Interpretation of NT-proBNP Results in Patients with Impaired Renal Function

Are There Limitations?

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NT-proBNP interpretation in renal disease

- The controversy between NT-proBNP and BNP: Does it still exist?
- Renal clearance and detection in the urine
- The correlations between NT-proBNP, BNP level and renal function
- Predicting cardiovascular disease
  - PCWP in the hospitalized patient
  - Heart failure in the dyspnea patient
  - Coronary disease, LVH and depressed LVEF in the asymptomatic patient
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  - Differences between NT-proBNP and BNP?

Renal function and natriuretic peptides

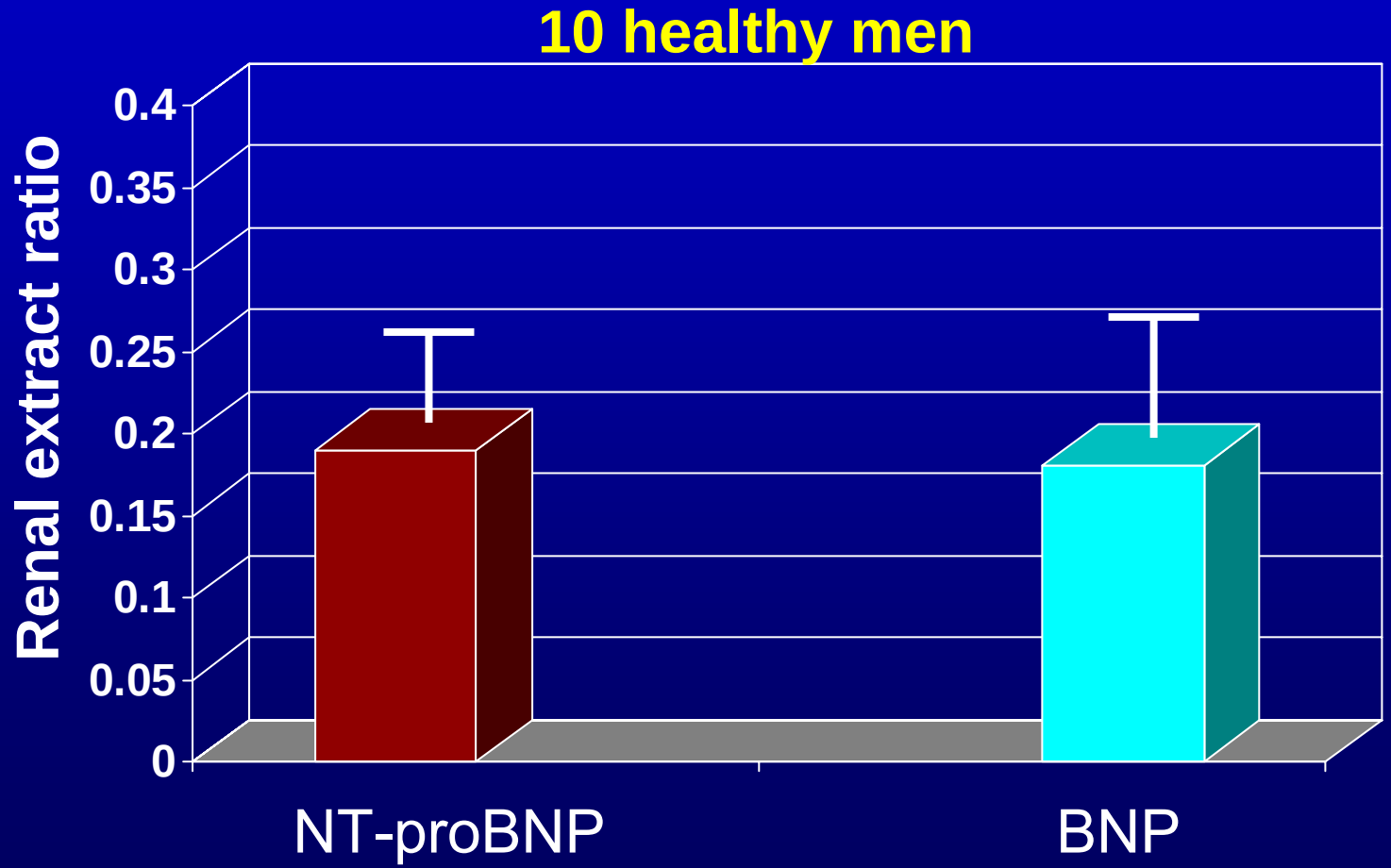
Was there ever really a controversy?

"It appears that both NP's offer considerable value to the clinician. The finding of this study suggest that the final decision as to which biomarker, BNP or NTproBNP, will be used will not necessarily be based on differences between the two peptides, but rather the presence of pre-existing laboratory equipment…."

Maisel. The coming of age of Natriuretic peptides
The emperor does have clothes! JACC 2006;47:61

McCullough, Rev Cardiovasc Med. *2003;4(suppl 4):S13–S19*

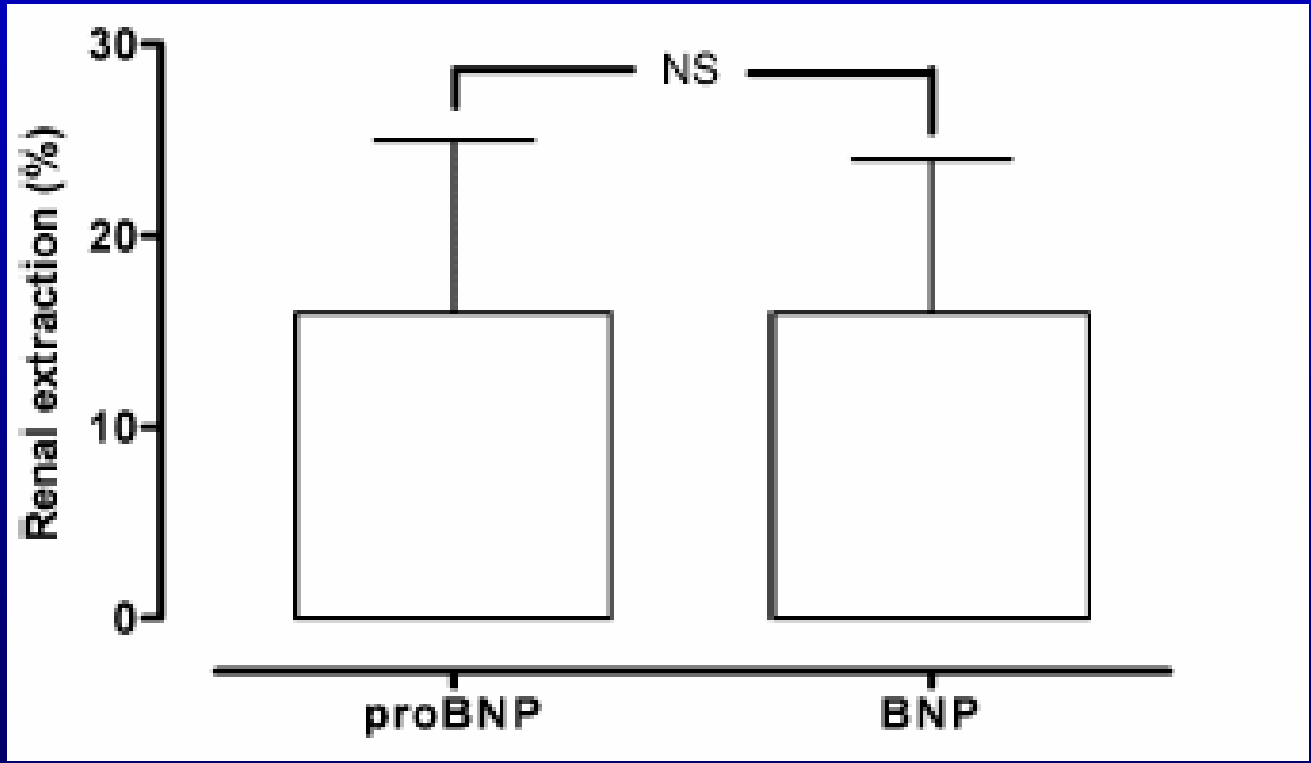
Kidneys extract BNP and NT-proBNP equally in healthy subjects



Schou M. J Appl Physiol 2005;99:1676

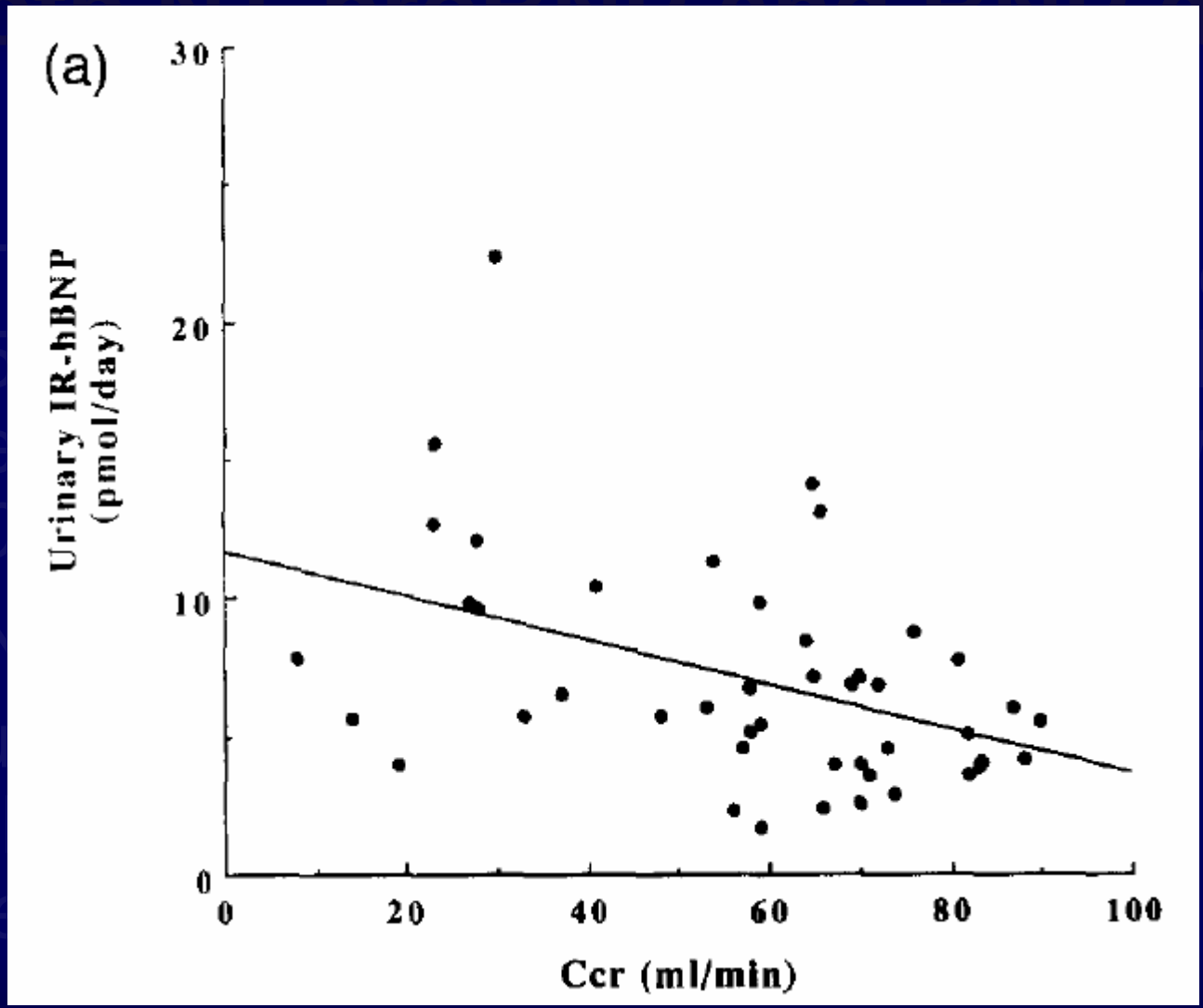
Identical renal extraction a consistent finding

Findings in a mixed cohort with advanced age



Patients with HTN, cirrhosis and controls, n=87

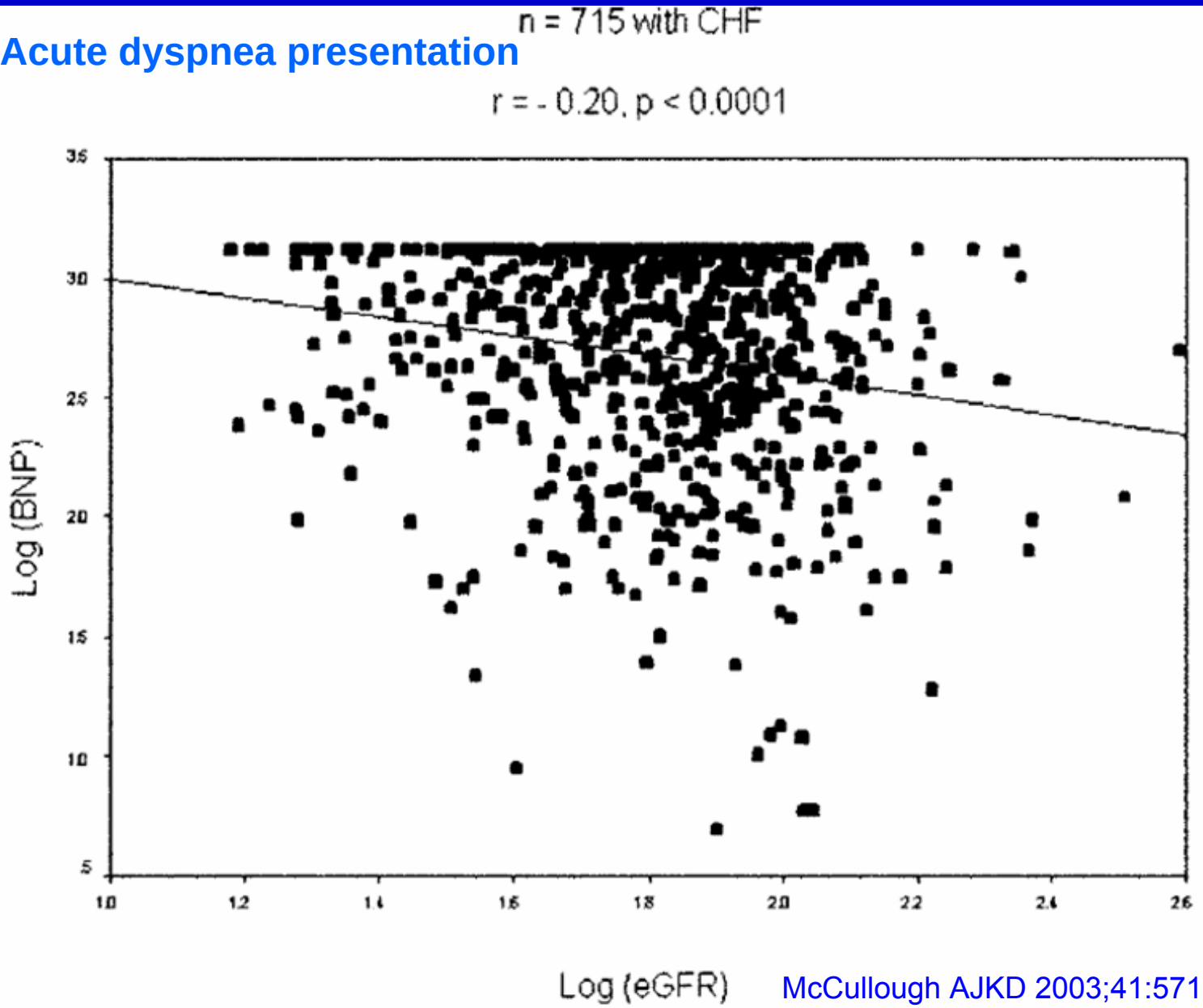
Eur J Clin Invest 2006; 36 (1): 8–15


(a)
Urinary IR-hBNP (pmol/day)
30
20
10
0
0
20
40
60
80
100
Ccr (ml/min)

Correlations between natriuretic peptide levels and GFR

Author	Population	NT-proBNP	BNP
Mark	Amb CKD		-0.40
deFilippi	Amb CKD	-0.31	
Khan	Amb CKD	-0.45	-0.38
Vickory	Amb CKD	-0.53	-0.36
Richards	Amb ICM	-0.51	-0.51
Anwaruddin	ED all dysp	-0.55 (log)	
deFilippi	ED all dysp	-0.42	-0.34
Anwaruddin	ED Dx HF	-0.34 (log)	
McCullough	ED Dx HF		-0.19
Kimmenade	Dx HF	-0.34	

Acute dyspnea presentation



McCullough AJKD 2003;41:571

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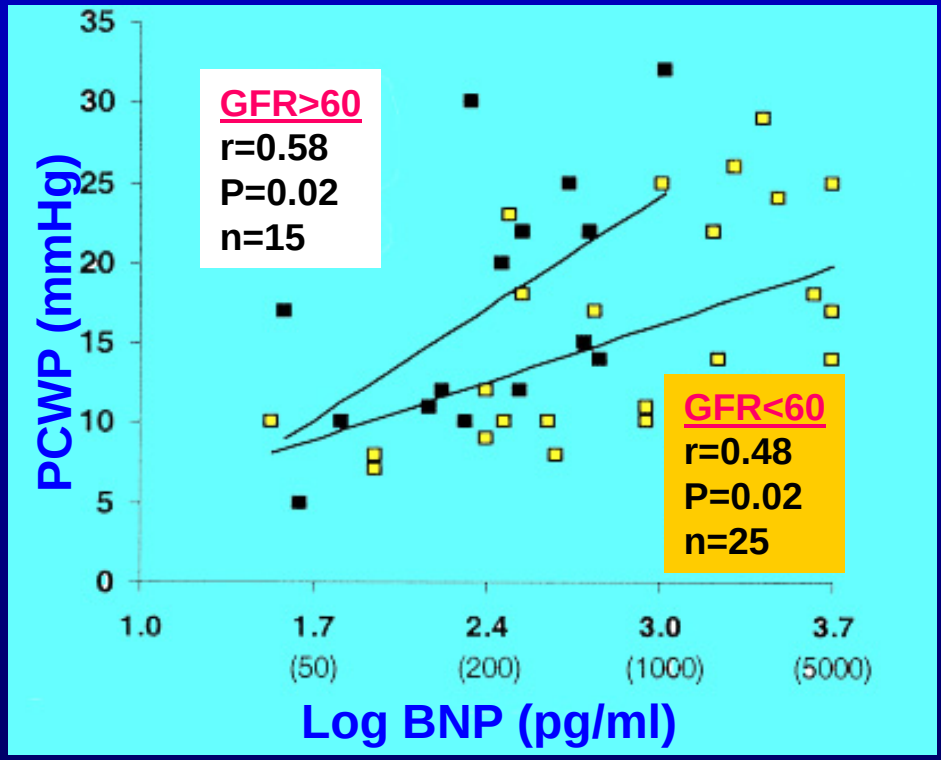
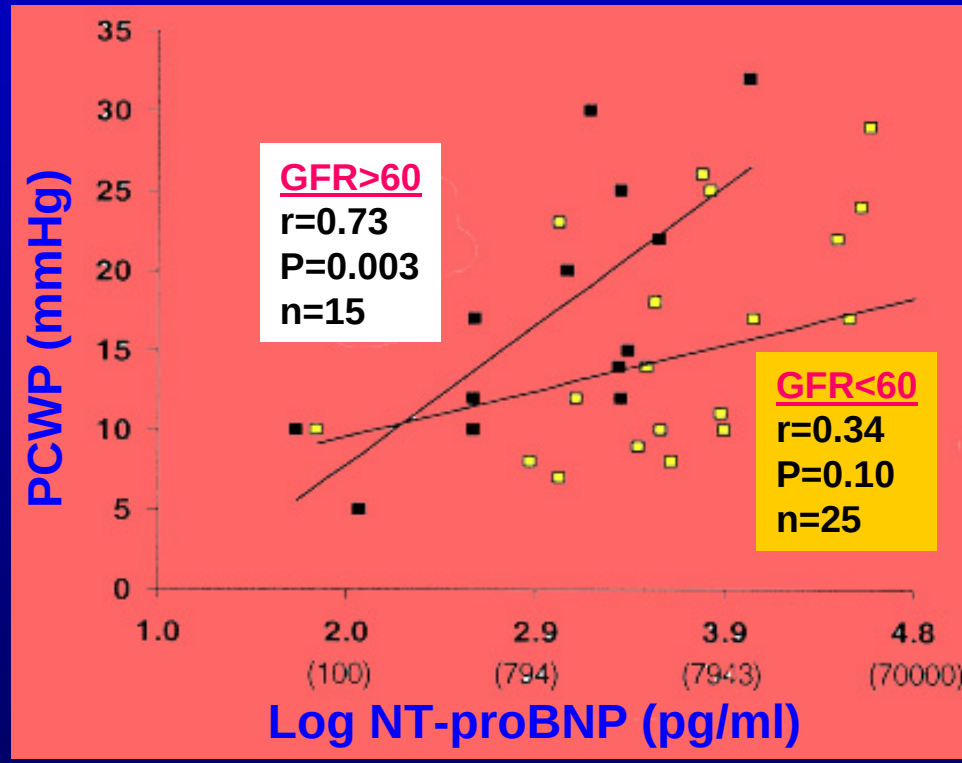
Renal function influences correlation of natriuretic peptide level with PCWP





Yellow boxes indicate patients with a GFR < 60 ml/min
Closed boxes indicate patients with a GFR >60 ml/min

Forfia et al. J Am Coll Cardiol 2005;45:1667

Diagnosing acute decompensated heart failure in the dyspnea patient

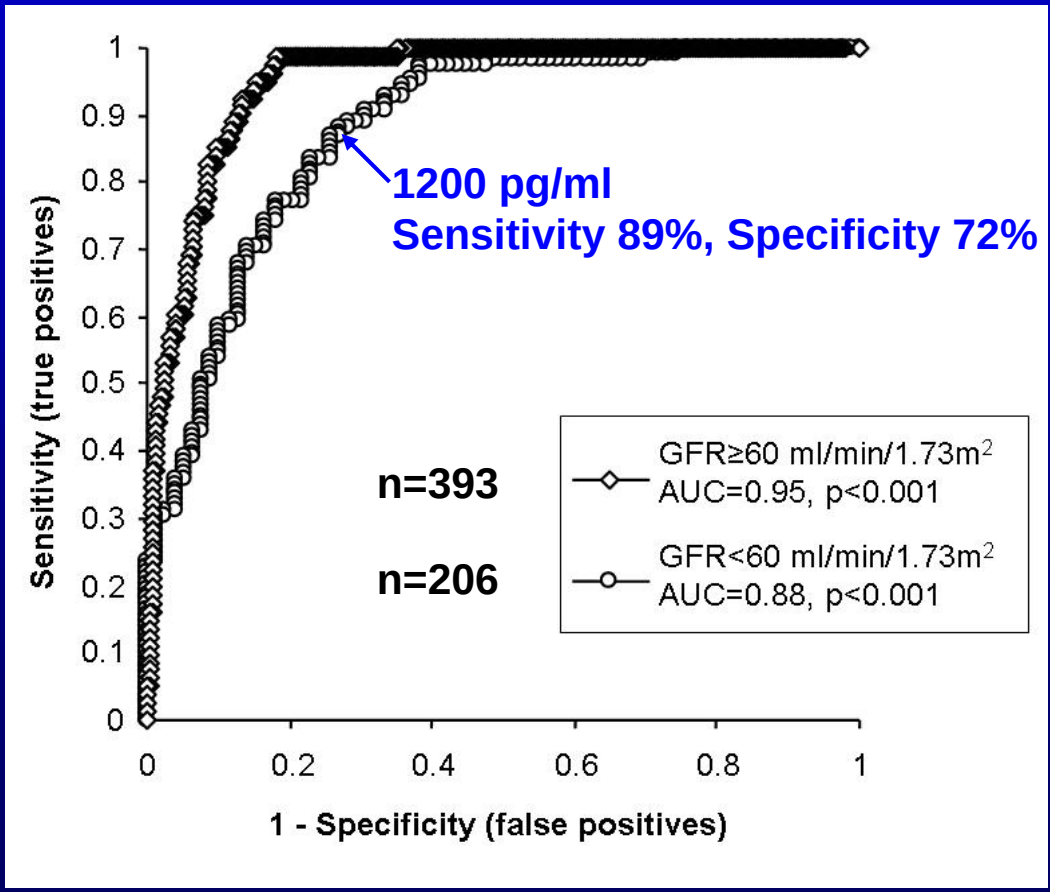
Impact of renal disease

BNP	eGFR (mL/min/1.73m^2)			
	>90	60-90	30-59	<30
AUC	0.91	0.90	0.81	0.86
Cut-off (pg/mL)	70.7	104.3	201.2	225

NT-proBNP	eGFR (mL/min/1.73m^2)	
	≥ 60	< 60
AUC	0.95	0.88
Cut-off (pg/mL)	900/450	1200

PRIDE revisited

Accuracy of NT-proBNP for HF Dx in dyspnea patient with renal disease



Anwaruddin J Am Coll Card 2006;47:91

Optimal NT-proBNP Cut-points

"Rule in"

Age strata	Optimal cut-point	Sensitivity	Specificity	PPV	NPV	Accuracy
All <50 years (n=184)	450 pg/ml	97%	93%	76%	99%	94%
All 50-75 years (n=537)	900 pg/ml	90%	82%	83%	88%	85%
All >75 years (n=535)	1800 pg/ml	85%	73%	92%	55%	83%
Overall average		90%	84%	88%	66%	85%

"Rule out"

	Optimal cut-point	Sensitivity	Specificity	PPV	NPV	Accuracy
Rule out	300 pg/ml	99%	60%	77%	98%	83%

Note: these cut-points are for ACUTE CHF DIAGNOSIS ONLY

Januzzi et al, Eurheartj 2005

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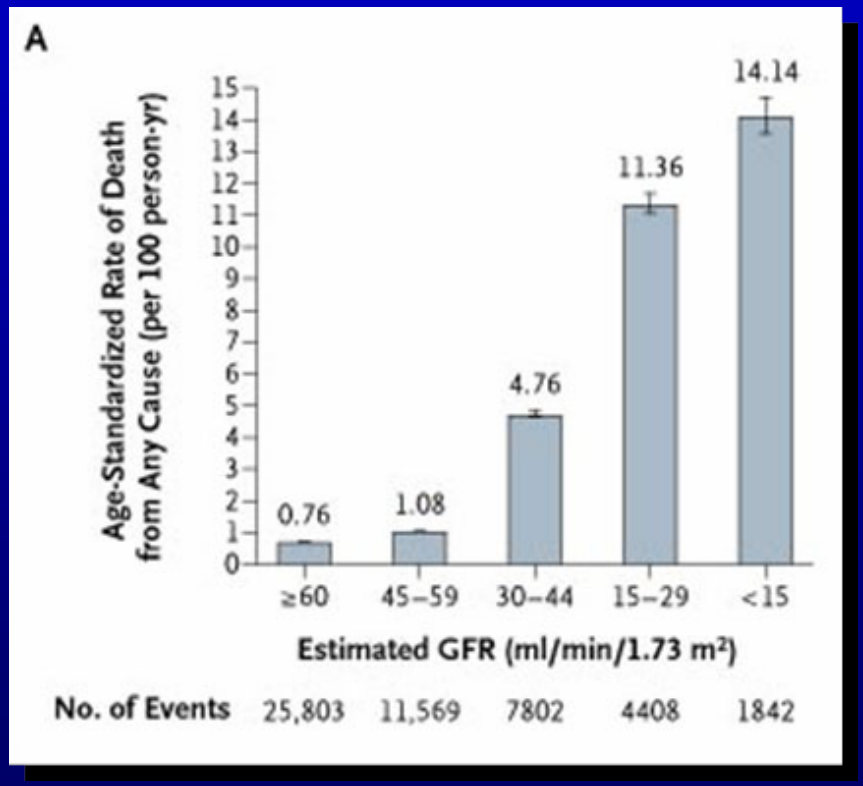
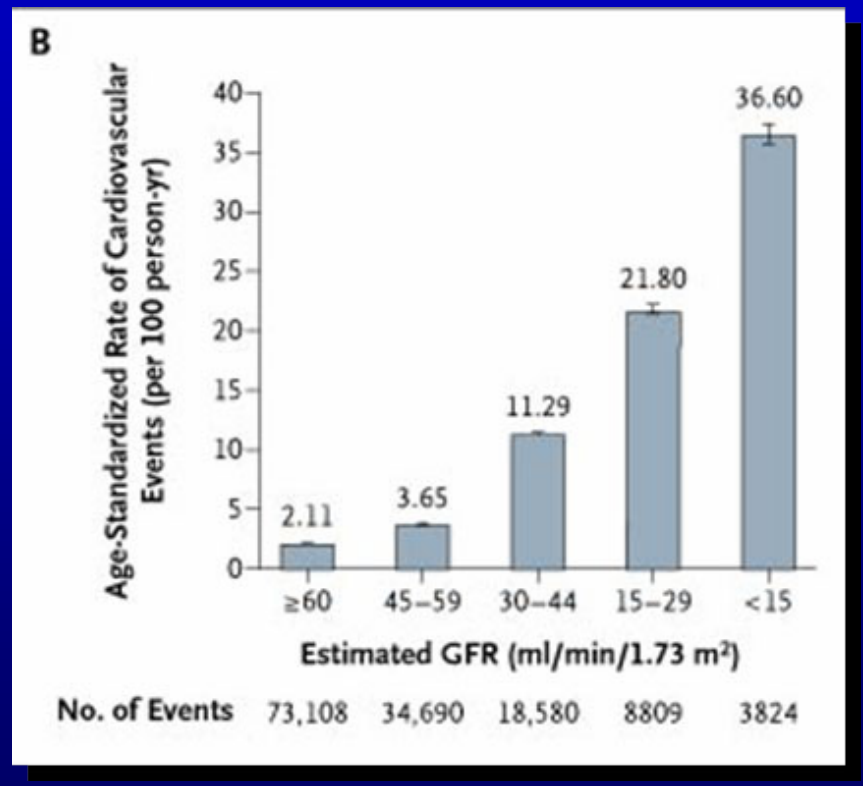
Chronic Renal Disease and Risk
The ambulatory outpatient





Go A, et al. N Engl J Med 2004; 351:1296

ProBNP level predicts CAD in chronic kidney disease patients

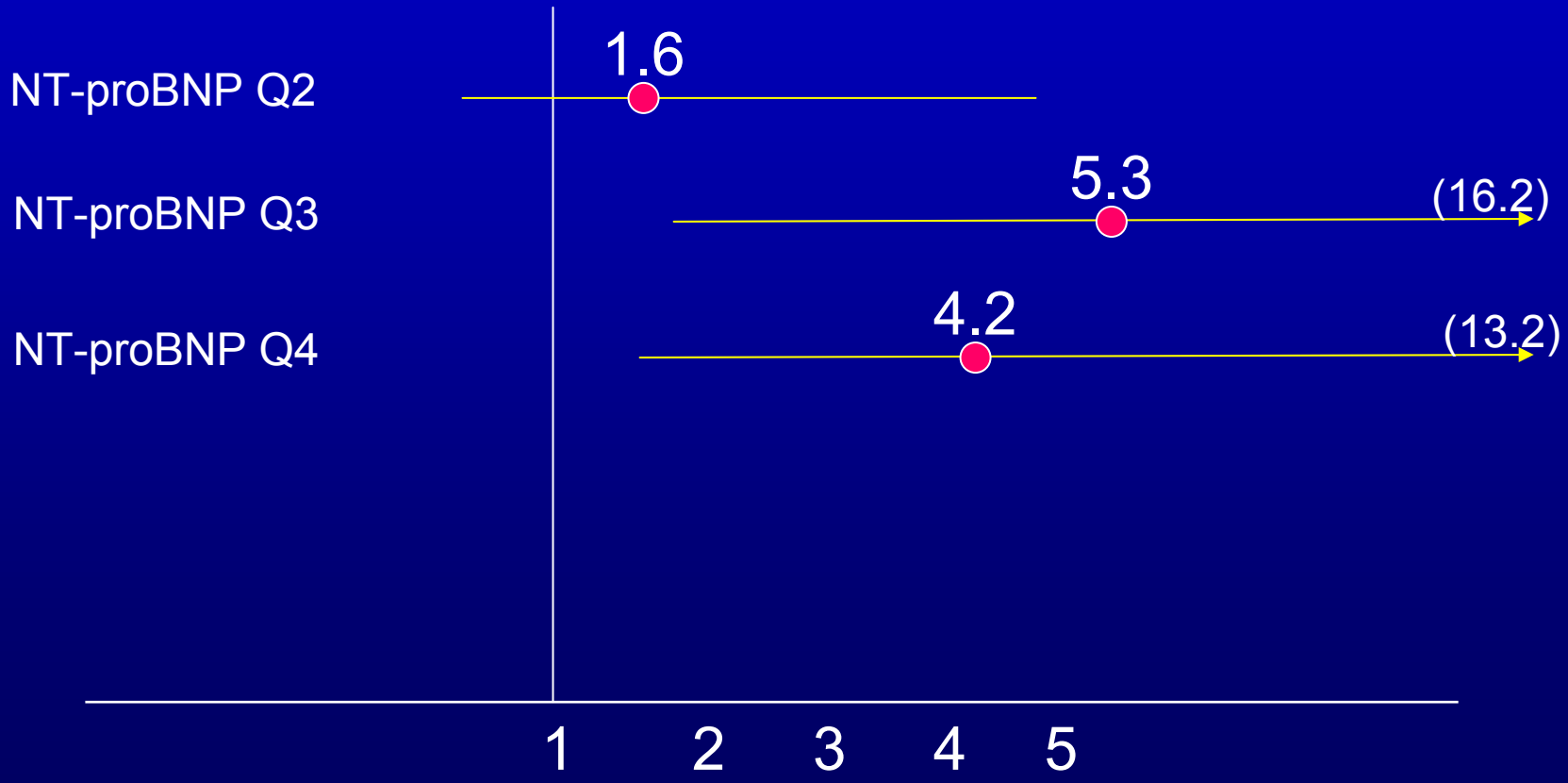
Quartiles of proBNP in asymptomatic patients with renal disease

	Q1 (4-116)	Q2 (122-490)	Q3 (490-1819)	Q4 (≥1976)	P for trend
	n=51	n=52	n=52	n=52	
Age (mean±SD)	5±15	64±13	67±12	67±13	<.001
Male n(%)	33(65)	26(50)	30(58)	32(62)	.94
Caucasian n(%)	11(22)	9(17)	13(25)	14(27)	.36
Diabetes n(%)	19(37)	25(48)	34(65)	30(58)	.03
Known CAD n(%)	6(12)	12(23)	27(52)	22(42)	<.001
GFR (mean±SD)	50±29	46±21	32±21	23±14	<.001
cTnT (>0.03ng/mL) n(%)	4(8)	6(12)	15(29)	24(46)	<.001

deFilippi et al., Am J Kidney Dis 2005

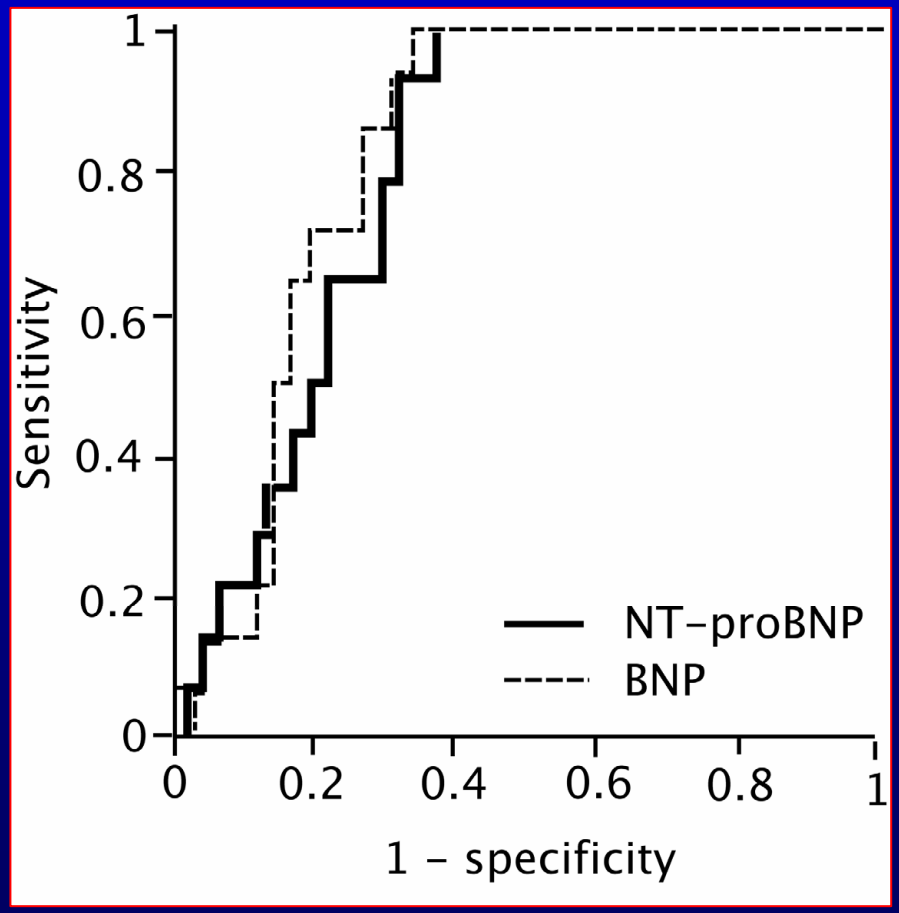
NT-proBNP level independently predicts CAD Dx in renal patients

Compared to Quartile 1, adjusted for age, GFR, diabetes and cTnT (n=207)



deFilippi et al. Am J Kidney Dis. 2005;46:35

NT-proBNP versus BNP
Ambulatory patients with CKD
Indicator of History of CAD



AUC for NT-proBNP=0.80, p=0.001
AUC for BNP=0.82, p=0.0004
P value for comparison of AUC=0.45
Prevalence of CAD Hx is 26%

Khan et al. Am J Card 2006

Factors that impact natriuretic peptide levels in patients with CKD

Multiple linear regression analysis

	BNP		NT-proBNP	
Variable	β Coefficient	*P*	β Coefficient	*P*
GFR	−0.0141	<0.0001	−0.0193	<0.0001
MABP	0.0102	0.0006	0.00746	0.0251
Age	0.00951	<0.0001	0.0088	0.001
Arteriopathic disease	0.312	<0.0001	0.386	<0.0001
PTH	0.000594	0.0292		
BMI			−0.0132	0.0187
Hemoglobin			−0.0471	0.0499
Calcium × phosphate product			0.123	0.0146
Addition of LV mass index to the model				
LV mass index	0.001408	0.0223	0.002131	0.0017

Vickery AJKD 2005;46:610

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  - ✓ The editorial- 2006
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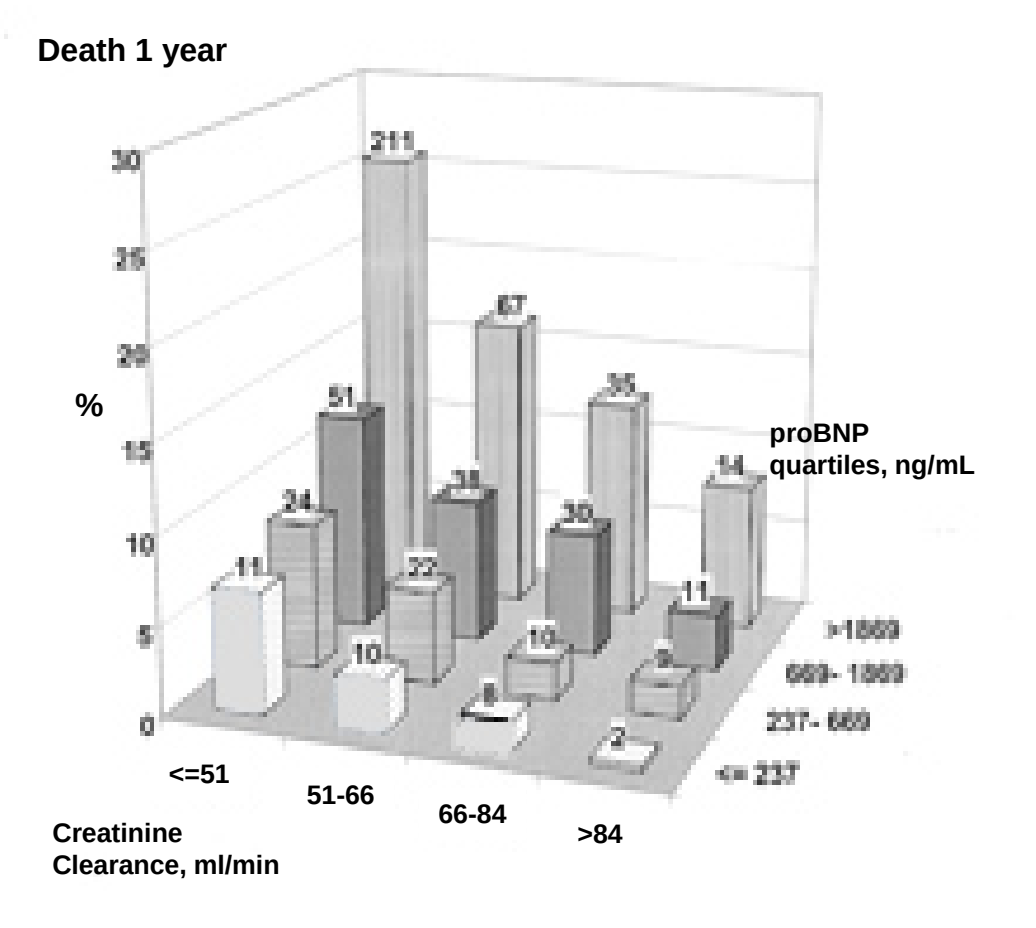
NT-ProBNP level and Renal Function

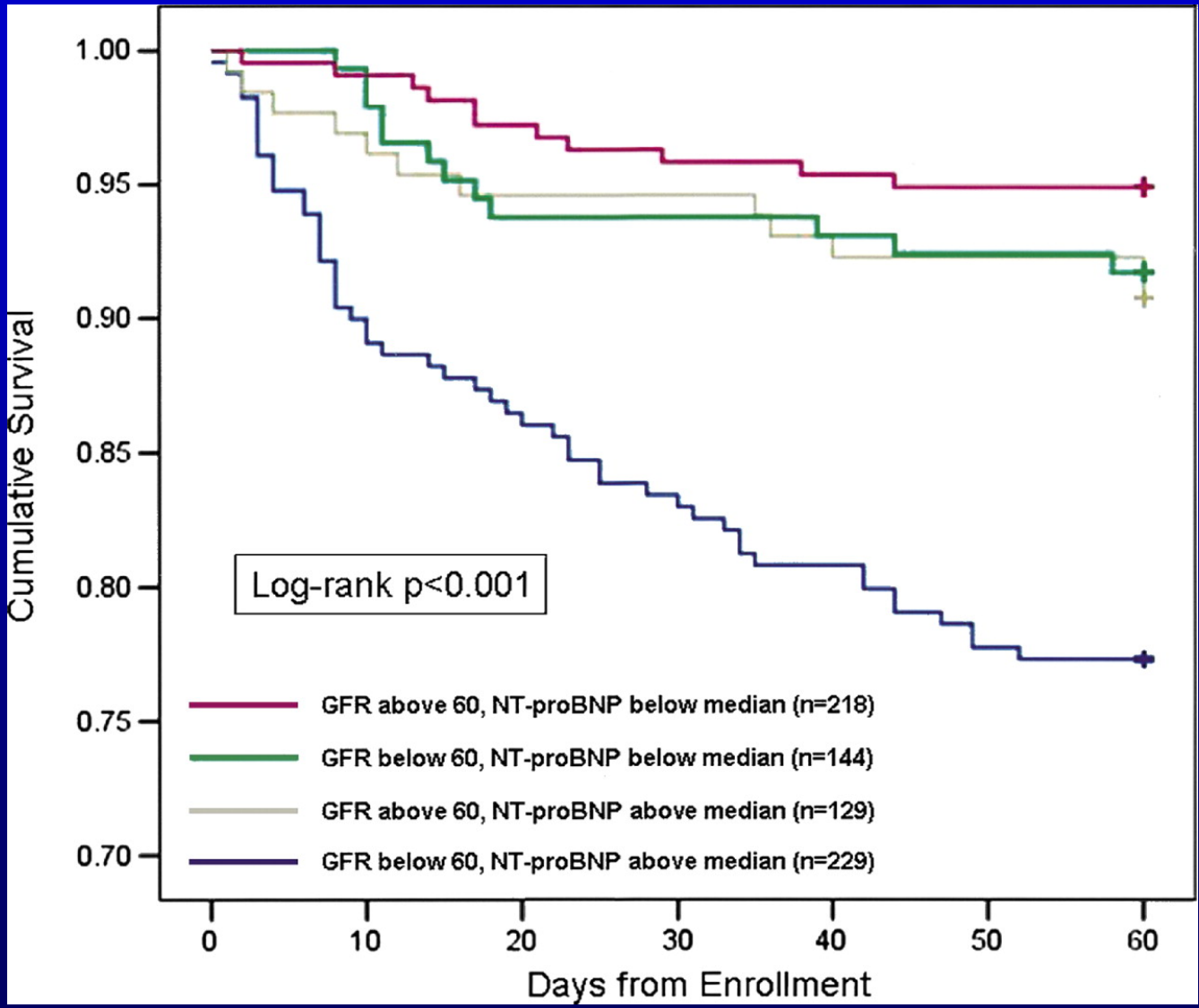
Complementary indices of risk in patients with acute coronary syndromes



1-year outcomes from the GUSTO-IV study

Circulation 2003;108:275

Survival curves of heart failure subjects in ICON as a function of GFR and NT-proBNP concentration on admission



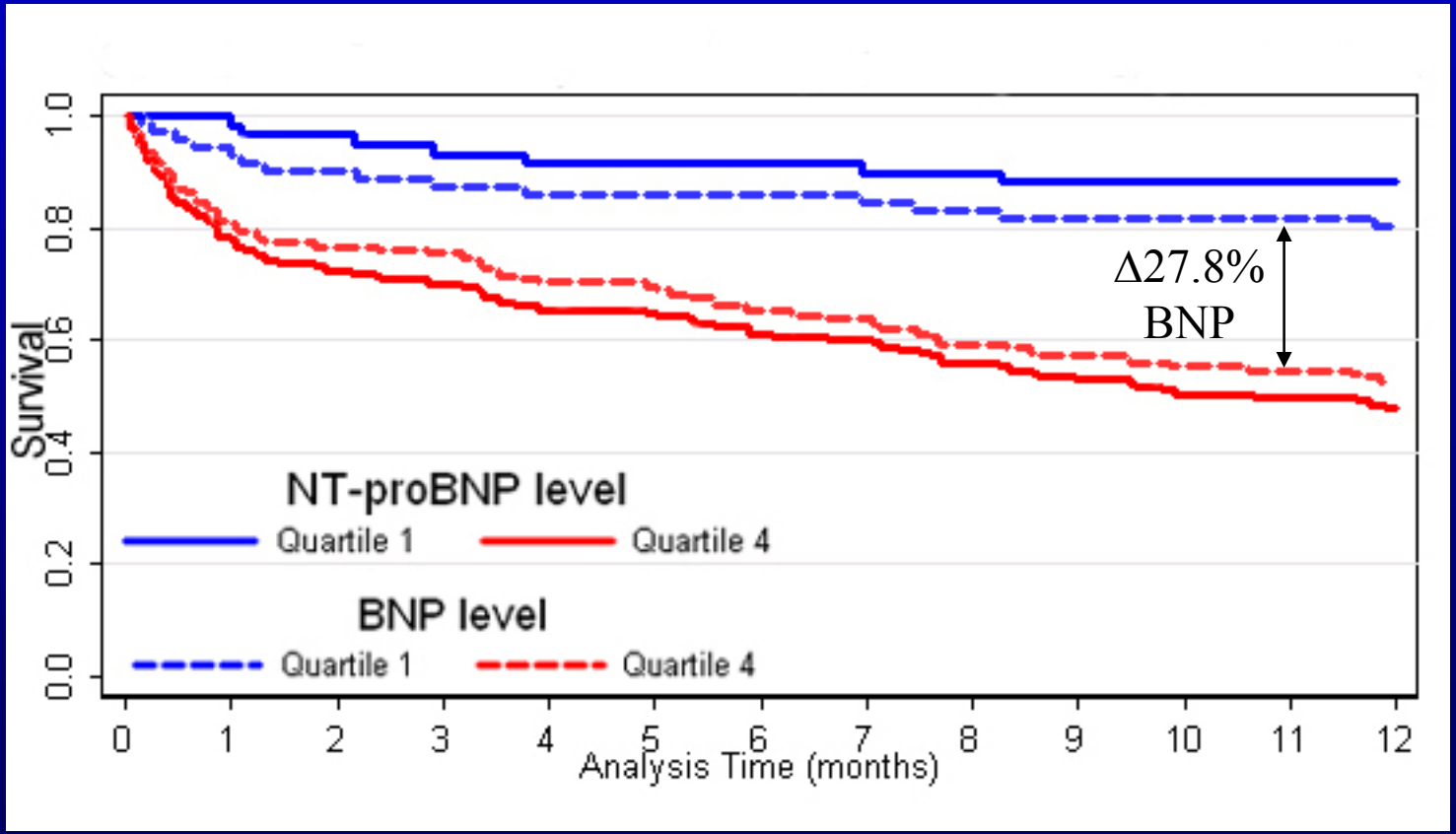
van Kimmenade J Am Coll Cardiol 2006;48:1621

JACC Journal of the American College of Cardiology

Survival in dyspnea patients with renal disease

Stratification by BNP vs. NT-proBNP

Carolinas outcome study



deFilippi et al. Clin Chem. 2007;53:1511-9.

Renal disease and dyspnea: NP association with one-year all-cause mortality (n=383)

	Adjusted* Hazard Ratio (95% CI)	Test of significance of biomarker
BNP		
Q1 (<88 ng/L)	Ref	$\chi^2(3)=13.5$; p=0.004
Q2 (83-333 ng/L)	1.3 (0.7, 2.7)	
Q3 (334-800 ng/L)	1.5 (0.7, 2.9)	
Q4 ≥800 ng/L)	2.6 (1.4, 4.8)	
NT-proBNP		
Q1 (<472 ng/L)	Ref	$\chi^2(3)=21.4$; p<0.001
Q2 (472-1728 ng/L)	2.0 (0.8, 4.9)	
Q3 (1729-6000 ng/L)	2.9 (1.0, 6.7)	
Q4 >6000 ng/L	4.5 (2.0, 10.2)	

* Adjusted for age, gender, race/ethnicity, eGFR, dialysis treatment, hypertension, diabetes, atrial fibrillation, coronary disease, prior heart failure, patient disposition, and diagnosis of acute decompensated heart failure.

deFilippi et al. Clin Chem. 2007;53:1511-9

Conclusions
In the Chronic Kidney Disease Patient

- ✓ NT-ProBNP and BNP are valuable adjuncts for the diagnosis and prognosis of decompensated HF in the renal patient with dyspnea
- ✓ Elevated natriuretic levels in the absence of HF may often represent other acute or chronic heart disease including ischemia heart disease.
- ✓ Additional future applications may include risk stratification in asymptomatic subjects and patients with concomitant renal disease