for all-cause mortality for proBNP (below median : above median) according to creatinine

Creatinine quartile	Risk ratio	95% C.I.	P-value (log rank test)
Quartile 1 (<111 U/L)	2.51	1.01-6.21	0.0397
Quartile 2+3 (111-148 U/L)	3.29	1.57-6.89	0.0008
Quartile 4 (>148 U/L)	3.64	1.27-10.44	0.0103

1013-77

Extent and Not Nature of Dysfunctional Myocardium Is the Main Determinant of B-Type Natriuretic Peptide in Patients With Ischemic Left Ventricular Dysfunction

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Background: B-type Natriuretic Peptide (BNP) reflects LV filling pressures, but the determinants of BNP release in ischemic LV dysfunction (eg. roles of global LV size and function, regional wall stress and myocardial viability) are unclear.

Methods: BNP (Biosite, San Diego) was measured in 32 pts (age 45 -75) with LV dysfunction after infarction. MRI was used to measure LVEDV, LVESV and LVEF, and identify dysfunctional myocardium. The LV was divided into 64 subsegments after dividing the 16 segts into 4 layers reflecting the transmural extent of infarction. Late contrast enhancement was used to identify infarcted (IM-late enhancement), viable (VM-regional dysfunction with no enhancement), and normal myocardium (NM). LV systolic global wall stress (WS) was calculated from LVESV, LV mass (both indexed by division with body surface area) and systolic BP.

Results: The strongest correlation of BNP was with total dysfunctional myocardium (ie numbers of segts with abnormal function). This was superior to correlations with infarcted and viable myocardium, and clearly superior to correlations with LVESV, LVEF and WS (Table). There was no meaningful correlation with a range of clinical factors. In a multivariate model, the only independent predictor of BNP was total dysfunctional myocardium (beta 0.63, p<0.0001)

Correlation Between Log BNP and Other Parameters

Total Dysfunctional Myocardium	IM	VM	NM	LVES V	LVEF	WS
r	0.580	0.561	-0.640	0.406	0.419	0.397
p	<0.0001	<0.0001	<0.0001	0.001	0.001	0.068

Conclusion: In patients with ischemic LV dysfunction, the amount of dysfunctional myocardium (rather than its nature) is an important determinant of BNP - more so than LVEF or even WS.

1013-78

Can the Presence of an S3 Predict Elevated B-Type Natriuretic Peptide Levels?

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Background: B-type natriuretic peptide (BNP) has been shown to be a sensitive and specific marker of congestive heart failure (CHF). Levels of this hormone demonstrate accurate correlation with left ventricular end-diastolic pressure and predict prognosis in heart failure patients. The presence of a third heart sound in older adults is thought to reflect left ventricular volume overload, with recent data demonstrating an adverse prognosis in CHF patients with this physical finding. An association between BNP levels and the presence of an S3 has not previously been studied. We hypothesized that auscultation of an S3 in older patients reflects elevated BNP levels.

Methods: BNP levels (Biosite, San Diego, CA) were measured in 75 consecutive patients visiting a general cardiology outpatient clinic. On the day that BNP was measured, a single experienced cardiologist (K.C.) blinded to BNP levels auscultated each patient in the supine and left lateral decubitus positions. The patients' primary diagnoses were determined by chart review, and the presence or absence of overt CHF was determined clinically on the day of the examination.

Results: 77% of the patients were male, 55% had coronary artery disease, and 11% had dilated cardiomyopathy. The mean age was 73 \pm 13 years and the mean BNP level was 263 \pm 257 pg/ml. 26% of patients were diagnosed with overt CHF, and 23% were found to have an S3. The mean BNP level of those with overt CHF was 502 pg/ml, and the mean BNP level of those without overt CHF was 185 pg/ml (p=0.00006). The mean BNP level of those with an S3 was 505 pg/ml, and the mean BNP level of those without an S3 was 192 pg/ml (p=0.00007). All patients with an S3 had overt CHF. A BNP level > 100 pg/ml was 100% sensitive and 50% specific for the presence of overt CHF. The presence of an S3 was 48% sensitive and 100% specific for a BNP level > 100 pg/ml.

Conclusion: In an elderly patient population with cardiovascular disease, the presence of an S3 is 100% specific for BNP levels > 100 pg/ml.

1013-79

Beside B-Type Natriuretic Peptide in the Emergency Diagnosis of Systolic and Nonsystolic Heart Failure: Results From the Breathing Not Properly (BNP) Multinational Study

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Background: Preserved systolic function is increasing common in patients presenting with symptoms of congestive heart failure (CHF), but is still difficult to diagnose. This study examines B-type natriuretic peptide (BNP) levels in patients with systolic versus non-systolic dysfunction presenting with shortness of breath. **Methods:** The BNP Multinational Study was a seven center, prospective study of 1586 patients who presented with acute dyspnea and had BNP measured upon arrival. A subset of 452 patients with a final adjudicated diagnosis of congestive heart failure who underwent echocardiography within thirty days of their visit to the emergency department were evaluated. An ejection fraction of greater than 45% was defined as non-systolic CHF. **Results:** Of the 452 patients with a final diagnosis of congestive heart failure, 165 (36.5%) had preserved left ventricular function on echocardiography while 287 (63.5%) had systolic dysfunction. Patients with non-systolic heart failure (NS-CHF) had significantly lower BNP levels than those with systolic heart failure (S-CHF) (413 pg/ml versus 821 pg/ml p <0.001). As the severity of heart failure worsened by NYHA, the percentage of S-CHF increased while the percentage of NS-CHF decreased. When patients NS-CHF were compared to patients without CHF (n=770), a BNP value of 100 pg/ml had a sensitivity of 86%, a negative predictive value of 96%, and an accuracy of 75% for detecting abnormal diastolic dysfunction. Using Logistic regression to differentiate S-CHF from NS-CHF, BNP entered first as the strongest predictor followed by oxygen saturation, history of myocardial infarction, and heart rate. **Conclusions:** We conclude that NS-CHF is common in the setting of the emergency department and that differentiating NS-CHF from S-CHF is difficult in this setting using traditional parameters. While BNP levels add modest discriminatory value in differentiating NS-CHF from S-CHF, its major role is still the separation of patients with CHF from those without CHF.

1013-80

N-T Pro-BNP and the Diagnosis of Heart Failure: A Pooled Analysis of Three European Epidemiological Studies

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Background: Many studies have reported the efficacy of BNP in diagnosing heart failure (HF) using the optimum concentration on ROC analysis as their cut-point. However, in routine clinical practice a cut-point reflecting abnormality has to be applied. This study reports the use of NT-pro-BNP (proBNP) in detecting HF in a meta-analysis of three epidemiological studies.

Methods: 3052 subjects were pooled from three European Population-Based studies of LV Dysfunction, which had collected compatible clinical information and measured plasma proBNP (MTP assay Roche). In particular 549 subjects were normal i.e. free of cardiovascular disease. As proBNP concentrations rose with age and were higher in women, an abnormal proBNP was defined as >95th centile, corrected for age and sex. HF was defined as a LVEF by echo cardiography \leq 2.5th centile for the normal range of each centre and symptoms of dyspnoea and/or loop diuretic therapy.

Results: The prevalences of HF and LVD were 3.1% and 10%. The median concentra-