

11:15 a.m.

888-4

Changes in Plasma Brain Natriuretic Peptide and Norepinephrine Over Time and Subsequent Mortality and Morbidity in Heart Failure: Results From Val-HeFT

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Background: Plasma brain natriuretic peptide (BNP) and norepinephrine (NE) are important predictors of heart failure (HF) mortality and morbidity (M&M). Whether changes in BNP and NE over time correspond to subsequent changes in M&M has not been studied. Val-HeFT evaluated the efficacy of valsartan in HF patients and measured BNP and NE at baseline (BL) and during follow-up. **Methods:** BL and % change from BL to 4 months in BNP (n=3740) and NE (n=3746) were analysed by quartiles (Q) for subsequent mortality and morbidity (death, sudden death with resuscitation, IV inotropic therapy, and hospitalisation for HF), using a Cox proportional hazard model with BL value as a covariate. The hazard risk ratio (RR) and 95% CI for changes between Q, using first Q as control was calculated for mortality and first morbid event in all patients, irrespective of treatment. **Results:** BL BNP and NE showed a significant quartile-dependent increase in M&M. Patients with the greatest % decrease in BNP and NE from baseline to 4 months (Q1) had the lowest, whereas patients with greatest % increase in BNP and NE had the highest subsequent M&M. (Table). Findings were similar for NE but RR were lower than for BNP. **Conclusions:** Plasma BNP and NE are not only important predictors of HF M&M, but changes in these neurohormones over time are associated with corresponding changes in subsequent M&M. These data further reinforce their role as significant surrogate markers in HF and underscore the importance of including their measurement in HF clinical trials.

Quartiles	% Mortality	RR vs Q1	95% CI	Cox P-value	% Morbidity	RR vs Q1	95% CI	Cox P-value
% change in BNP								
Q1 (<-45)	13.6	1.00			21.5	1.0		
Q2 (-45 to -13)	15.5	1.30	1.03-1.66	0.03	25.5	1.37	1.33-1.65	0.001
Q3 (-13 to +30)	15.1	1.36	1.07-1.74	0.014	28.1	1.65	1.37-2.00	<0.0001
Q4 (>+30)	19.1	1.92	1.52-2.43	<0.0001	33.0	2.24	1.86-2.69	<0.0001
% change in NE								
Q1 (<-24)	14.4	1.00			25.9	1.00		
Q2 (-24 to +4.5)	16.0	1.23	0.97-1.55	0.09	26.3	1.12	0.93-1.33	0.23
Q3 (+4.5 to +41)	15.7	1.28	1.01-1.62	0.04	27.4	1.24	1.04-1.48	0.018
Q4 (>+41)	17.5	1.48	1.17-1.87	0.001	29.2	1.41	1.18-1.68	0.0002

11:30 a.m.

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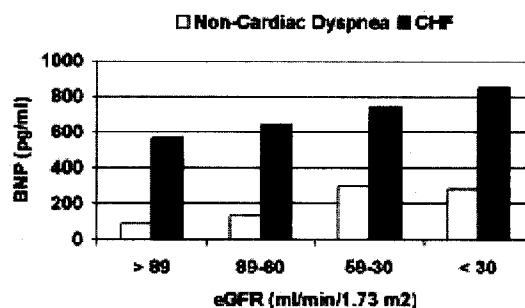
B-Type Natriuretic Peptide and Renal Function in the Diagnosis of Heart Failure: An Analysis From the BNP Multinational Study

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Background B-type natriuretic peptide (BNP) and renal function are prognostic indicators of survival in patients with congestive heart failure (CHF). We sought to define the relationships between BNP and renal function.

Methods and Results—The Breathing Not Properly Multinational Study was a prospectively designed, diagnostic test evaluation study conducted in seven centers. Of 1586 participants who presented with acute dyspnea, 1452 (91.6%) had both BNP and baseline estimated glomerular filtration rate (eGFR) available. Patients with eGFR < 15 ml/min/1.73 m² and those on dialysis were excluded. The final diagnosis was CHF in 715 (49.2%). The raw, and log-log transformed correlations between BNP and eGFR were $r = -0.19$ and $r = -0.17$, and $r = -0.20$ and $r = -0.31$, for those with and without CHF, both $p < 0.0001$ for $r \neq 0$. There were graded increases in BNP for those with and without CHF with decreasing renal function (Figure). The following variables, in ranked order, were found to be most independently predictive of CHF as a final diagnosis: 1) log (BNP), OR = 13.5, 95% CI 10.1-18.4, $p < 0.0001$; 2) history of CHF, OR 5.0, 95% CI 3.6-7.0, $p < 0.0001$; 3) S₃, OR = 6.0, 95% CI 2.8-12.7, $p < 0.0001$; 4) diabetes, OR = 1.6, 95% CI 1.1-2.3, $p = 0.01$; 5) log (eGFR), OR 0.5, 95% CI 0.2-1.0, $p = 0.07$.

Conclusions With decreasing eGFR, there are graded increases in BNP among those with and without CHF. Despite a weak correlation between BNP and eGFR, BNP is a strong and independent predictor of CHF after taking renal function into consideration.



11:45 a.m.

888-6

What Is the Normal Range for N-Terminal Pro-Brain Natriuretic Peptide Levels in the Community?

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Background: Heart failure (HF) is placing an increasing burden on society. Data suggests that N-terminal pro-Brain Natriuretic Peptide (NTB) is secreted from the ventricles of subjects with HF and that its serum concentration may help diagnose HF. Serum NTB levels can now be measured by autoanalyser in the laboratory. Little data has been collected on normal serum NTB values and differences with age and gender in healthy subjects in the community.

Methods: Accordingly, 1403 subjects ≥ 45 years old were chosen at random from 7 representative local general practices and invited to attend for echocardiography, venesection for serum NTB levels (Elecys, Roche Diagnostics) and a questionnaire. Subjects were classified as normal if they had no prior ischaemic heart disease, diabetes, cerebrovascular disease, peripheral vascular disease or hypertension; were normotensive, and had normal systolic and diastolic function, normal valves and no left ventricular hypertrophy on echocardiography.

Results: 734 subjects (52%) attended. 290 subjects (40%) were classified as normal. Serum NTB levels in normal subjects are shown below. NTB levels increased with age ($p < 0.001$ age 45-54 vs 65+, $p = 0.003$ age 55-64 vs 65+). NTB levels were higher in females than males at each age cut off ($p < 0.001$ age 45-54, $p < 0.001$ age 55-64, $p = 0.03$ age 65+).

Conclusion: Thus in normal healthy subjects serum NTB levels increase with age and female gender, requiring age and gender specific cutoffs to be used when using NTB in clinical practice.

Serum NTB levels (pg/ml) stratified for age and gender

	Males Age 45-54	Females Age 45-54	Males Age 55-64	Females Age 55-64	Males Age 65+	Females Age 65+
Median NTB levels (pg/ml)	19.5	48	17	61	42	83.5
Mean NTB levels (pg/ml)	25.9	60.6	24.1	78.8	62.4	111
Mean +2SD NTB levels (pg/ml)	75.8	152	71.2	186	157	265
97.5th Centile NTB levels (pg/ml)	98.8	183	-	243	-	-
Number subjects	76	90	37	45	20	22