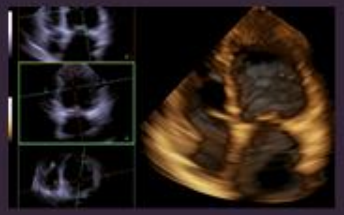


EuroValve
March 10-11, 2016

Asymptomatic MR: Neuro-Hormones

Dr Julien Magne, PhD

CHU Limoges, France

CHU Centre hospitalier universitaire Limoges

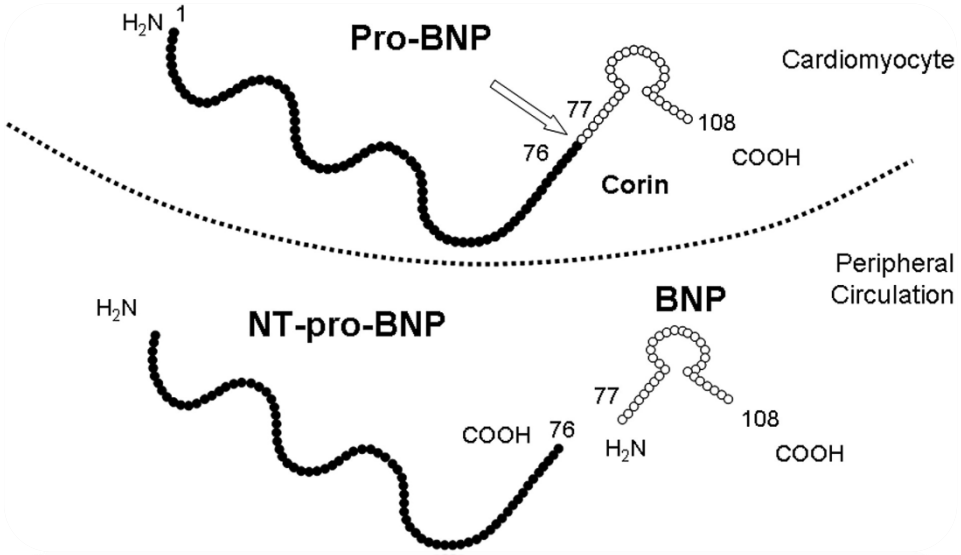
Université de Limoges

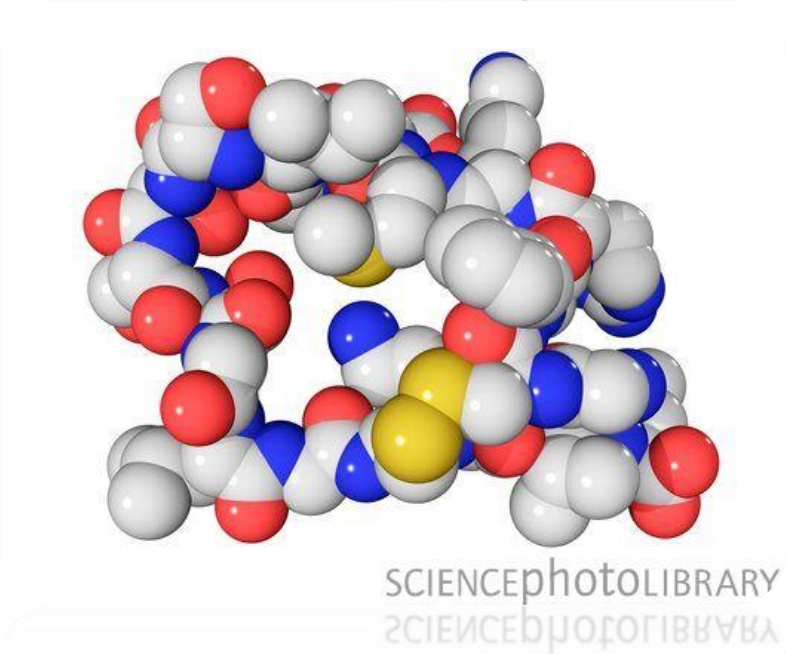
www.eurovalvecongress.com

BNP Molecular Forms and Processing

Brain Natriuretic Peptide: Sudoh et al, *Nature*, 1988

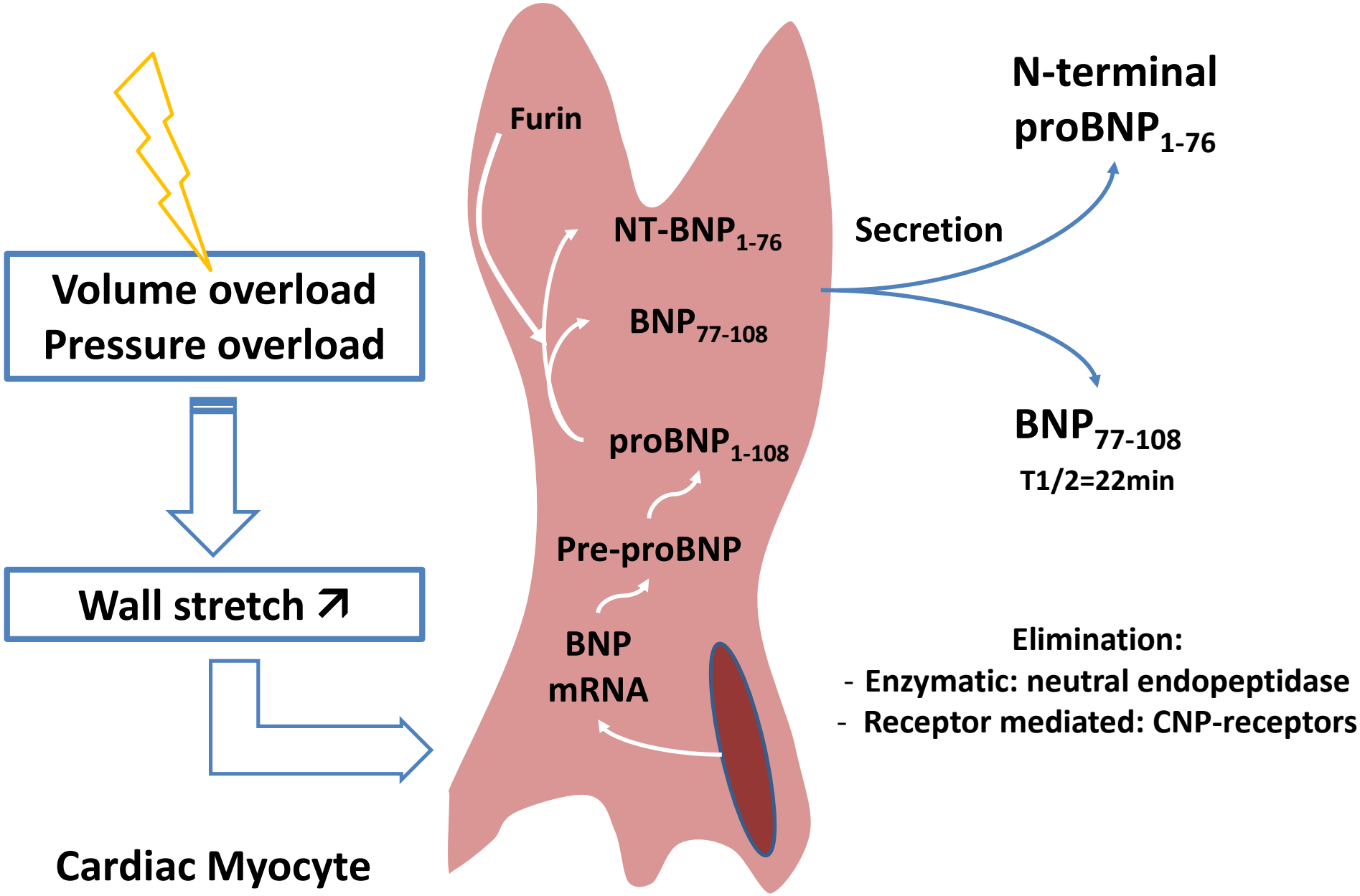
BNP and its inactive amino terminal portion are neurohormones released by the ventricles in response to increased LV wall stress





Lam et al. JACC, 2007

BNP Release Activation



Characteristics of an ‘ideal’ biomarker

Specific

- **High myocardium/serum ratio**
- **Not present in non-cardiac tissue, even pathologically**

Sensitive

- **Zero baseline**
- **Marker of ‘early,’ reversible cardiotoxicity**
- **Immediate release with injury** 👌

Predictive

- **Long half-life in blood**
- **Release proportionate to extent of injury** 👌

Robust

- **Rapid, simple, and accurate** 👌

Non-invasive / accessible / unexpensive 👌

The Place of BNP in current VHD Guidelines

ESC 2012: General comments on biomarkers in MR

"B-type natriuretic peptide (BNP) serum level has been shown to be related to functional class and prognosis, particularly in AS and MR."

"Low-plasma BNP has a high negative predictive value and may be helpful for the follow-up of asymptomatic patients"

ACC/AHA 2014:

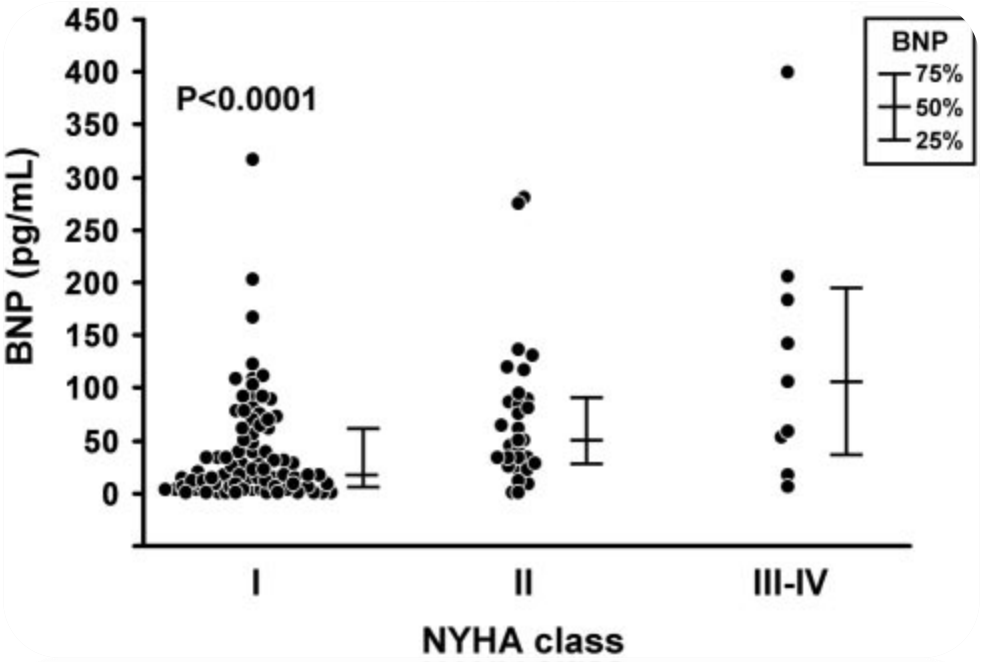
"Although the data are preliminary, the finding of a rising B-type natriuretic peptide could be helpful as another factor in deciding the optimal timing of mitral surgery."

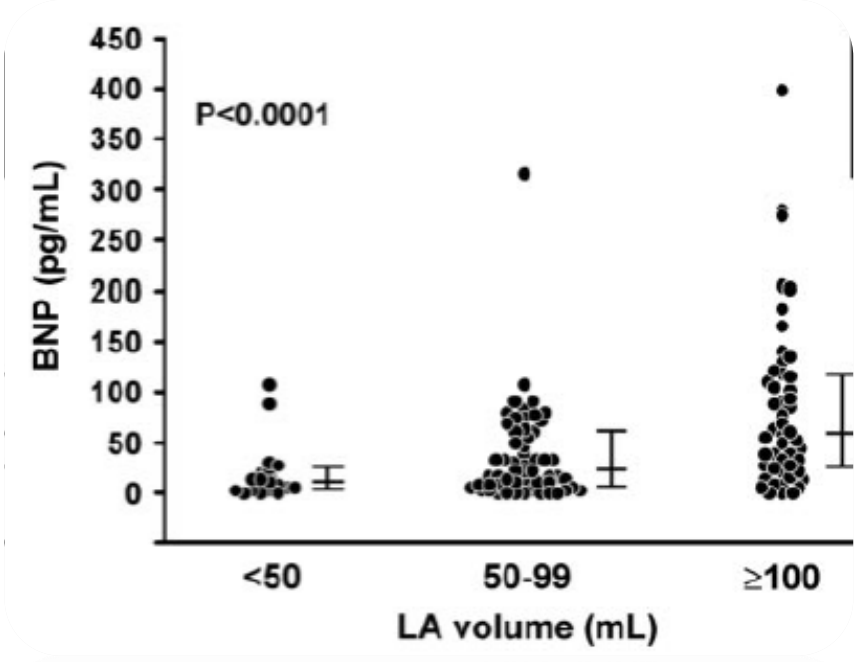
Vahanian et al. EHJ, 2012
Nishimura, Otto et al. JACC, 2014

BNP level in Mitral Regurgitation

BNP level is not related to MR itself but to the atrial and ventricular consequences of MR

124 patients with primary MR; BNP vs. MR severity (ERO): r=0.17, p=0.06





Detaint et al. Circulation, 2005

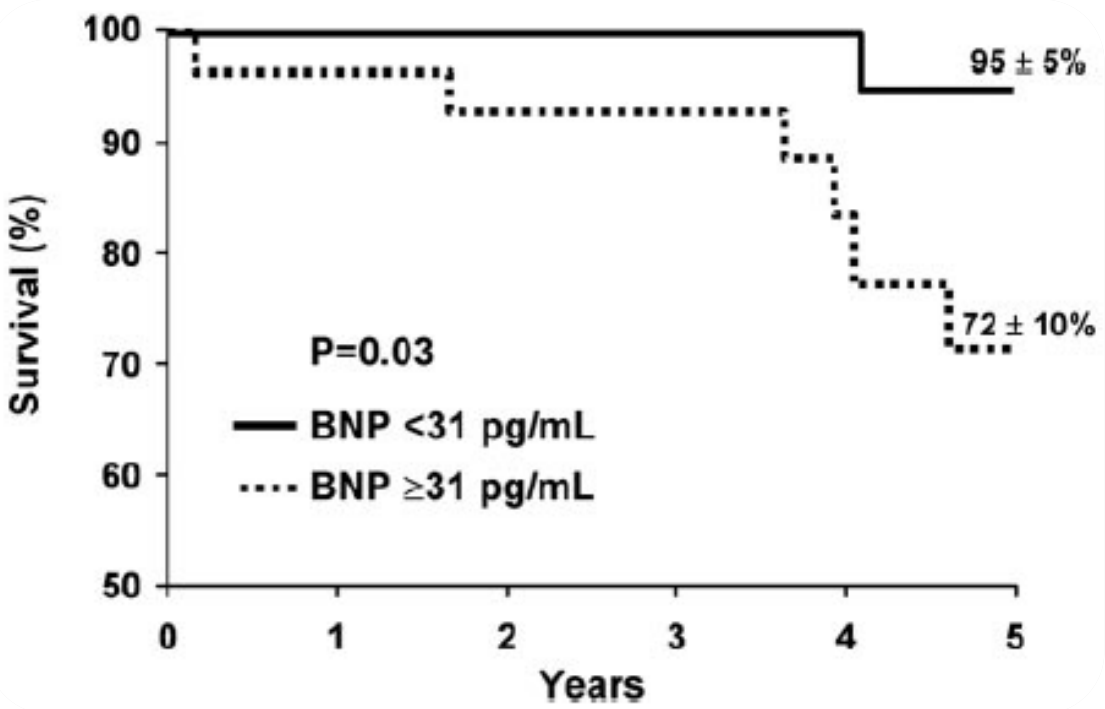
BNP level in Mitral Regurgitation

Determinants of BNP level

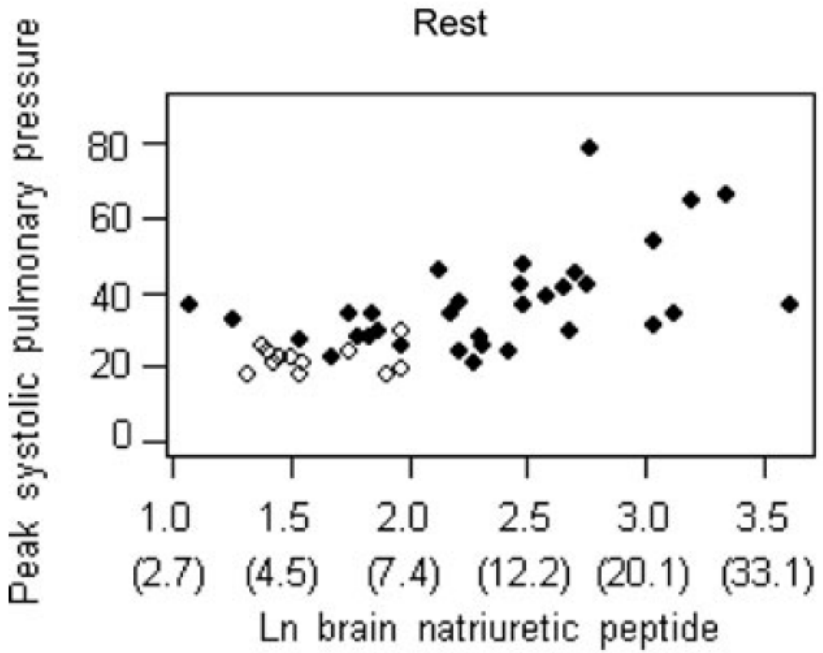
Variable	BNP, Multivariate Analysis (*P*)
LA volume	0.0001
AF	0.006
ESVI	0.02
NYHA class	0.01
Sex	0.01
Age	0.0003

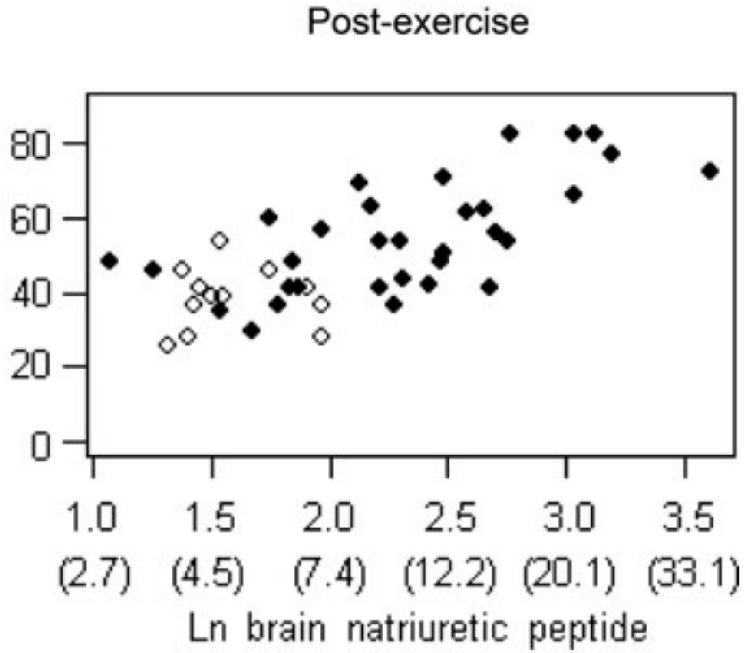
Detaint et al. Circ, 2005

Impact of BNP level on survival

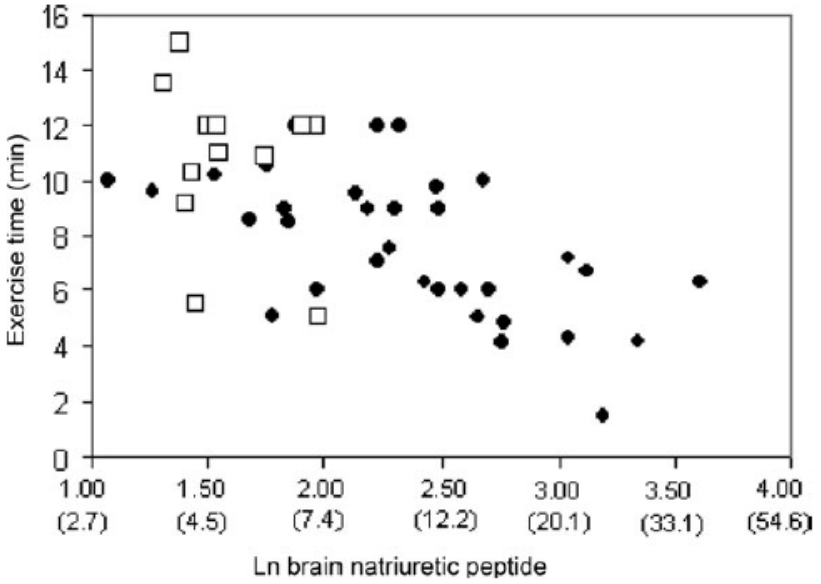


BNP level and Exercise Parameters





n=33 asymptomatic or mild symptoms, moderate to severe MR, LVEF>60%



Kerr et al. EHJ, 2008

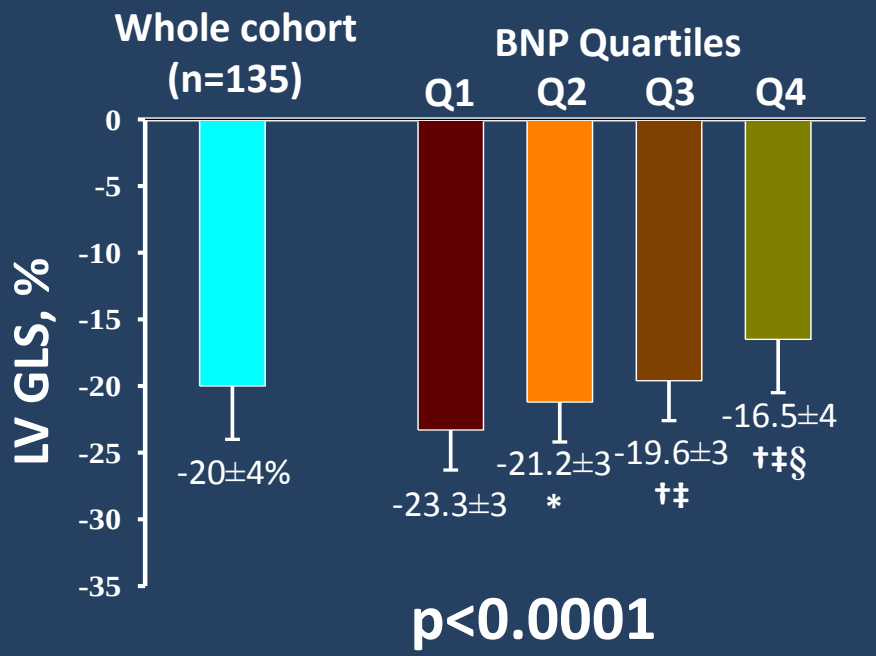
LV Longitudinal Function and BNP Level

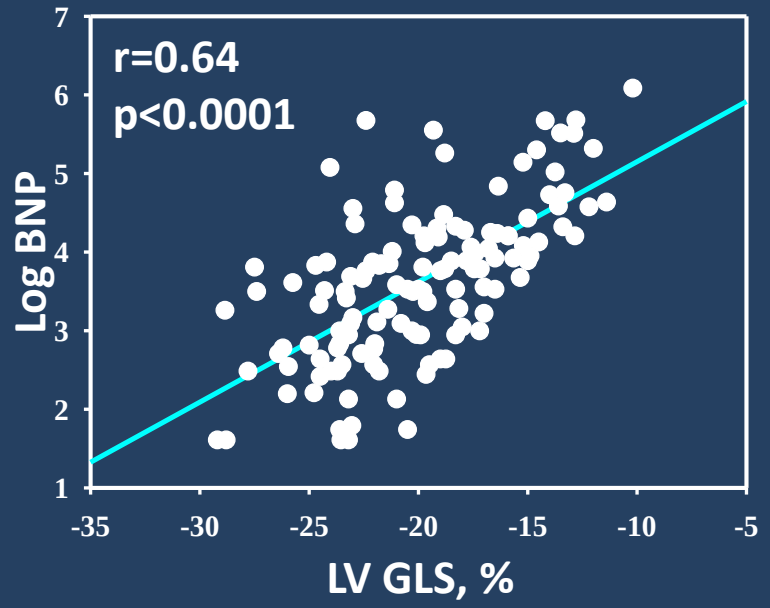
ORIGINAL ARTICLE

Prognostic importance of brain natriuretic peptide and left ventricular longitudinal function in asymptomatic degenerative mitral regurgitation

Julien Magne,[1] Haifa Mahjoub,[2] Luc A Pierard,[1] Kim O'Connor,[1,2] Charles Pirlet,[1] Philippe Pibarot,[2] Patrizio Lancellotti[1]

Bi-centric study, n=135 asymptomatic MR (moderate & severe) with no LV dysfunction/dilatation





Magne et al. Heart 2012

Determinants of BNP Level

Variables	Log BNP			BNP ≥40 pg/ml		
	β	SE	p Value	OR	95% CI	p Value
Age, per years	0.01	0.01	0.10	1.01	0.97 to 1.06	0.56
Male gender*	0.03	0.12	0.82	2.17	0.65 to 7.2	0.20
iLVES diameter, per mm/m^2	0.03	0.02	0.12	1.01	0.86 to 1.8	0.92
E/Ea ratio	0.20	0.13	0.12	1.22	0.44 to 3.35	0.70
Deceleration time, per ms	0.01	0.002	0.003	1.02	1.0 to 1.03	0.043
iLA volume, per ml/m^2	0.01	0.004	0.008	1.05	1.00 to 1.09	0.034
SPAP, per mm Hg	0.01	0.01	0.12	1.01	0.95 to 1.08	0.73
Global longitudinal strain, per %	0.13	0.020	<0.0001	1.33	1.12 to 1.59	0.0010

LV diastolic function + Disease chronicity + Longitudinal function + …
= BNP level

BNP level in Asymptomatic MR

	Derivation Set			Validation Set		
	BNP <105 pg/ml (n = 130)	BNP ≥105 pg/ml (n = 37)	p Value	BNP <105 pg/ml (n = 75)	BNP ≥105 pg/ml (n = 27)	p Value
Age (yrs)	61 ± 6	66 ± 8	0.07	62 ± 5	65 ± 7	0.09
Male	77 (59)	24 (64)	0.38	47 (63)	18 (65)	0.94
Atrial fibrillation	12 (9)	5 (13)	0.17	5 (6.6)	3 (7.4)	0.77
Hypertension	20 (15)	8 (21)	0.22	9 (12)	3 (10)	0.82
Systolic arterial pressure (mm Hg)	139 ± 22 (93–170)	135 ± 18 (90–155)	0.27	137 ± 28 (91–160)	136 ± 21 (90–150)	0.77
Heart rate (beats/min)	76 ± 10 (62–98)	69 ± 11 (55–89)	0.15	75 ± 10 (60–101)	70 ± 12 (55–94)	0.45
NFL, n (%)	2 (1.5)	4 (10)	0.001	1 (1.3)	1 (3.7)	0.02
Exercise capacity (METs)	9.5 (8.5–11)	9.0 (8.0–12)	0.39	9.0 (8.0–14)	8.5 (7.5–11)	0.45
Ejection fraction (%)	68 (65–72)	65 (63–68)	0.04	68 (65–70)	66 (63–69)	0.04
End-diastolic diameter/BSA (mm/m^2)	33 (25–38)	40 (29–46)	0.08	32 (24–37)	39 (31–45)	0.09
End-systolic diameter/BSA (mm/m^2)	18 (14–23)	24 (19–29)	0.001	18 (14–22)	25 (21–30)	0.01
Regurgitant volume (ml/beat)	65 (63–70)	76 (66–84)	0.01	66 (62–71)	76 (68–86)	0.01
Regurgitant fraction (%)	49 (46–55)	58 (49–64)	0.01	49 (45–57)	60 (52–67)	0.01
EROA (mm^2)	53 (46–61)	65 (47–74)	0.0001	46 (44–57)	67 (49–81)	0.001
AV/BSA (cm^3/m^2)	65 (42–73)	76 (49–84)	0.03	64 (40–69)	77 (48–82)	0.02
Pulmonary artery systolic pressure (mm Hg)	24 (18–30)	32 (24–38)	0.04	25 (15–29)	35 (22–39)	0.037

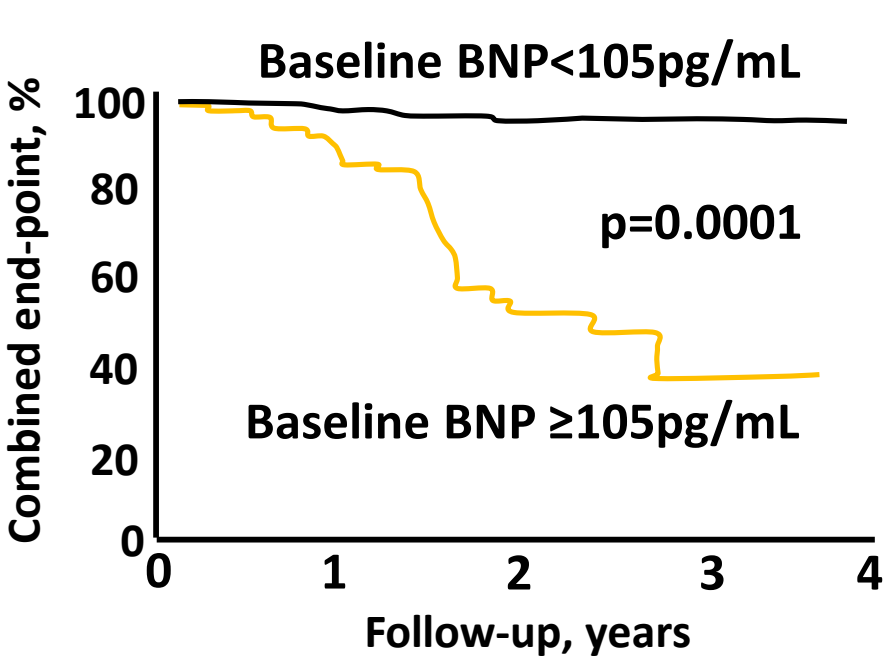
⇨BNP is a good marker of advanced stage of the disease

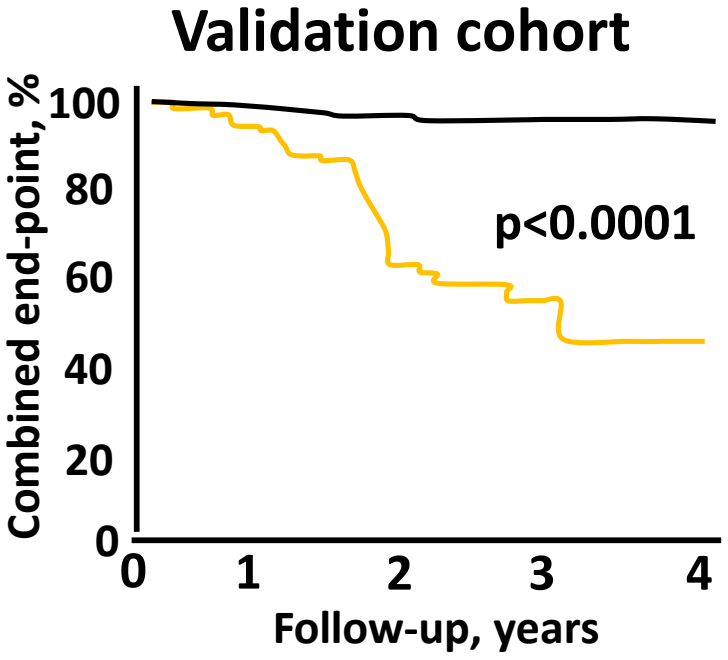
Pizarro et al. JACC, 2009

BNP level in Asymptomatic MR

Multivariate predictor of combined end-point

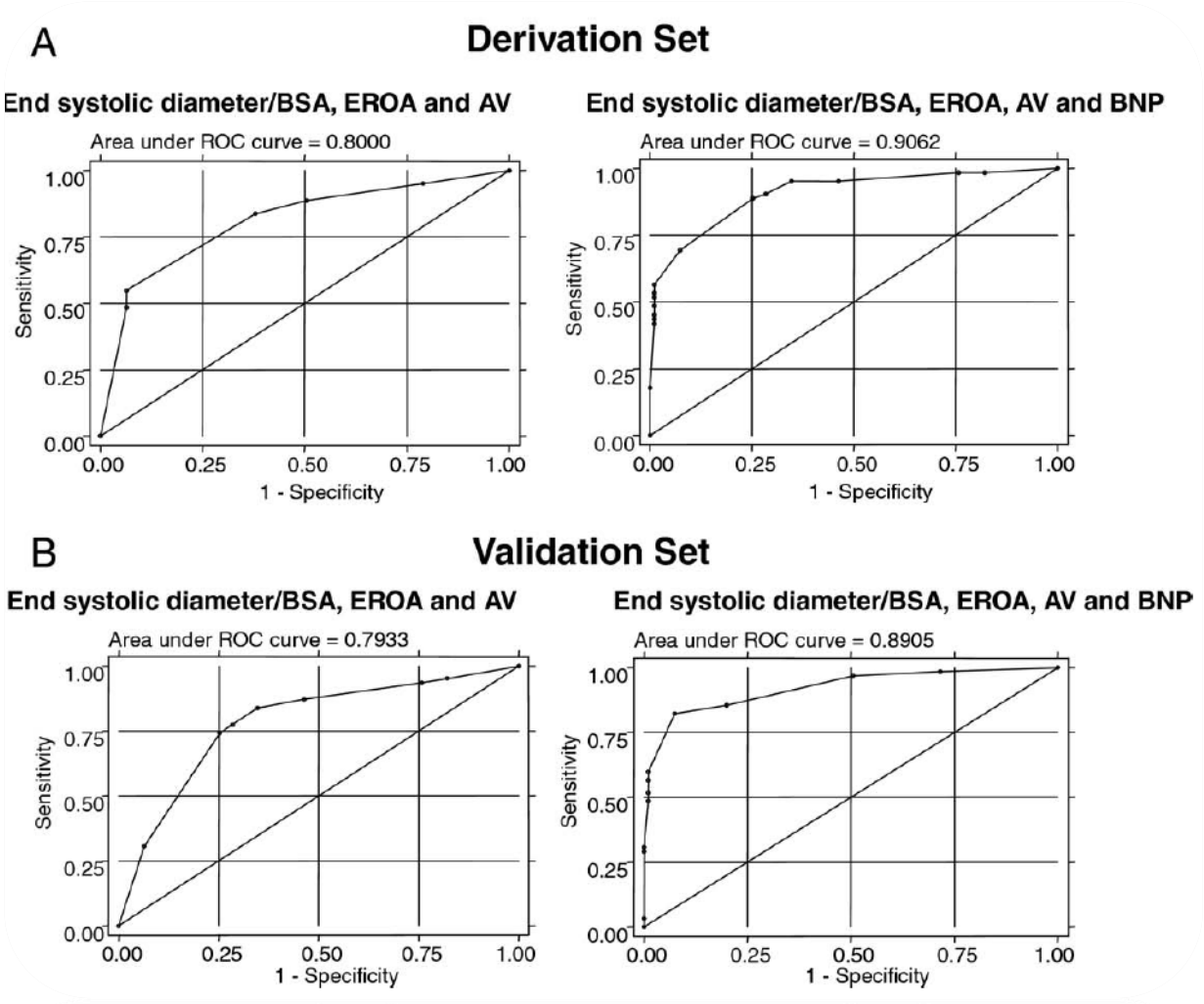
	OR (95% CI)	p Value
BNP ≥105 pg/ml	4.6 (2.7–11.6)	0.0001
End-systolic diameter/BSA >22 mm/m^2	3.4 (1.6–10.7)	0.01
EROA >55 mm^2	4.2 (2.1–11.4)	0.001





Pizarro et al. JACC, 2009

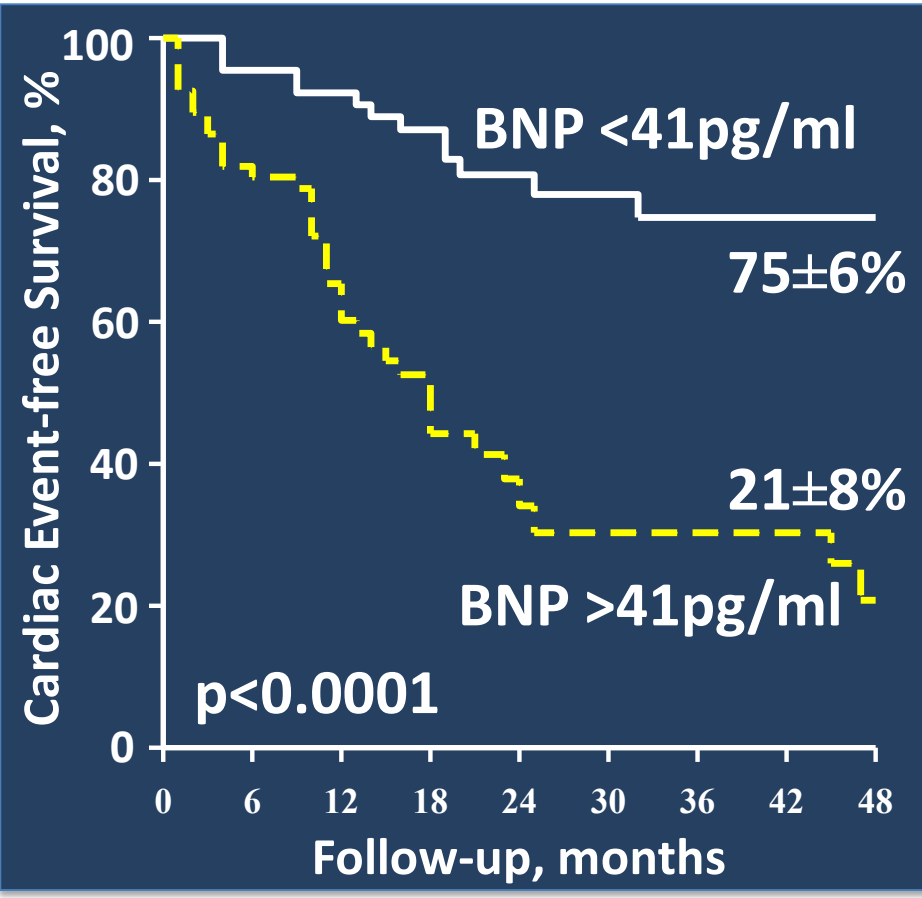
BNP level in Asymptomatic MR



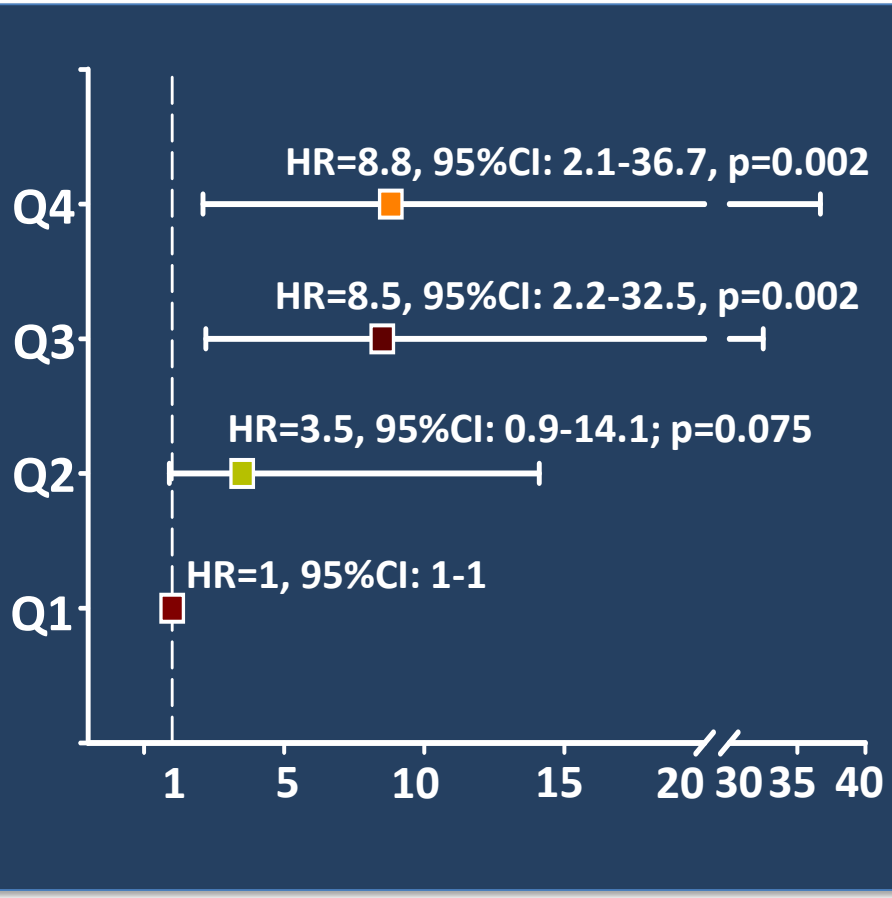
Pizarro et al. JACC, 2009

BNP and Impact on Outcome

KM curves: median of BNP



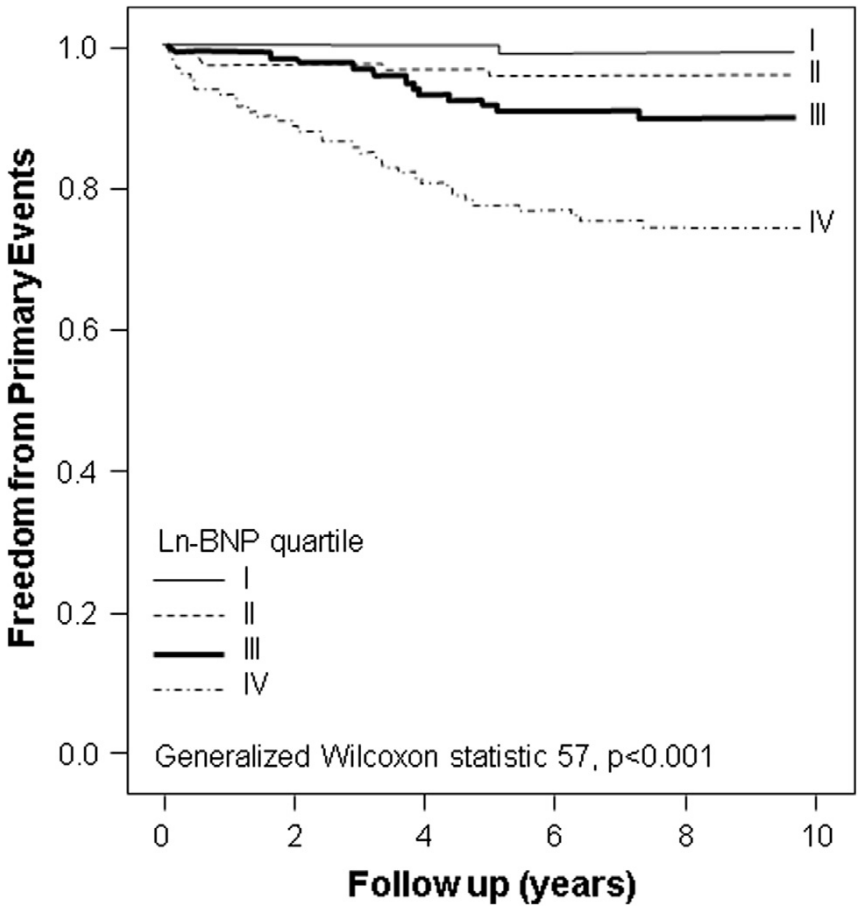
Multivariable Analysis

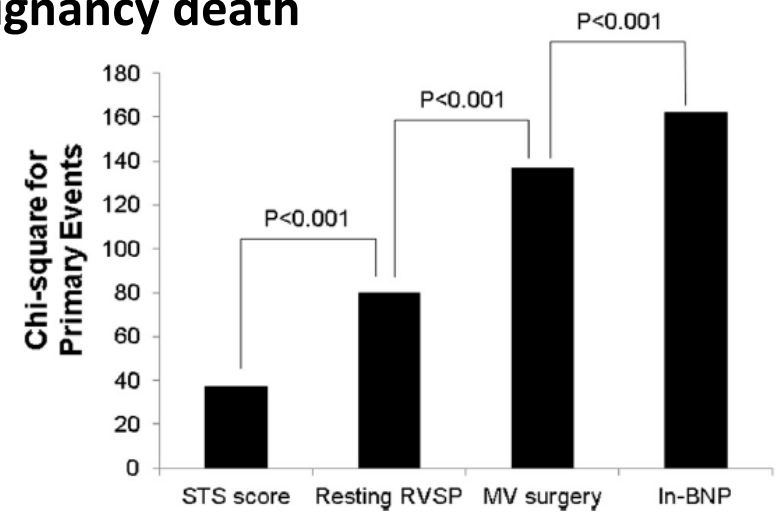


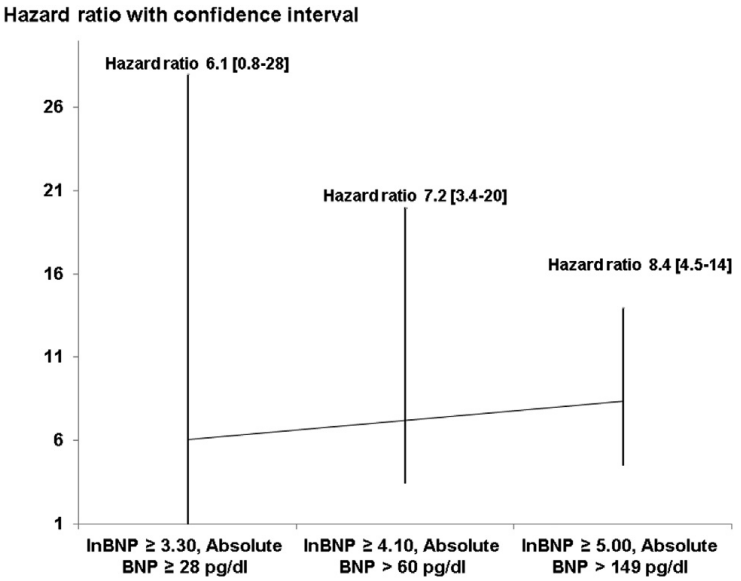
HR=3.5, 95%CI: 1.7-7.2, p=0.001

BNP and Impact on Outcome

n=548 asymptomatic patients, preserved LVEF, moderate to severe MR, primary end-point= non-malignancy death



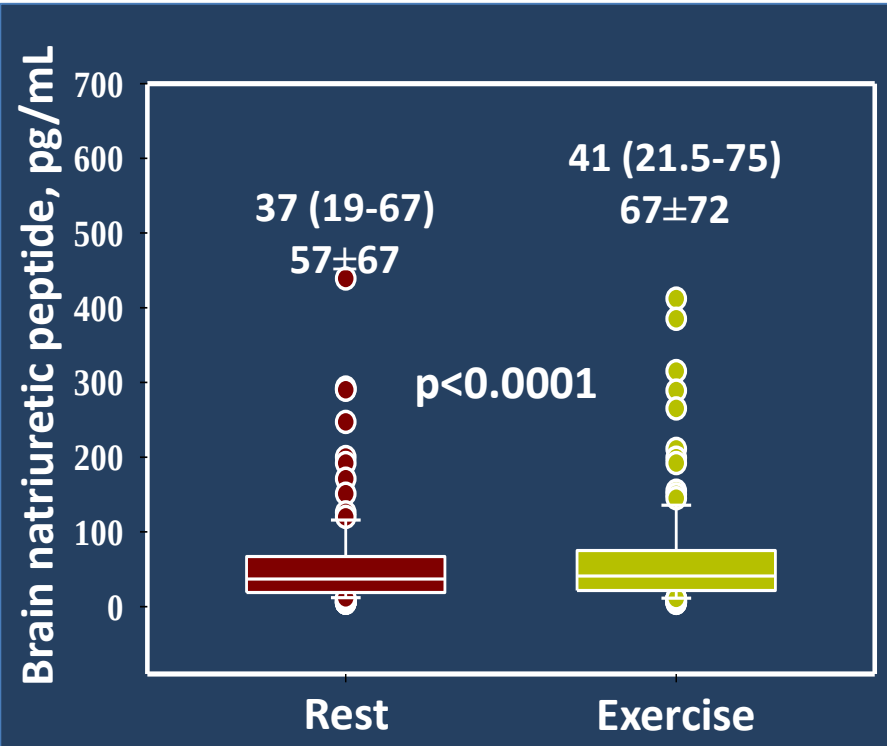




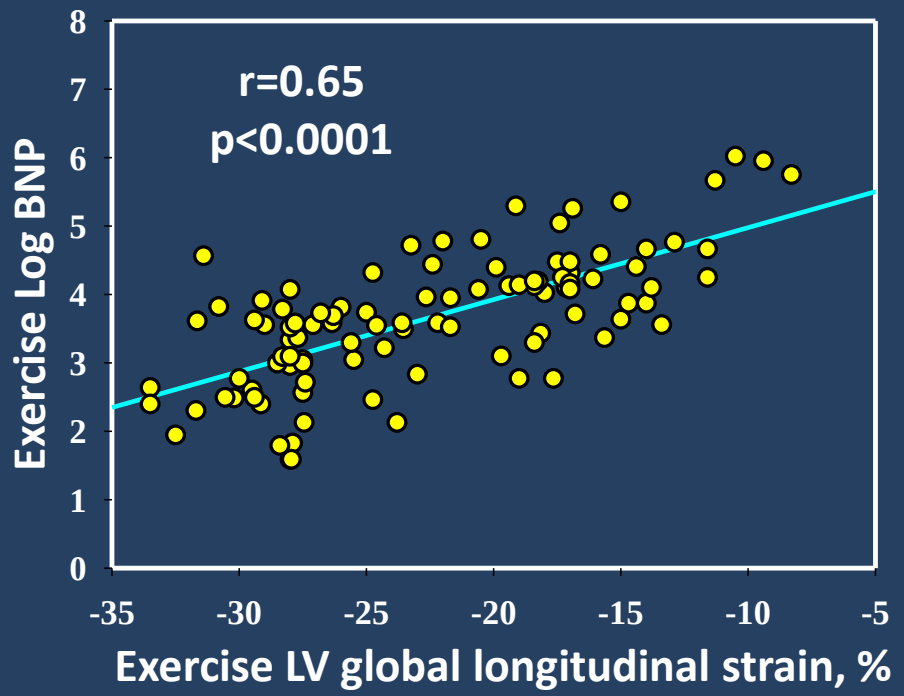
Mentias et al. AJC, 2016

Exercise BNP and Impact on Outcome

BNP level significantly increase during exercise



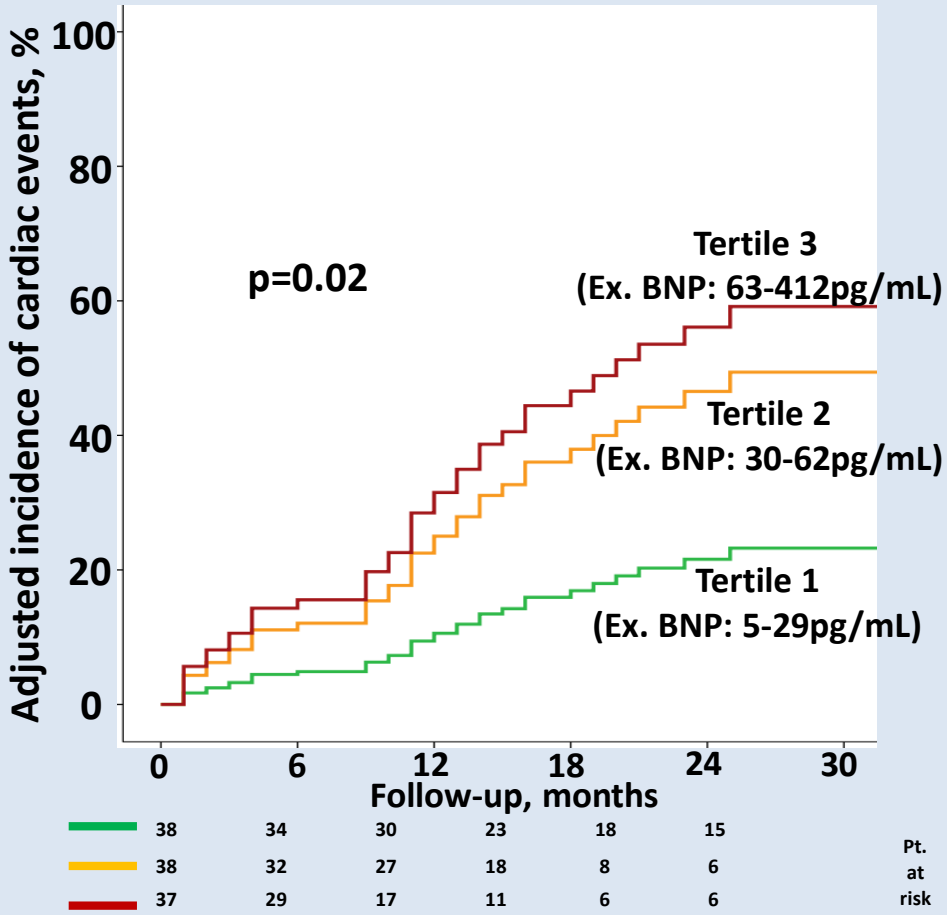
Exercise BNP is determined by ex. LV longitudinal function



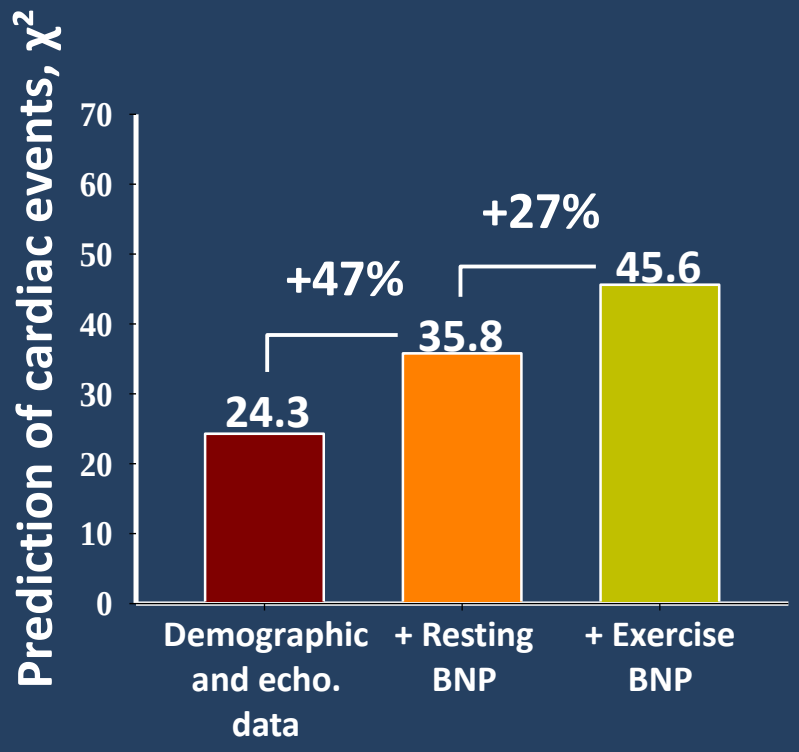
Magne et al. Eur J HF, 2012

Exercise BNP and Impact on Outcome

Exercise BNP level and outcome



Incremental prognostic value of exercise BNP



Magne et al. Eur J HF 2012

Take Home Messages!

- **Despite lack of recommendation, BNP level is of high clinical and prognostic importance in asymptomatic patients with MR**
- **LV diastolic dysfunction, LA, Longitudinal function…are determinants of BNP level**
- **Exercise BNP level may have incremental prognostic value**
- **In asymptomatic patients with severe MR, no LV dysfunction/dilatation, and high BNP level…follow-up should be shorten/surgery could be discussed…**

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