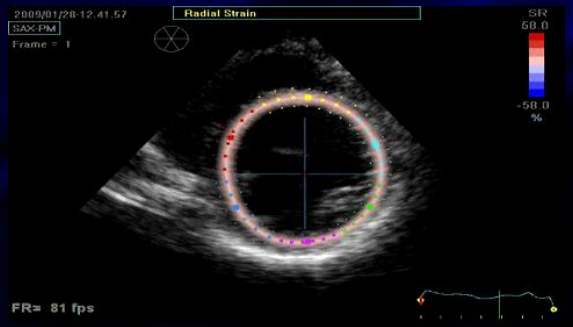
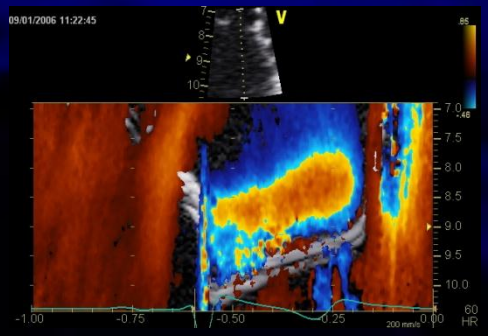
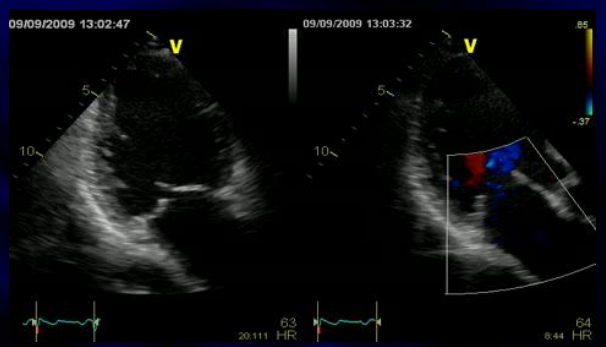
B-type Natriuretic Peptide in VHD: a Non-imaging Helper for the Cardiologist







Dr. Julien Magne, PhD

Sart Tilman Liège, BELGIUM

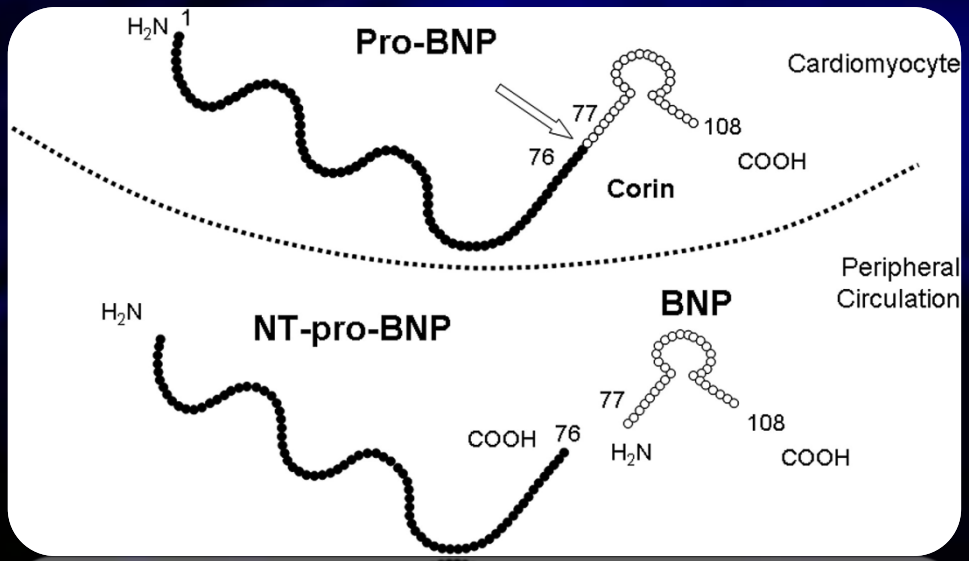
Conflict of Interest Disclosure

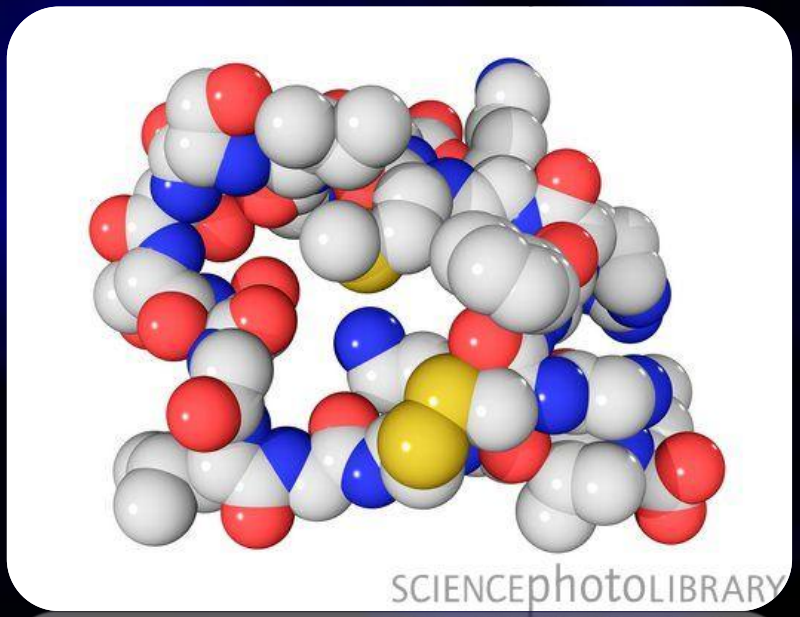
None

BNP Molecular Forms and Processing

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

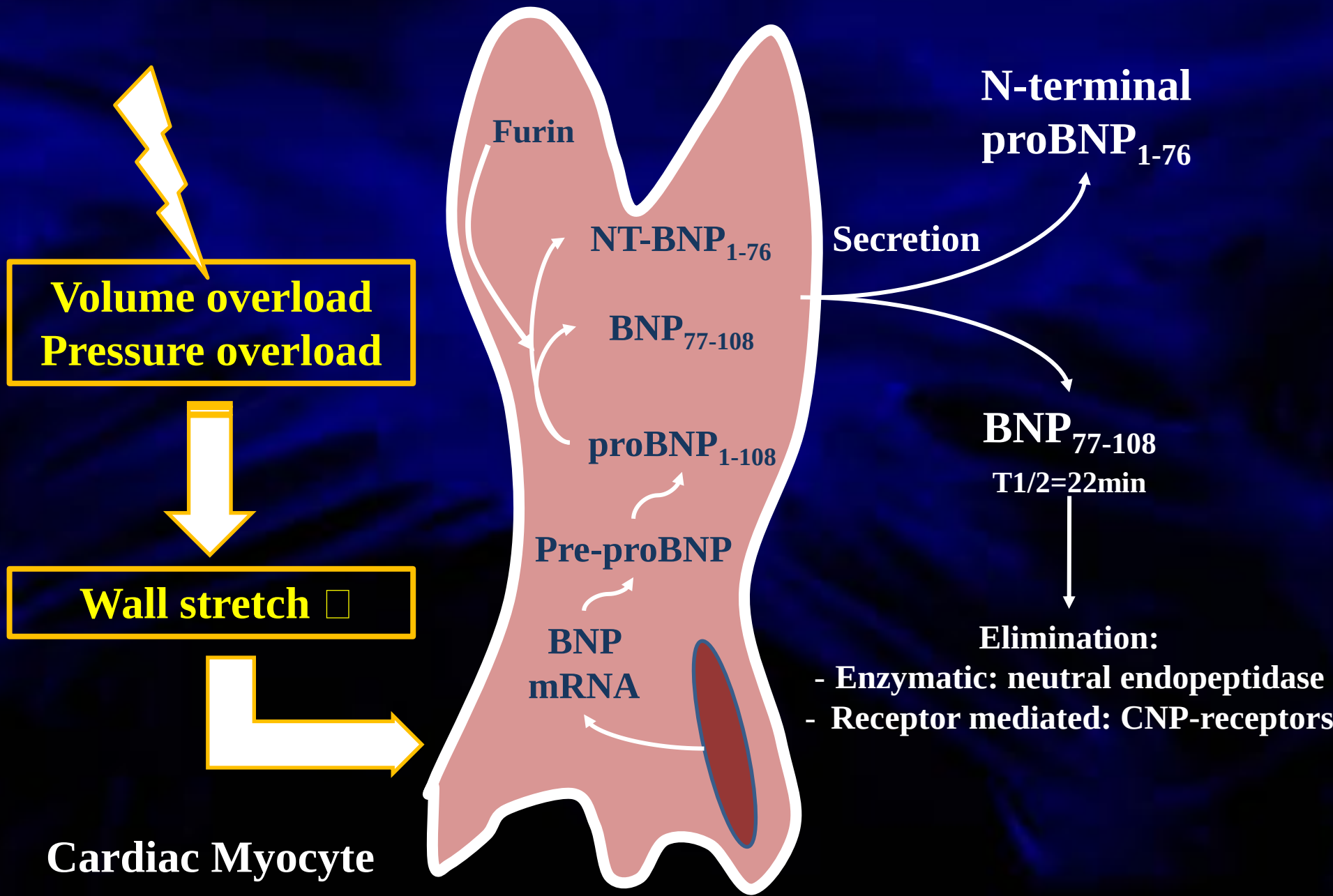
BNP and its inactive amino terminal portion are neurohormones released by the ventricles in response to increased LV wall stress





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 Guidelines

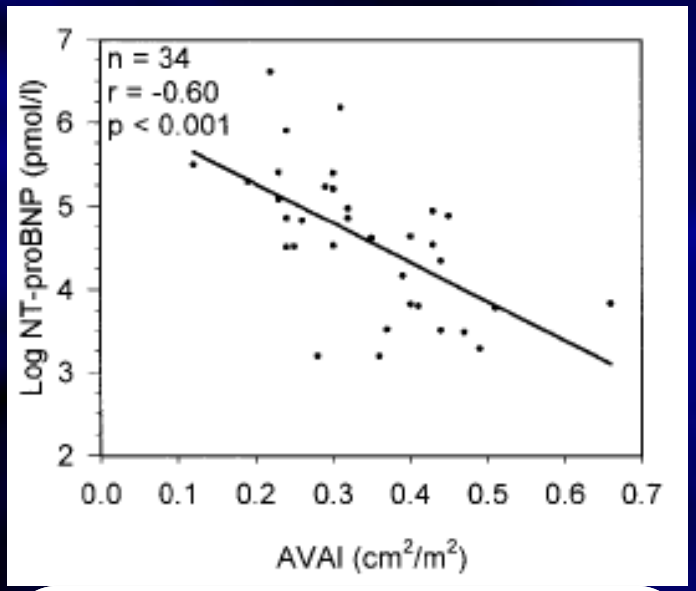
In Aortic stenosis:

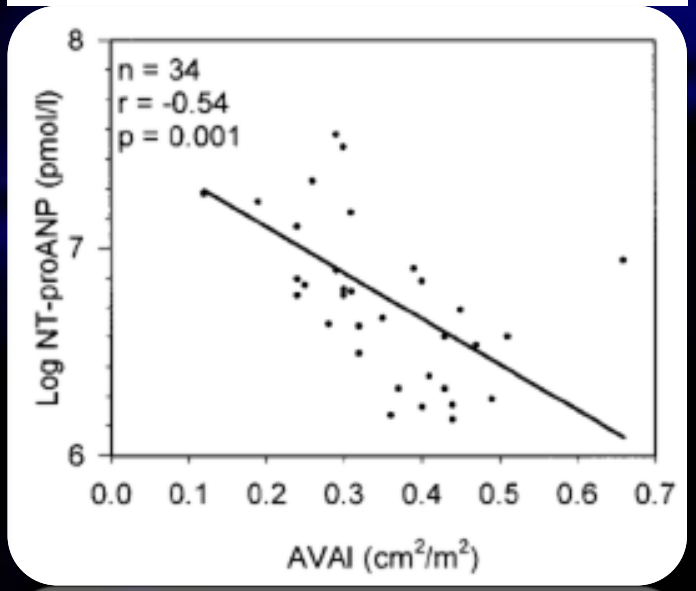
"Natriuretic peptides have been shown in preliminary studies to predict symptom-free survival in AS."

In Mitral regurgitation:

"Preliminary series have also suggested the value of elevated BNP levels as predictors of long-term outcome but this also remains to be validated"

BNP level in AS

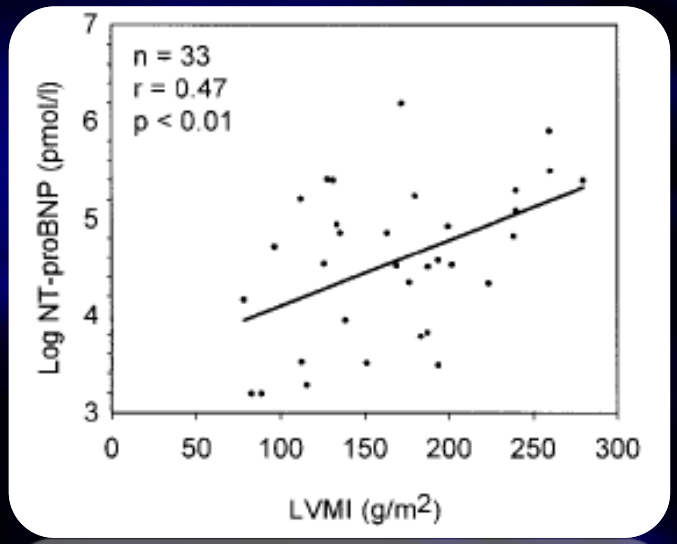




BNP level is correlated with AS severity:

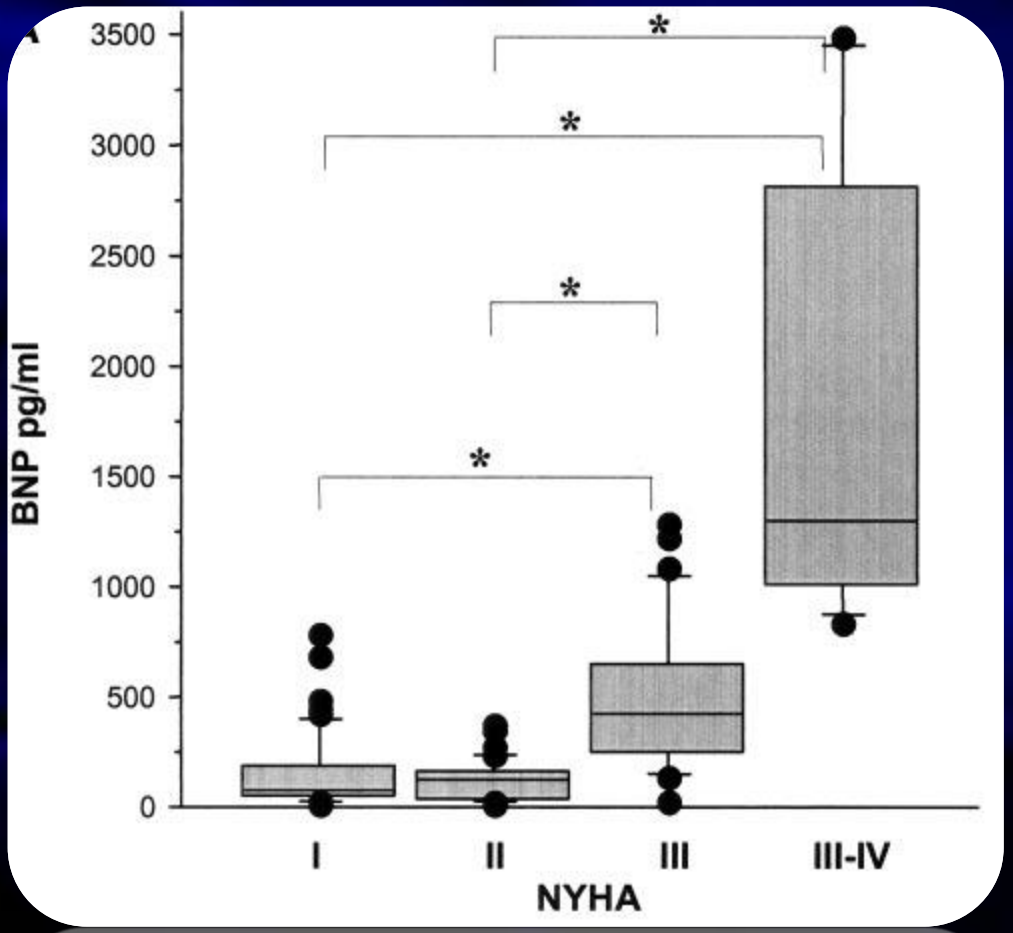
- **++ with AVA**
- **+- with pressure gradient**

BNP is correlated with the consequences of AS on LV



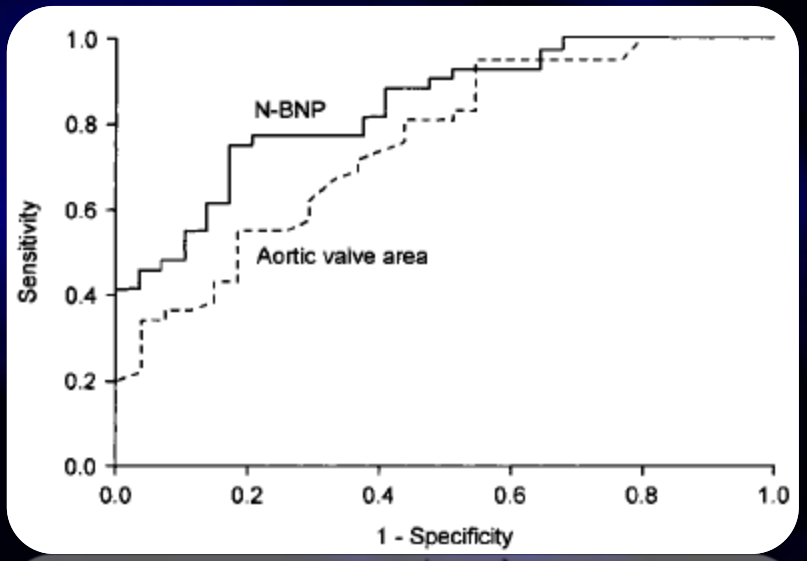
Qi et al. AHC 2001
Gerber et al. Circulation, 2003
Lim et al. Eur Heart J, 2004

BNP level in AS



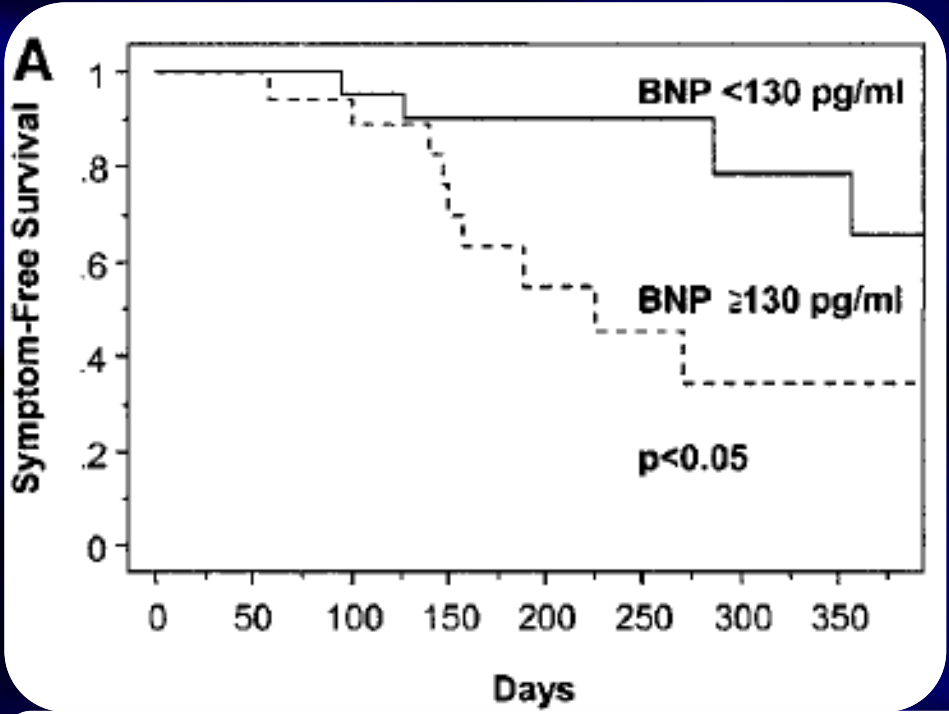
Bergler-Klein et al. Circulation 2004

BNP level is well associated with the symptomatic status



Gerber et al. Circulation 2003

BNP level and Symptoms in AS



- **BNP is more powerful than AS severity parameters to identify symptoms**
- **BNP level may predict the occurrence of symptoms:**

	Baseline			Follow-Up		
	Patients Developing Symptoms (n=14)	Patients Remaining Asymptomatic (n=29)	*P*	Patients Developing Symptoms (n=14)	Patients Remaining Asymptomatic (n=29)	*P*
BNP, pg/mL	188 (56–420)	64 (27–161)	<0.001	486 (83–738)	64 (43–115)	<0.01
NtBNP, pmol/L	131 (50–202)	31 (19–56)	<0.001	136 (37–739)	32 (18–67)	<0.01

Bergler-Klein et al. Circulation 2004

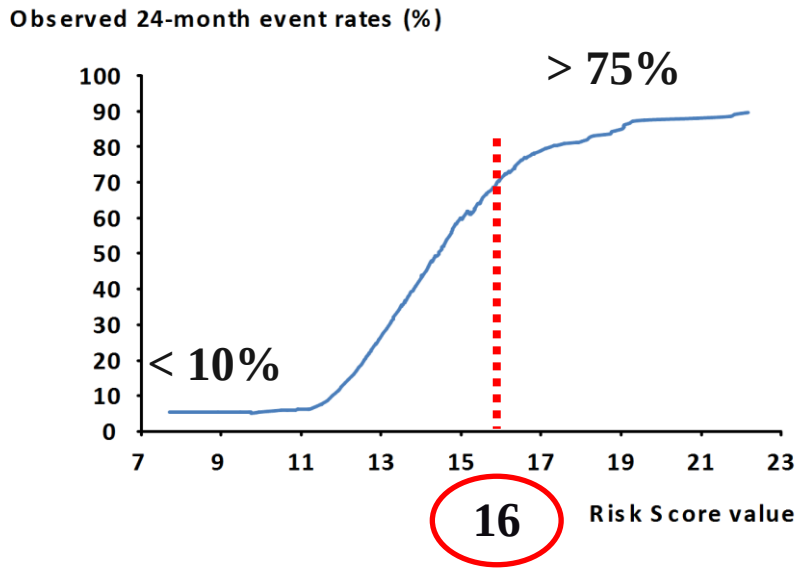
BNP for Risk Stratification in asymptomatic AS

Risk Score for Predicting Outcome in Patients With Asymptomatic Aortic Stenosis

Jean-Luc Monin, MD, PhD; Patrizio Lancellotti, MD, PhD; Mehran Monchi, MD; Pascal Lim, MD; Emmanuel Weiss, MD; Luc Piérard, MD, PhD; Pascal Guéret, MD

- **107 pts followed in Créteil**
- **Risk score according to independent variables**
- **Validation in Liège (107 pts)**

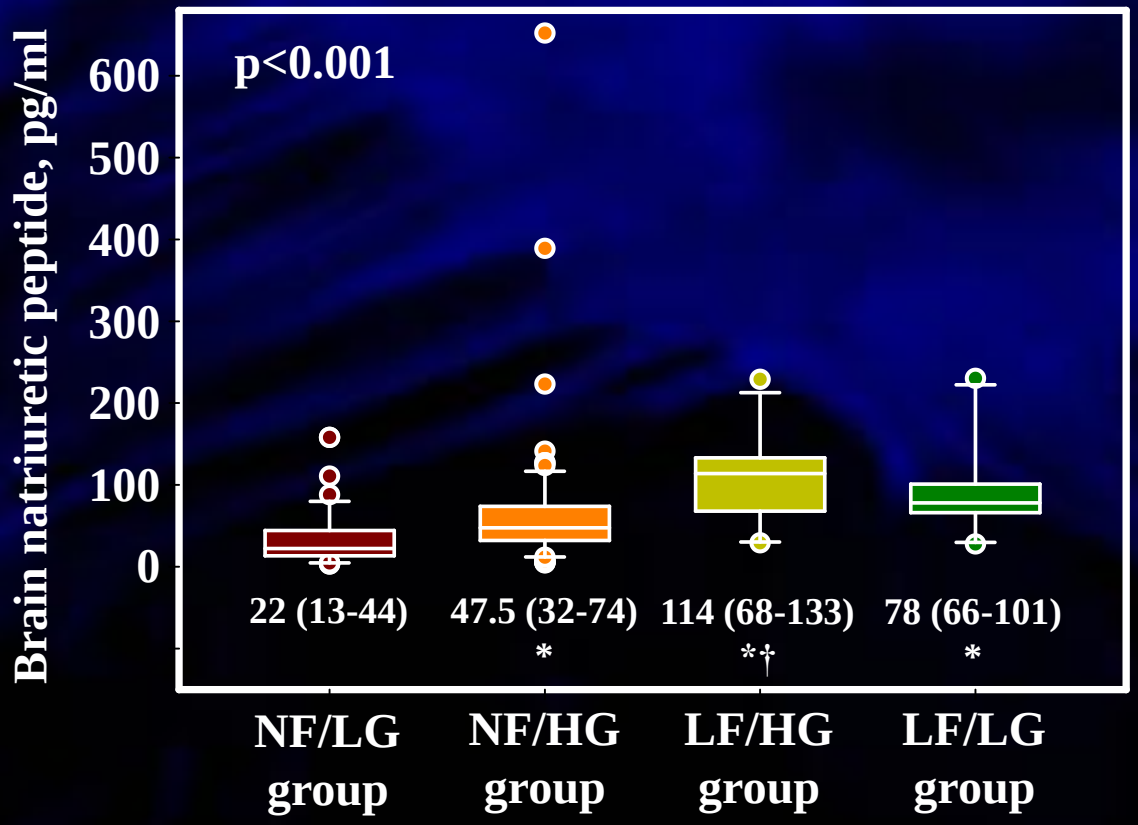
Score = (Peak velocity x 2) + (nat log BNP x 1.5) + 1.5 (if female)



Monin et al. Circulation, 2009

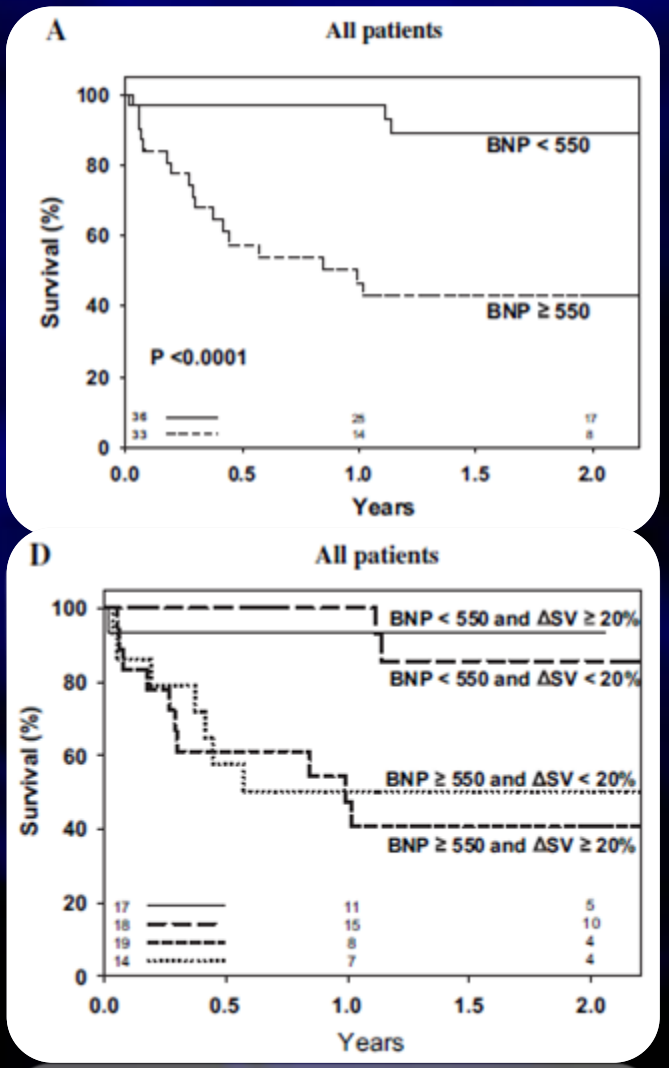
BNP level in LF/LG AS

BNP is significantly elevated in LF AS, even in paradoxical LF/LG AS.
BNP level >550pg/mL strong predictor of outcome in LF/LG AS



Lancellotti, Magne et al. JACC, 2012

TOPAS study

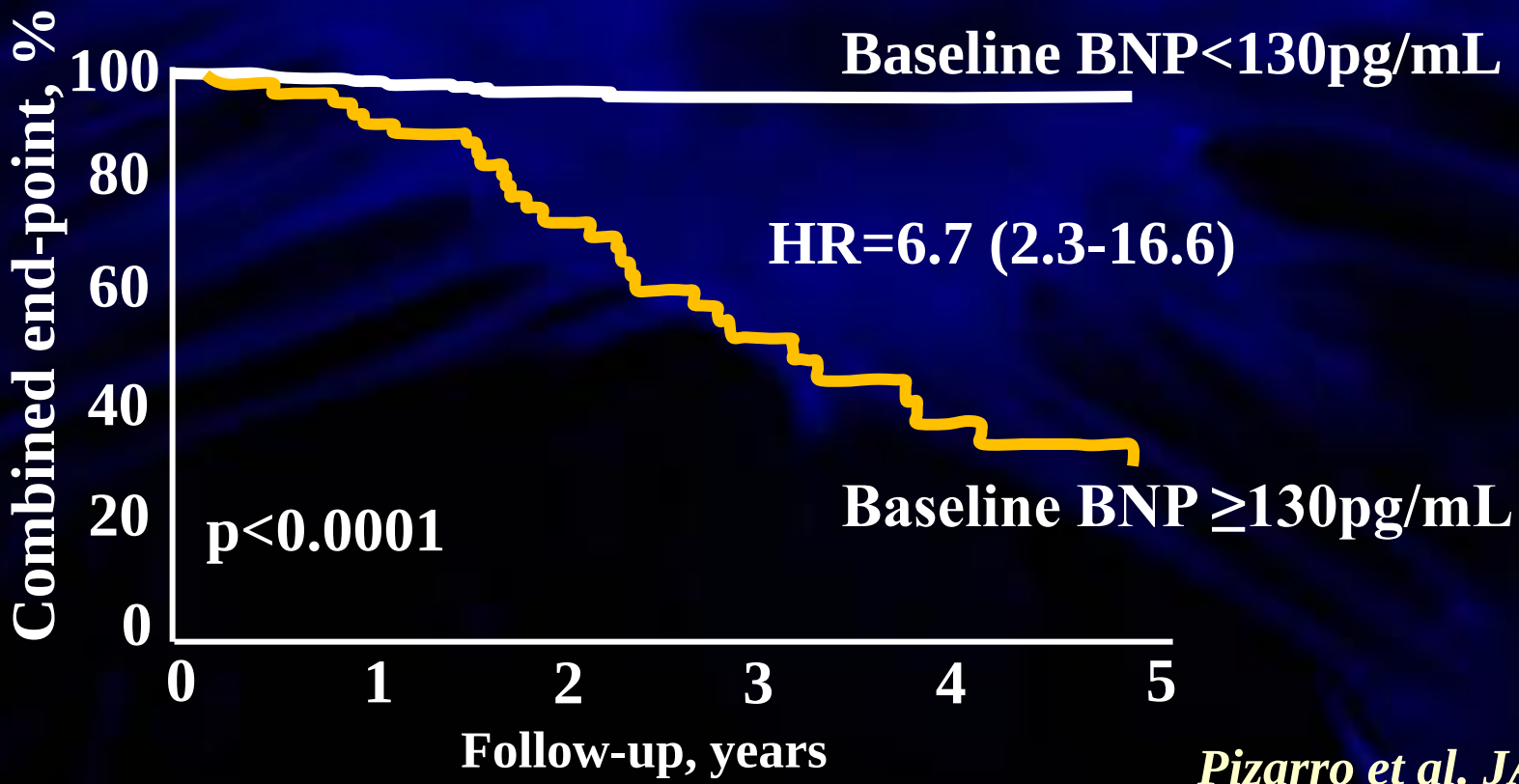


Bergler-Klein et al. Circulation, 2007

BNP level in Aortic Regurgitation

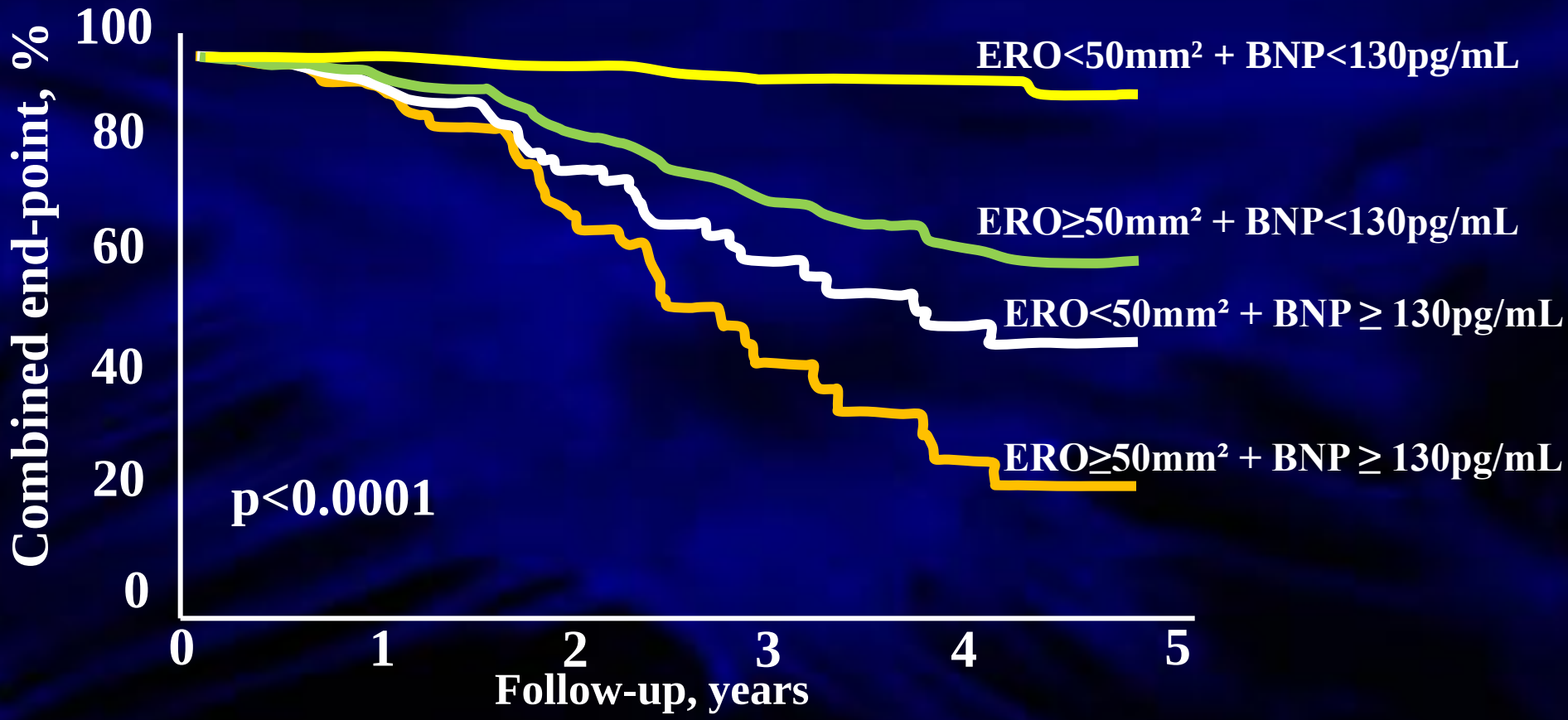
Derivation (n=160) and validation (n=134) cohorts of asymptomatic severe AR and no LV dilatation/dysfunction

Combined end-point defined as LV dysfunction, symptoms or death



Pizarro et al. JACC, 2011

BNP level in Aortic Regurgitation



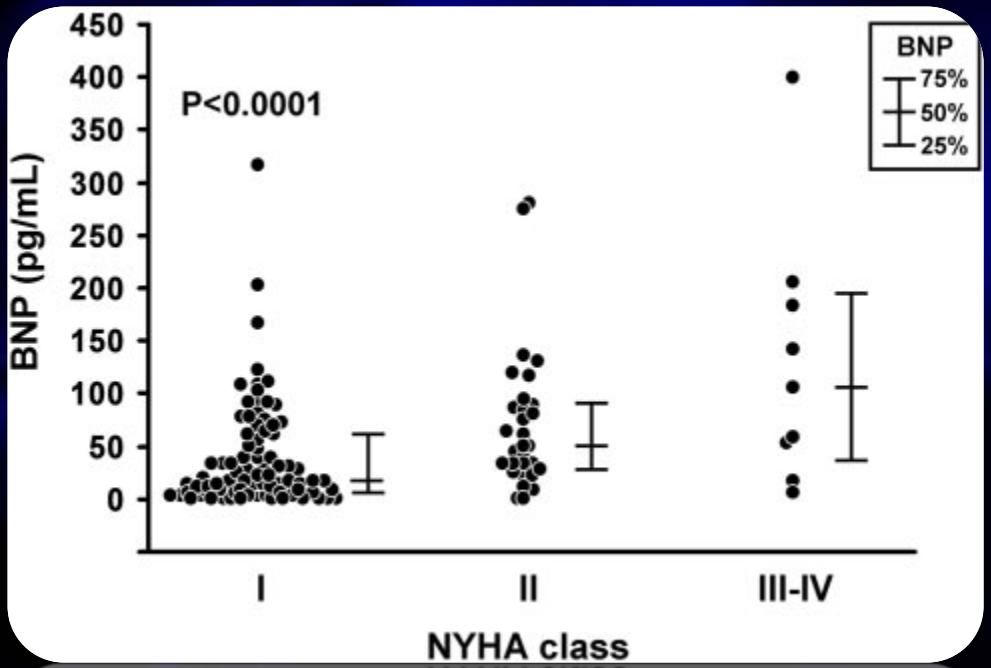
Endpoint	OR (95% CI)	p Value
BNP ≥130 pg/ml	6.9 (2.52–17.57)	0.0001
ESD/BSA ≥24 mm/m^2	3.4 (1.88–11.9)	0.01
EROA ≥50 mm^2	4.3 (2.4–12.4)	0.001
EDD ≥35 mm/m^2	2.1 (0.88–13.7)	0.09

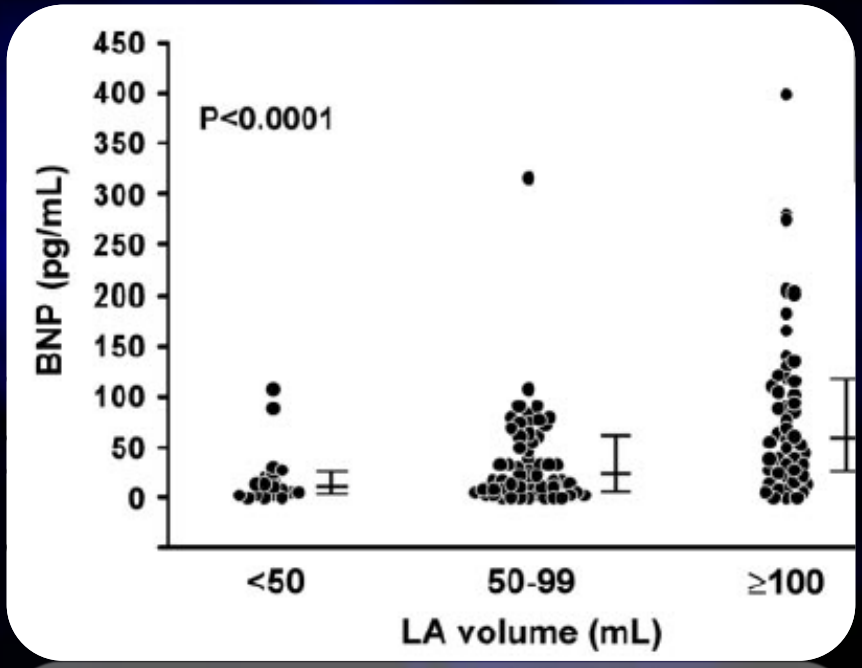
Multivariate predictors of Cardiac events

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

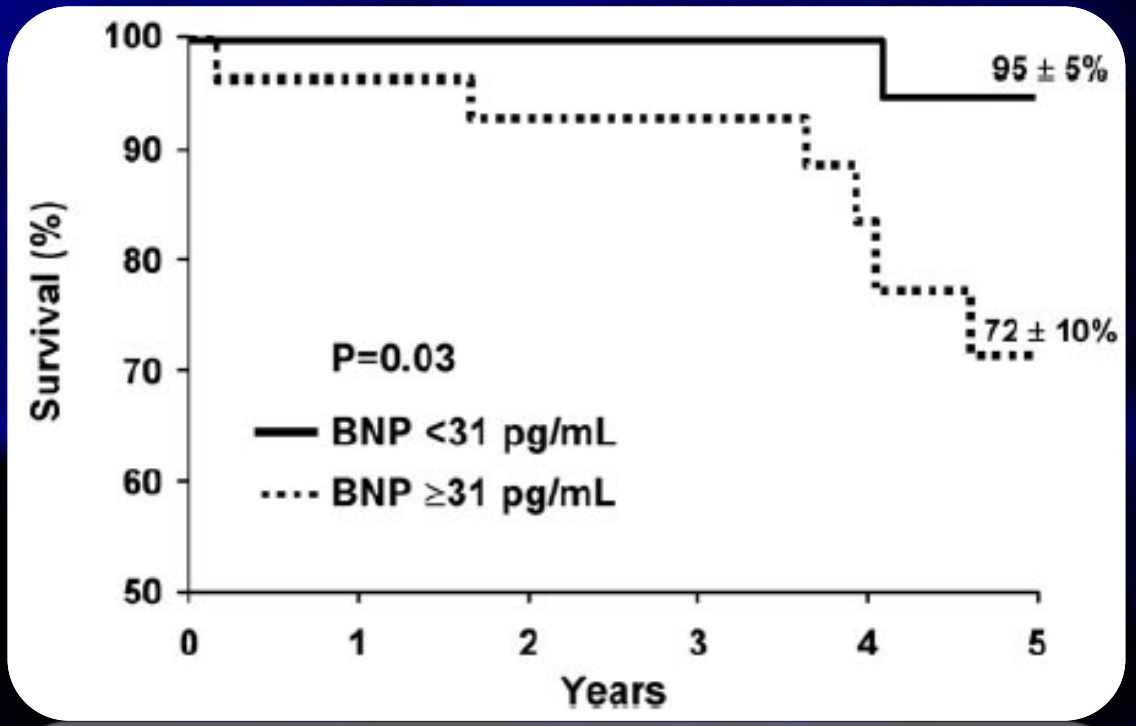
BNP level in Mitral Regurgitation

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 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

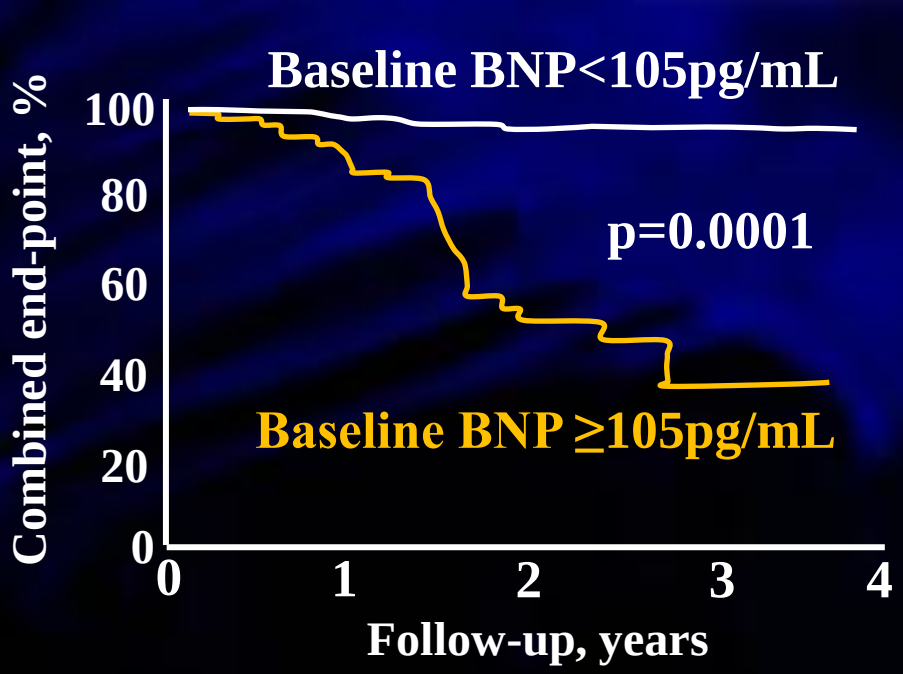
- BNP is a good marker of advanced stage of the disease

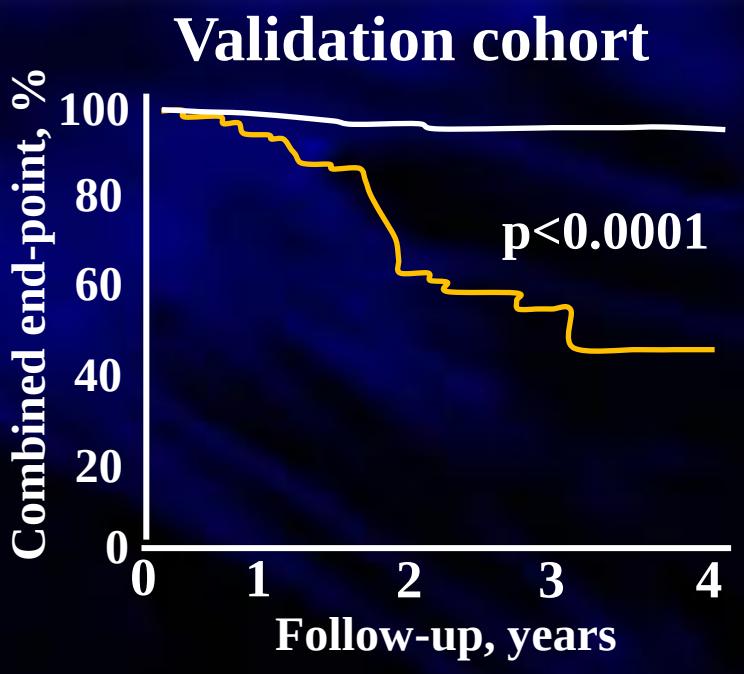
Pizarro et al. JACC, 2009

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

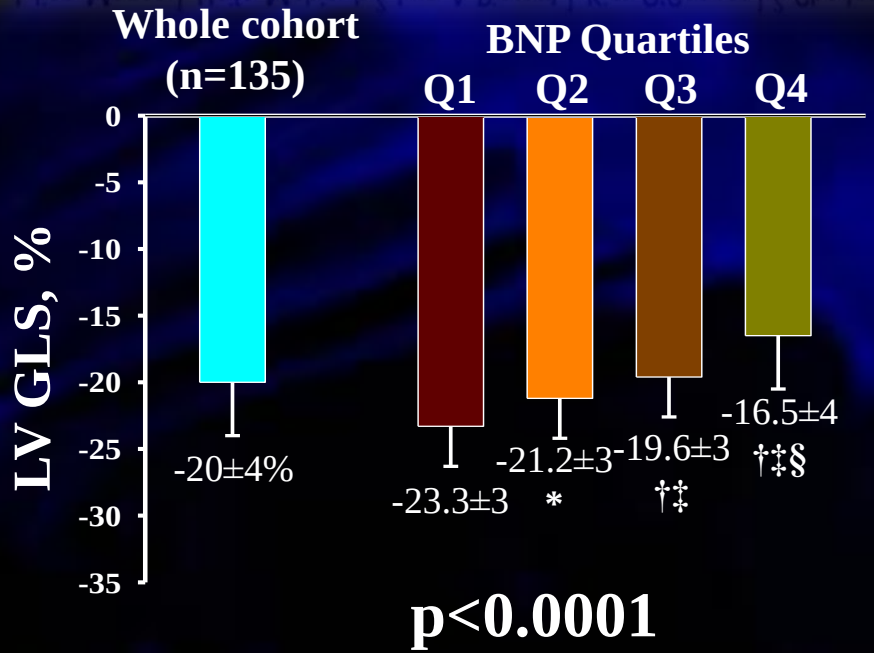
LV Longitudinal Function and BNP Level

ORIGINAL ARTICLE

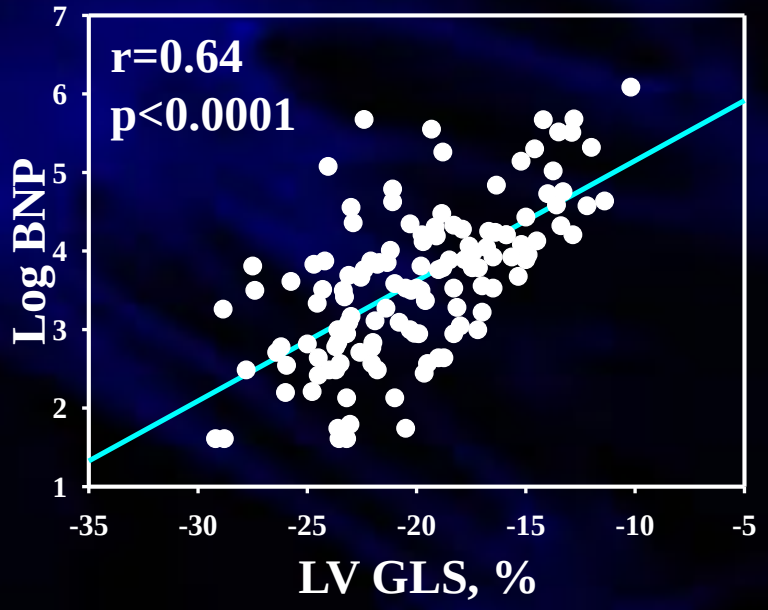
Prognostic importance of brain natriuretic peptide and left ventricular longitudinal function in asymptomatic degenerative mitral regurgitation

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



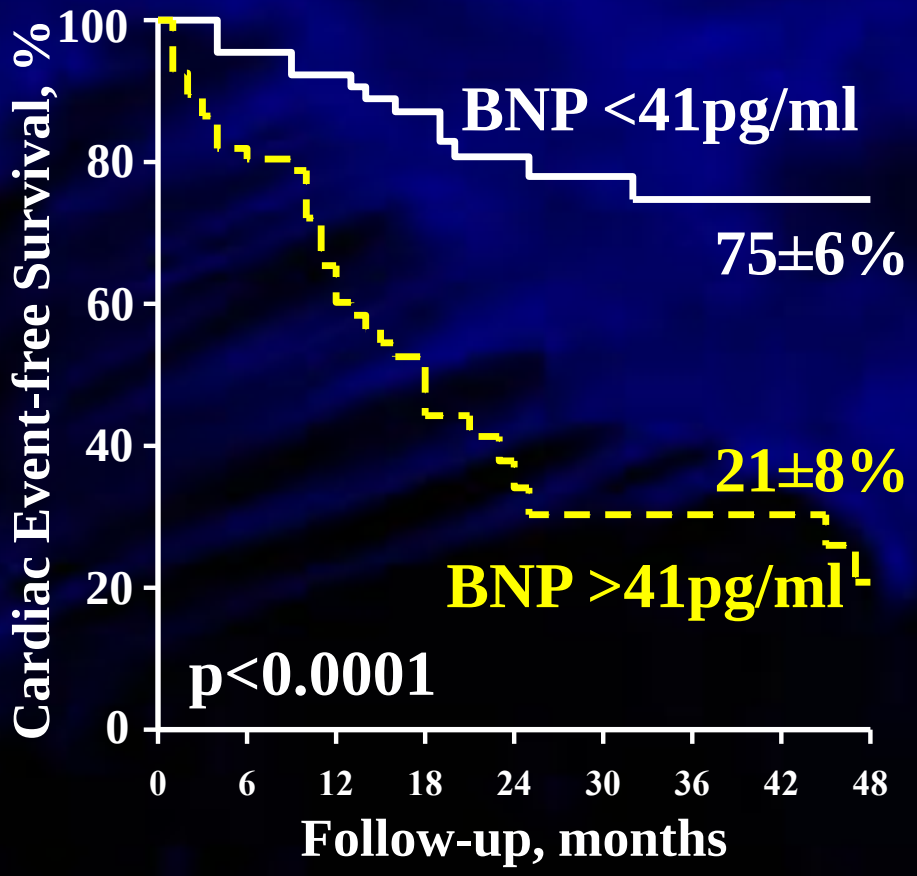
p<0.0001



Magne et al. Heart 2012

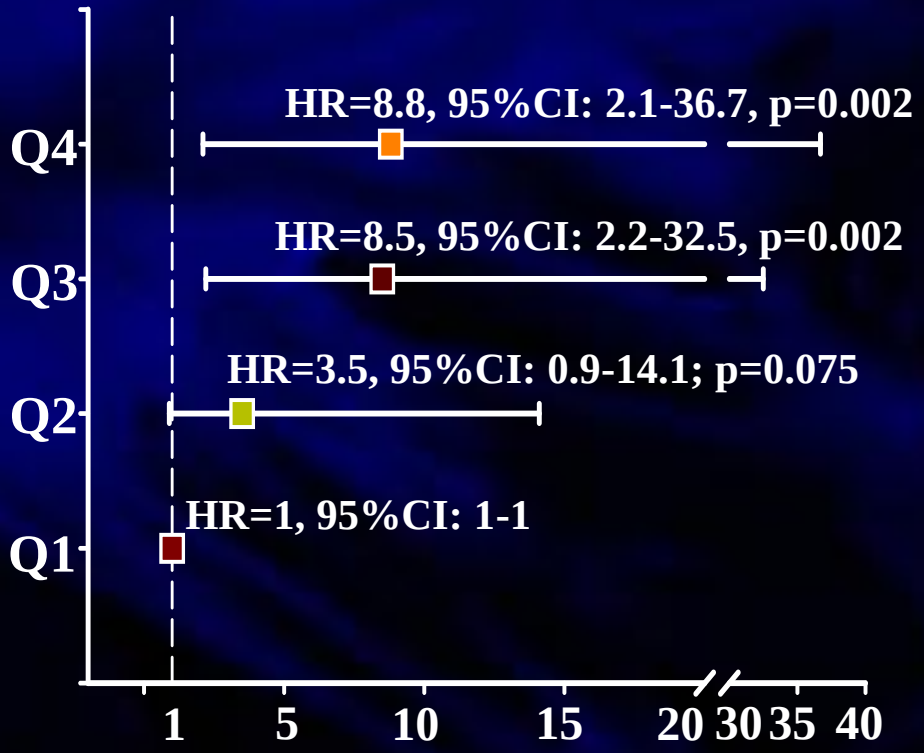
BNP and Impact on Outcome

KM curves: median of BNP



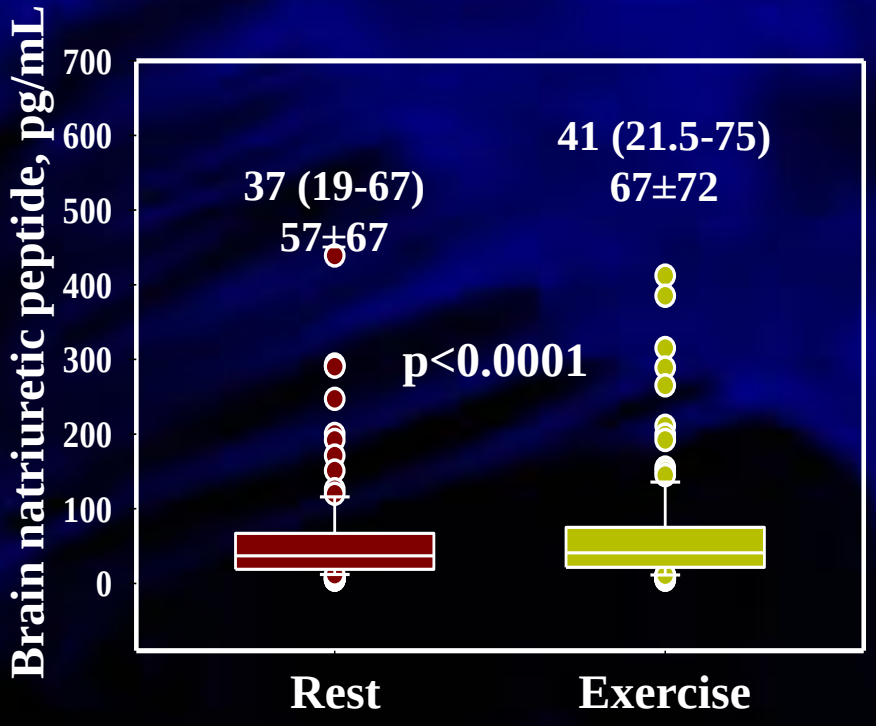
HR=3.5, 95%CI: 1.7-7.2, p=0.001

Multivariable Analysis

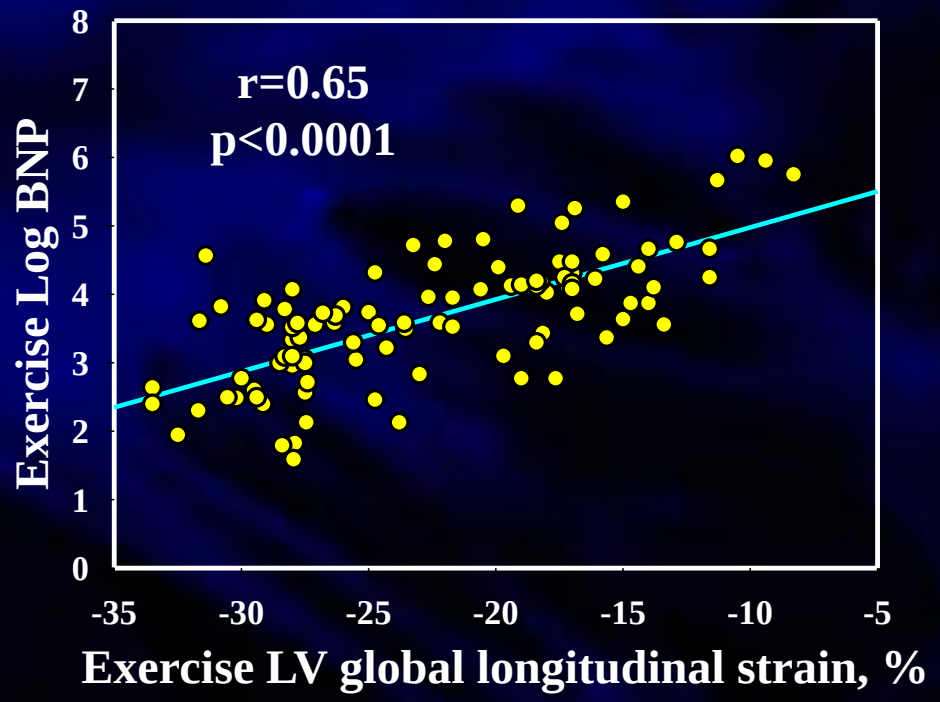


Exercise BNP and Impact on Outcome

BNP level significantly increase during exercise



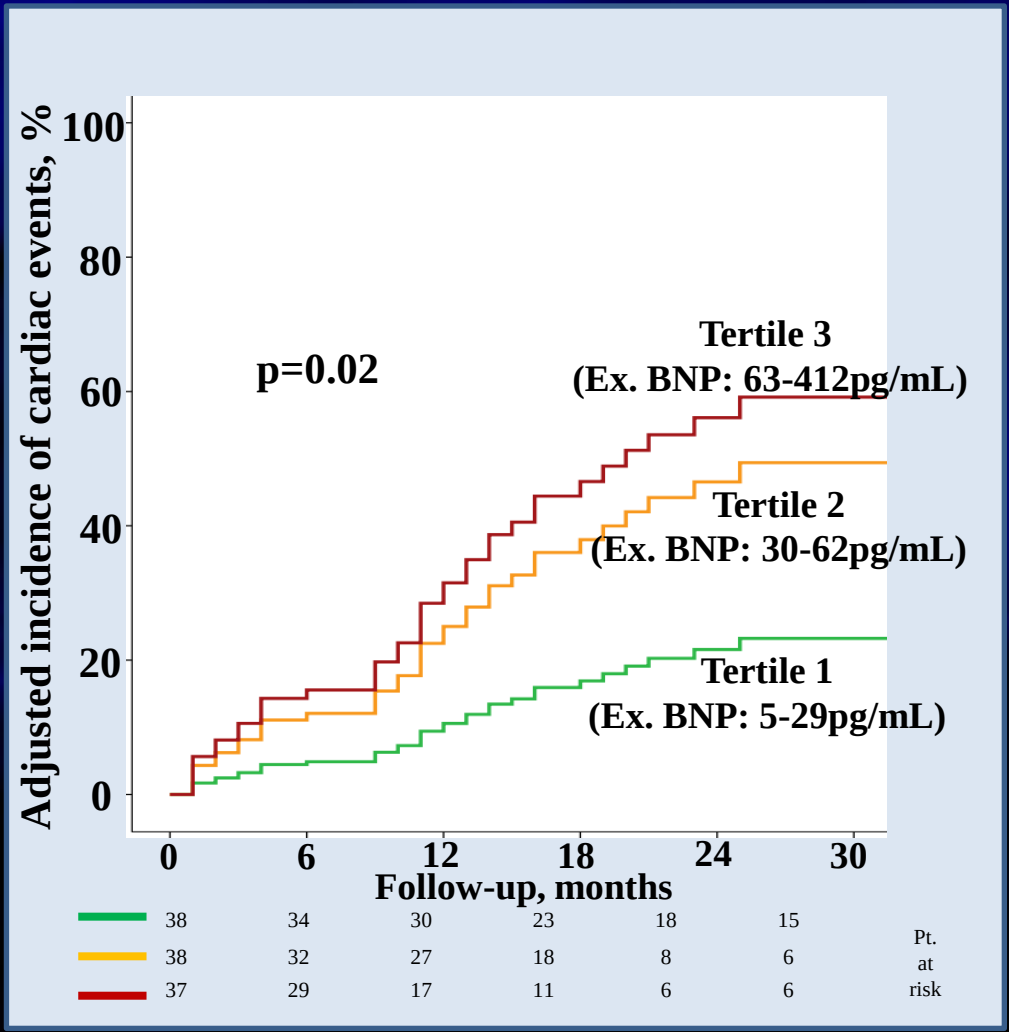
Exercise BNP is determined by ex. LV longitudinal function



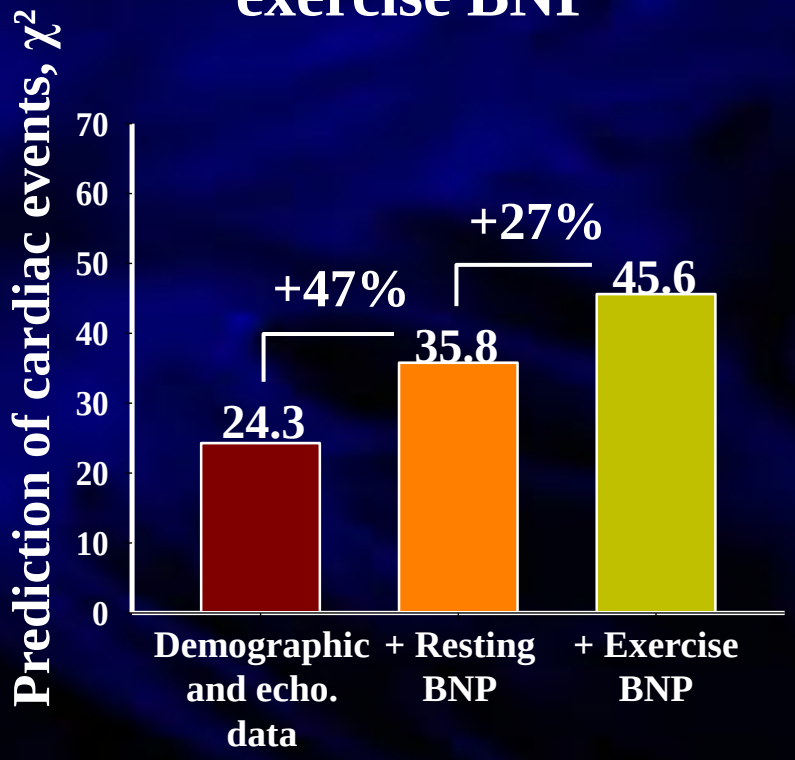
Magne et al. Submitted 2012

Exercise BNP and Impact on Outcome

Exercise BNP level and outcome



Incremental prognostic value of exercise BNP



Magne et al. Submitted 2012

BNP in VHD: Take Home Messages

- **In severe AS, BNP is a powerful predictor of the occurrence of symptoms and of poor outcome in asymptomatic pts (when combined with AS severity and gender)**
- **In LF/LG AS, BNP>550pg/mL is associated with significant reduced survival.**
- **In severe AR, BNP>130pg/mL multiplies by 7 the risk of cardiac events.**
- **In severe primary MR, BNP>105pg/mL multiplies by 4.5 the risk of cardiac events.**
- **In asymptomatic primary MR, exercise BNP level may have important incremental prognostic value.**

DON'T MISS

5-8 December 2012
MAICC – Athens, Greece

Abstract submission deadline
31 May

Early bird registration
30 September

Thank you for your attention.

Fonds Léon Fredericq

"In these matters the only certainty is that nothing is certain."

Pliny The Elder, 23 AD-79 AD

fnrs
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