UniversitätsKlinikum Heidelberg

How will new high sensitive troponins affect the criteria?

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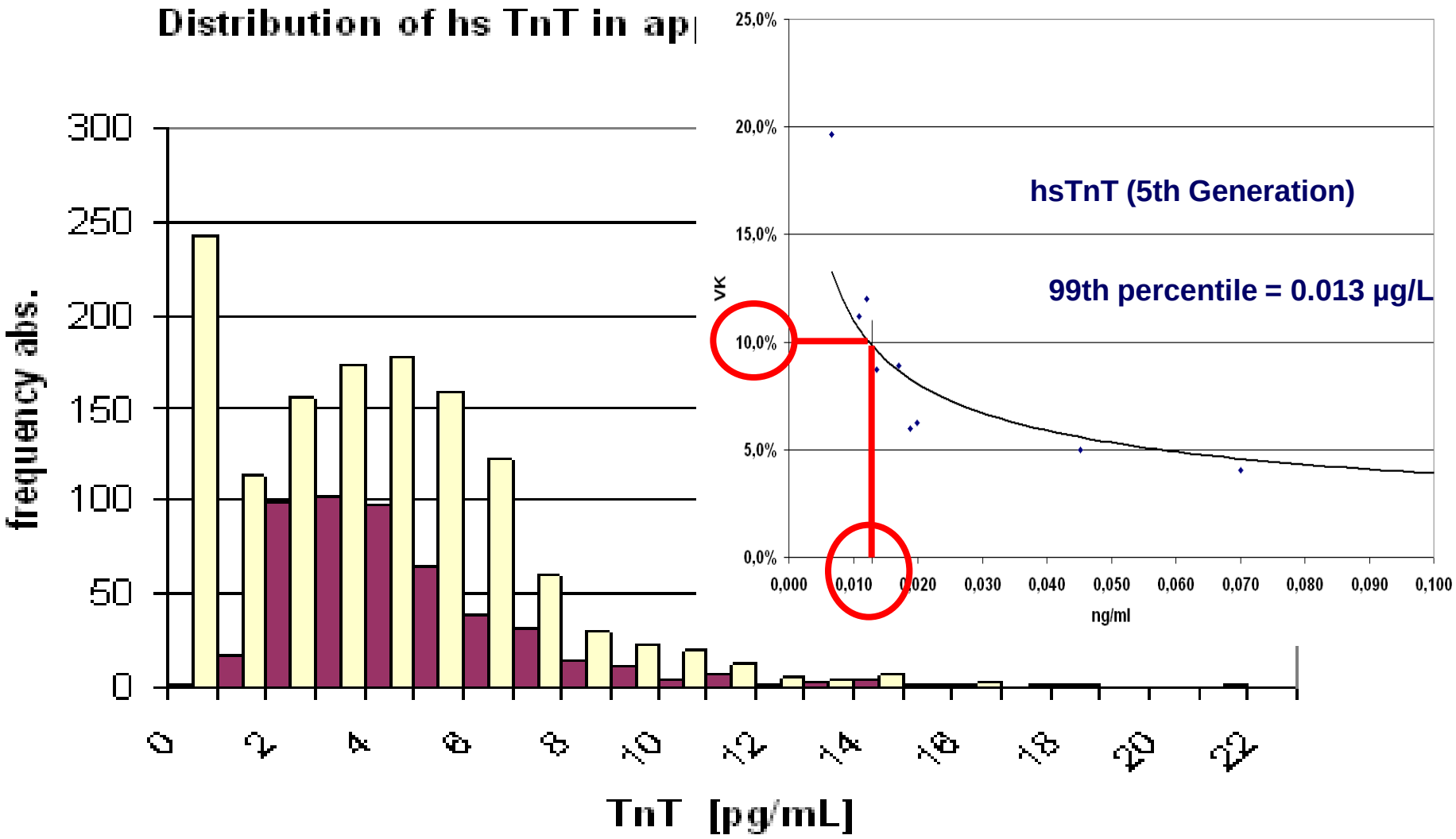
Kardiologie, Angiologie, Pulmologie

Universitätsklinikum Heidelberg

Even more sensitive: The new Troponin T assay hs



Giannitsis et al Clin Chem 2010

Universal Definition of Myocardial Infarction

Criteria of Myocardial Infarction

Myocardial necrosis:

Detection of rise and/or fall of cardiac biomarker (preferably troponins) with at least one value above the 99th percentile of the upper reference limit

With evidence of myocardial ischemia with at least one of the following:

- **Symptoms of ischemia**
- **New ST-T changes or LBBB**
- **Development of new Q-waves**
- **Imaging evidence of new loss of viable myocardium**
- **or new regional wall motion abnormality**

Sub-Classification of AMI

Type 1 **Spontaneous myocardial infarction related to ischemia due to a primary coronary event such as plaque erosion or rupture, fissuring or dissection**

Type 2 Myocardial infarction secondary to ischemia due to imbalance between oxygen demand and supply e.g. coronary spasm, anemia, or hypotension

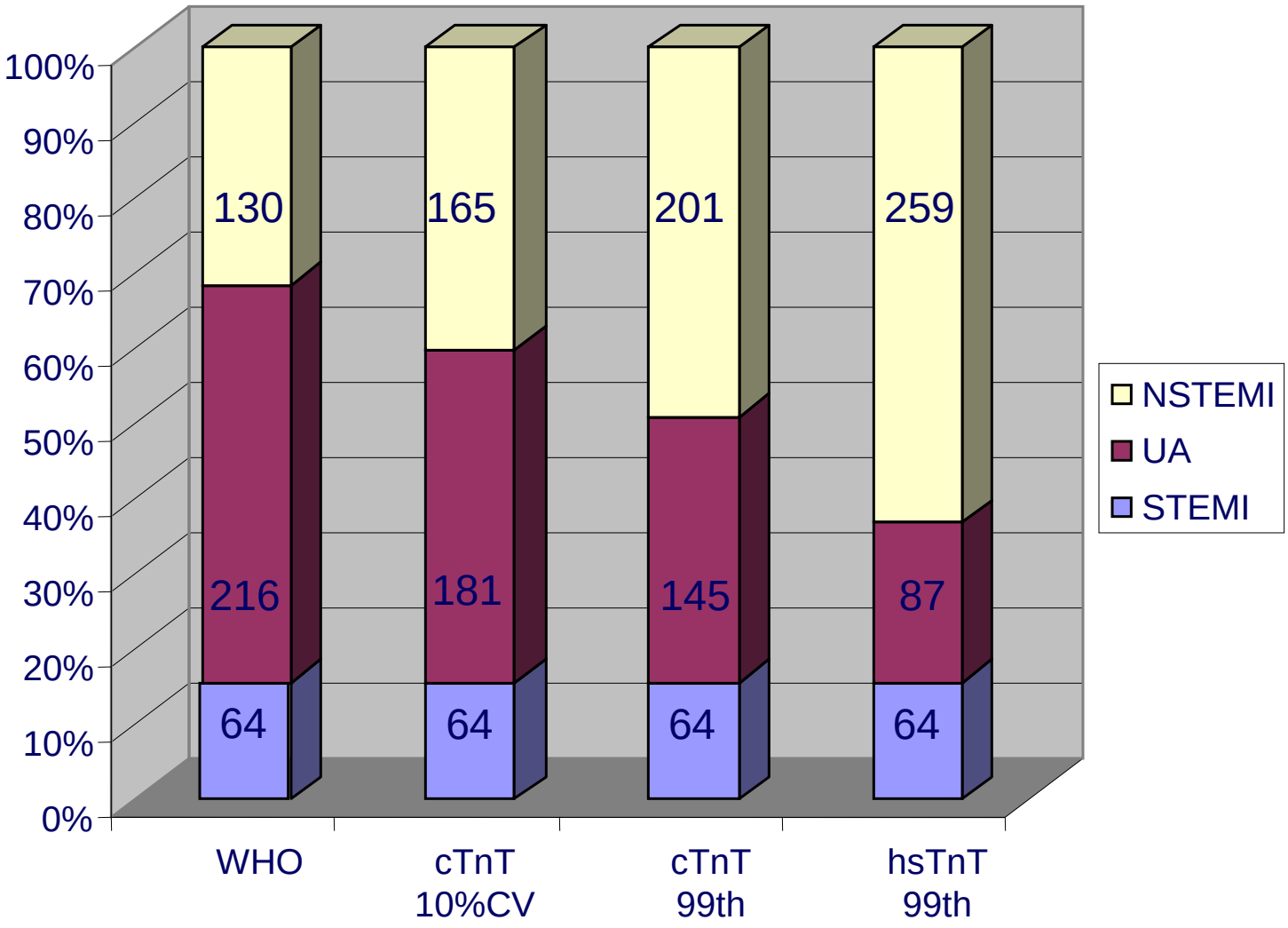
Type 3 Sudden cardiac death with symptoms of ischemia, accompanied by new ST elevation or LBBB, or verified coronary thrombus by angiography or autopsy, but death occurring before blood samples could be obtained

Type 4a Myocardial infarction associated with PCI

Type 4b Myocardial infarction associated with verified stent thrombosis

Type 5 Myocardial infarction associated with CABG

Applying the Universal Definition of MI: What Has Happened with the Diagnosis of Unstable Angina?



unpublished

Diagnostic performance of serial blood sampling using 99th percentile in evolving MI

Higher delta improves specificity

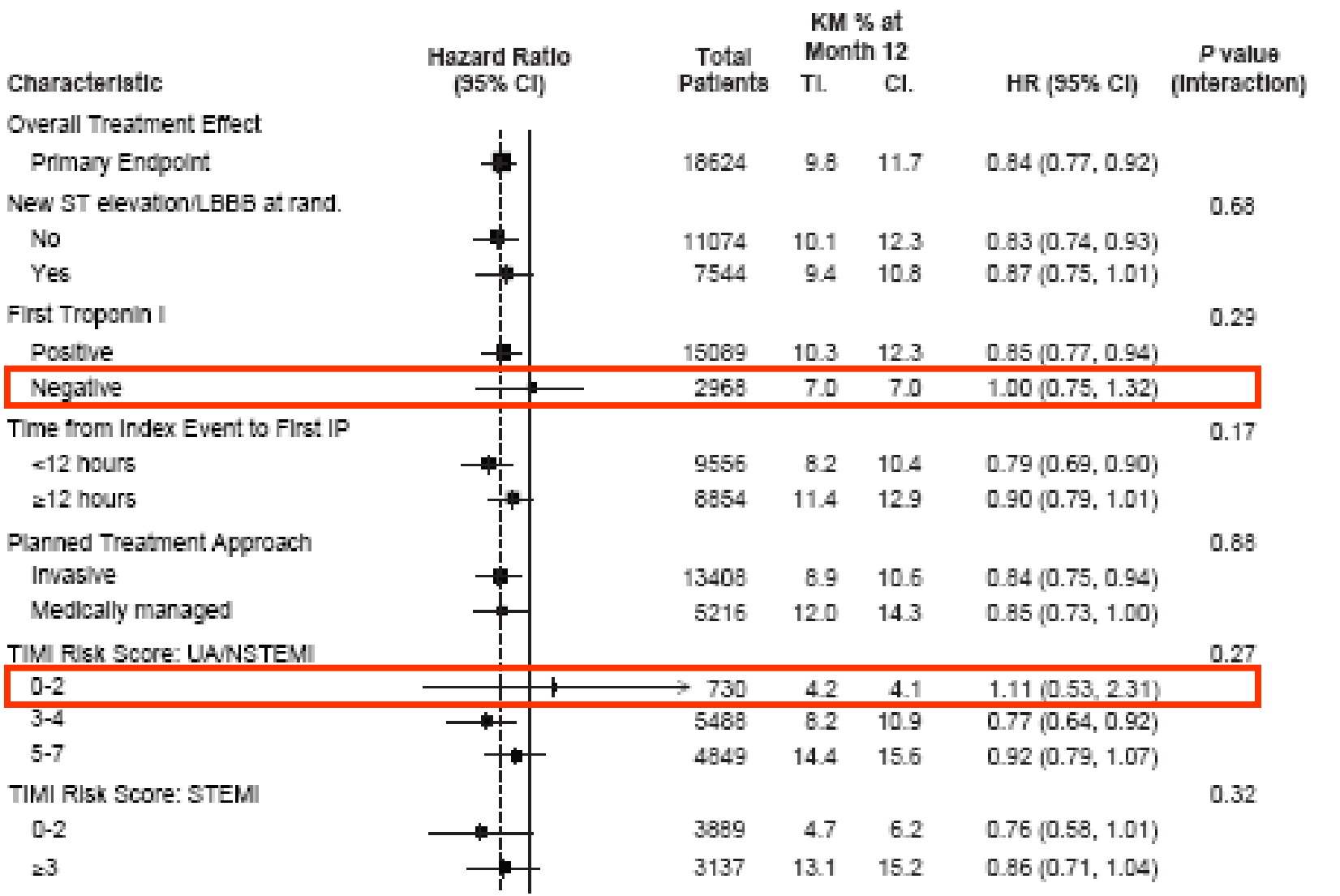
	Sens %	Spec %	PPV	NPV
Baseline sample >99th	62	77	69	71
FU sample 3hours >99th	100	77	65	100
FU sample >99th + 20%delta	85	57	79	67
FU sample >99th + 117%delta	69	100	100	88

Giannitsis E, et al. Clin Chem 2010

Predictors of Death at 3 years FU

N=1530	HR	95%CI	p-value
TnThs ≥14 pg/ml	7.591	1.006-57.3	0.049
Age ≥ 75 years	2.753	1.448-5.233	0.002
GFR <60 ml/min/1.73m^2	2.318	1.364-3.938	0.002
TIMI Risk Score by Tertiles	1.193	0.876-1.626	0.263
NT-proBNP > 2399 pg/ml (ROC-optimized)	5.698	3.252-9.983	<0.001
cTnT ≥ 0.03 µg/l	1.752	0.778-3.947	0.176

Unstable angina and treatment options



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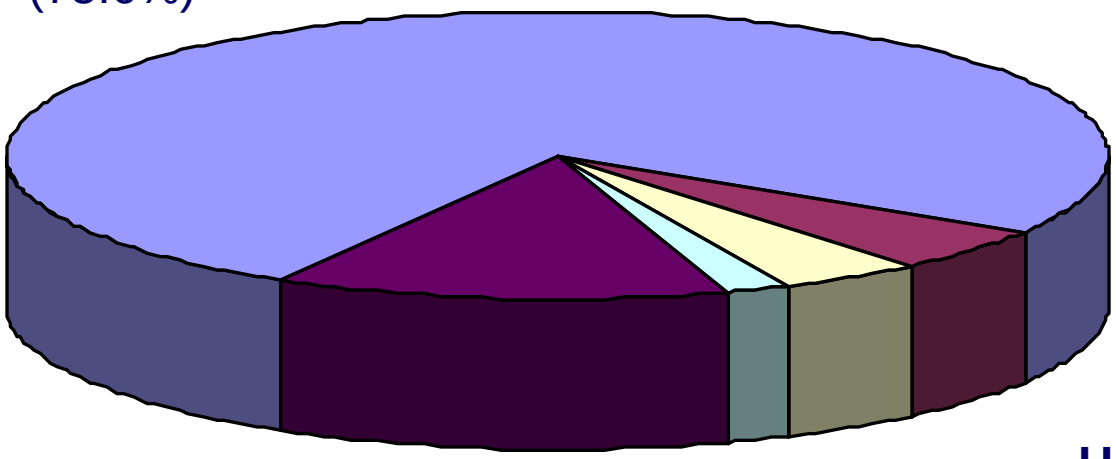
Diagnoses in Chest Pain Patients

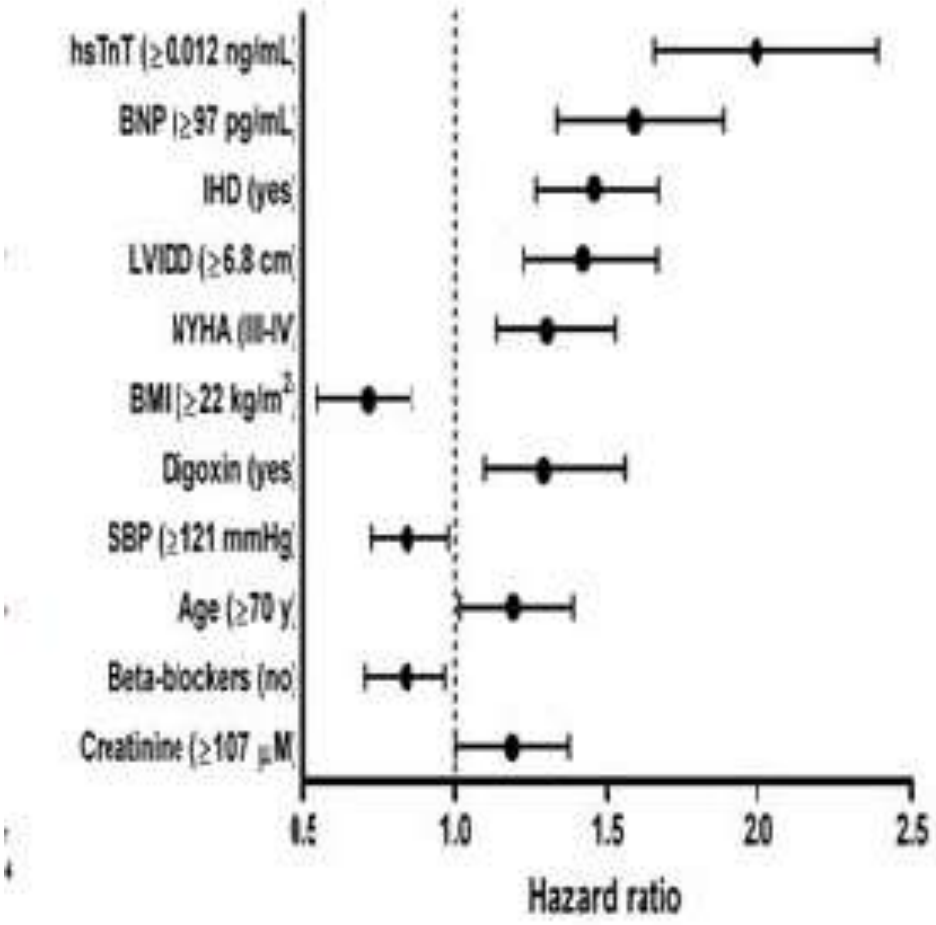
CPU Registry Heidelberg (n=3,327)
8.6.2009 – 30.11.2009 (6-months)



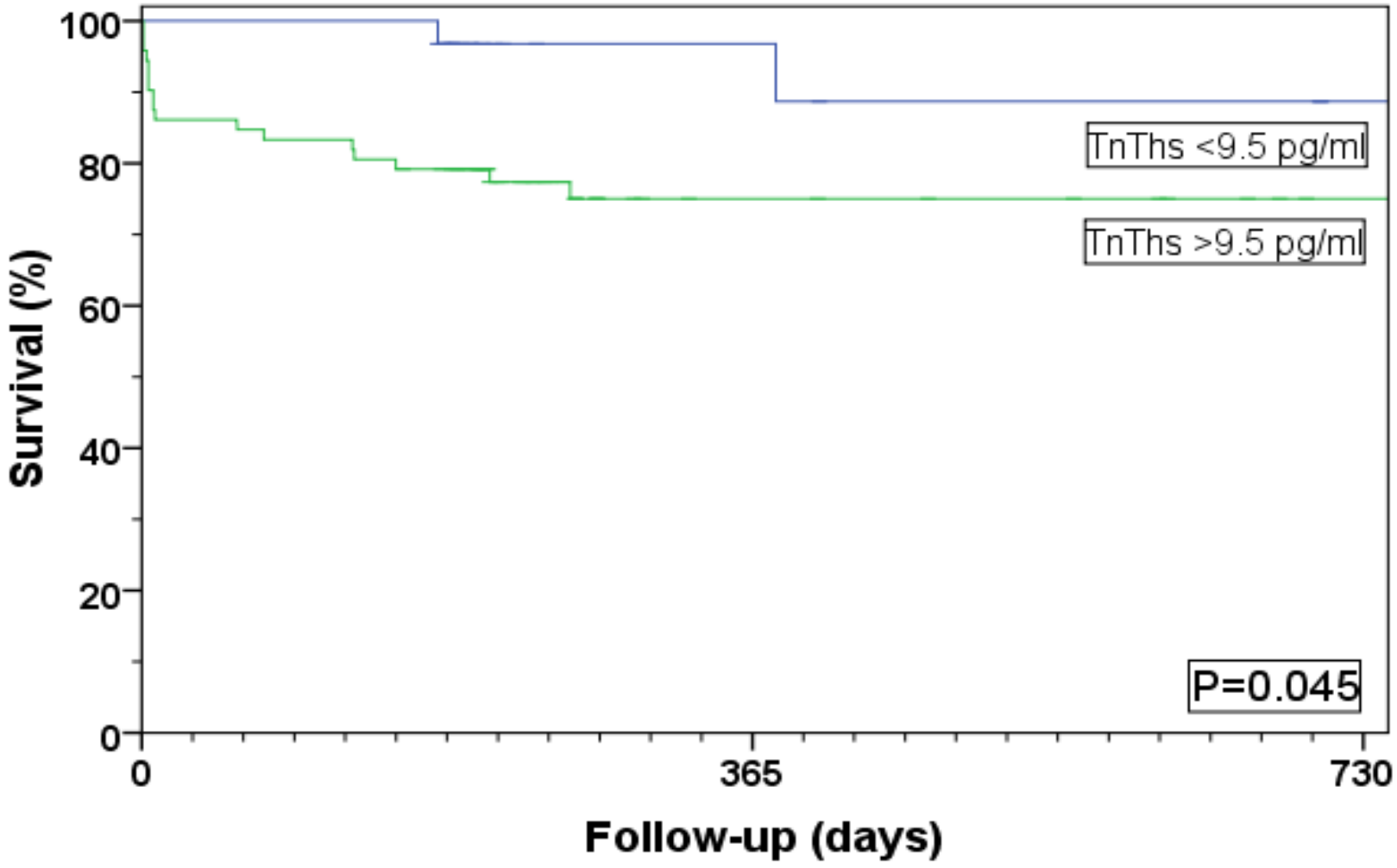
Median number of TnThs measurements 3 (IQR 3-5, range 2-6)

20% of consecutive pts admitted to CPU TnThs positive !!
69% elevations are not due to clinical ACS !!

High Sensitive Troponin T is a Strong Predictor of Outcomes in Patients with Chronic Heart Failure - A Study from the Val-HeFT Trial

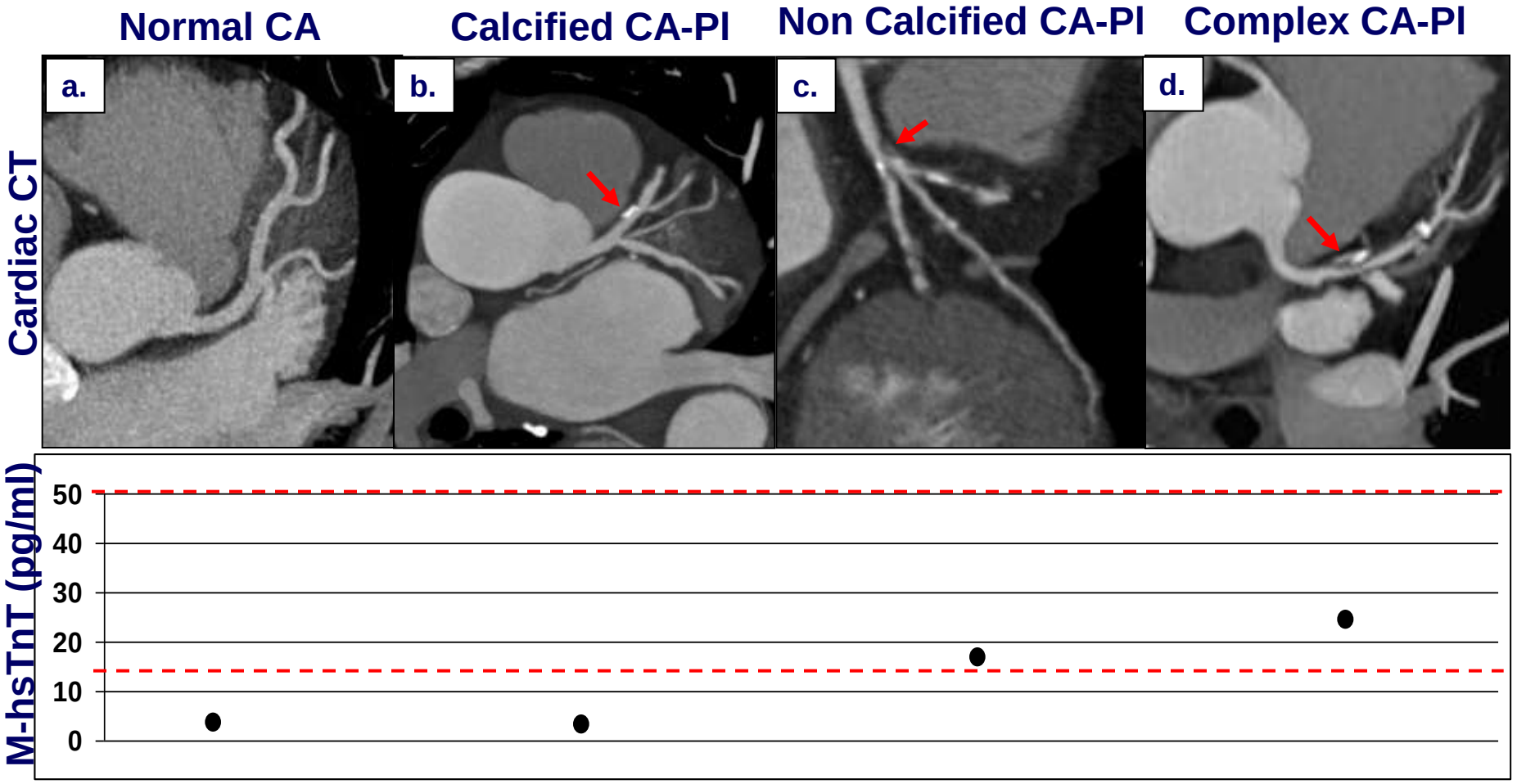


Acute Pulmonary Embolism
Probability of Long-Term Survival



Lankeit M,….Giannitsis E, Katus HA, Konstantinides SDGK 2009; Poster

hsTnT and Plaque Morphology in Stable Coronary Artery Disease



CT angiography and biomarkers in subjects without ACS as a function of hsTnT

Characteristic	hsTnT ≥13 pg/mL (N=38)	hsTnT <13 pg/mL (N=302)	*P*
Coronary CT angiography			
Segments with calcified plaque	4.4 (±4.0)	1.5 (±3.0)	<.001
Segments with non-calcified plaque	1.8 (±3.0)	0.8 (±2.0)	.05
Segments with mixed plaque	1.4 (±2.5)	0.5 (±1.4)	.04
Segments with plaque	4.8 (±5.0)	1.7 (±3.0)	.001
Segments with significant stenosis	0.4 (±1.0)	0.06 (±0.3)	.04
Vessels with significant stenosis	0.2 (±0.5)	0.05 (±0.3)	.09
Vessels with plaque	2 (±1.8)	0.9 (±1.3)	.001
Cardiac chamber size and function			
Left atrial diastolic volume, mL	107 (±33.0)	95 (±24.0)	.02
Left atrial systolic volume, mL	69 (±31.0)	55 (17.0)	.01
Left ventricular end diastolic volume, mL	122 (±45.0)	117 (±30.0)	.50
Left ventricular end systolic volume, mL	48 (±41.0)	38 (±16.0)	.20
Left ventricular mass	173 (±60.0)	147 (±39.0)	.01
Left ventricular ejection fraction, %	65 (±14.0)	68 (±9.0)	.30
Regional left ventricular dysfunction	8 (22%)	24 (8%)	.008
Biomarkers besides TnT			
NT-proBNP, pg/mL, median (interquartile range)	248 (92-492)	42 (23-86)	<.001
Cystatin-C, mg/L, median (interquartile range)	0.93 (0.75-1.07)	0.82 (0.73-0.92)	.05

Januzzi et al, 2009, Submitted

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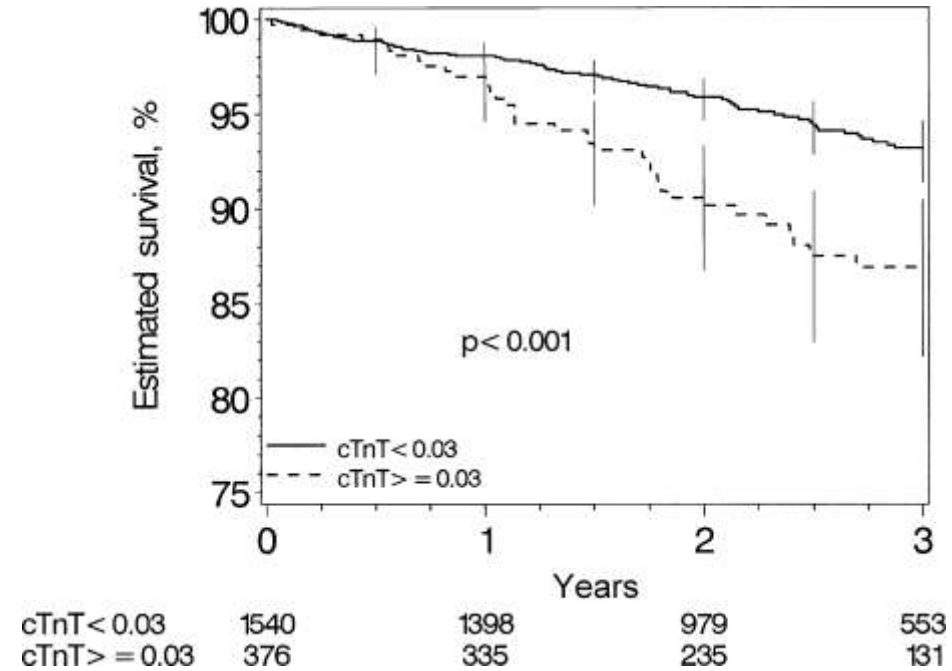
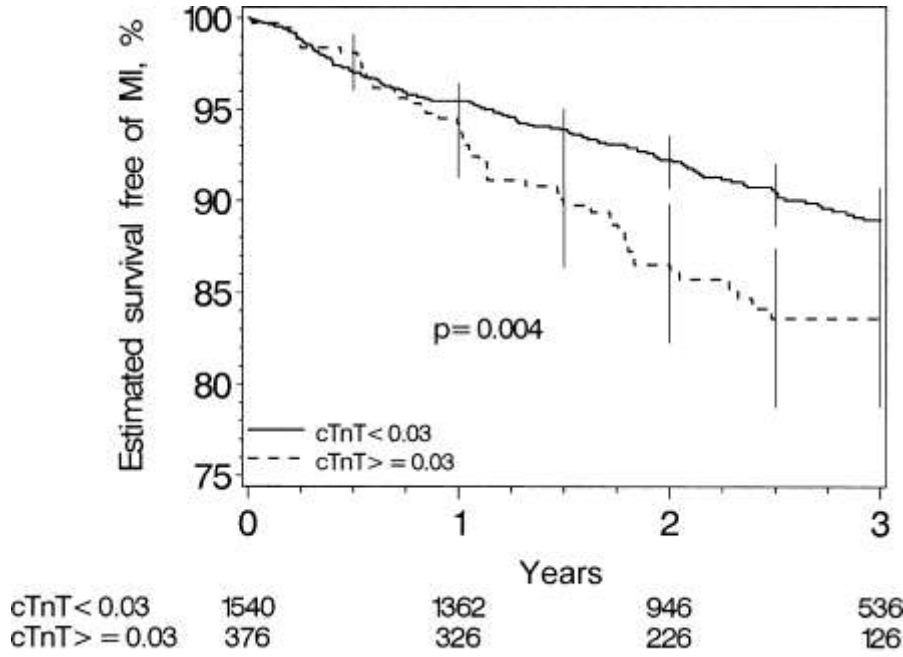
Kaplan-Meier survival estimates for those with (TnT >=0.03) and without (TnT)

1,949 patients from the Mayo Clinic registry

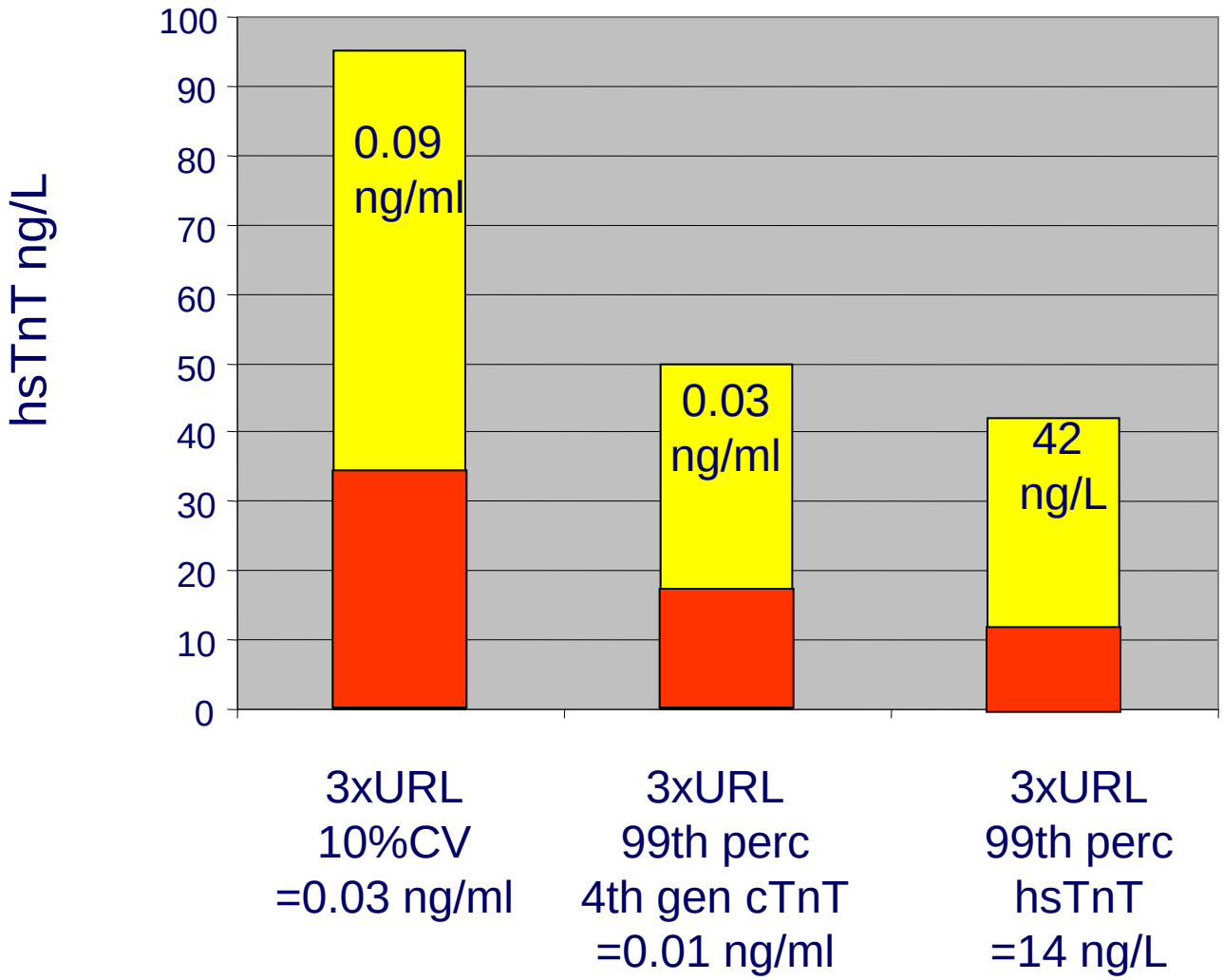
All had normal CK-MB after the procedure
383 (19.6%) patients with elevated cTnT





Prasad, A. et al.
J Am Coll Cardiol 2006;48:1765-1770

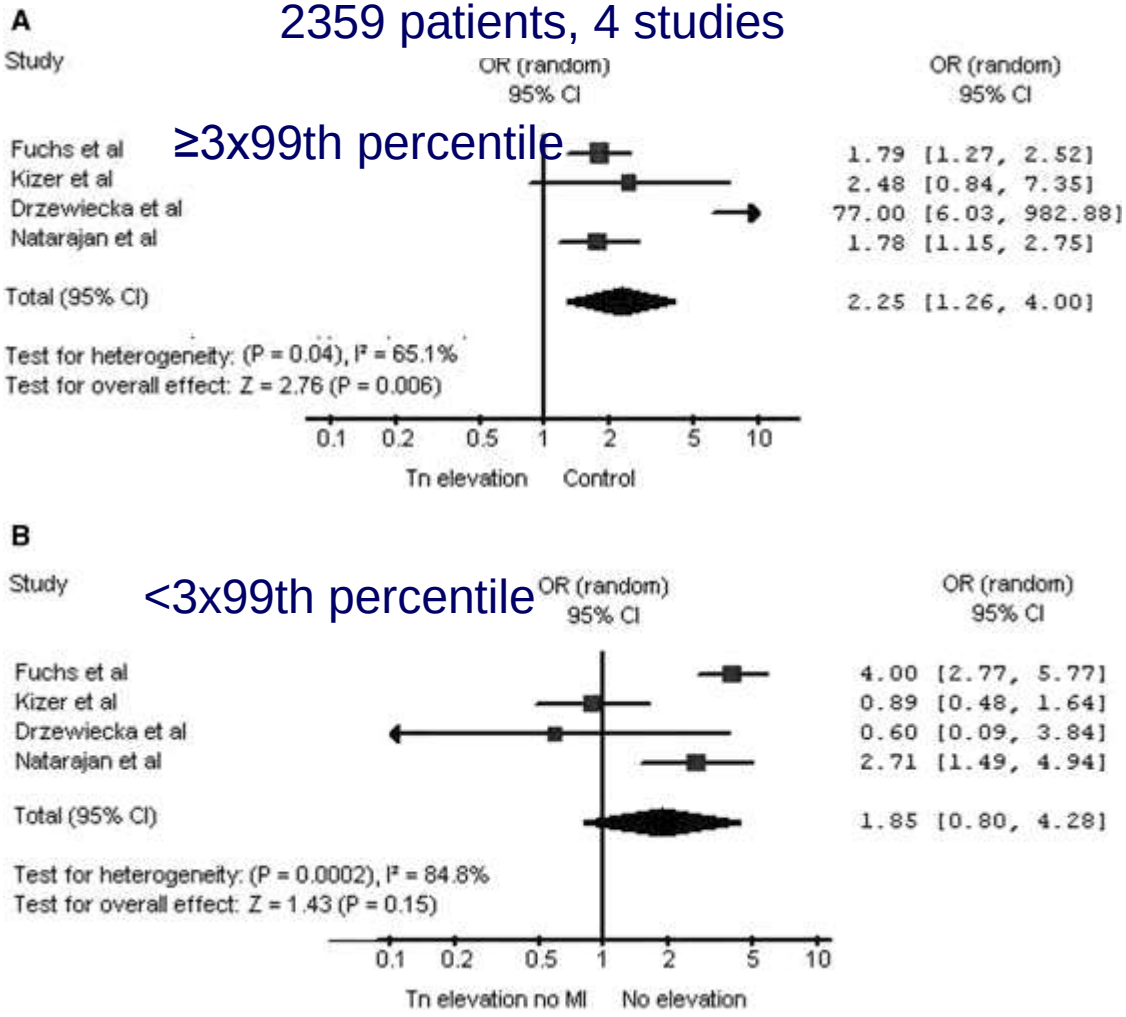
Cutoff concentrations for diagnosis of periprocedural MI



Incidence and prognostic role of Universal Definition Type IV MI

Meta-analysis 15 studies, 7578 patients

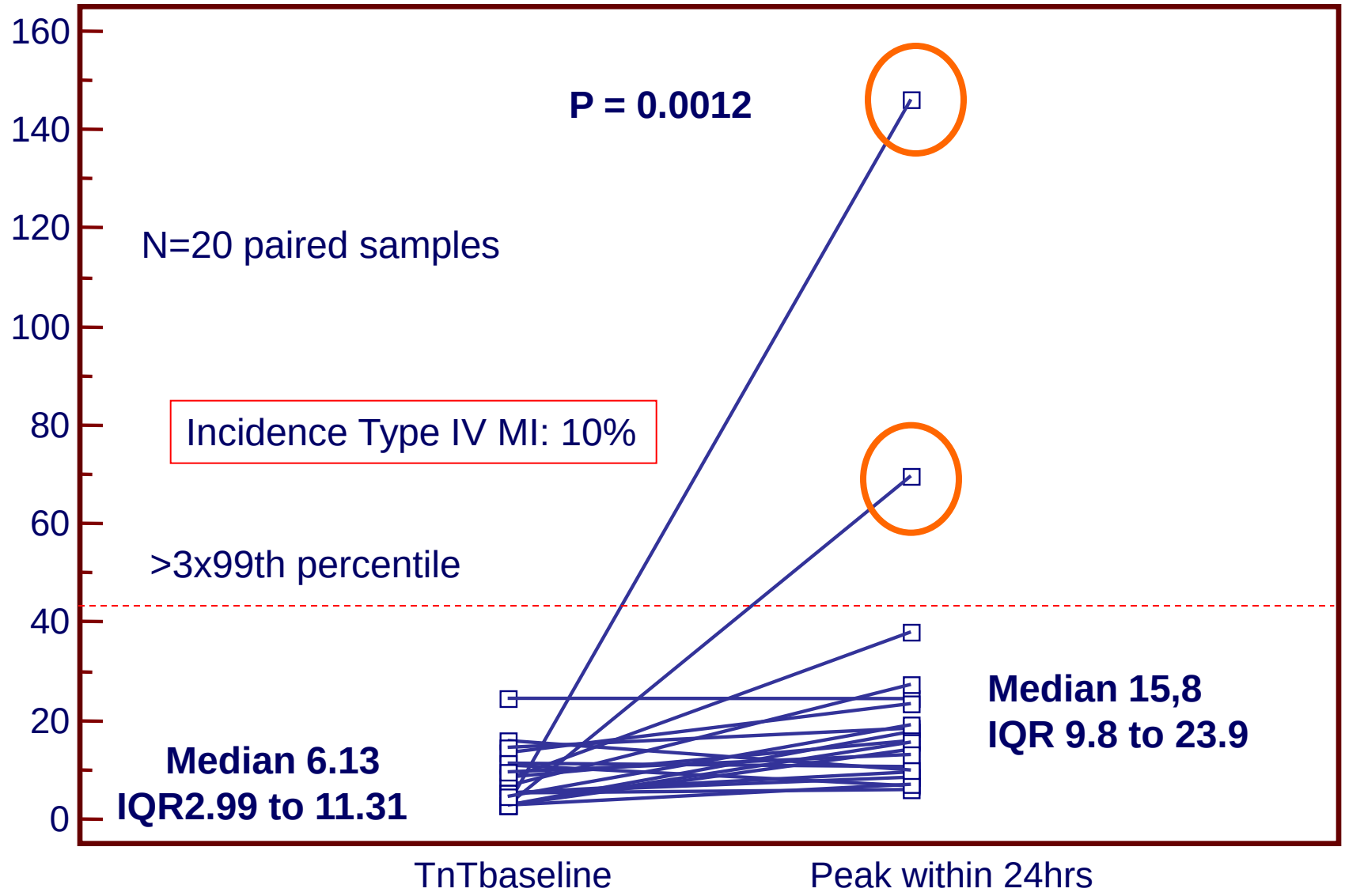
Elevation of troponin after scheduled PCI: 28.7%
PCI-related MI by Universal definition: 14.5%.



Type IV MI: Death OR 17.25 (2.71–109.96), *P* = 0.003,
Re-PCI OR 10.86 (3.2–36.94), P<0.001

Testa L et al. QJM 2009;102:369-378

Type 4 MIs after Elective PCI (> 3x 99th percentile = 42 pg/ml)



Prognostic significance of preprocedural cardiac troponin elevation among patients with stable CAD undergoing PCI: The EVENT Registry

	cTn Positive (n=142)	cTn Negative (n=2240)	*P*
Death or MI, n (%)	19 (13.4)	126 (5.6)	<0.001
Death, n (%)	1 (0.7)	0 (0.0)	0.060
MI, n (%)	19 (13.4)	126 (5.6)	<0.001
Urgent repeat PCI, n (%)	2 (1.4)	5 (0.2)	0.061
Urgent CABG, n (%)	1 (0.7)	6 (0.3)	0.35
Stent thrombosis, n (%)	0 (0.0)	5 (0.2)	1.00
Any angiographic complication, n (%)*	16 (7.5)	121 (4.0)	0.012

CABG indicates coronary artery bypass grafting.

*Lesion-based analysis.

7592 consecutive patients
142 (6.0%) cTnT + at baseline

Jeremias A, et al.Circulation 2008

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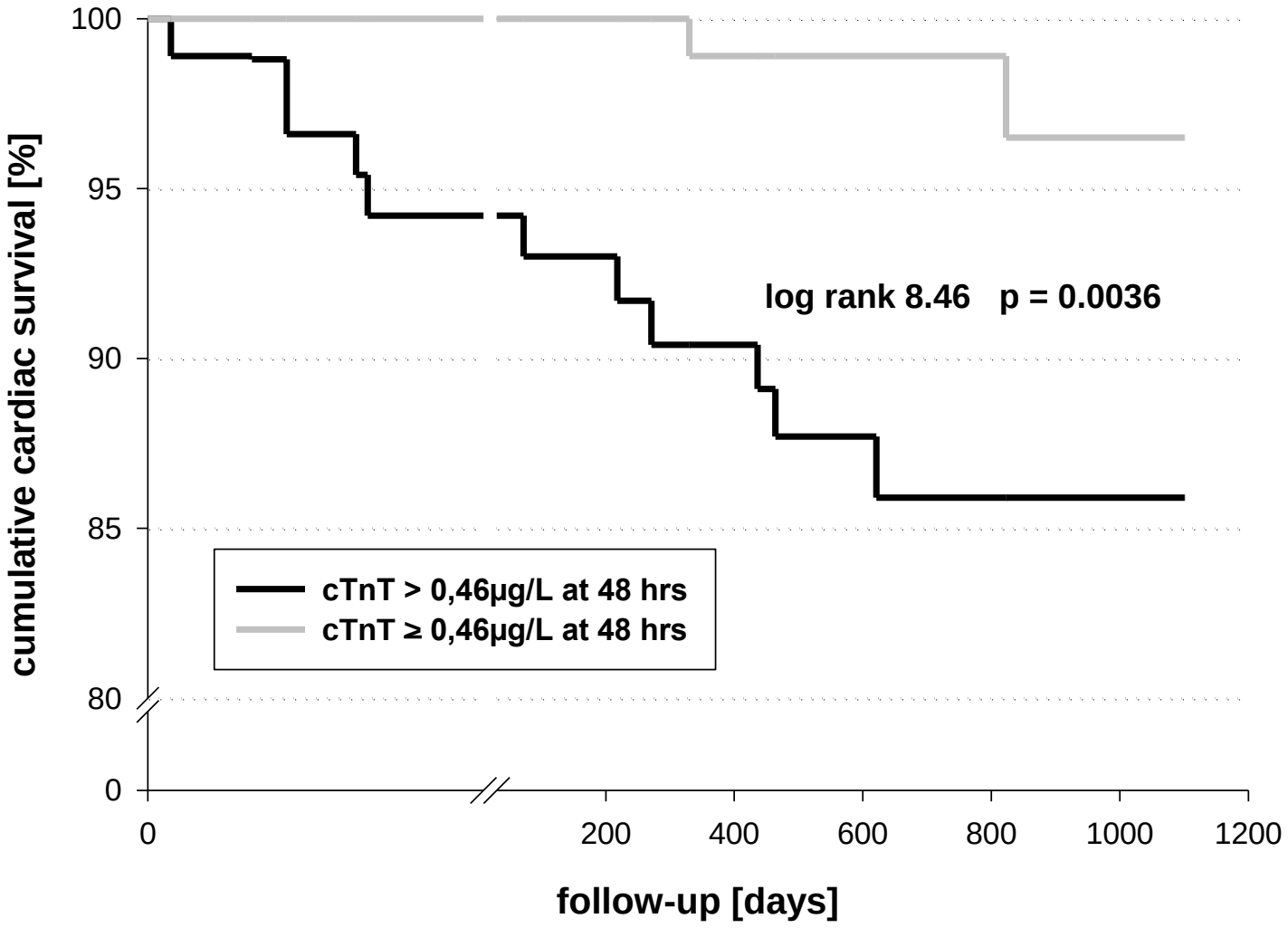
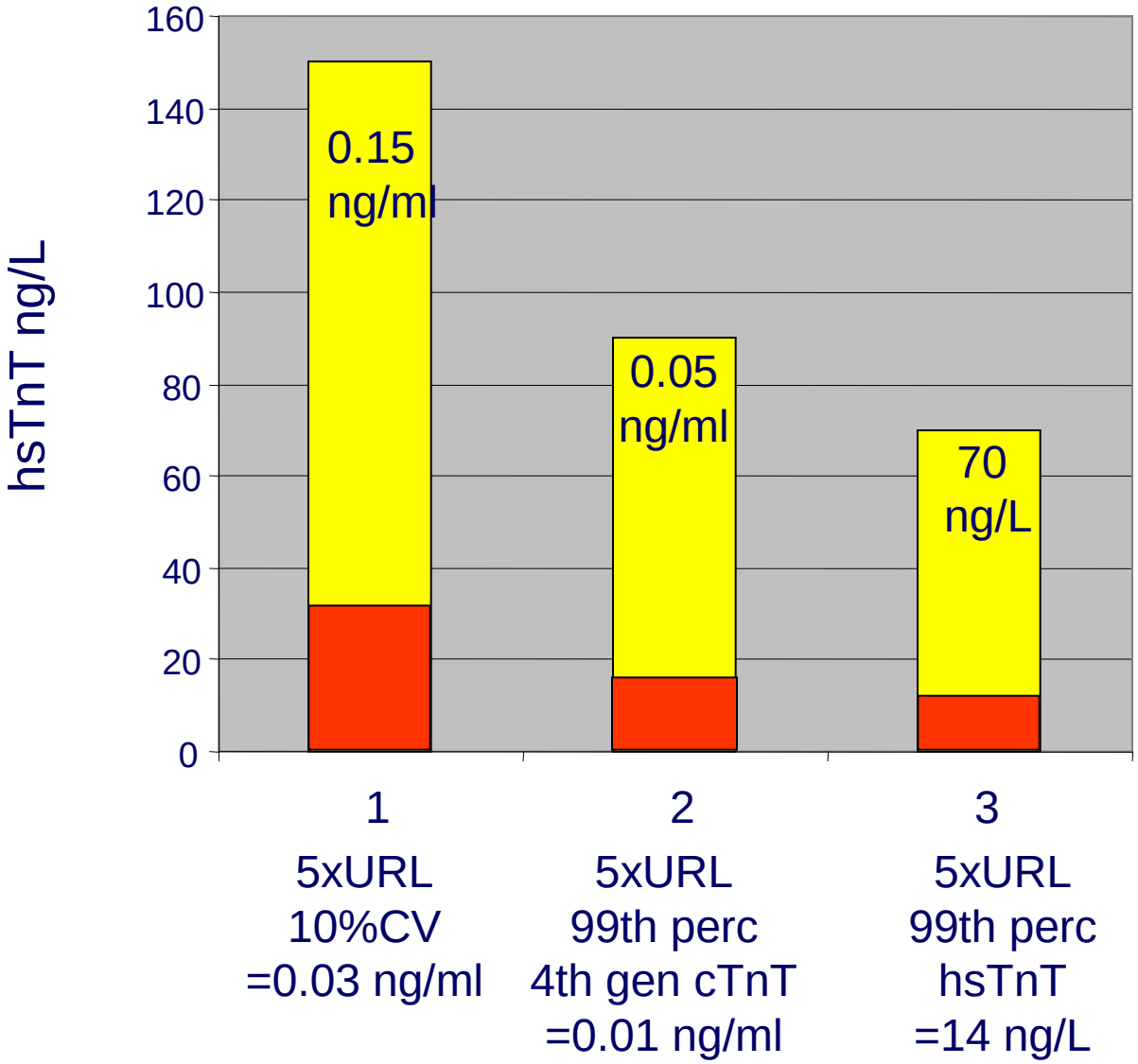
CTnT and Out-Come Following CABG-Surgery



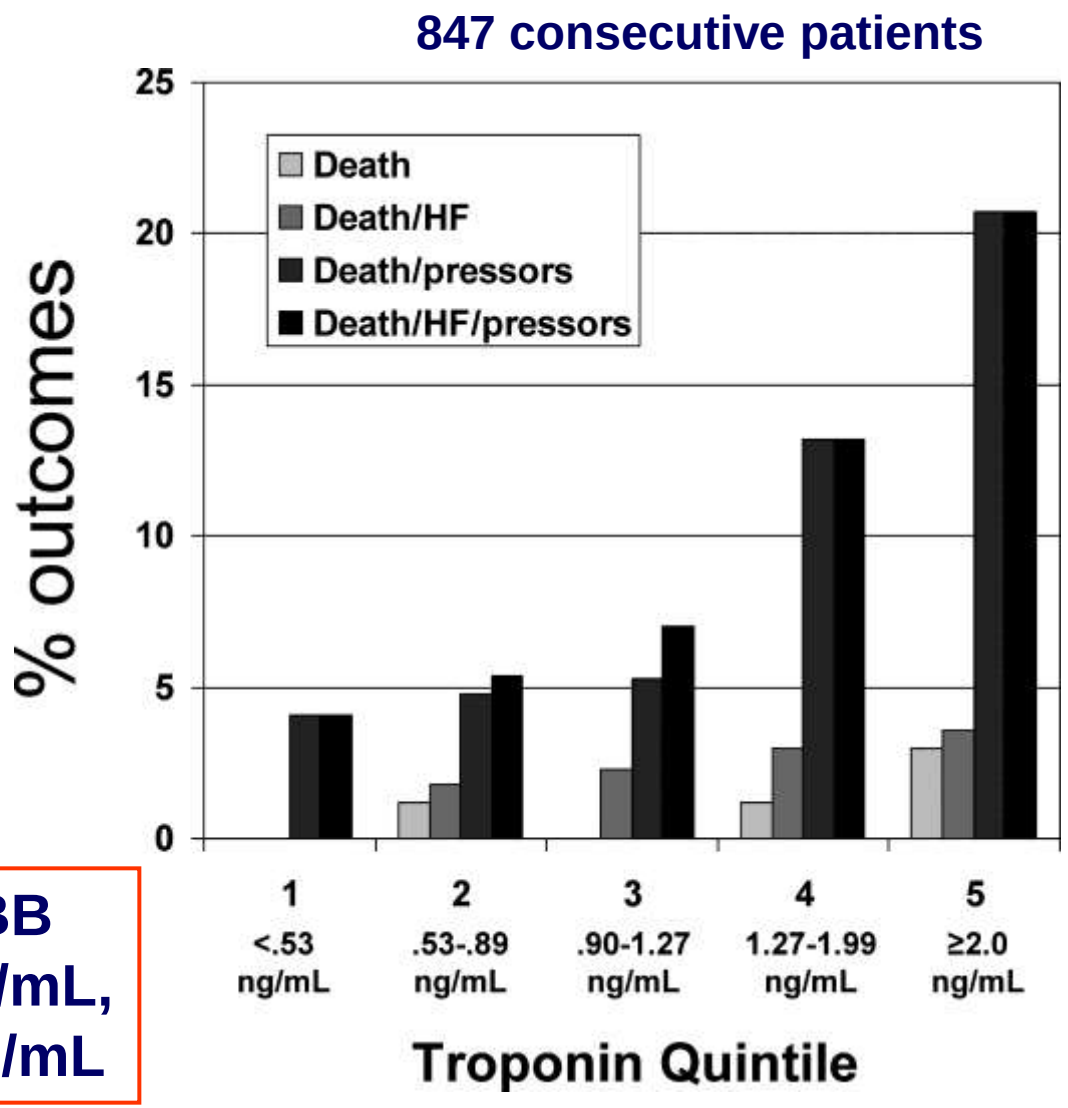
Cutoff concentrations for diagnosis of MI post CABG



Magnitude of cTnT release after CABG postoperative complications

Universal MI definition:
Type V MI (Periprocedural MI)
If cTn >5x99th percentile

= 0.07 ng/mL



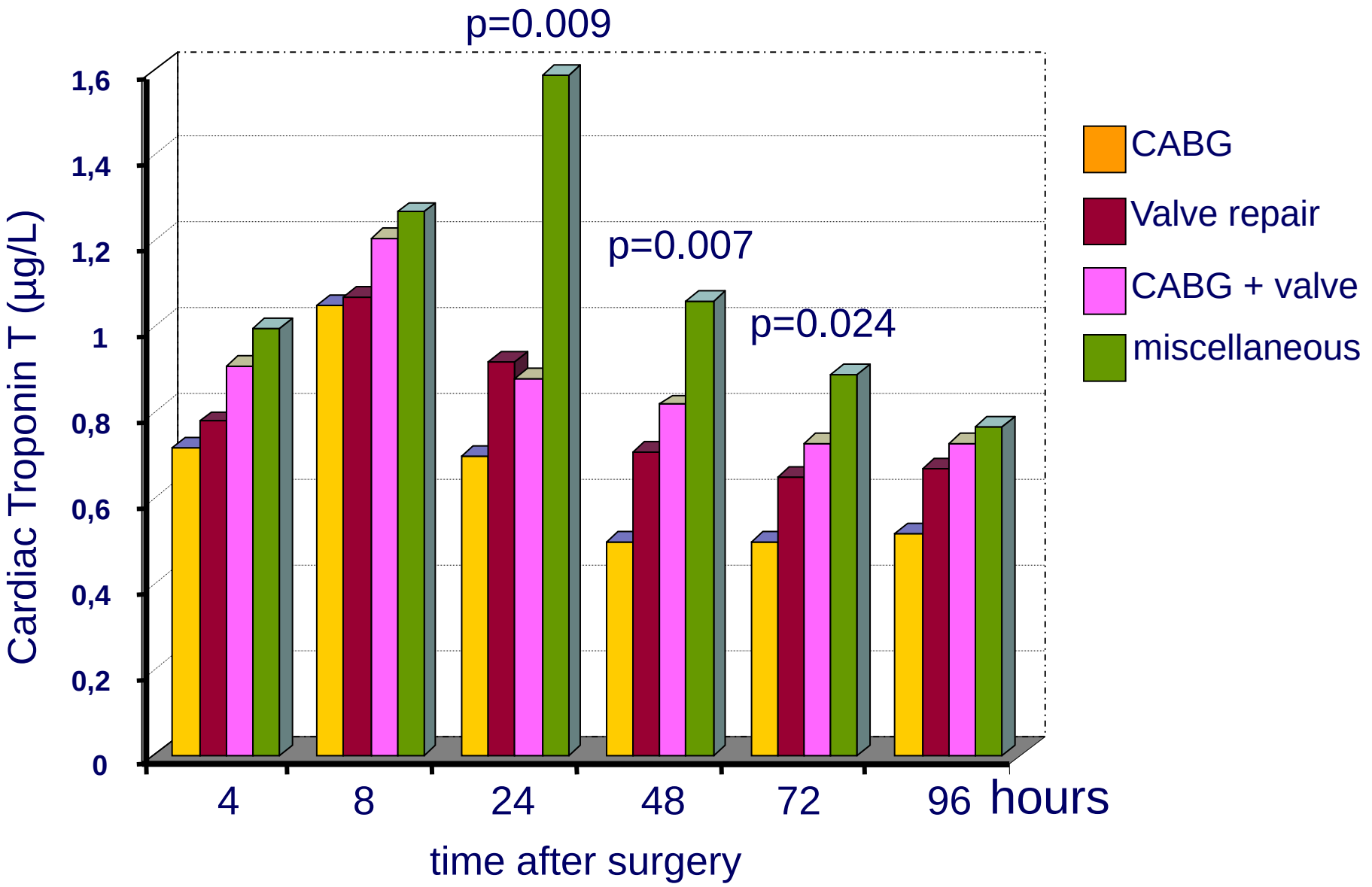
2% new Q-waves or LBBB
98.9% had a cTnT 0.03 ng/mL,
97.5% had a cTnT 0.10 ng/mL

Mohammed, A. A. et al.
Circulation 2009;120:843-850

Impact of hsTn on AMI Diagnosis/ Criteria

- **Type 1: Many more patients rule in for AMI, prevalence of unstable angina will diminish but risk prediction will be improved**
- **Type 2 AMIs will remain a diagnostic challenge**
- **Type 4 AMI will be observed in 10-40% of elective PCIs. The prognostic impact of minor marker increases needs to be tested prospectively**
- **Type 5 AMI will need revision due to extra-ordinarily high rate of peri-operative AMI diagnoses and lack of prognostic information at low levels**

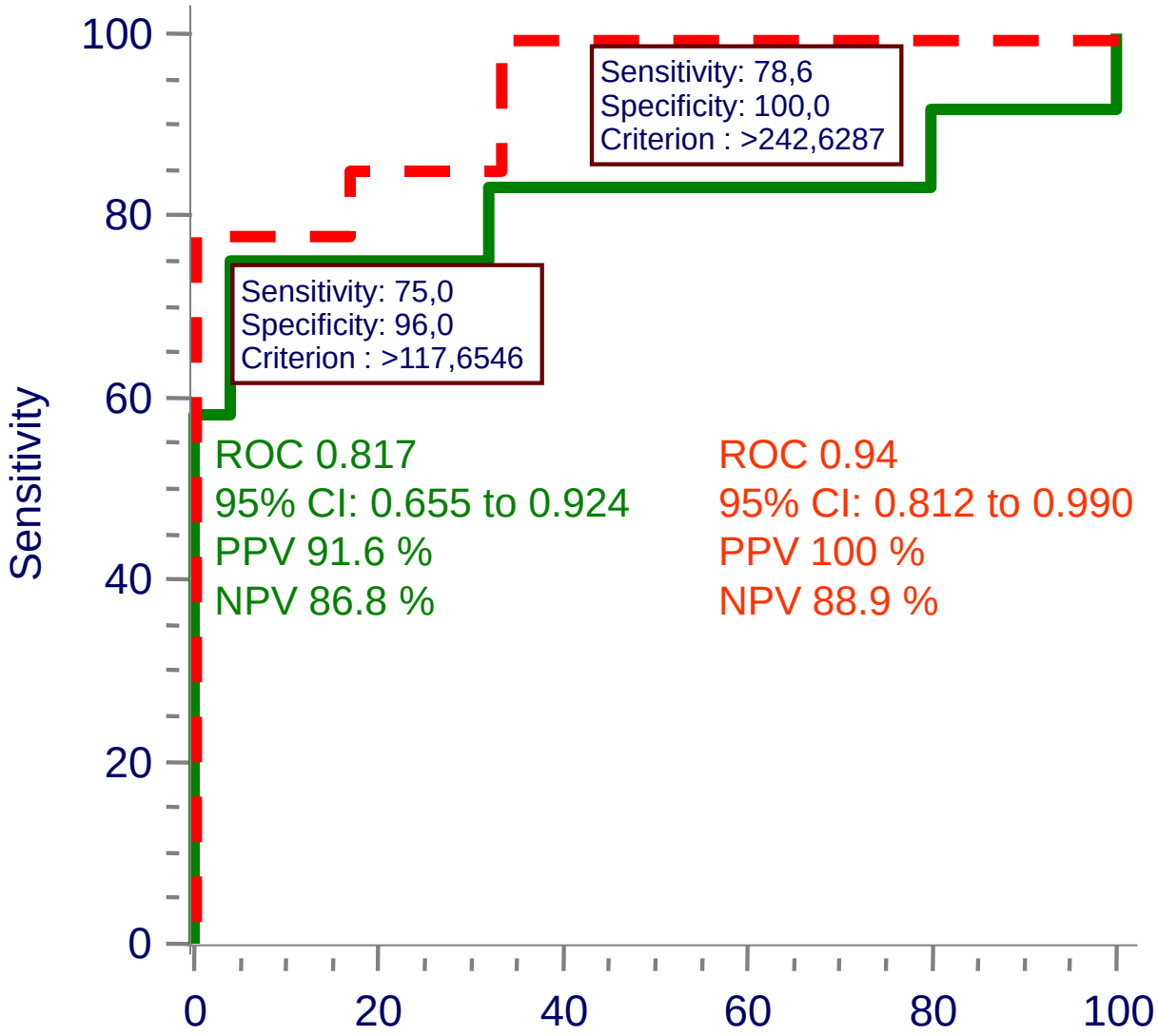
Troponin Release: Type of Surgery



Short- and long-term biological variation in hscTnT

Variable	Short-term (0-4 h)	Long-term (0-8 weeks)
Analytical variation		
$CV_{A, \%}$ *	53.5	98
Biological variation		
$CV_{I, \%}$	48.2	94
$CV_{G, \%}$	85.9	94
Index of Individuality	84.5	19.6
RCV, lognormal increase, %	84.6	315
Mean Delta Increase, %	58	103.4
Mean Delta Decrease, %	57.5	87

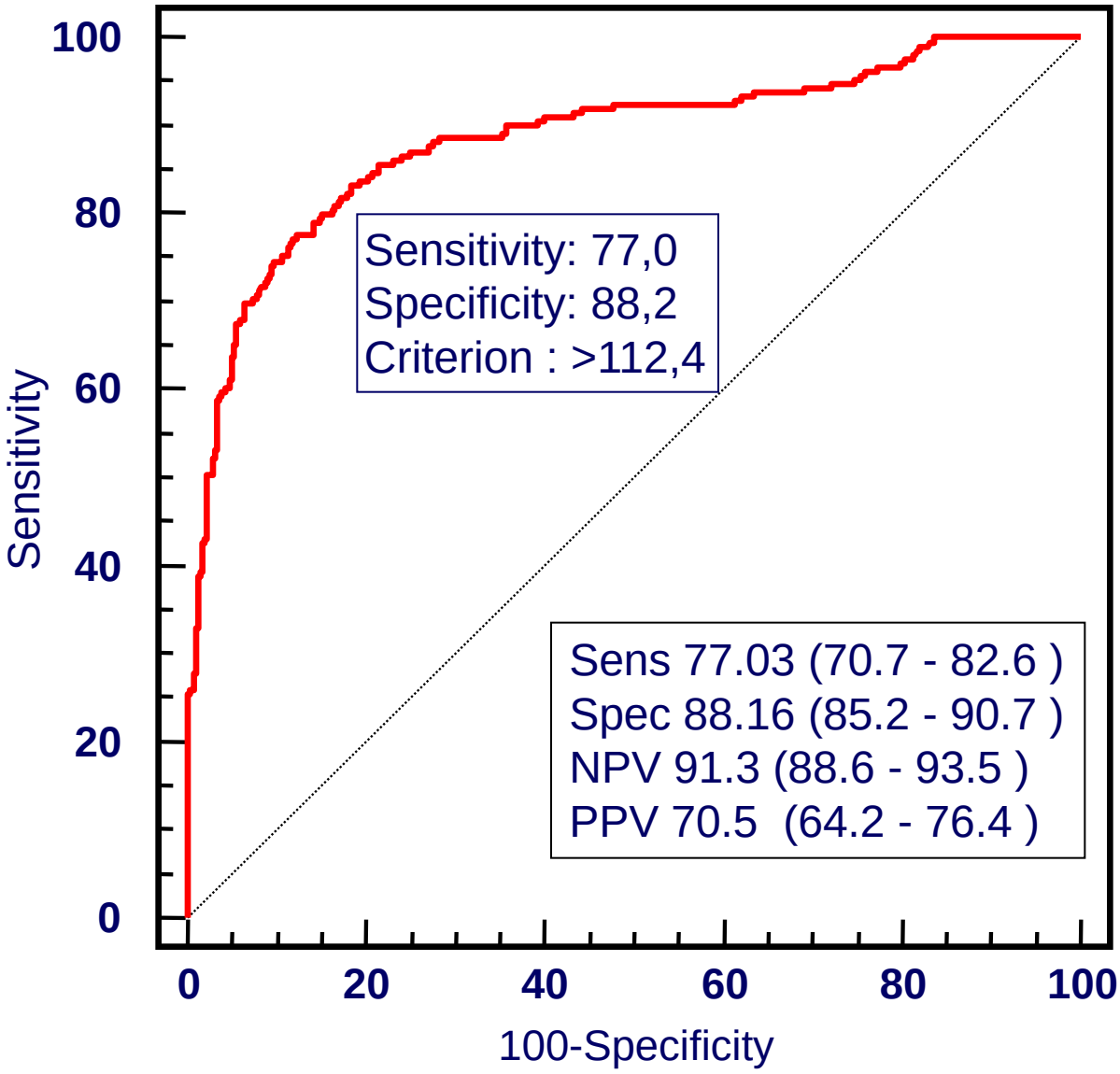
Optimal delta change for prediction of evolving NSTEMI*



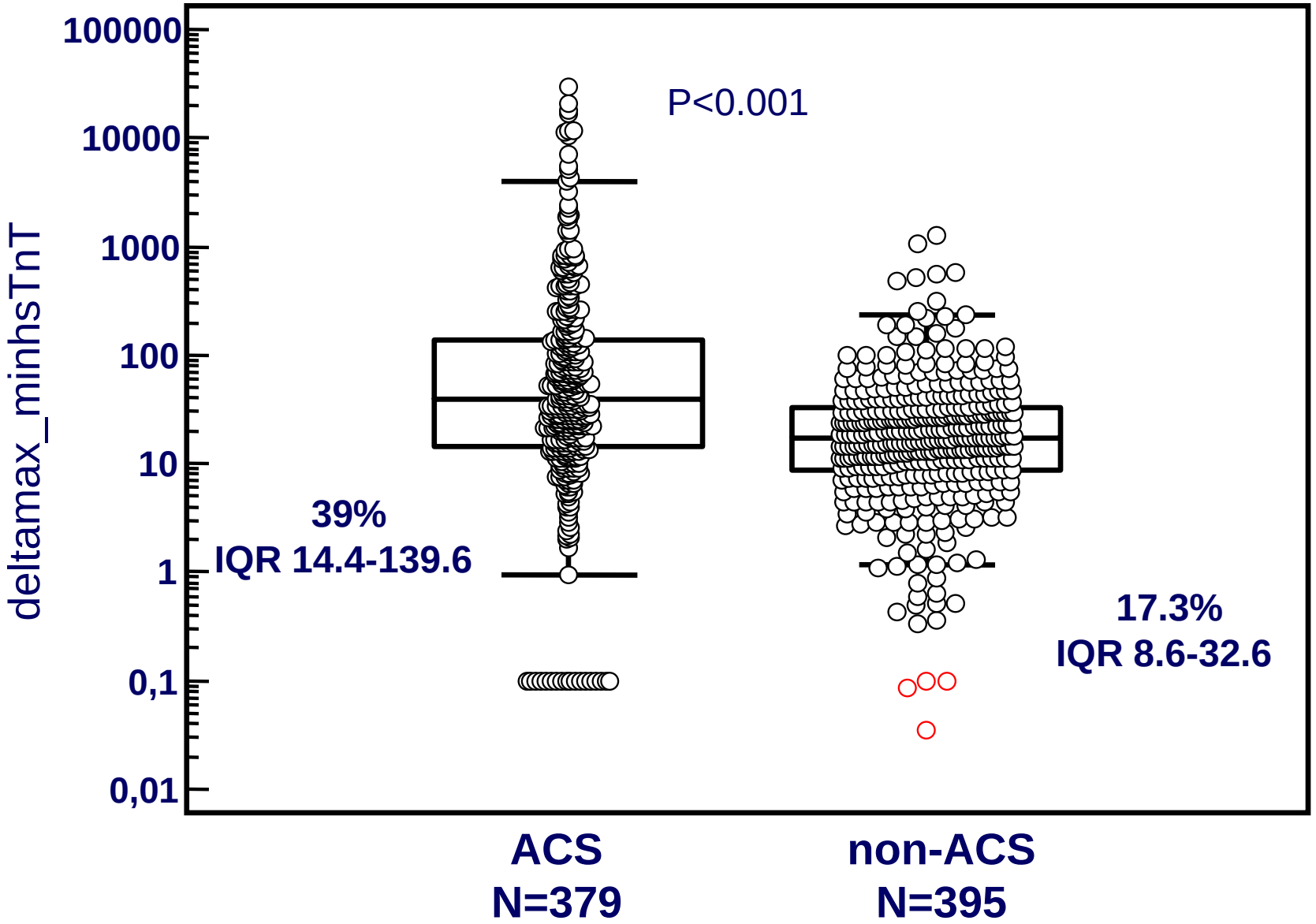
*MI defined by 4th gen. cTnT

Giannitsis et al. Clin Chem 2010

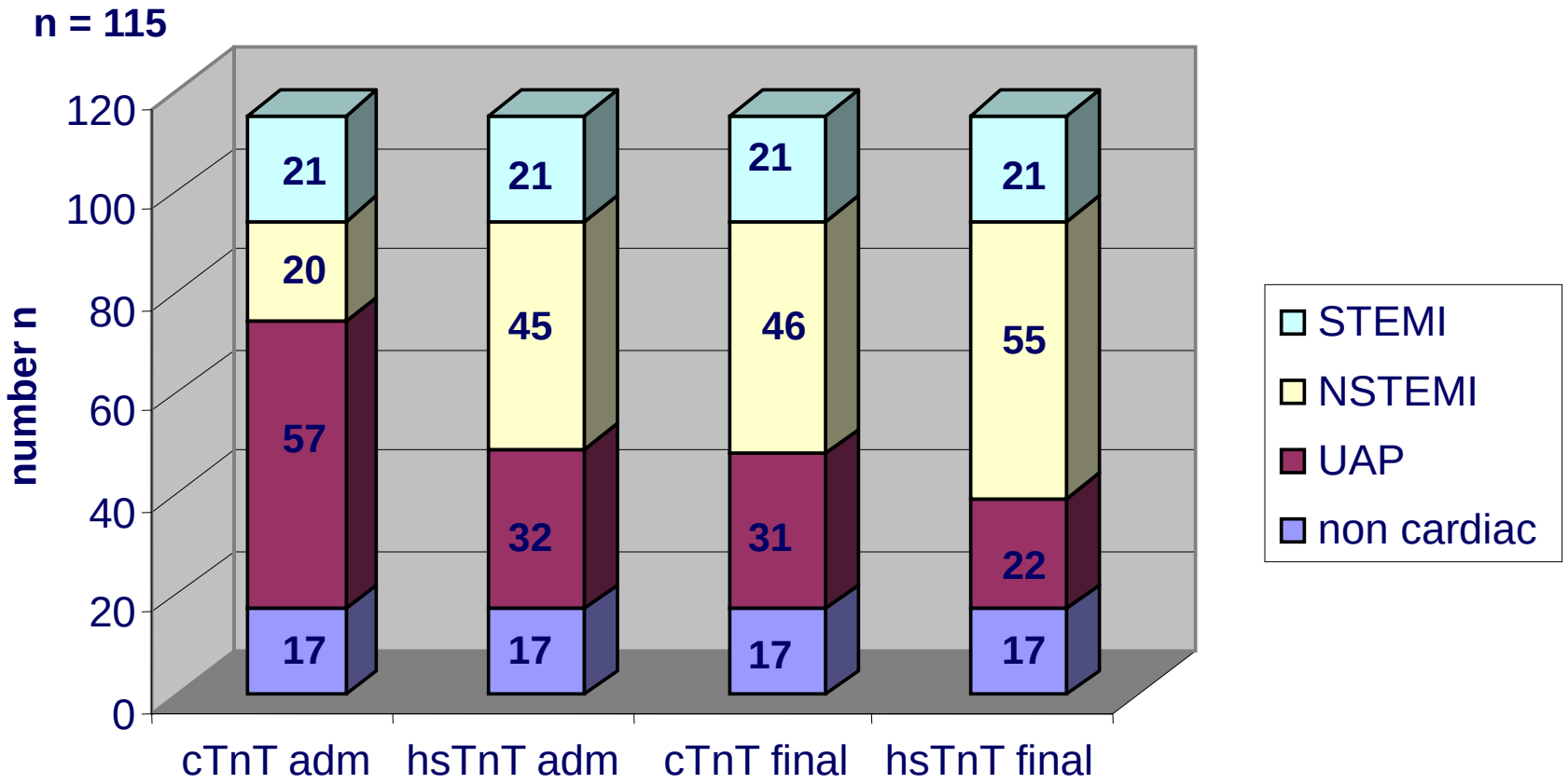
Maximal hsTnT within 6 hours for prediction of MI



Early delta change in ACS versus TnThs-positive non-ACS patients



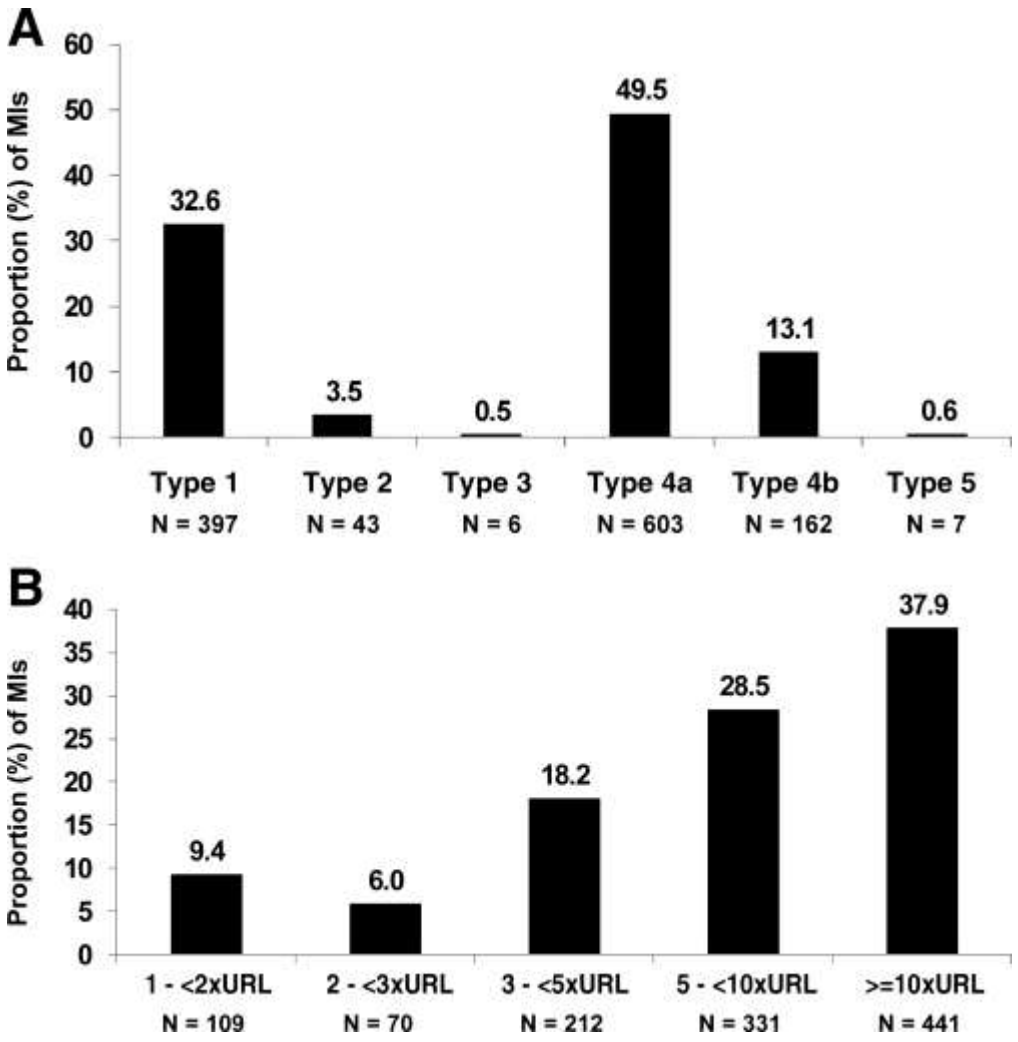
Diagnostic sensitivity of TnT hs compared to cTnT



p between cTnT adm and hsTnT adm (UAP/NSTEMI) < 0.0001
p between cTnT final and hsTnT final (UAP/NSTEMI) < 0.0001
p between cTnT adm and cTnT final (UAP/NSTEMI) = 0.0003
p between hsTnT adm and hsTnT final (UAP/NSTEMI) = 0.0008

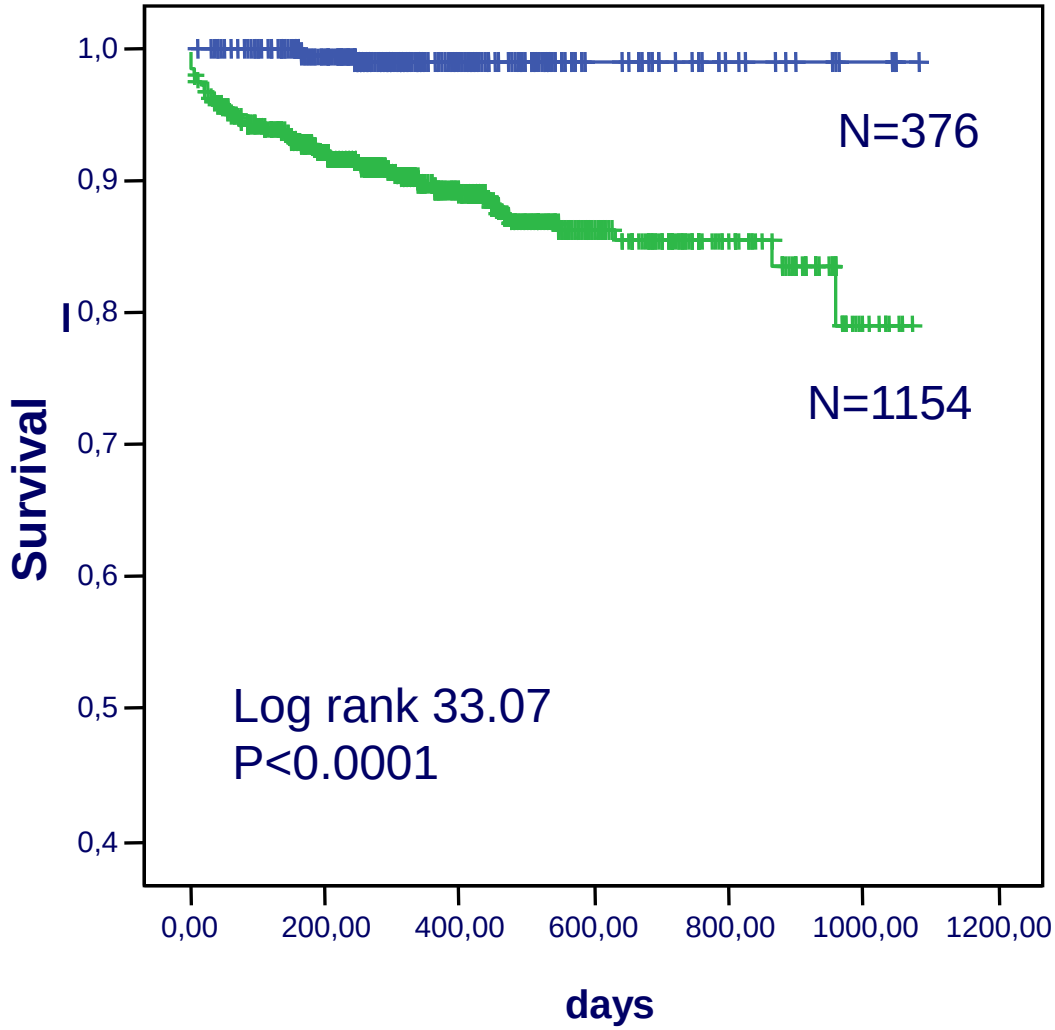

Dank Kontrastmittel
sah ich mein Herz und dessen Kranz
sah ich Kalk darin gelagert
sah die Arterie
Wunder tat - und sah

Distribution of new or recurrent MIs (n=1218) by the universal definition of MI clinical classification



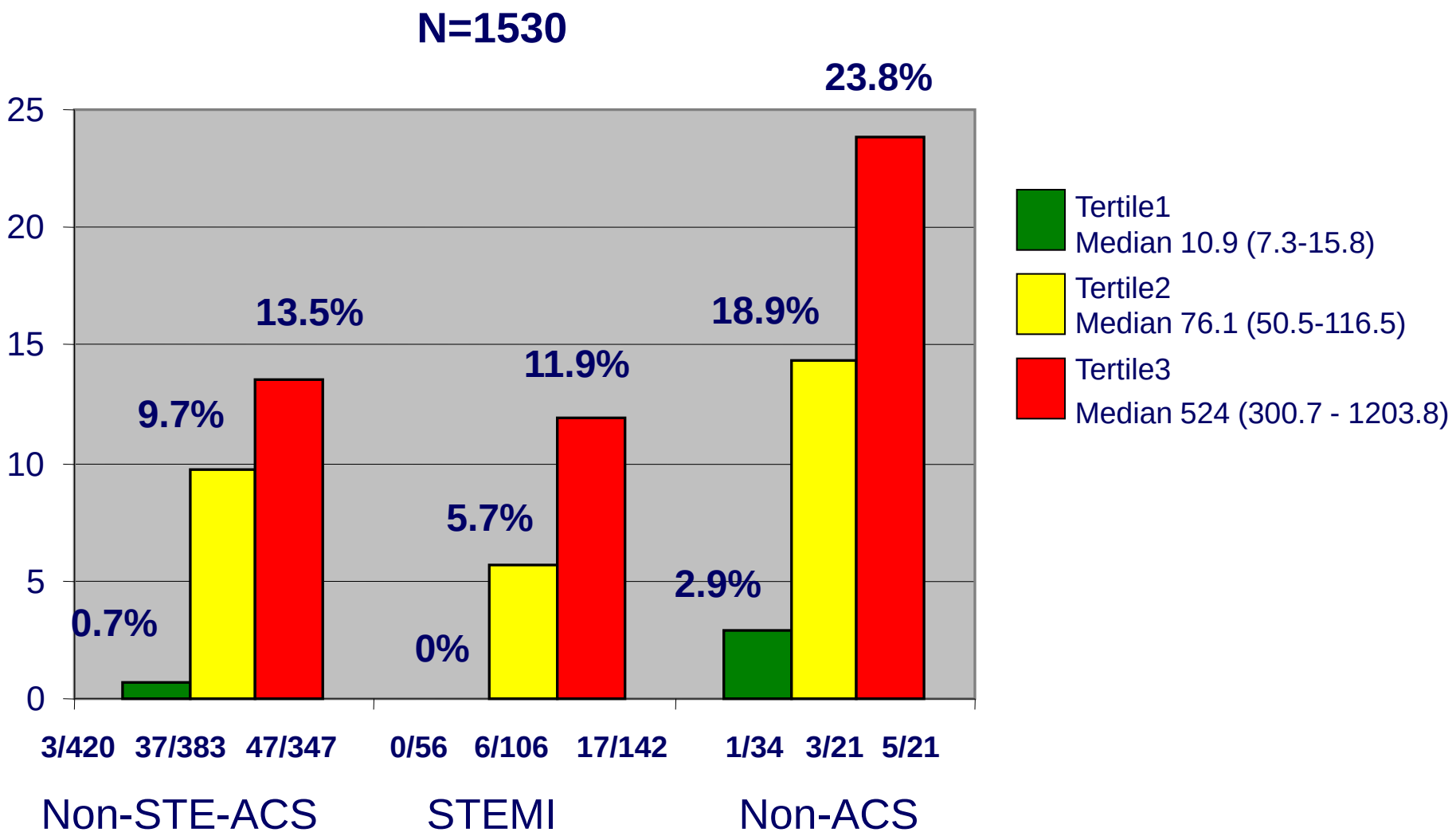
Morrow, D. A. et al.
Circulation 2009;119:2758-2764

All-cause Death by TnThs 99th percentile

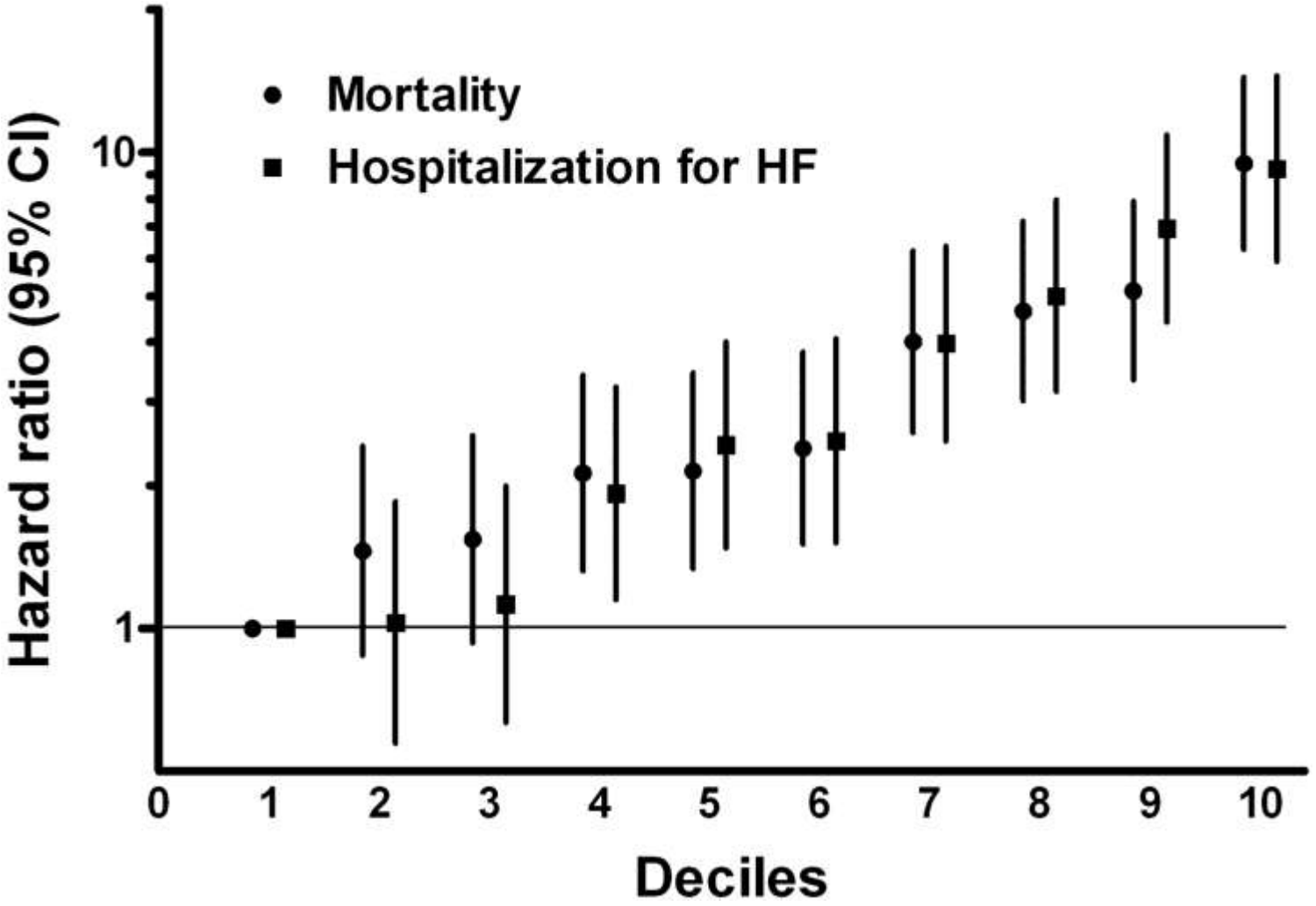


N=1530

All-cause mortality at 3yrs follow up cTnThs tertiles by diagnosis



HsTnT and Outcomes in Heart Failure: The Valheft-Trial



Latini R. et al. Circulation 2007;116

Case 4: A 78 year old female

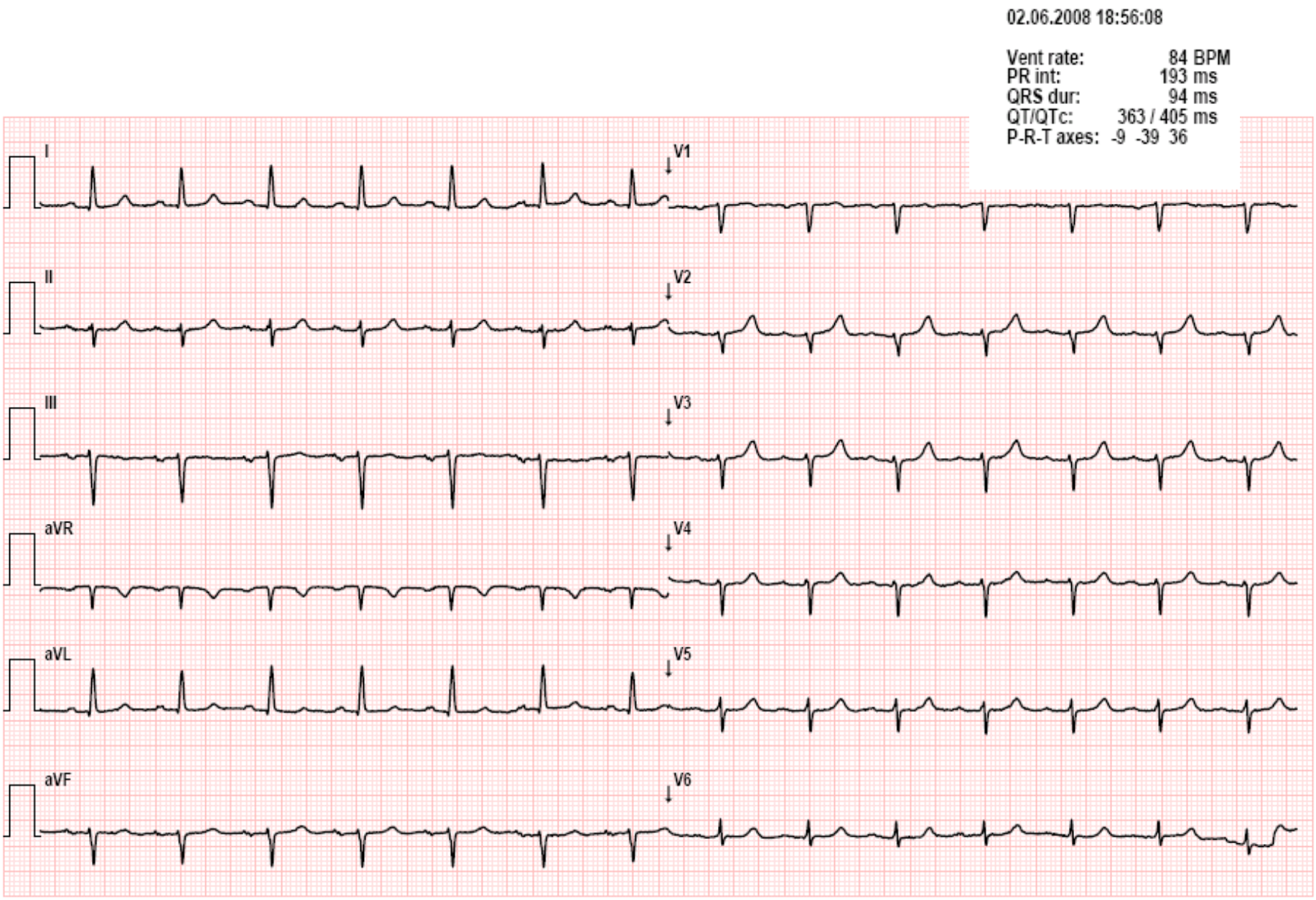
History:

- referred to our chest pain unit with dizziness, vomiting and nausea
- no typical cardiac chest pain
- discrete shortness of breath and decrease of performance
- known diseases: subtle renal failure (MDRD 50 ml/min/1.73m^2)
- CVRF: hypertension, hypercholesterolemia
- medication: ASS 100mg 0-1-0, candesartan 16mg 1-0-1, hydrochlorothiazid 12,5mg 1-0-1, nebivolol 5mg ½-0-½, pravastatin 20mg 0-0-1, estrogen 0,6mg 1-0-0

Physical examination:

- 67.0 kg, 1.70 cm, BMI 23 kg/m^2,
- RR adm 130/60mmHg, HR adm 80/min, 36.1 °C
- Auscultation: Cor/Pulmo: unsuspicious

Case 4: EKG

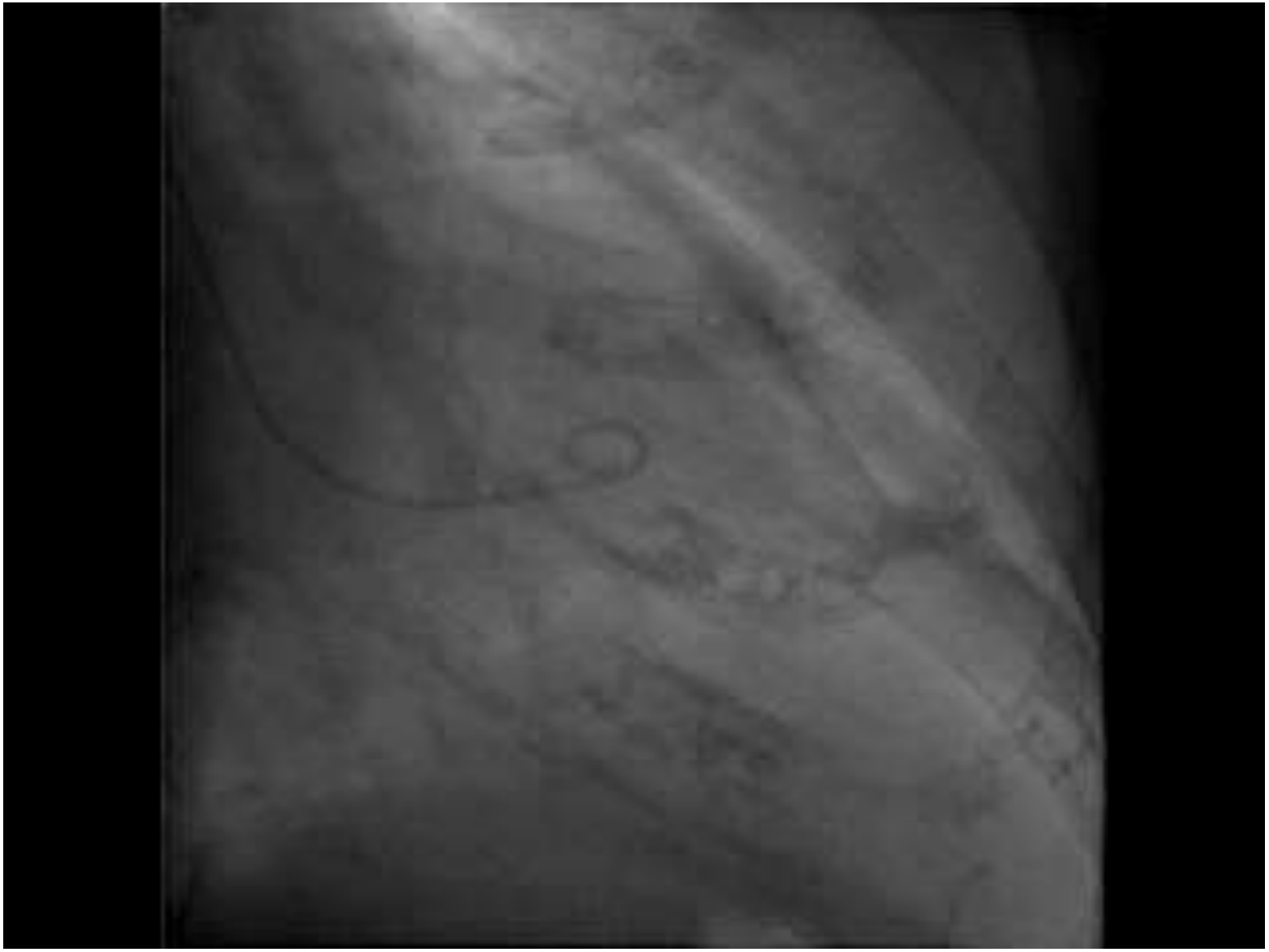

02.06.2008 18:56:08
Vent rate: 84 BPM
PR int: 193 ms
QRS dur: 94 ms
QT/QTc: 363 / 405 ms
P-R-T axes: -9 -39 36
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6

Case 4: Laboratory Results

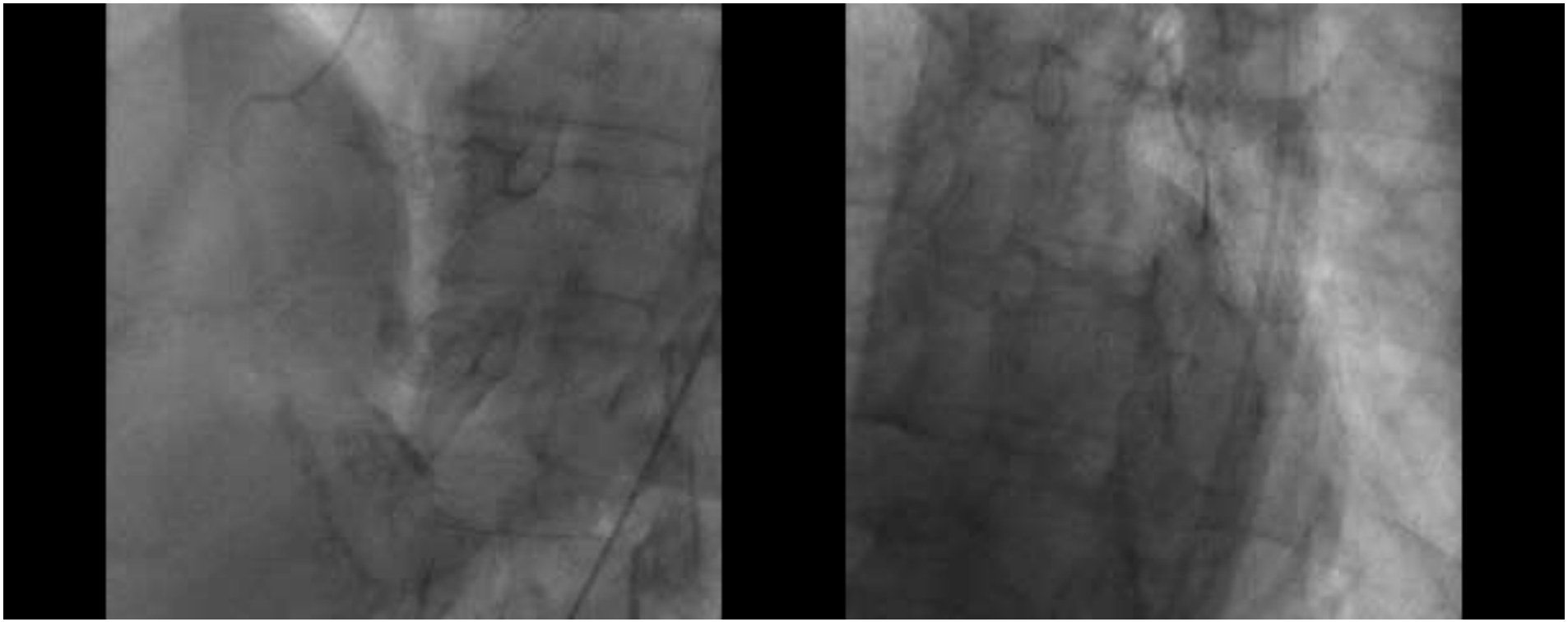
	admission		after 24h		(norm)
• creatinine	1.75		1.44		(1.1-1.3) mg/dl
• urea	100		80		(-45) mg/dl
• glucose	158		111		(70-110) mg/dl
• Hb	11.0		10.2		(12-15) g/dl
• platelets	233		231		(150-440) /nl
• white blood cells	9.34		7.82		(4-10) /nl
• C-reactive protein	9.9		8.7		(-5) mg/dl
• cTnT	0.02	0.04	0.02		(-0,03) µg/l
• hsTnT	40	60	50	30	(-14) pg/ml
• CK	44		70		(-170) U/l
• NTproBNP	na				(-450) ng/l

• normal values for sodium, potassium, GOT, GPT, LDH

Case 4: Left Ventricular Angiography



Case 4: Coronary Angiography



Postoperative cTnT results as a function of outcome after CABG