



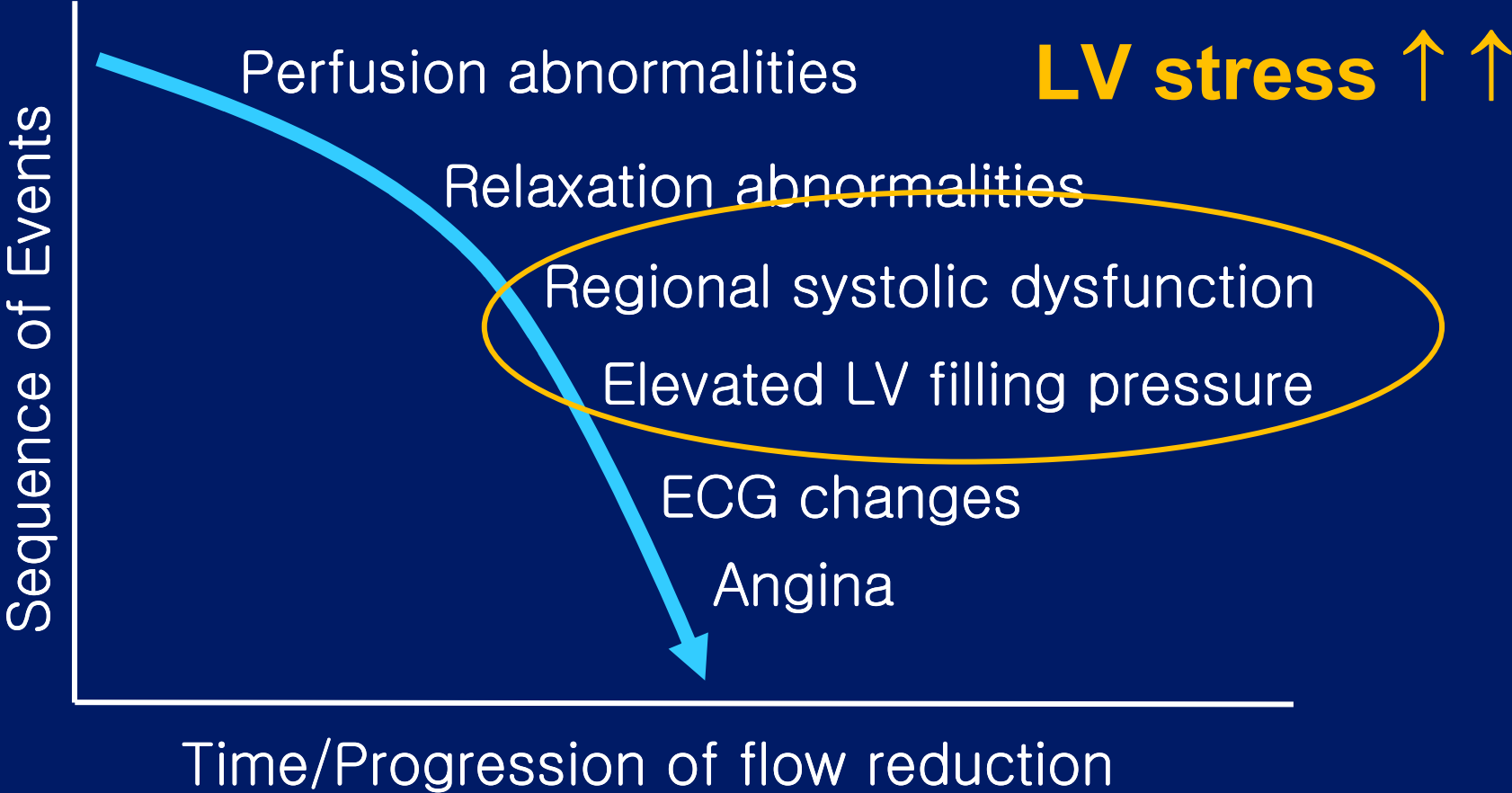
BNP in Vascular Disease

신준한
아주의대 순환기내과

Diseases Related to Elevated BNP

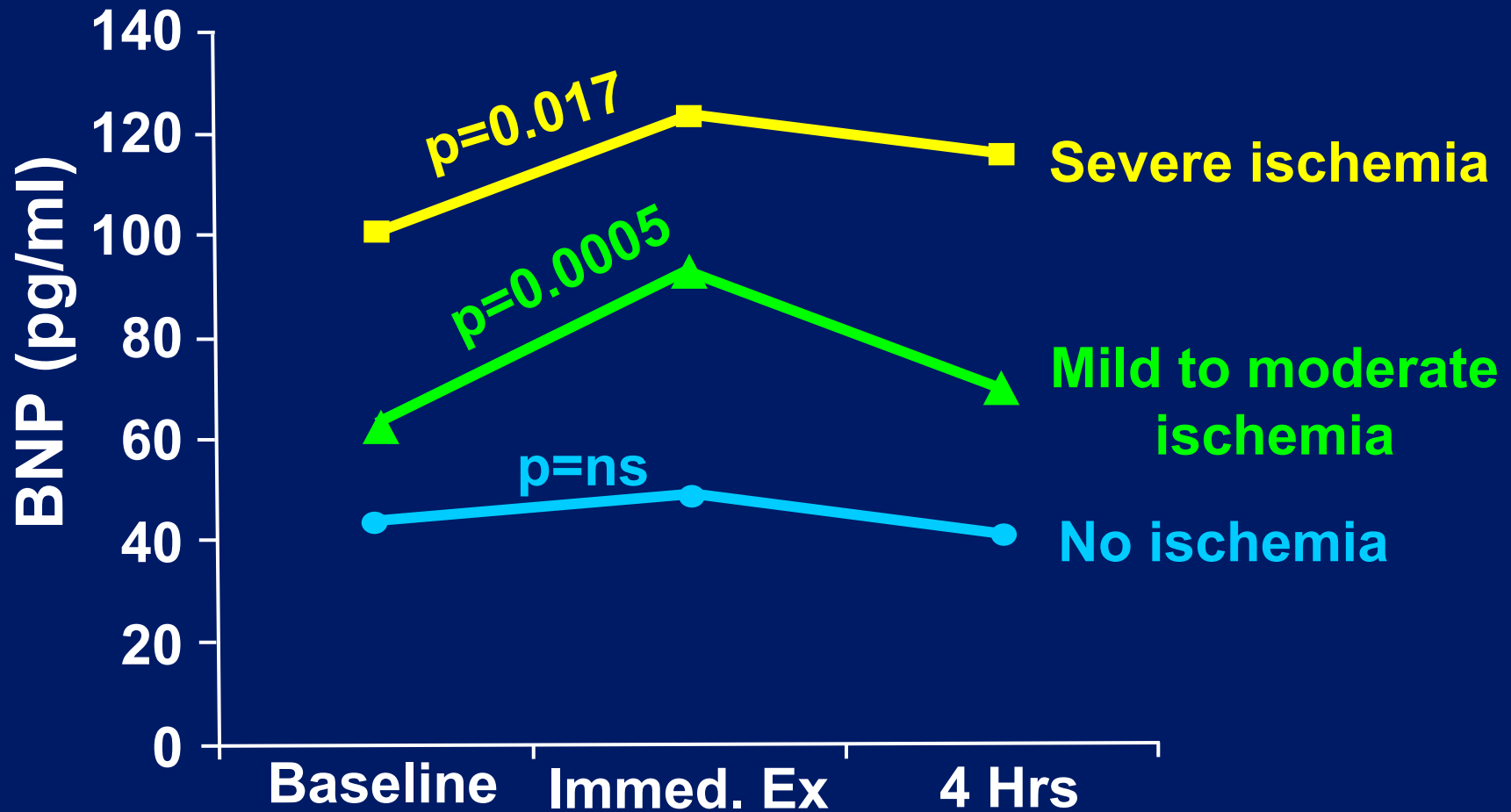
Cardiac	Non-Cardiac
<ul style="list-style-type: none">• Heart failure• Coronary artery disease• Diastolic dysfunction• LV hypertrophy• Hypertrophic CM• Restrictive CM• Constrictive pericarditis• Valvular heart disease• Atrial fibrillation• Cardiac amyloidosis	<ul style="list-style-type: none">• COPD• Pulmonary embolism• Pulmonary hypertension• Sepsis• Hypertension• Subarachnoid hemorrhage• Renal failure

Ischemic Cascade

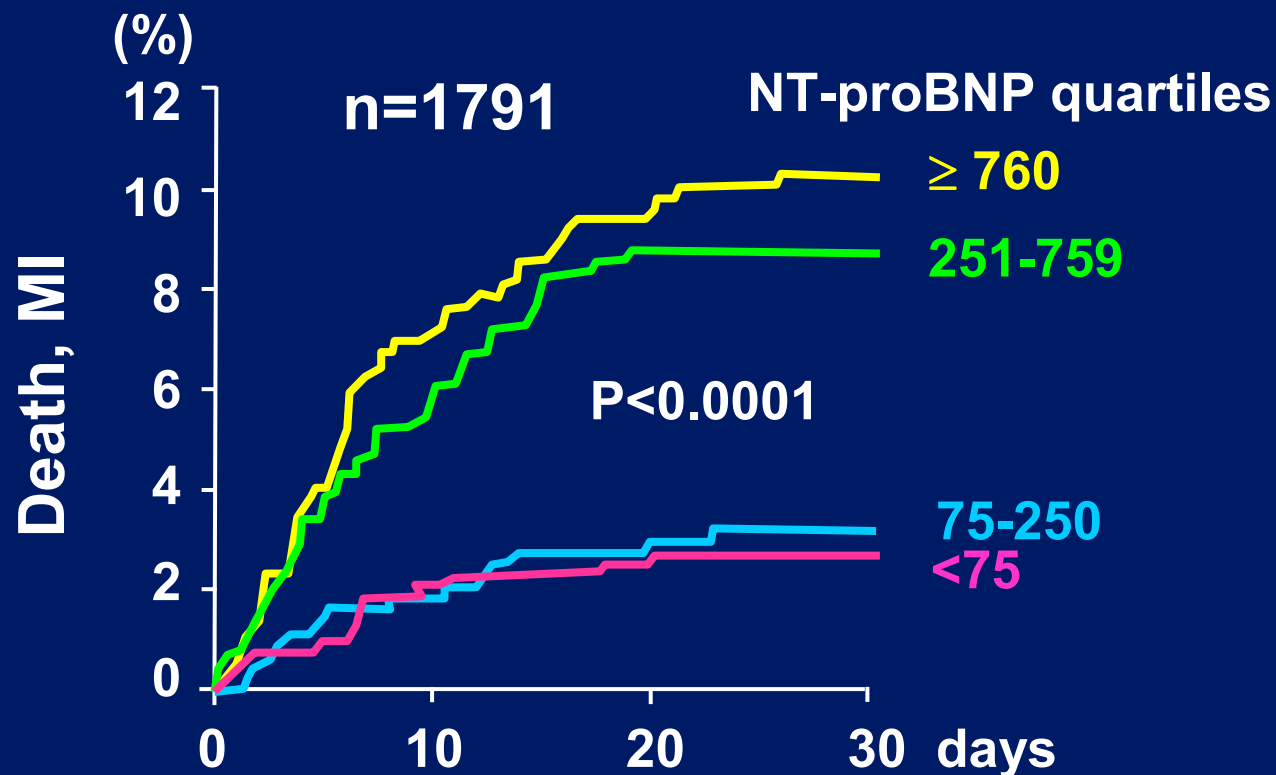


BNP in relation to myocardial ischemia

Exercise PET study



Prognostic Value of BNP in Acute Coronary Syndrome



PRISM investigators. Circulation 2004;110:3206-3212

Multivariate Analysis for Prognosis

BNP is a powerful and independent determinant beyond conventional risk markers in ACS

Variable	Risk Ratio (95% CI)	P value
Age > 66 yr-old	2.5 (1.4 – 4.3)	0.001
LVEF < 47%	1.9 (1.1 – 3.1)	0.01
Killip class >1	3.2 (1.9 – 5.5)	<0.0001
BNP > 545 pmol/L	2.1 (1.1 – 3.9)	0.02

Large Studies to Confirm the Prognostic Value of BNP in Acute Coronary Syndrome

Study	No.	Sampling time	measurement
OPUS-TIMI 16	2525	40 h post Sx	BNP
Jernberg et al.	775	Adm	NT-proBNP
TACTICS-TIMI 18	1676	Adm	BNP
FRISC II	2019	39 h post Sx	NT-proBNP
GUSTO IV	6809	9.5 post Sx	NT-proBNP
Richards et al.	666	1-4 d post Sx	both
ICTUS	1141	Adm	NT-proBNP

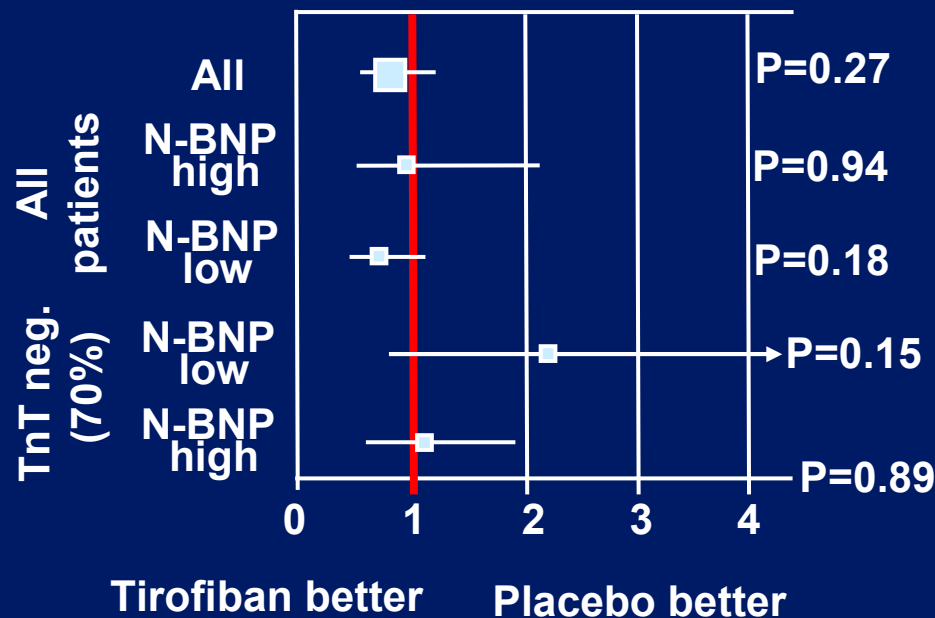
Diagnostic Value of BNP for Chest Pain Potential ACS in Emergency Setting (n=426)

Tests	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Acute MI (cutoff 51 pg/ml)	87.2	62.3	18.8	98.0
Myoglo, CKMB, cTnl + BNP	97.4	47.8	15.8	99.5
All ACS (cutoff 31 pg/ml)	75.2	61.8	20.6	93.9
Myoglo, CKMB, cTnl + BNP	88.1	43.9	18.0	95.5

Useful adjunct to conventional markers in chest pain with non-diagnostic test

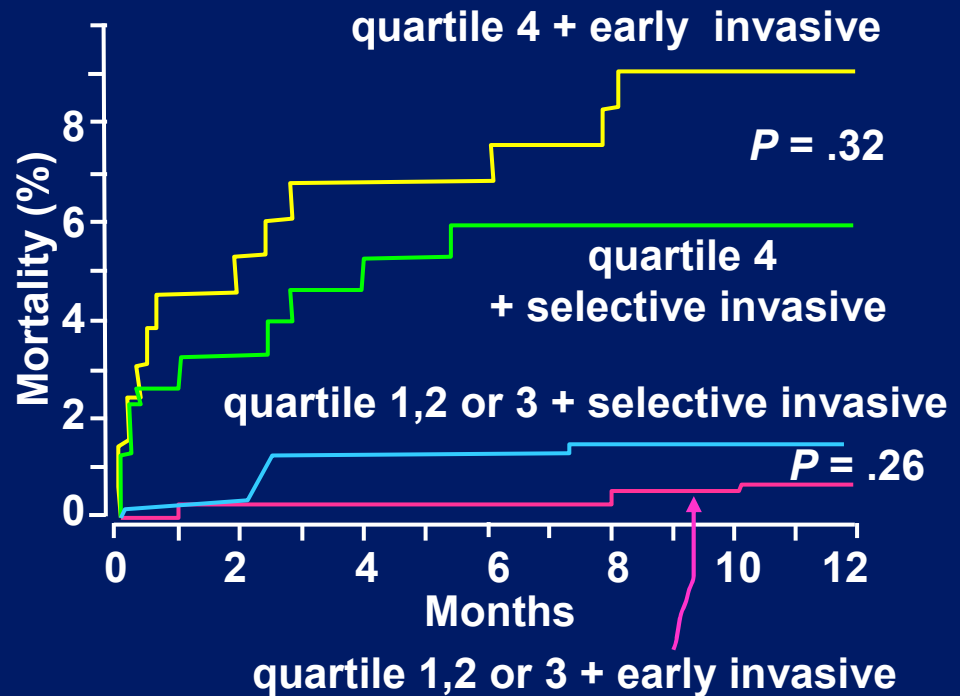
Implication of BNP on Therapeutic Strategy

GpIIb/IIIa



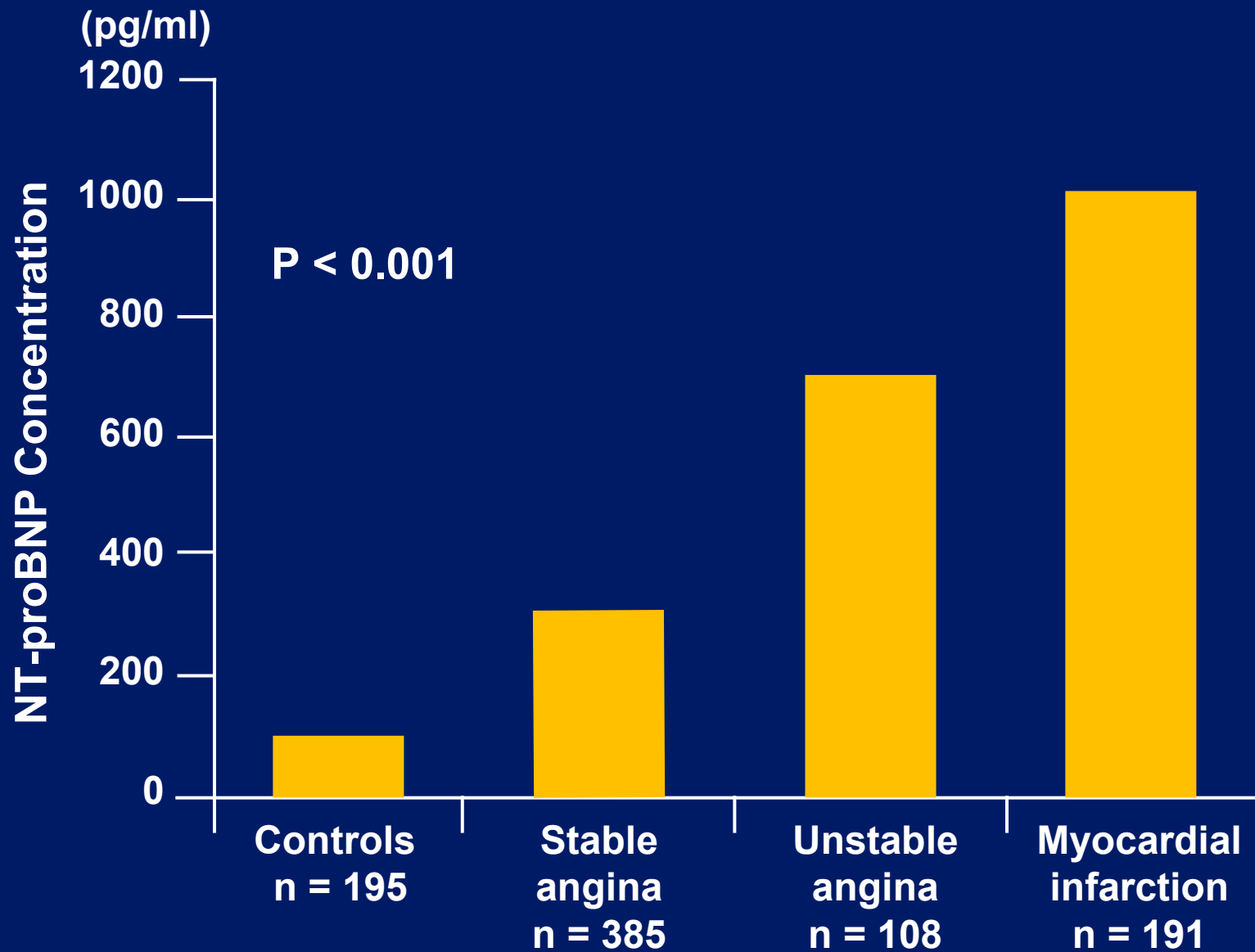
PRISM substudy
Circulation 2004;110:3206

Invasive Therapy



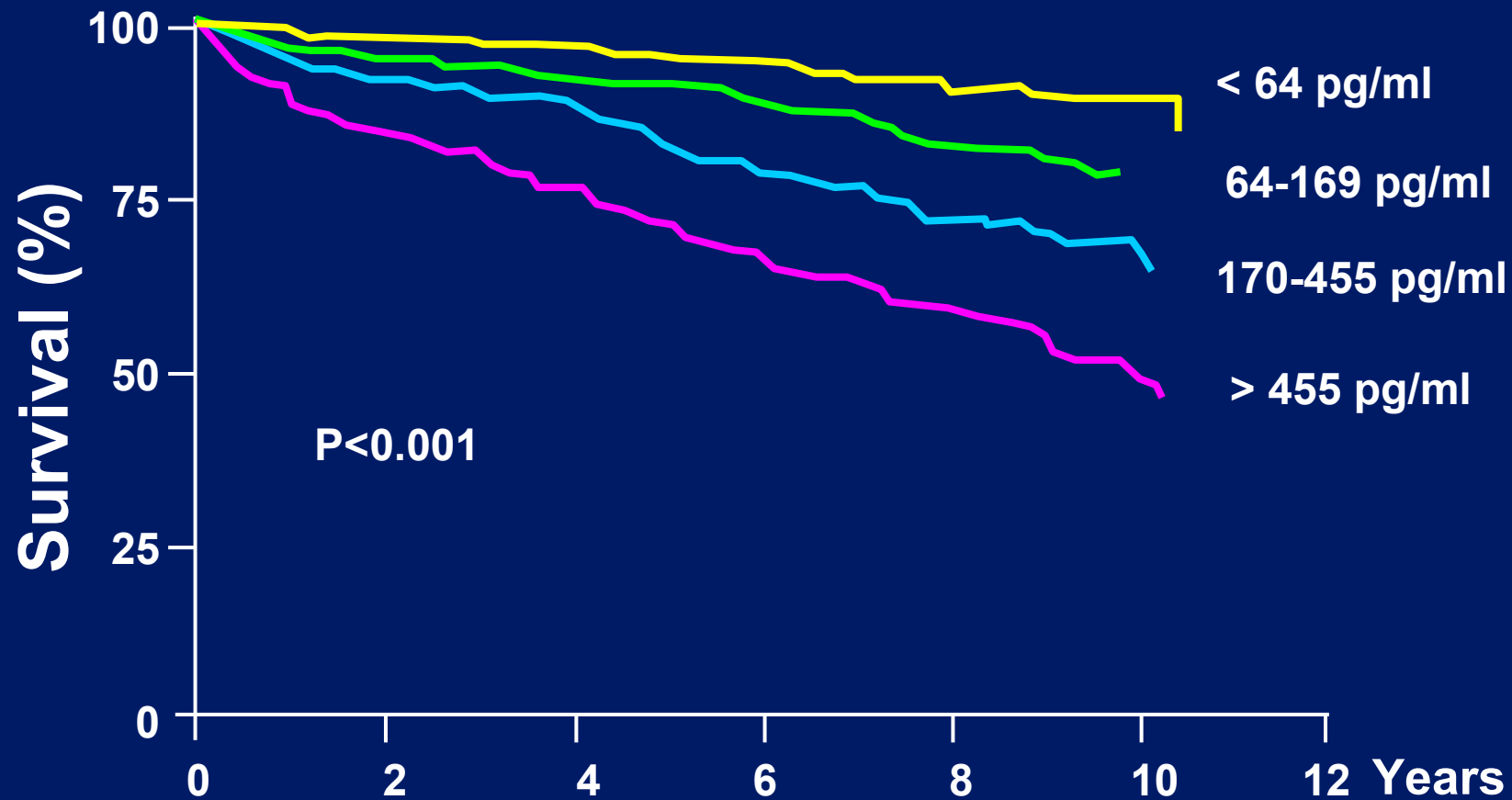
ICTUS substudy
Am Heart J 2007;153:485-92

BNP According to CAD Activity



BNP in Stable Angina

NT-ProBNP is a Marker of Long-Term Mortality
in Patients with Stable Angina (n=1034)



Kragelund C et al. NEJM 2005;352;666-675

Multivariate Analysis for Mortality

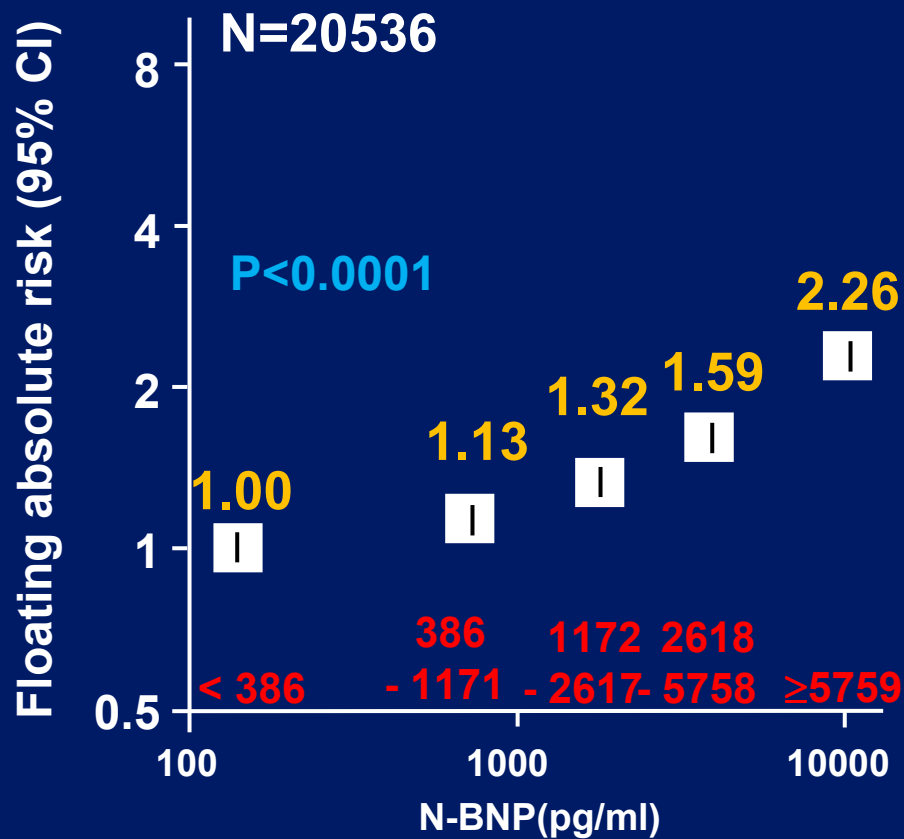
Variable	Hazard Ratio (95% CI)	P Value
NT-pro-BNP (4th vs. 1st quartile)	2.4 (1.5-4.0)	<0.001
Age (per 10-yr increase)	1.6 (1.4-1.9)	<0.001
Diabetes	1.7 (1.3-2.2)	<0.001
Cigarette smoking	1.6 (1.2-2.0)	<0.001
CAD (severe vs. none)	1.8 (1.2-2.6)	0.002
LVEF (per 10% decrease)	1.2 (1.1-1.4)	<0.001
Suspected heart failure	1.8 (1.4-2.4)	<0.001

Large Studies to Confirm the Prognostic Value of BNP in Stable Coronary Disease

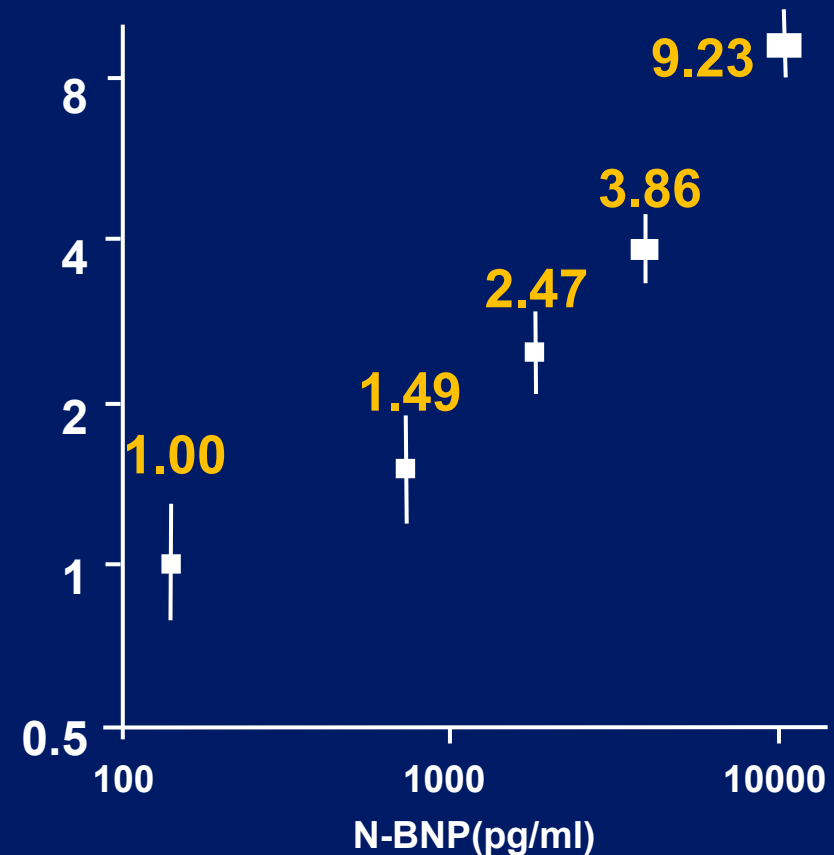
Study	No.	outcome	measurement
Richards et al.	1049	Mortality, HF	Both
Rothenbacher	1051	CVD events	NT-proBNP
PEACE	3761	Mortality, HF	Both
Heart and Soul S.	987	Mortality	NT-proBNP
Heart Protection S.	20536	Vascular events	NT-proBNP
HOPE	3199	CVD events	NT-proBNP
Marz et al.	1641	Mortality	NT-proBNP

NT-proBNP as a Strong Indicator of Future Vascular Events (Heart Protection Study)

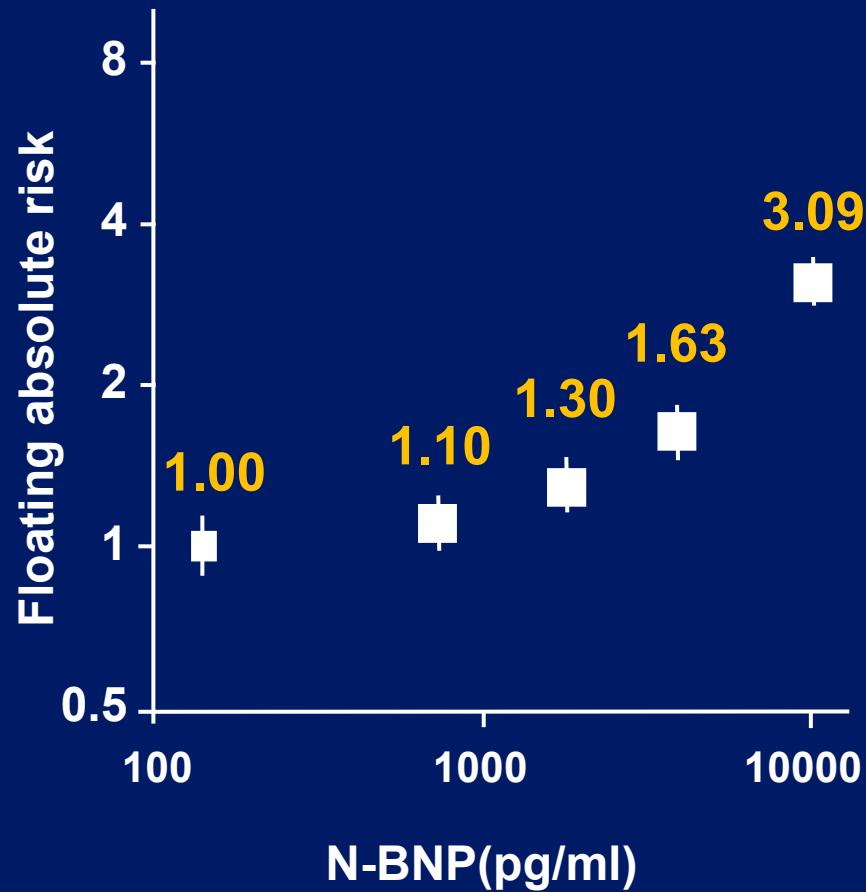
Major Vascular Events



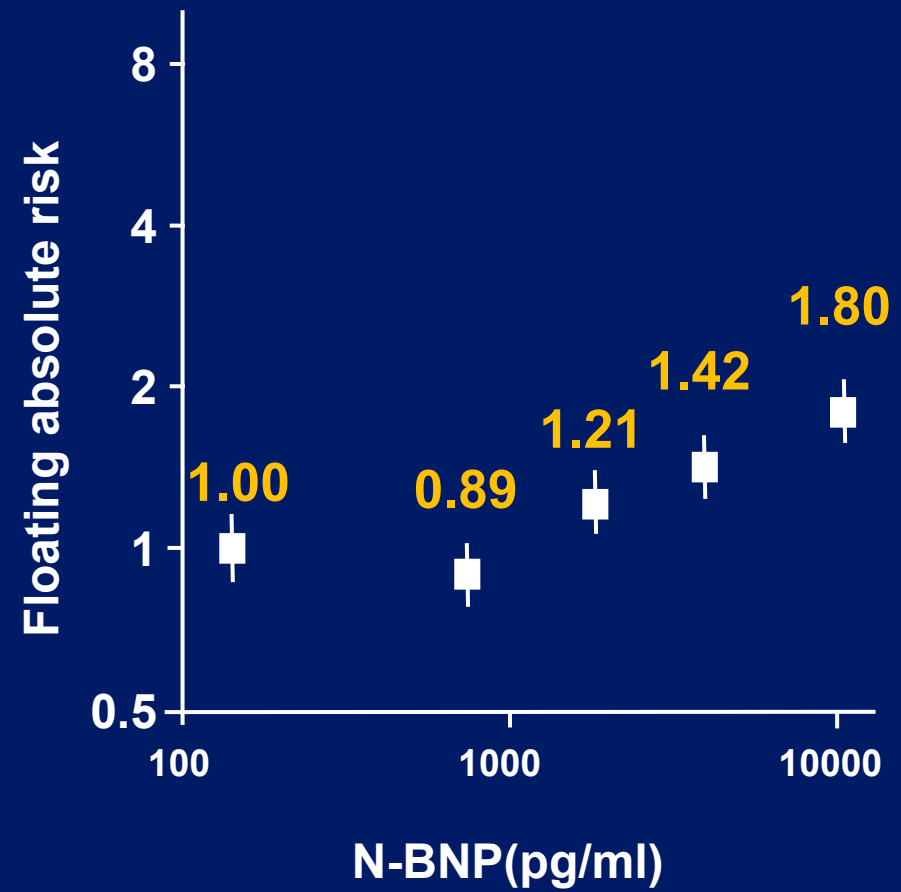
Heart Failure



Major coronary event



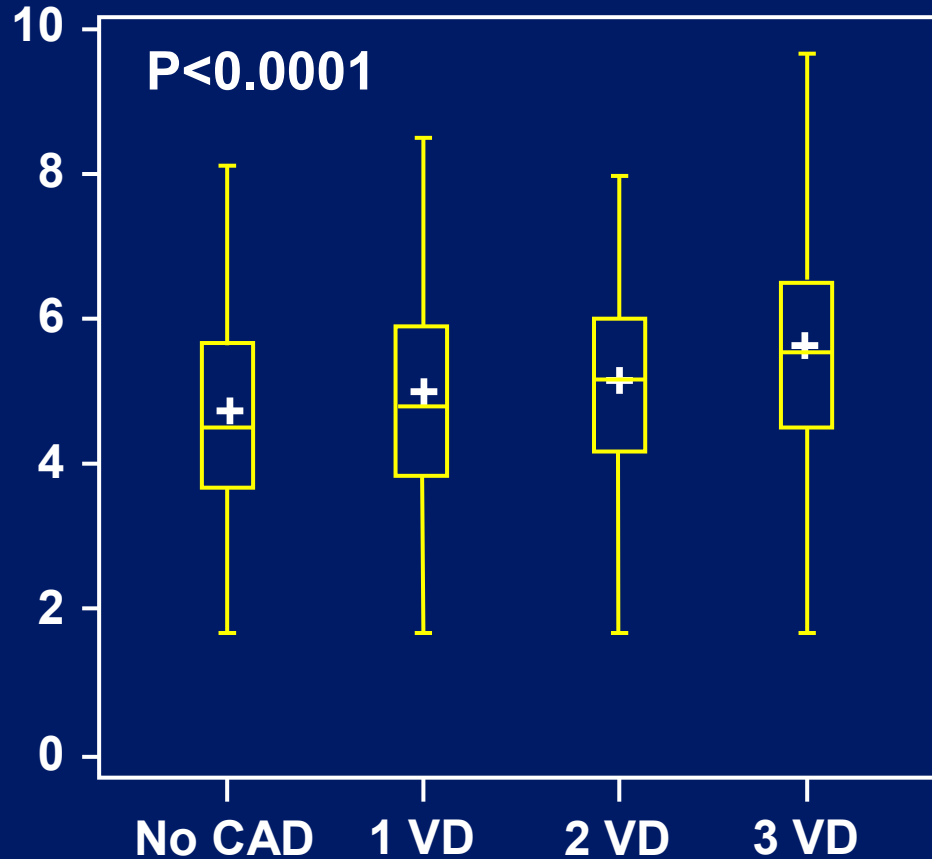
Stroke



BNP as a screening test to diagnose CAD

N = 1034

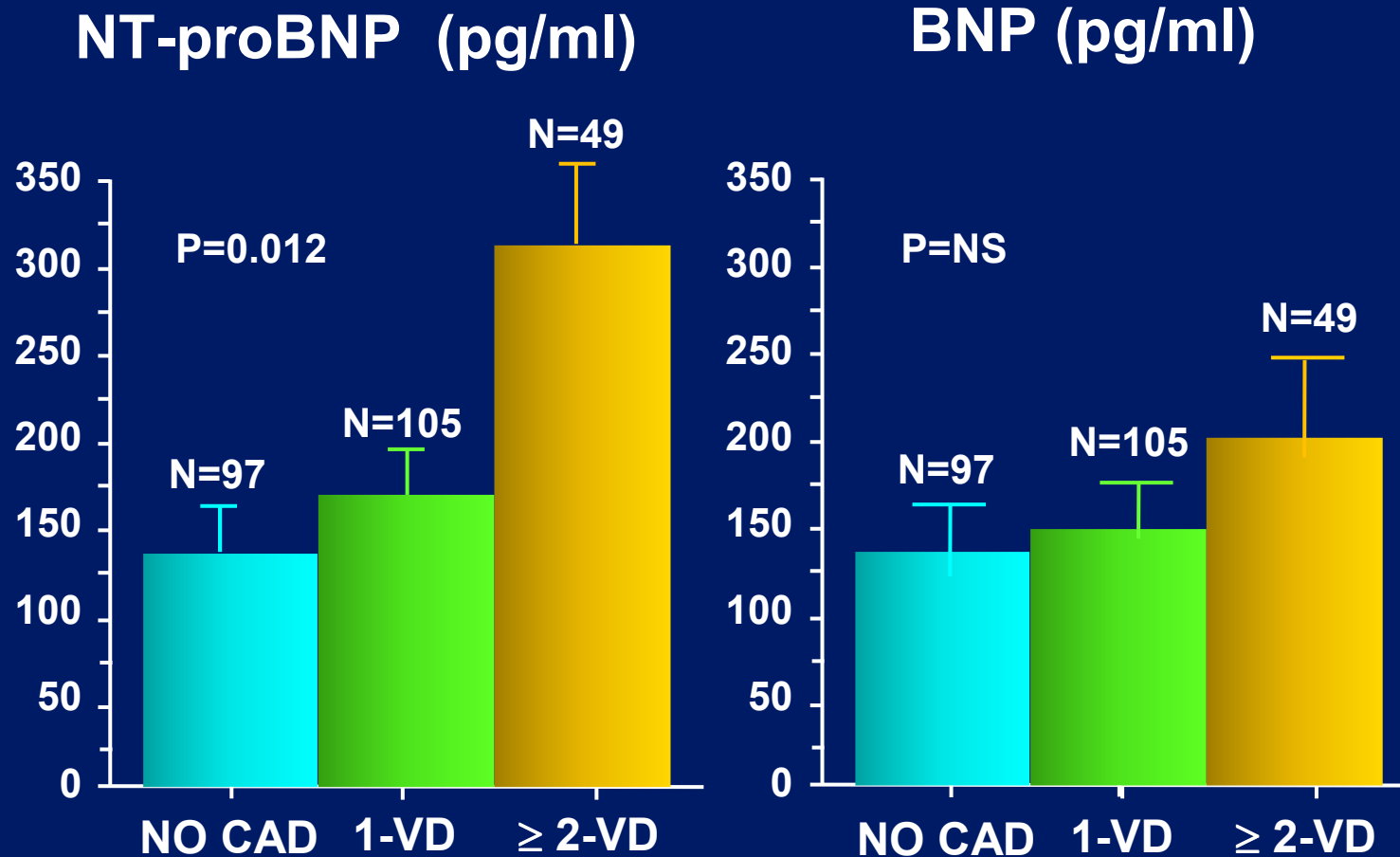
Log(NT-proBNP)



NT-ProBNP (pg/ml)	Sensitivity(%)	Specificity(%)	Accuracy(%)
125	61	60	61
100	66	52	73
70	76	42	69
45	86	28	74
30	91	20	77

BNP or NT-ProBNP ?

Plasma NT-proBNP might be superior to BNP to assess disease severity of CAD (n=251)

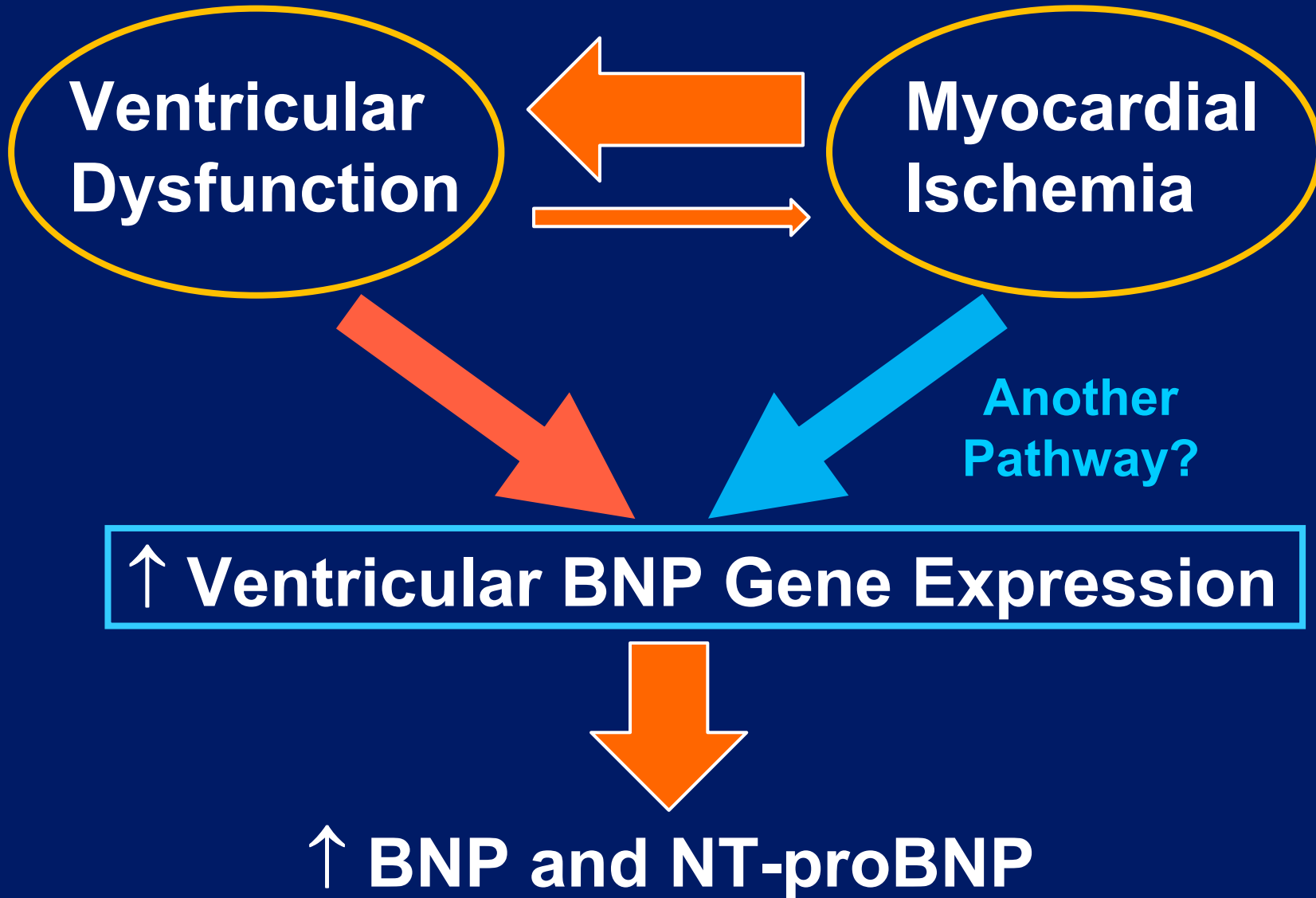


BNP or NT-ProBNP ?

Multivariate Analysis in PEACE Trial

Outcome	BNP		NT-ProBNP	
	HR(95%CI)	p value	HR(95%CI)	p value
Cardiovascular mortality	1.06 (0.87-1.28)	0.57	1.69 (1.38-2.07)	<0.001
Fatal/nonfatal MI	0.91 (0.77-1.07)	0.24	1.02 (0.87-1.19)	0.84
Fatal/nonfatal CHF	1.62 (1.32-1.97)	<0.001	2.35 (1.86-2.98)	<0.001
Fatal/nonfatal stroke	1.15 (0.91-1.45)	0.24	1.63 (1.26-2.12)	<0.001

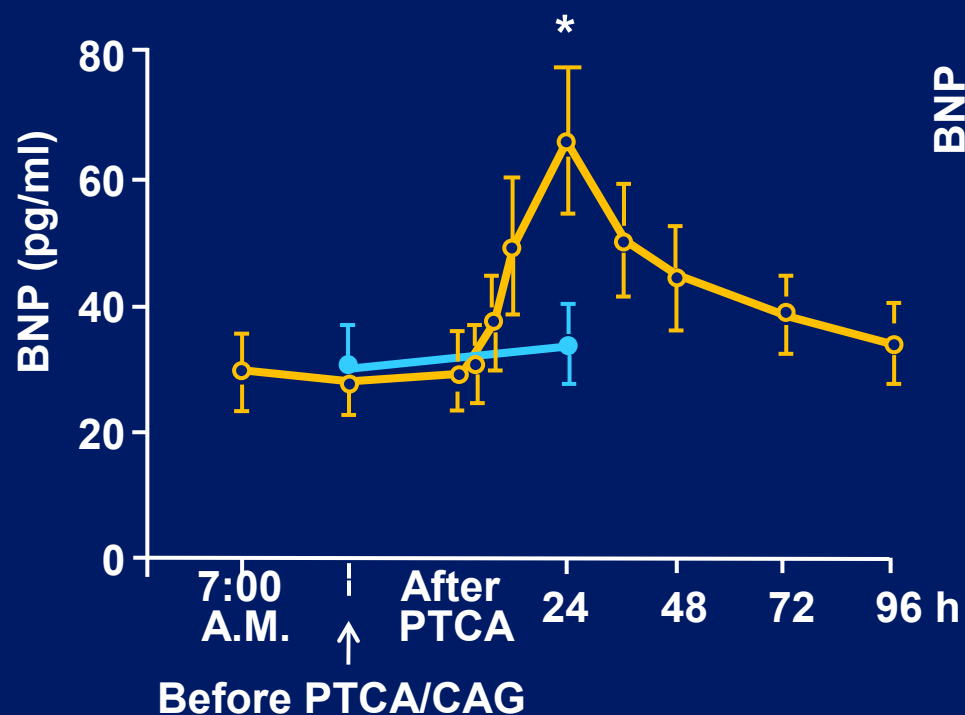
Elevated BNP in Myocardial Ischemia



Myocardial Ischemia vs LV filling pressure

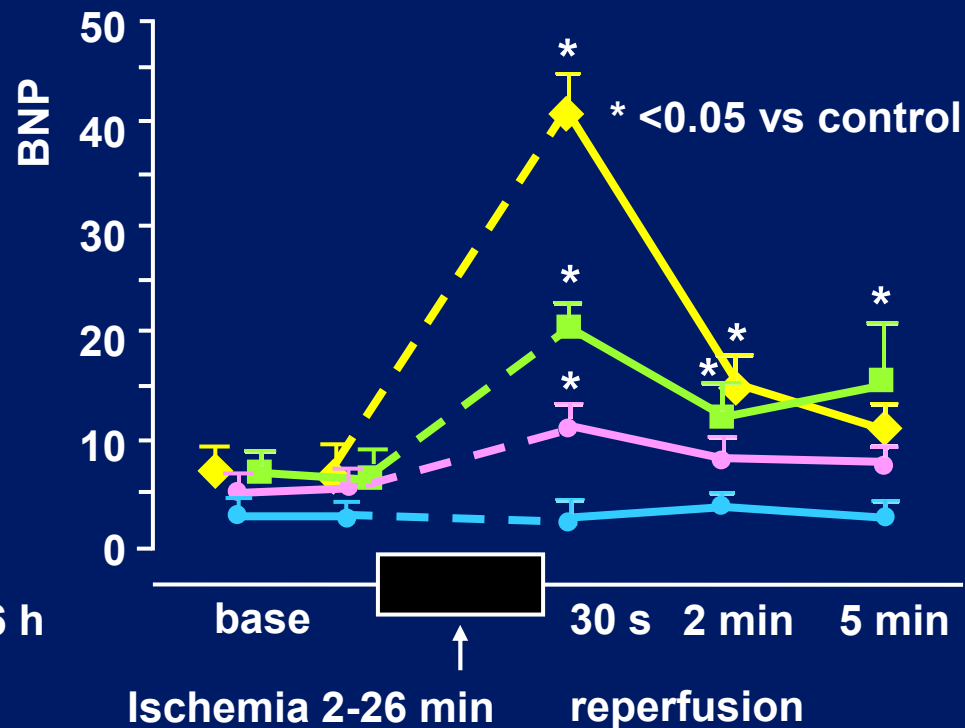
- PTCA(n=30); pcwp 9±3 mmHg
- CAG (n=49); pcwp 8±4 mmHg

- 20 min ischemia ΔLVEDP > 10 mmHg
- 5 min ischemia ΔLVEDP ; no change
- 2 min ischemia ΔLVEDP ; no change
- no ischemia ΔLVEDP ; no change



Tateish J et al.

Clin Cardiol 2000;23:776-780



D'Souzs SP et al.

Am J Physiol 2003;284:H1592-H1600

Suggested Reason for Elevated BNP in Myocardial ischemia and CAD

- ◆ **Myocardial ischemia augment BNP gene expression and release (Cardioprotection ?)**
- ◆ **Atherosclerotic plaques stimulate BNP synthesis and release (protective effect ?)**

Schirger JA et al. JACC 2000;35:796-801

- ◆ **Hypoxia is a direct stimulus for BNP release from human cardiac myocyte**

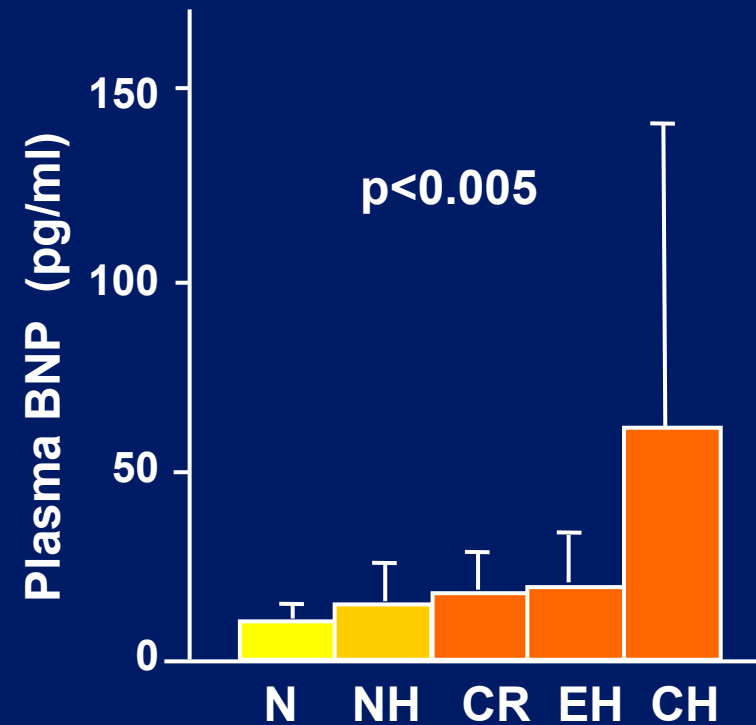
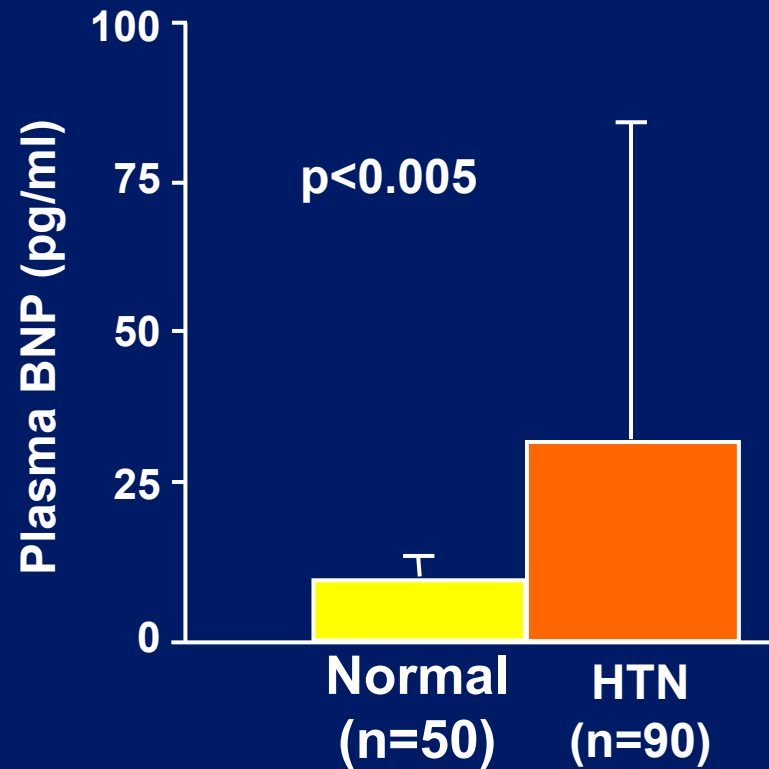
Hopkins WE et al. Circulation 2004;109:2872-2877

Summary

Role of BNP in Coronary Disease

- ◆ **BNP has a strong prognostic value in CAD**
- ◆ **To diagnose ACS, BNP is useful in case of non-diagnostic conventional markers**
- ◆ **Elevation of BNP in CAD may related to both LV wall stress and myocardial ischemia itself**
- ◆ **Threshold of BNP and sampling time have to be resolved for future studies**

Impact of LV Geometry on Plasma BNP in Patients with Essential Hypertension



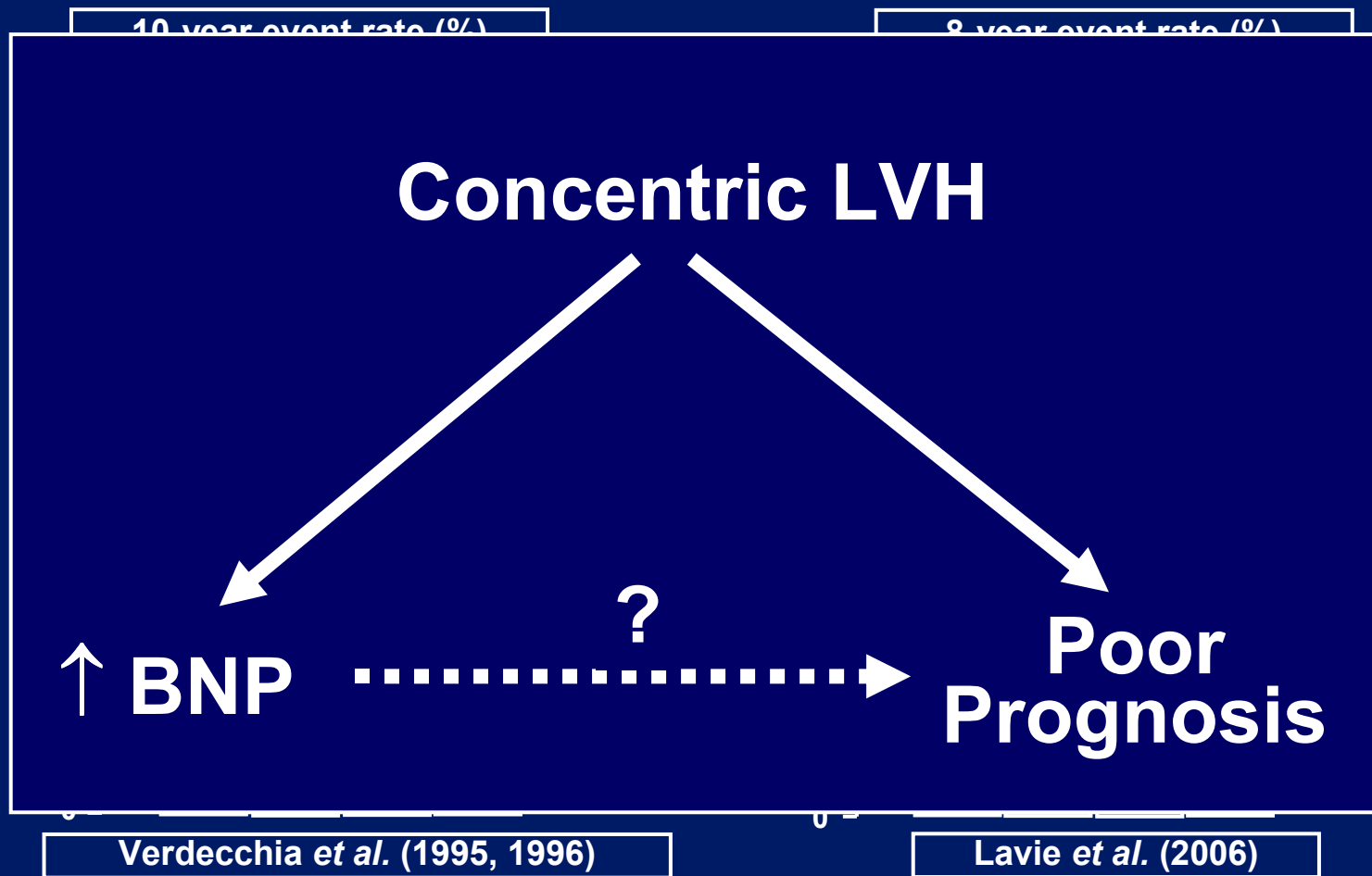
N	no HTN
NH	HTN with normal geometry
CR	Concentric remodeling
EH	Eccentric LVH
CH	Concentric LVH

Nishikimi T et al.
Hypertension 1996;28:22-30

Prognostic Value of 4 Different LV Geometry

■ Concentric LVH
■ Concentric remodeling

■ Eccentric LVH
■ Normal



BNP as a Prognostic Marker in Hypertension

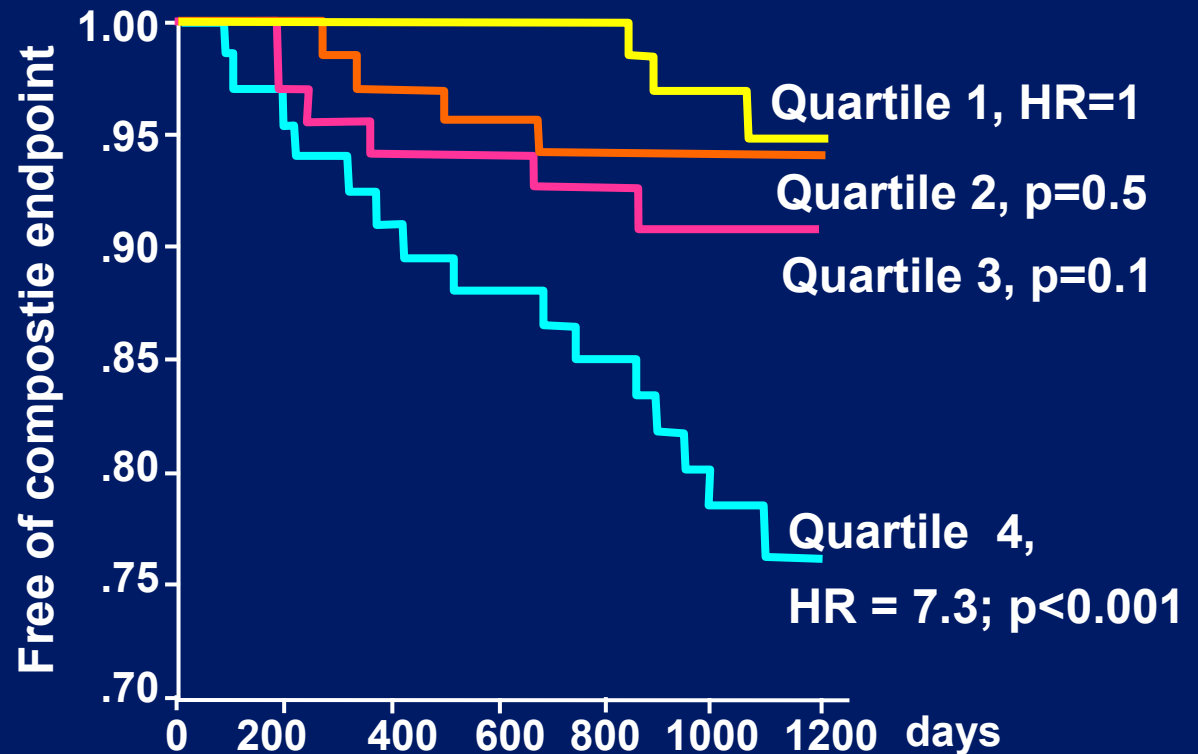
N=569; 50-89 yr-old

EF > 50%

Composite End-Point
stroke/TIA

MI

All cause death

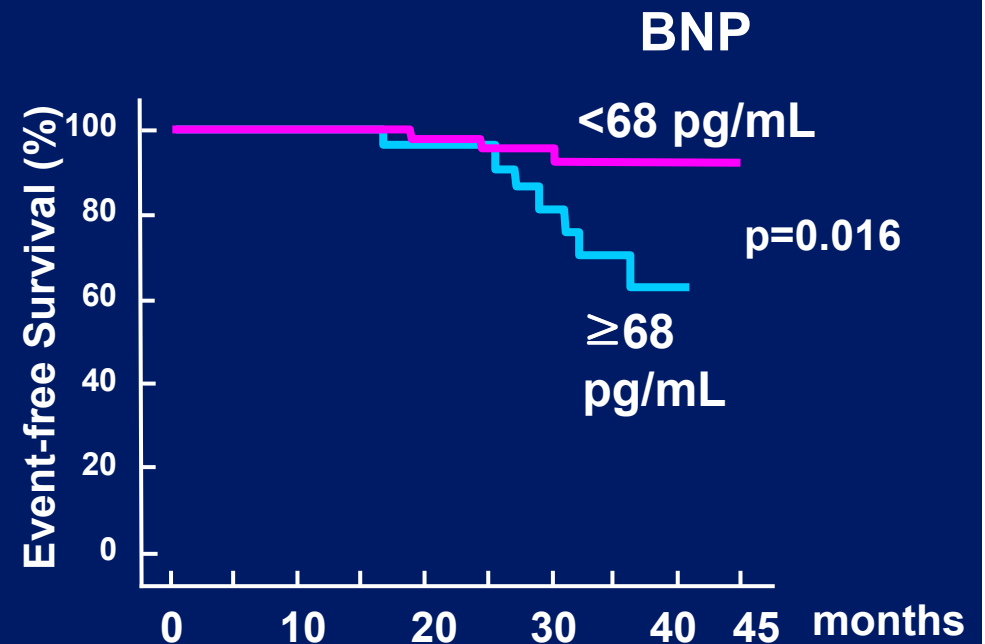


BNP as a Prognostic Marker in Hypertension

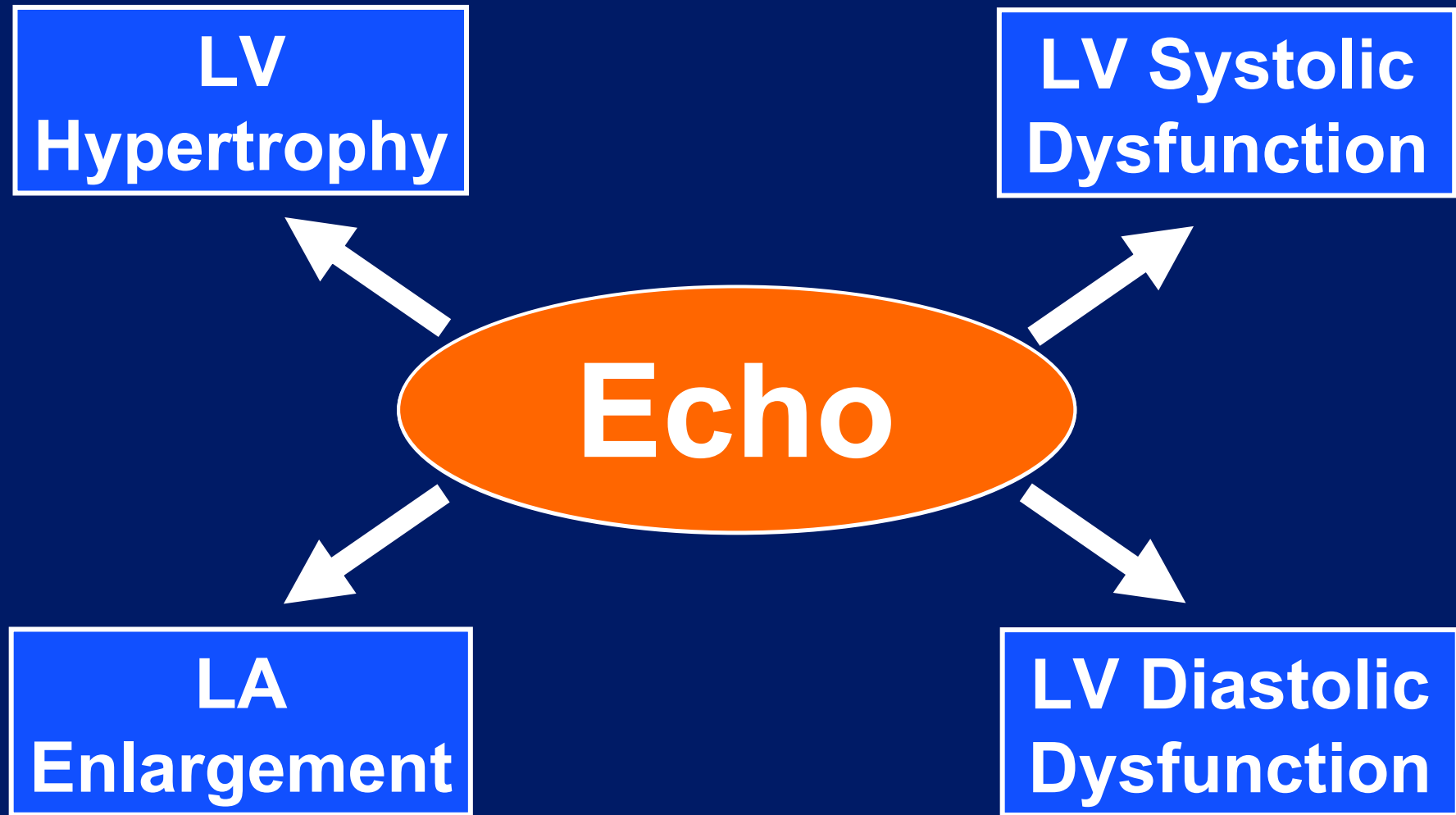
Multivariate Analysis for cardiovascular events

	Risk Ratio (95% CI)	P value
Pulse pressure	1.050 (1.009-1.091)	0.015
LVMi	1.020 (1.000-1.040)	0.049
BNP	1.011 (1.004-1.017)	0.001

Survival curve in old age with hypertrophy



Cardiac Influence of Hypertension



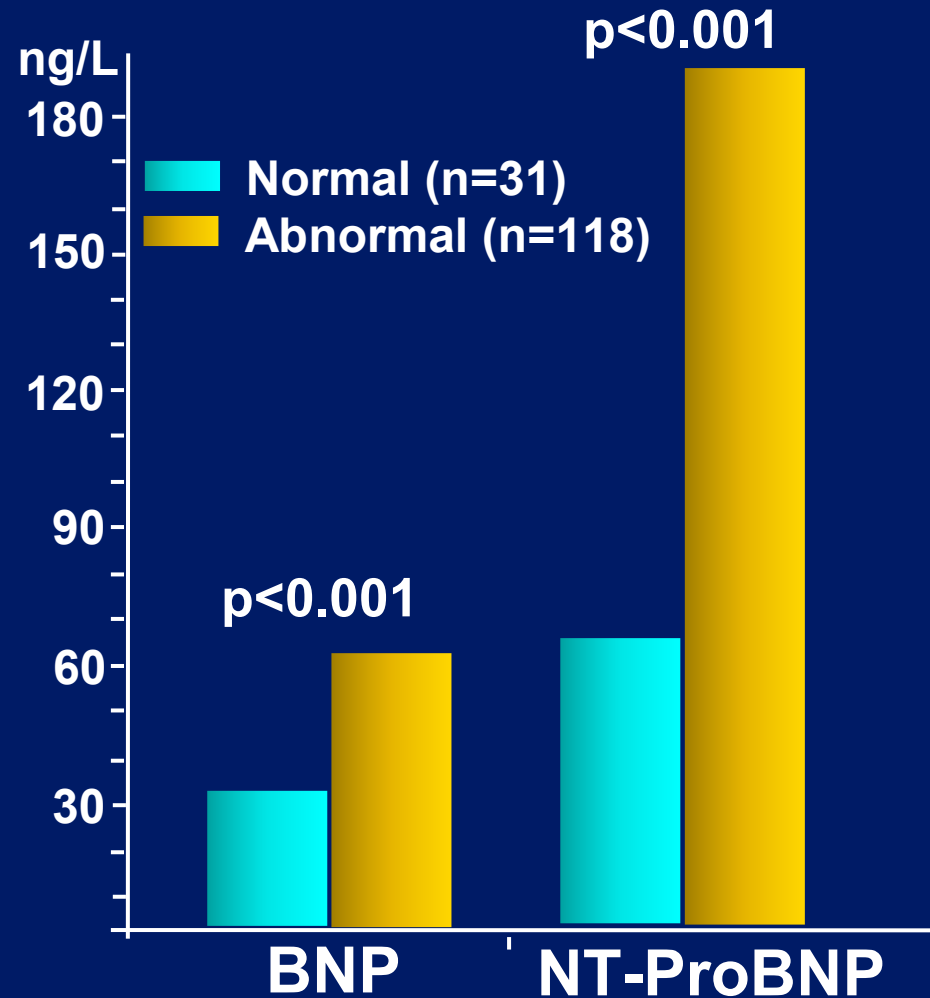
Screening Strategy of BNP Indicating Structural Abnormalities in Hypertension

N = 149

Asymptomatic HTN

Structural Abnormalities

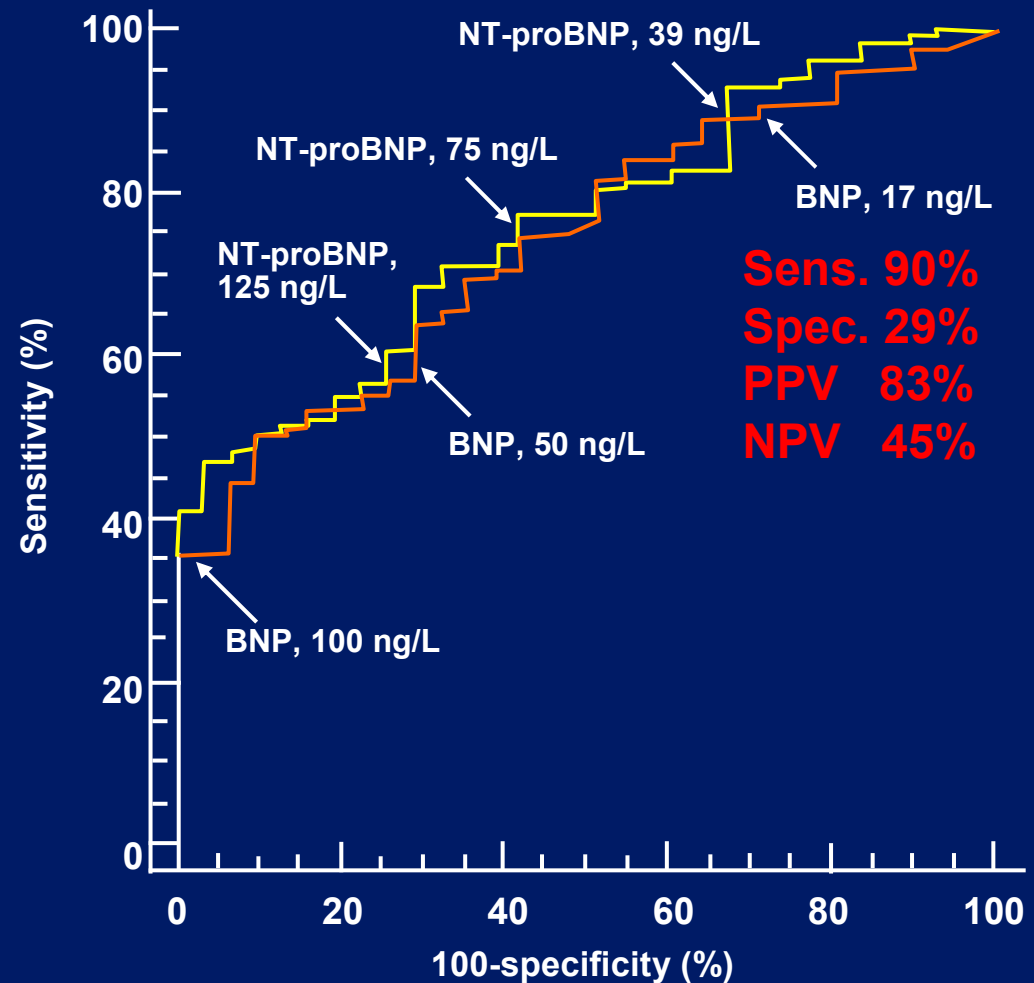
- Systolic dysfunction
- Diastolic dysfunction
- LA enlargement
- LV dilatation
- LV hypertrophy
- Pulmonary hypertension



BNP might have limited value for screening of cardiac abnormalities in hypertensives

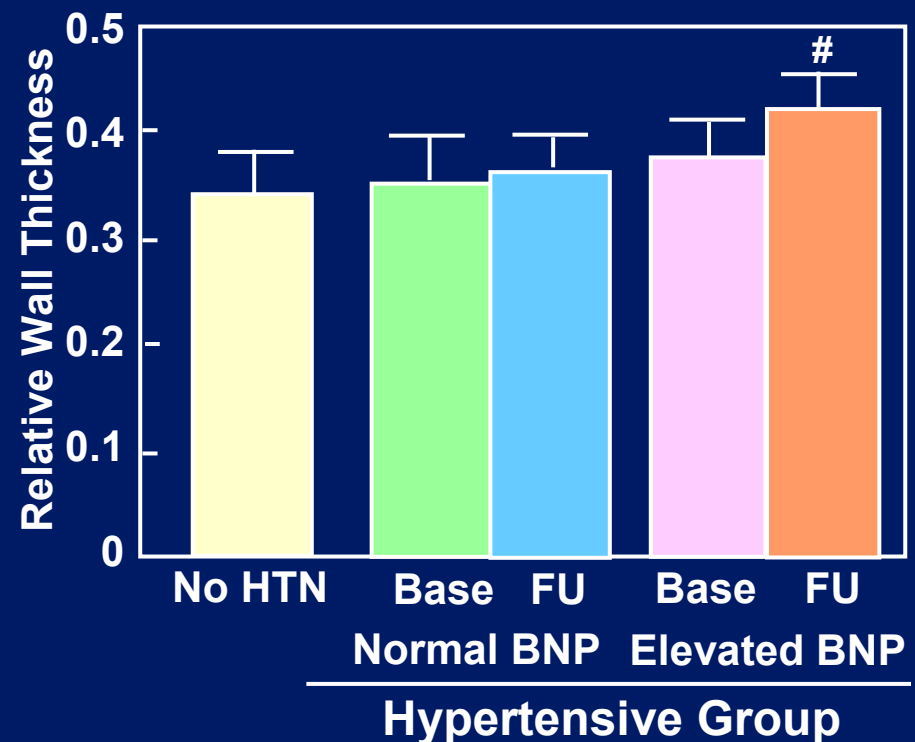
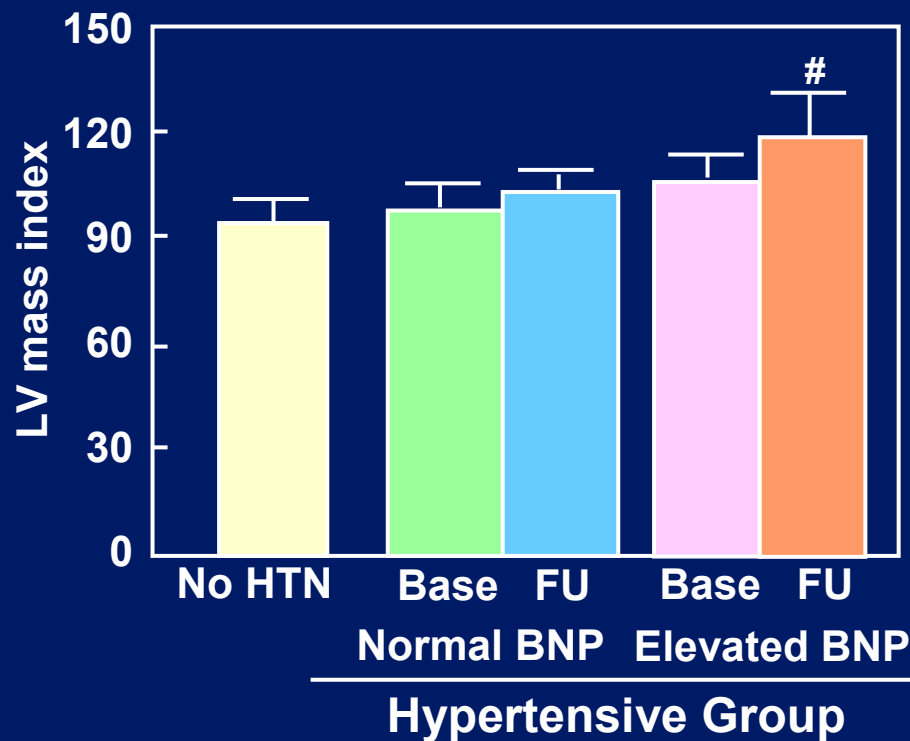
AUC of BNP
0.740 (CI 0.662-0.808)

AUC of NT-ProBNP
0.762 (CI 0.685-0.828)



Progression of LVH Related to Baseline BNP in Hypertensive Patients (n=82)

Multivariate analysis showed only BNP at baseline were independently related with progression of LVH ($r=0.78$; $p<0.01$) after adjusting various clinical parameters



BNP and BP Tracking (Framingham HS)

Higher BNP in non-hypertensives is associated with increased risk of BP progression in men but not women (4 year follow-up, n=1801)

Plasma BNP Category	Men Odd Ratio	Women Odd Ratio
C 1	1.0 (referent)	1.0 (referent)
C 2	0.68 (0.43-1.07)	0.98 (0.67-1.44)
C 3	1.51 (0.99-2.28)	1.09 (0.75-1.60)
C 4	1.37 (0.89-2.12)	0.92 (0.61-1.36)
Trend across categories	1.15 (1.00-1.32) <i>P</i> =0.046	0.99 (0.87-1.12) <i>P</i> =0.82

Summary

Role of BNP in Hypertension

- ◆ BNP is elevated in HTN, especially associated with structural changes including LVH
- ◆ BNP is a prognostic marker in HTN
- ◆ Elevated BNP in HTN predicts LVH progression and in normotension predicts HTN progression
- ◆ Screening strategy of BNP, however, in HTN is not recommended.