Troponins in Acute Myocardial Infarction: Beyond the Diagnosis

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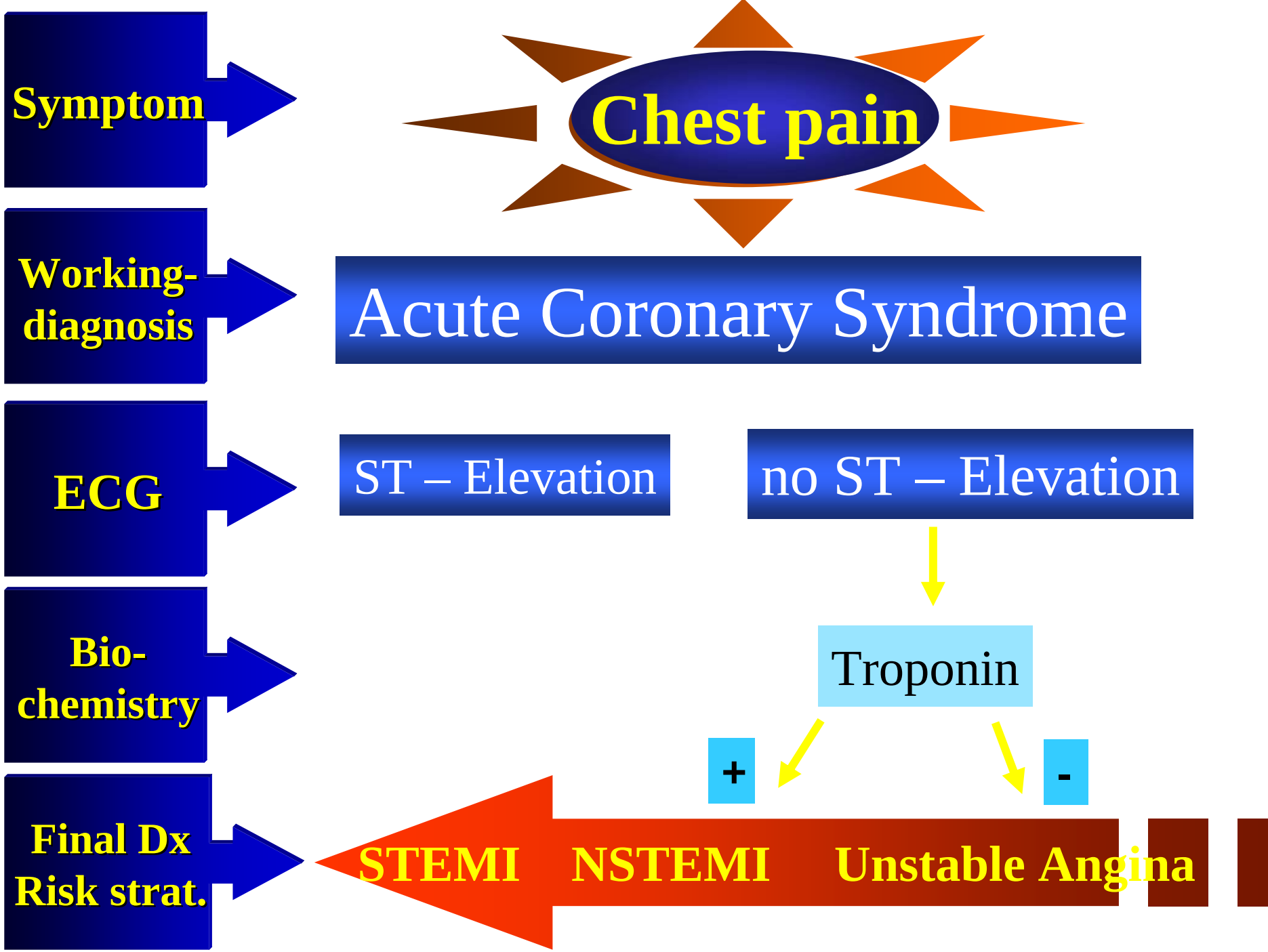
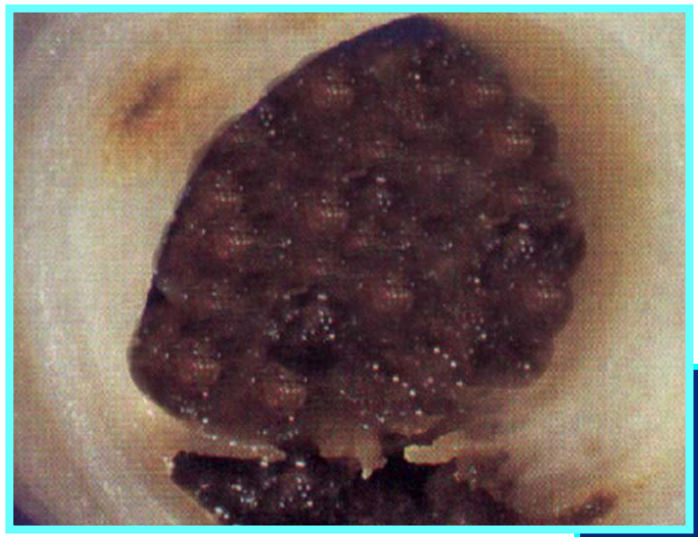
Kardiologie, Angiologie, Pulmologie

Universitätsklinikum Heidelberg

Heidelberg

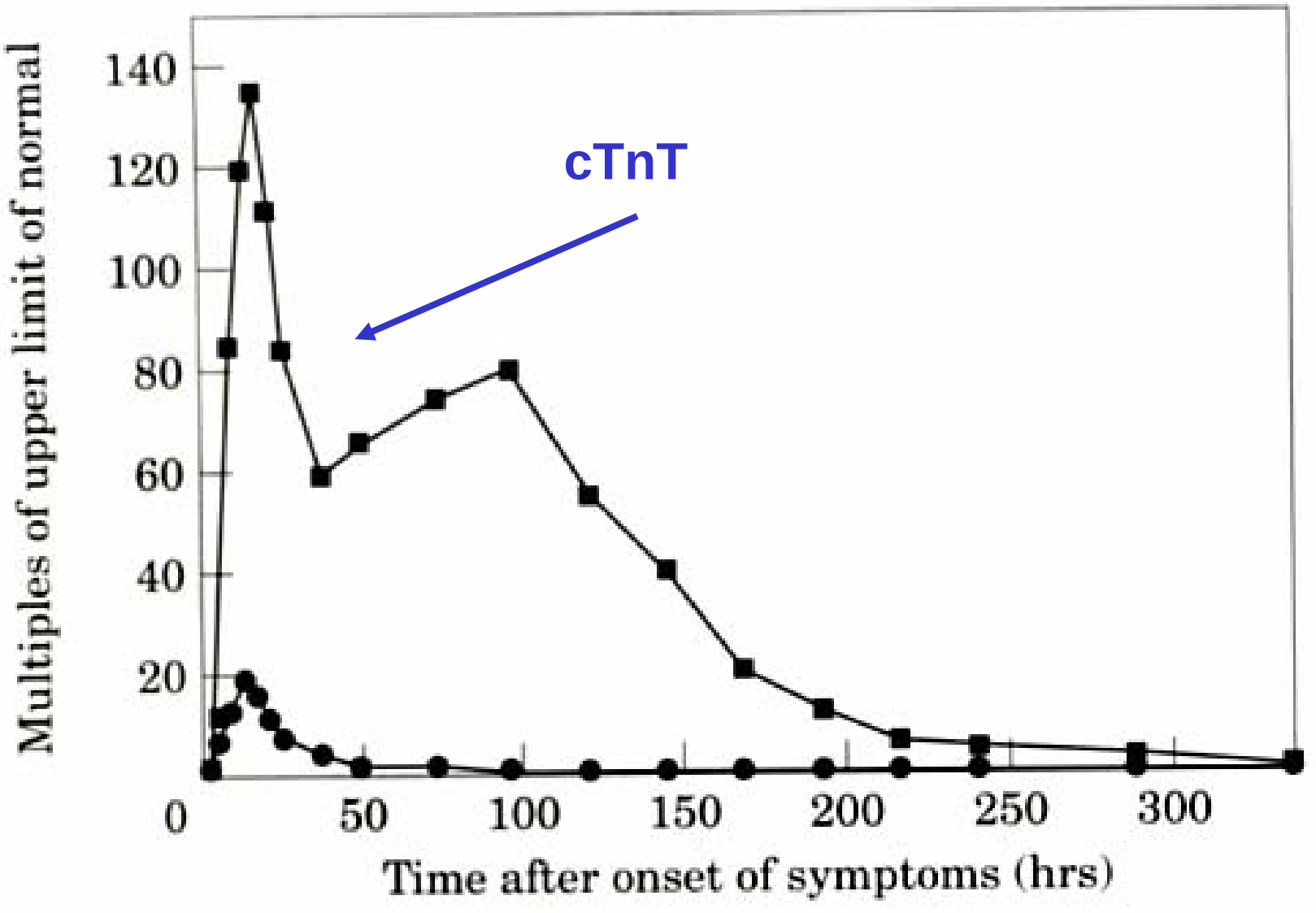

Symptom
Chest pain
Working-diagnosis
Acute Coronary Syndrome
ECG
ST – Elevation
no ST – Elevation
Bio-chemistry
Troponin
+
-
Final Dx Risk strat.
STEMI
NSTEMI
Unstable Angina

ST-segment elevation AMI



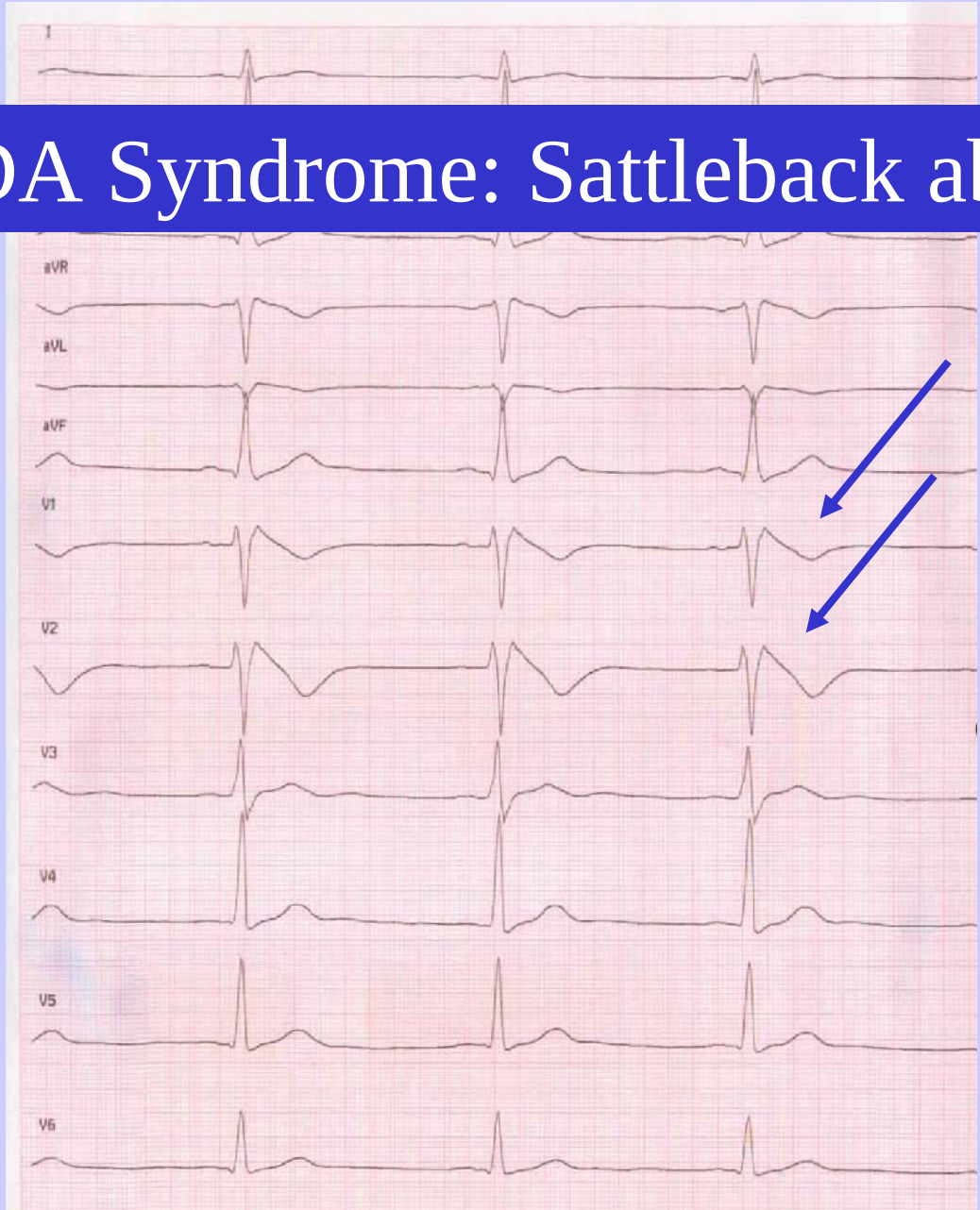
Diagnosis is straithforward in 90 % of cases

Retrospective Confirmation



Confounders and Non-interpretable ECG

BRUGADA Syndrome: Sattleback abnormality



Beyond the Diagnosis

Less well established indications for troponin testing in STEMI:

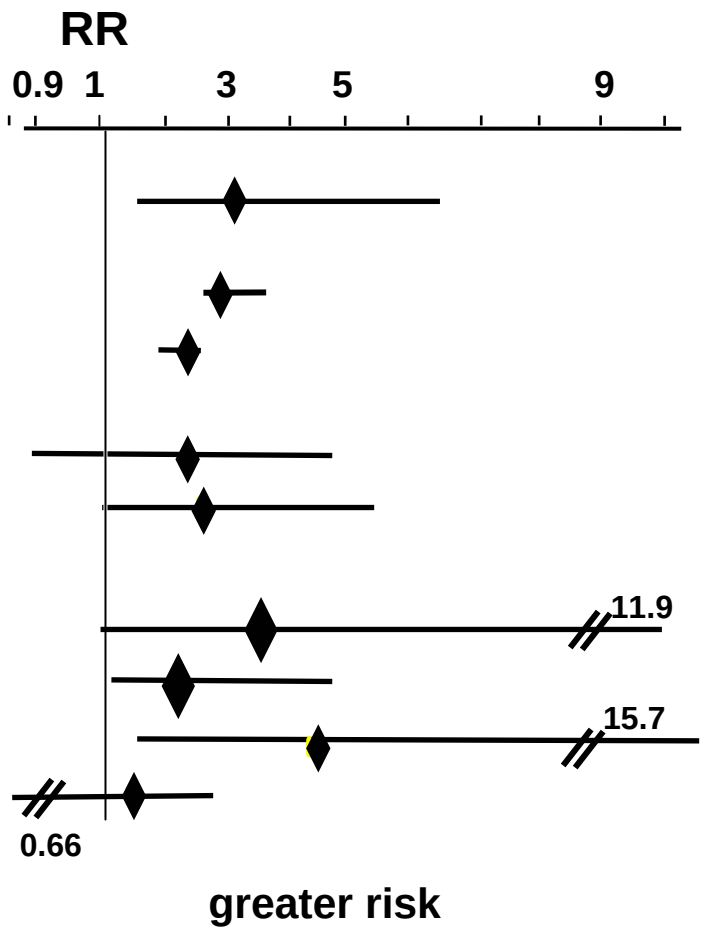
- Risk stratification
  - Troponin on admission
  - other timepoints

- Assessment of Reperfusion

  - After Thrombolysis
  - After Primary PCI

- Assessment of Infarct Size

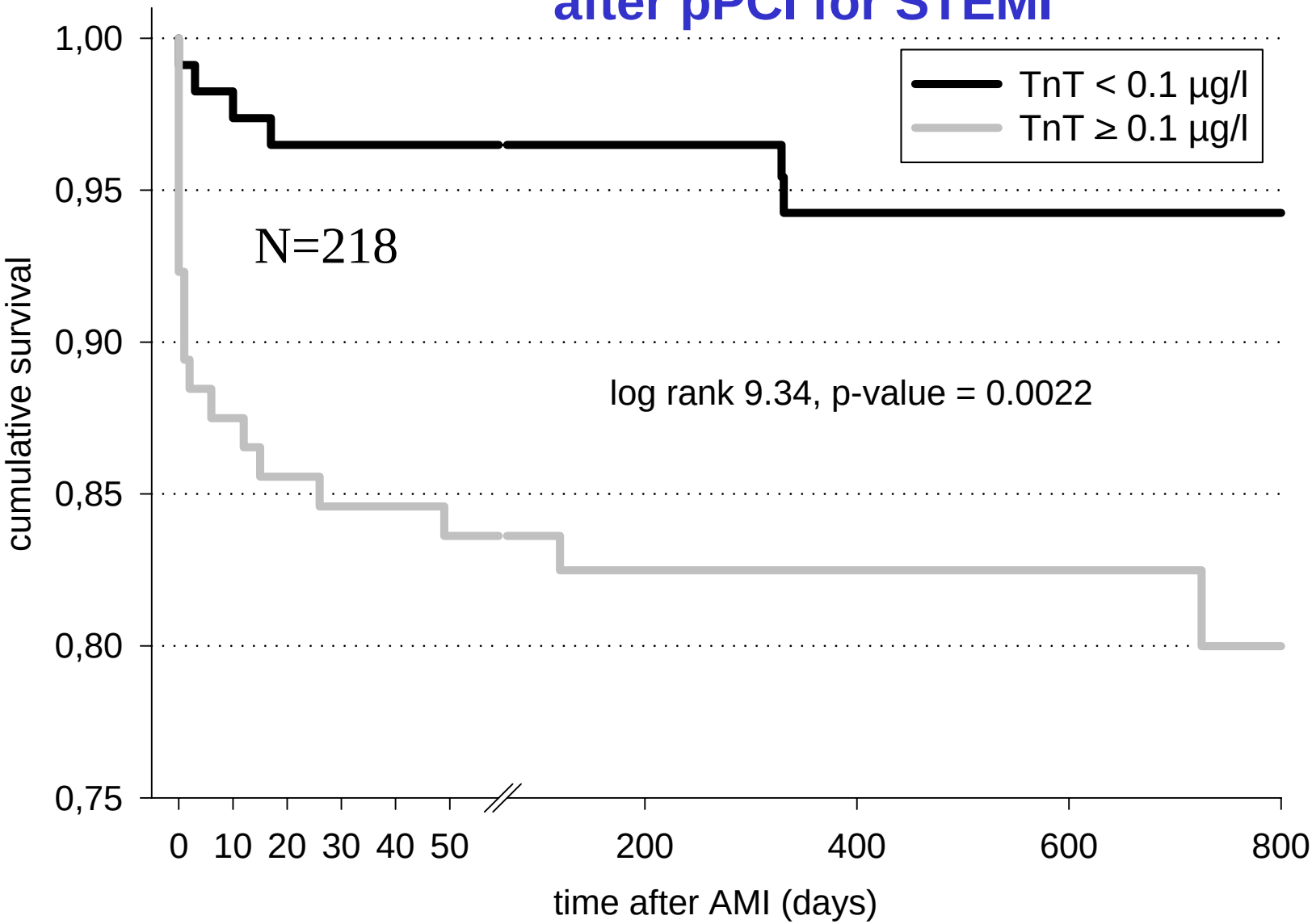
cTnT on Admission and Prognosis in STEMI



Trial	Endpoint	cTn pos	cTn neg
GUSTO II-A	Death	13 %	4.7 %
GUSTO III	Death	15.7 %	6.2 %
Trop-T-Substudy	Death/AMI	18.8 %	9.3 %
Stubbs	Death	35.5 %	21.2 %
	Death/AMI	41.9 %	23.1 %
Matetzky	Death	11 %	0 %
	Death/AMI	19 %	5.4 %
	Death/AMI/TVR	32 %	14 %
Giannitsis	Death	17.2 %	4.5 %
	Death/AMI/TVR	30.1 %	24.2 %

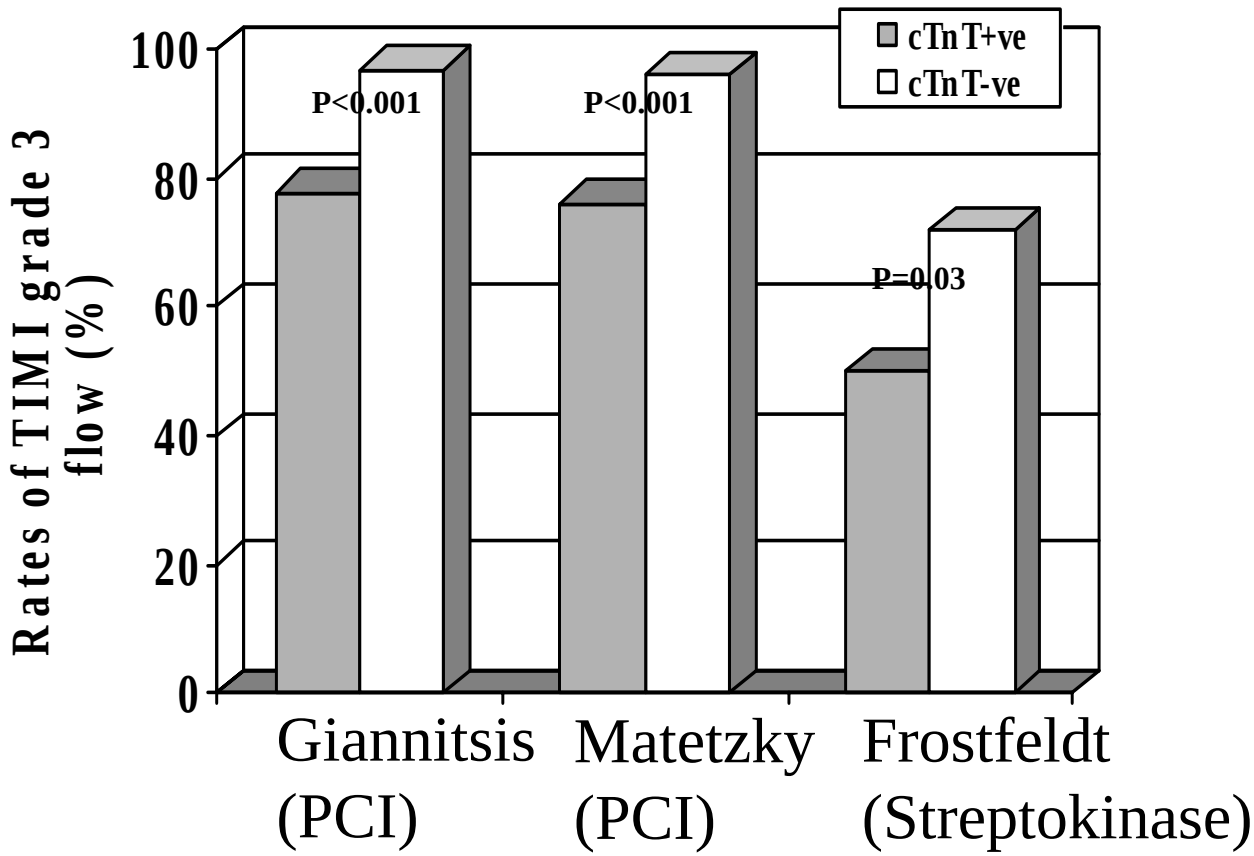
Lehrke S, et al. 2002

Impact of Admission cTnT despite TIMI 3 flow after pPCI for STEMI



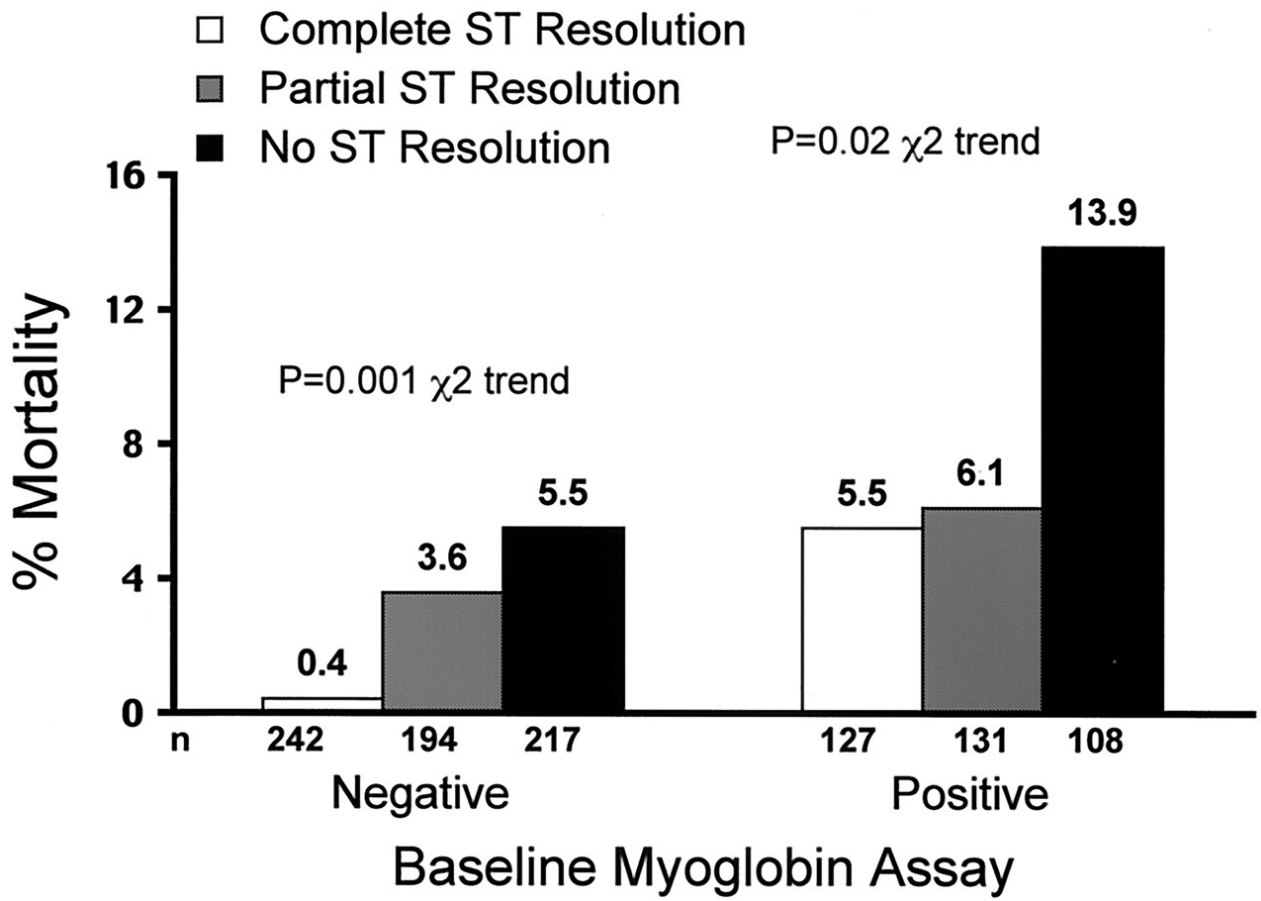
Kurowski V et al.
Crit Care Med 2003

cTnT on Admission and Prognosis in STEMI



Lehrke S, et al. 2002

Baseline Myoglobin for Prediction of Prognosis



Giugliano RP, et al.
Am Heart J 2000

Beyond the Diagnosis

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  - other timepoints
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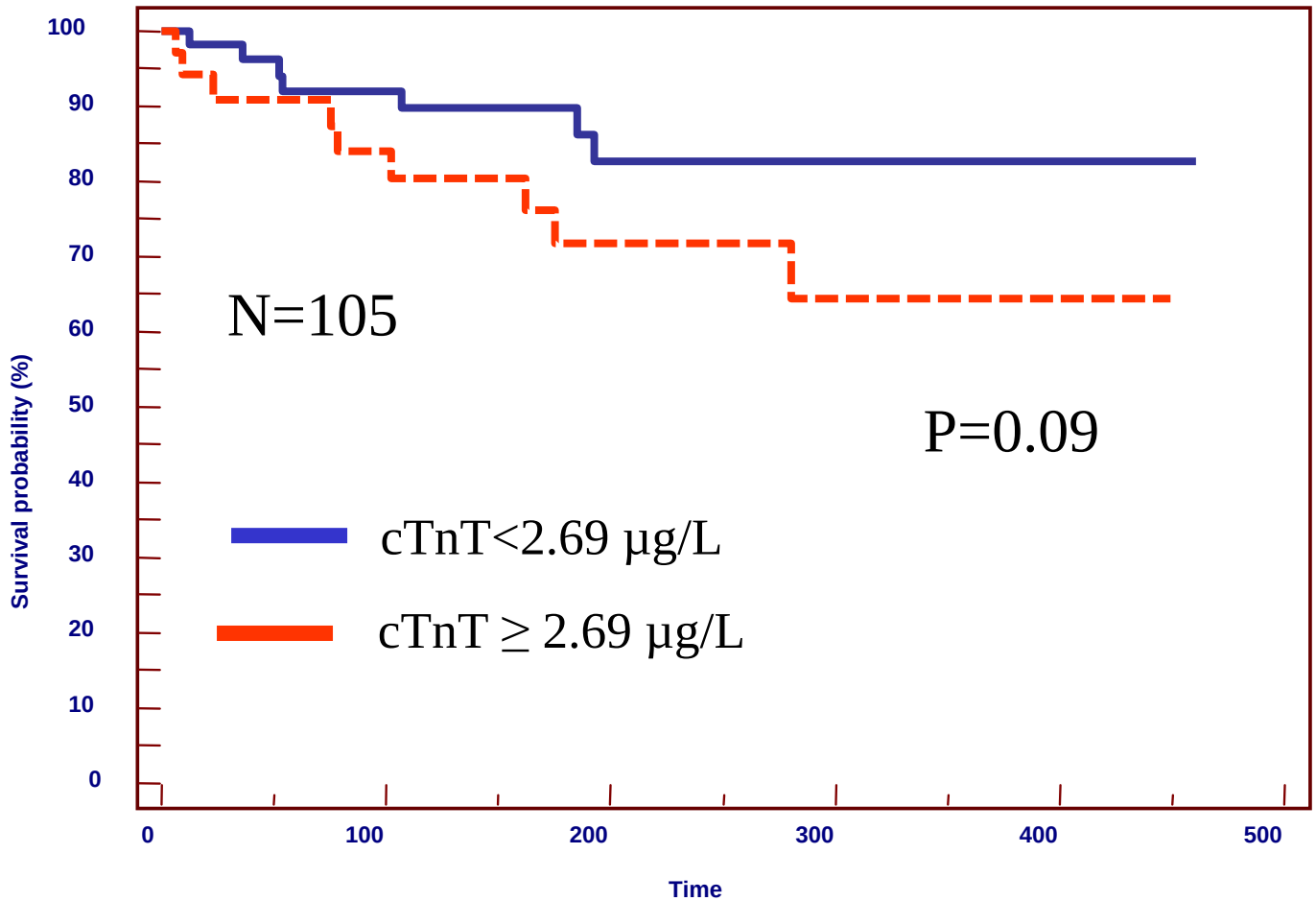
  - After Primary PCI
- Assessment of Infarct Size

Prognostic Role of cTnT on Day 4 in STEMI

Composite Endpoint: Death, MI, TVR



Beyond the Diagnosis

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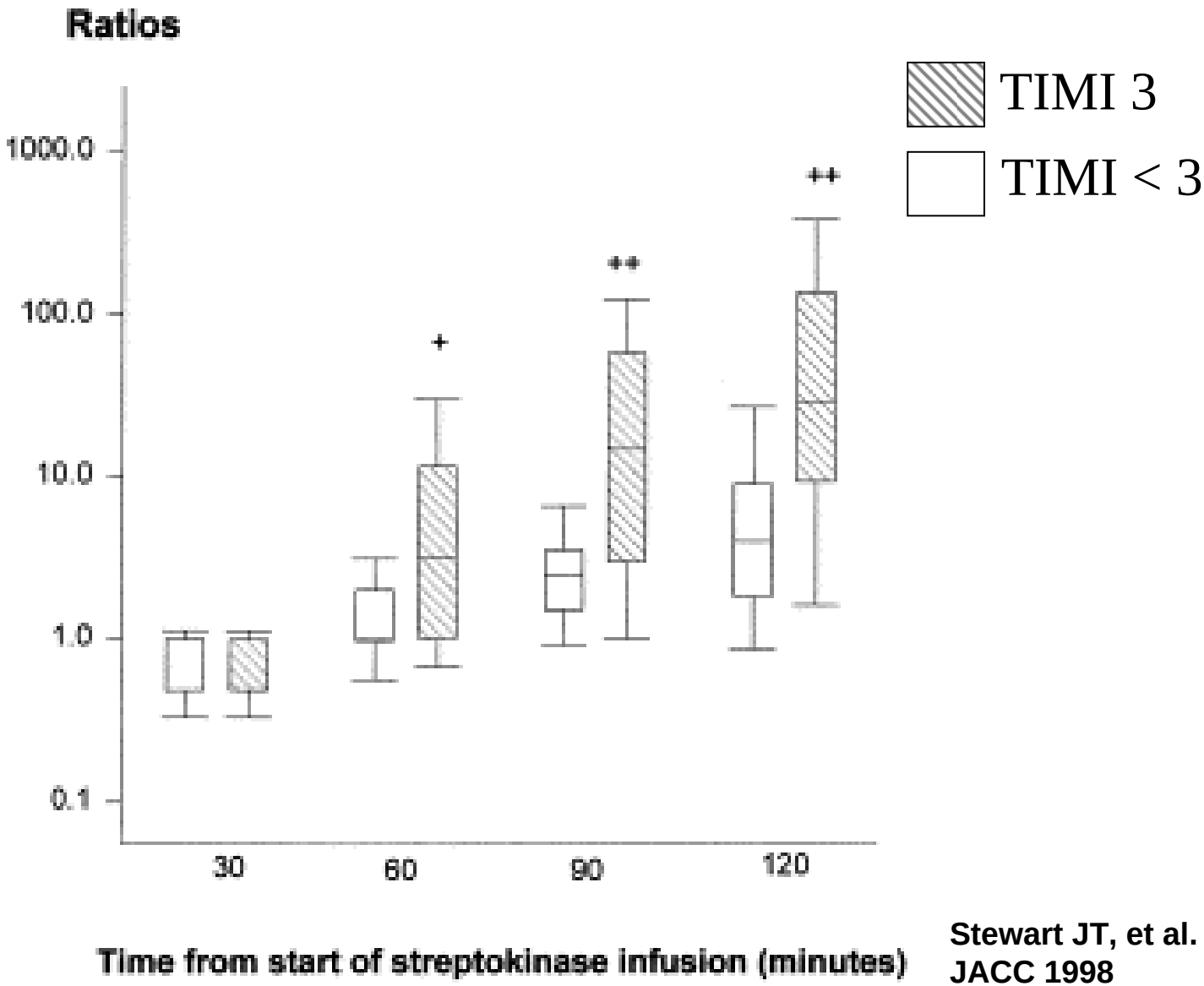
cTnT Ratio after Streptokinase



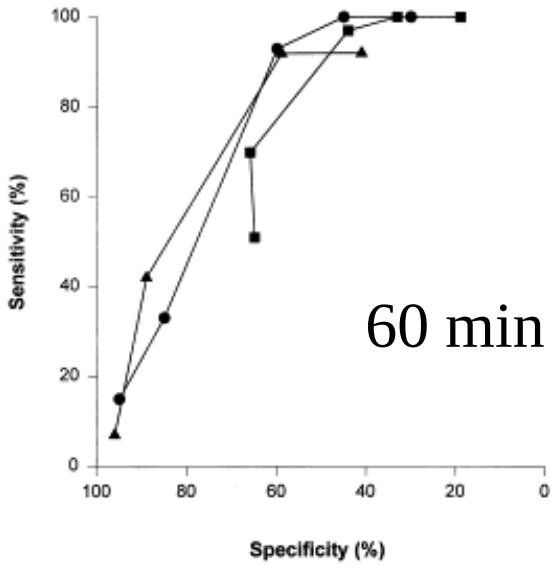
Stewart JT, et al.
JACC 1998

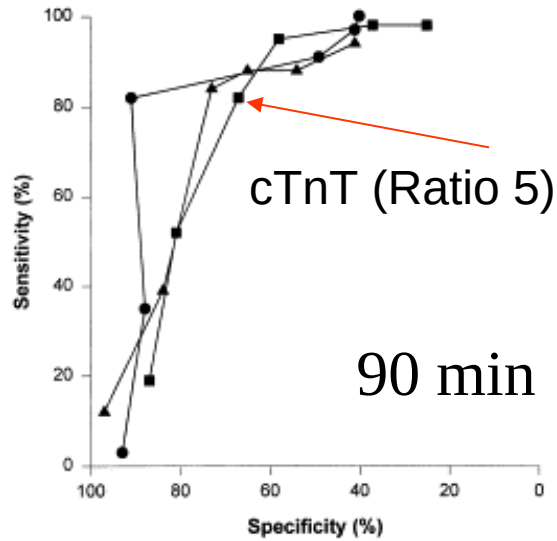
Sensitivity and Specificity of Marker Ratios for Detection of TIMI 0-2 Flow

Predictors of Reperfusion Failure

Factor	RR	P-value
ST recovery < 70 %	4.15 (1.43.12.06)	0.009
Baseline CK-MB >4µg/L	3.11 (1.06-9.08)	0.039
Baseline myo > 85 µg/L	2.77 (1.01-7.58)	0.048
Troponin T ratio $\leq$ 5	16.49 (3.5-77.73)	<0.001

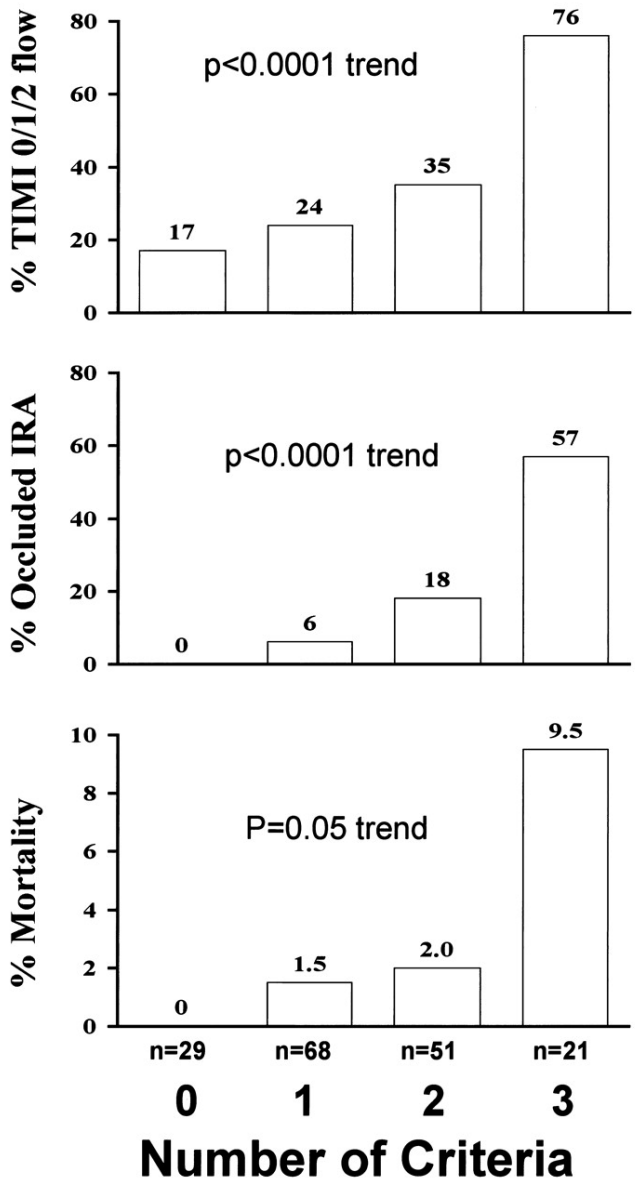
French JK, et al.
Am Heart J 2003





Stewart JT, et al.
JACC 1998

Combination of ST-resolution with other Predictors of Failed Reperfusion

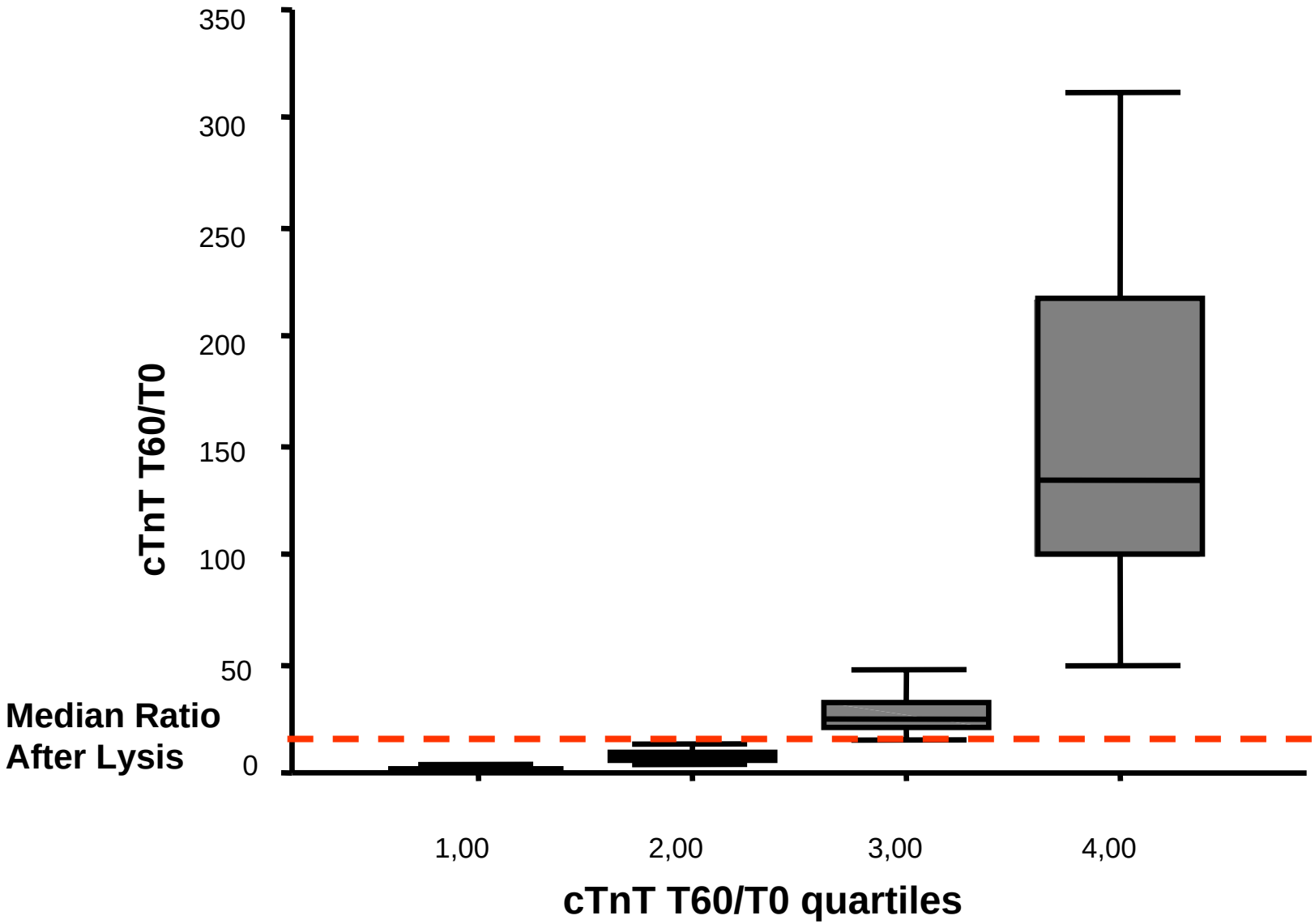


Criteria:

1. ST resolution <50 % at 90 min
2. 60 min/baseline ratio of serum myoglobin < 4
3. Persistent chest pain at angiography

De Lemos, et al.
Am J Cardiol 2001

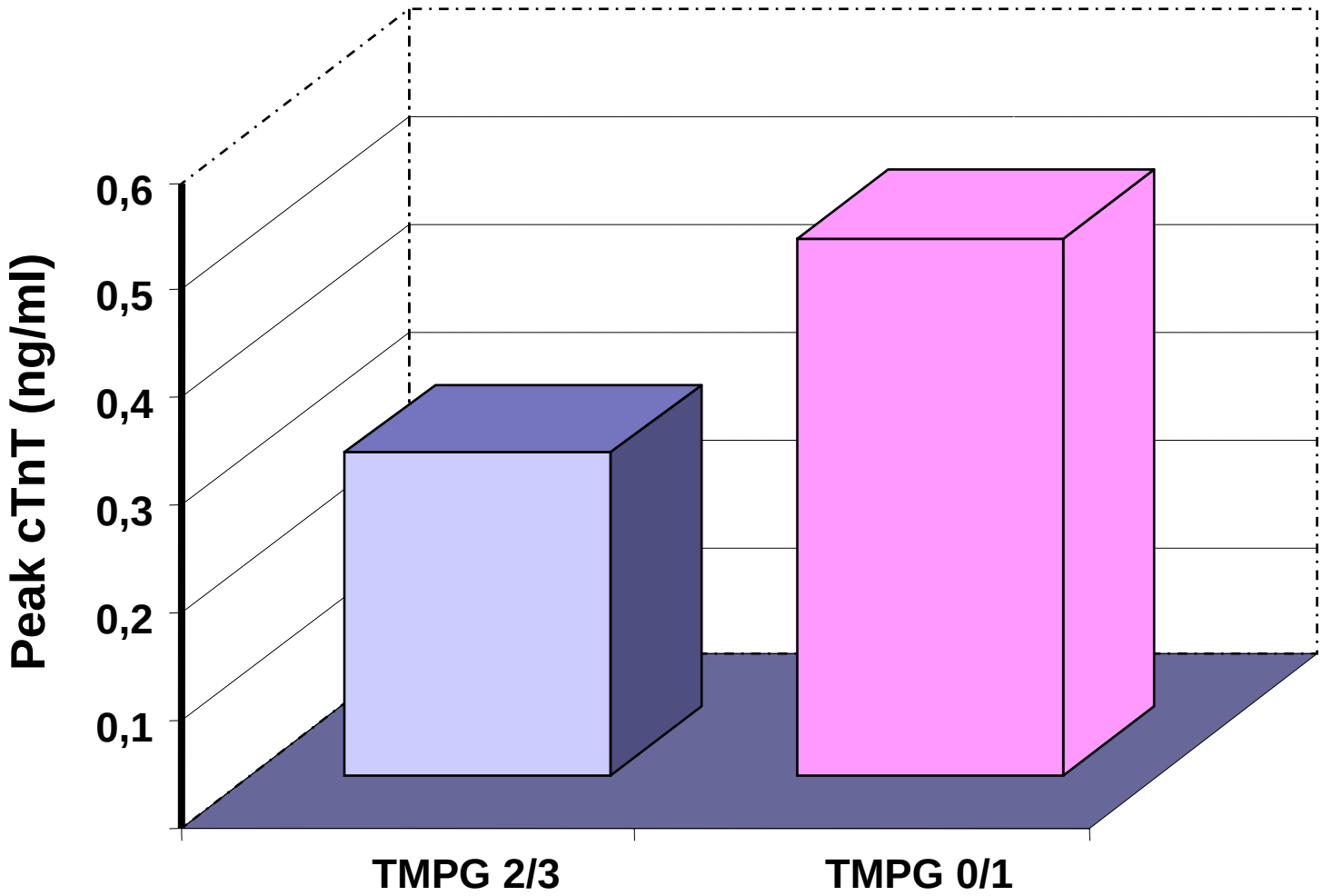
Cardiac Troponin T: Wash-out After pPCI



MRT
-Microvascular obstruction-

Peak-cTnT stratified by TMPG Status

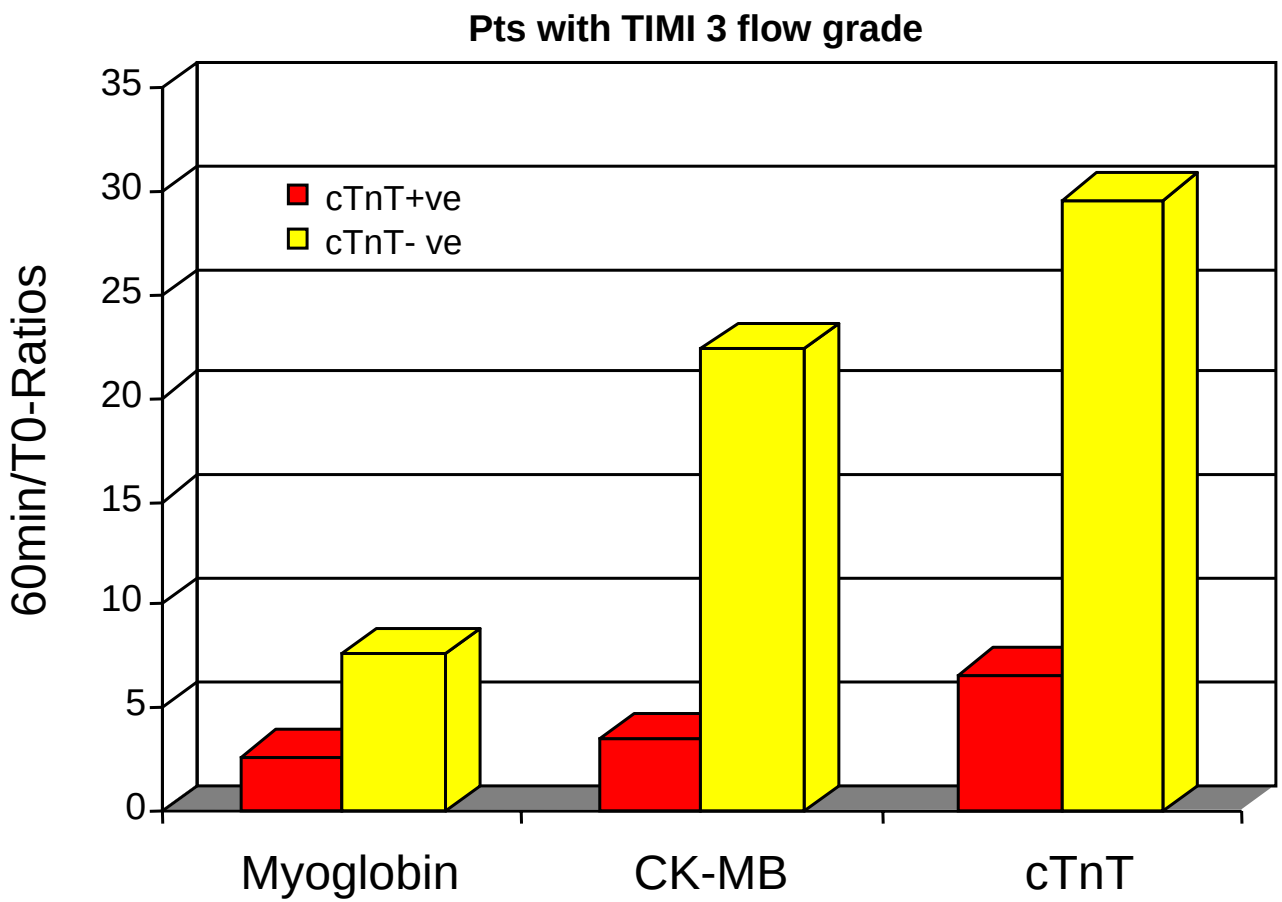
TACTICS-TIMI-18 Substudy: 310 pts with NSTE-ACS



Wong GC et al, Circulation 2002

Clinical Significance of Troponin T Status on Admission

Microvascular Flow

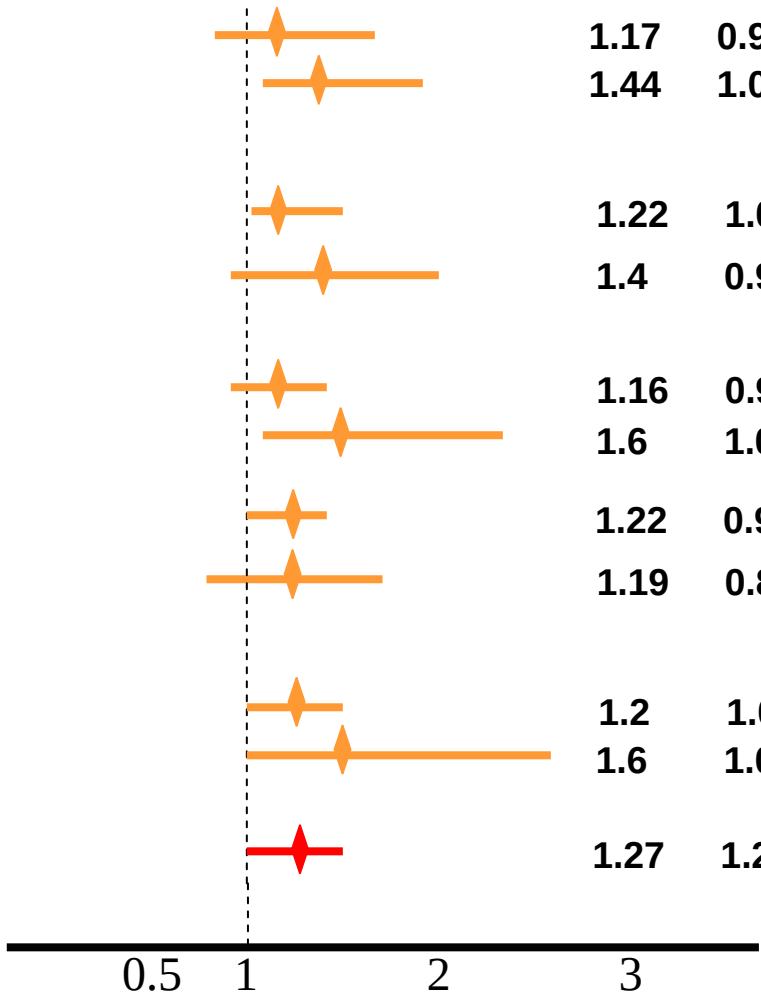


n=118

Giannitsis, Circulation 2001

Effects of Reopro on Microvascular Flow After Primary PCI

	No. of pts	%		Standard better / abciximab better	OR	95 % CI
cTnT neg	88	88.6	75.5		1.17	0.9-1.4
cTnT pos	57	86.4	60		1.44	1.05-1.98
DM neg	112	85.7	70		1.22	1.01-1.49
DM pos	33	93.3	66.7		1.4	0.98-1.99
Age < 70	110	84.1	72.7		1.16	0.95-1.4
Age > 70	35	92.3	59.1		1.6	1.07-2.3
Male	108	84.1	68.8		1.22	0.99-1.51
Female	37	86.6	70.8		1.19	0.8-1.7
Latency < 6h	118	86.9	72.2		1.2	1.0-1.44
Latency > 6h	27	90.9	56.3		1.6	1.01-2.6
All patients	145	145	145		1.27	1.27



Lowest vs. upper 3 quartiles of cTnT ratios

Lehrke S, et al.
Haemost Thromb 2004

Beyond the Diagnosis

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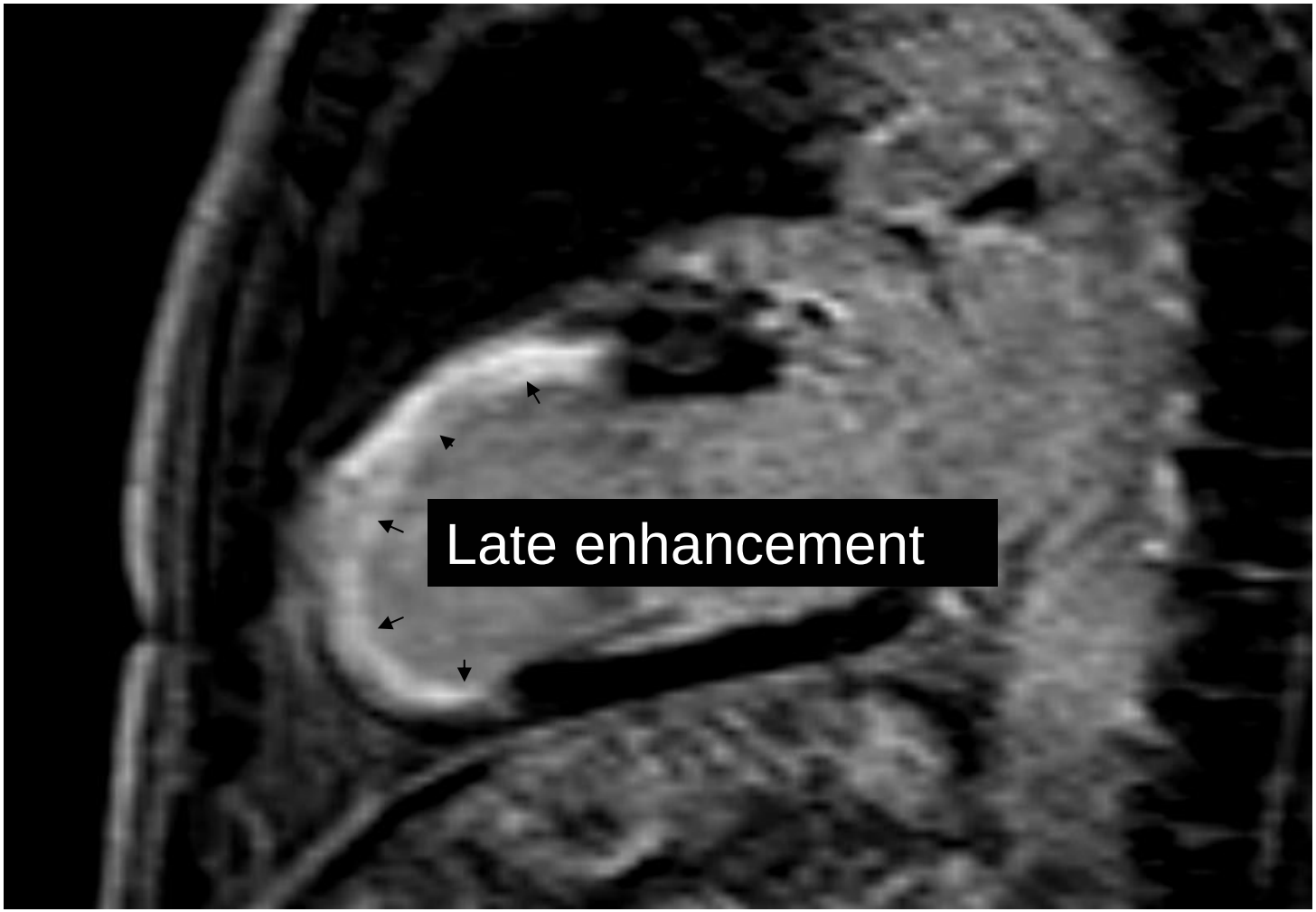
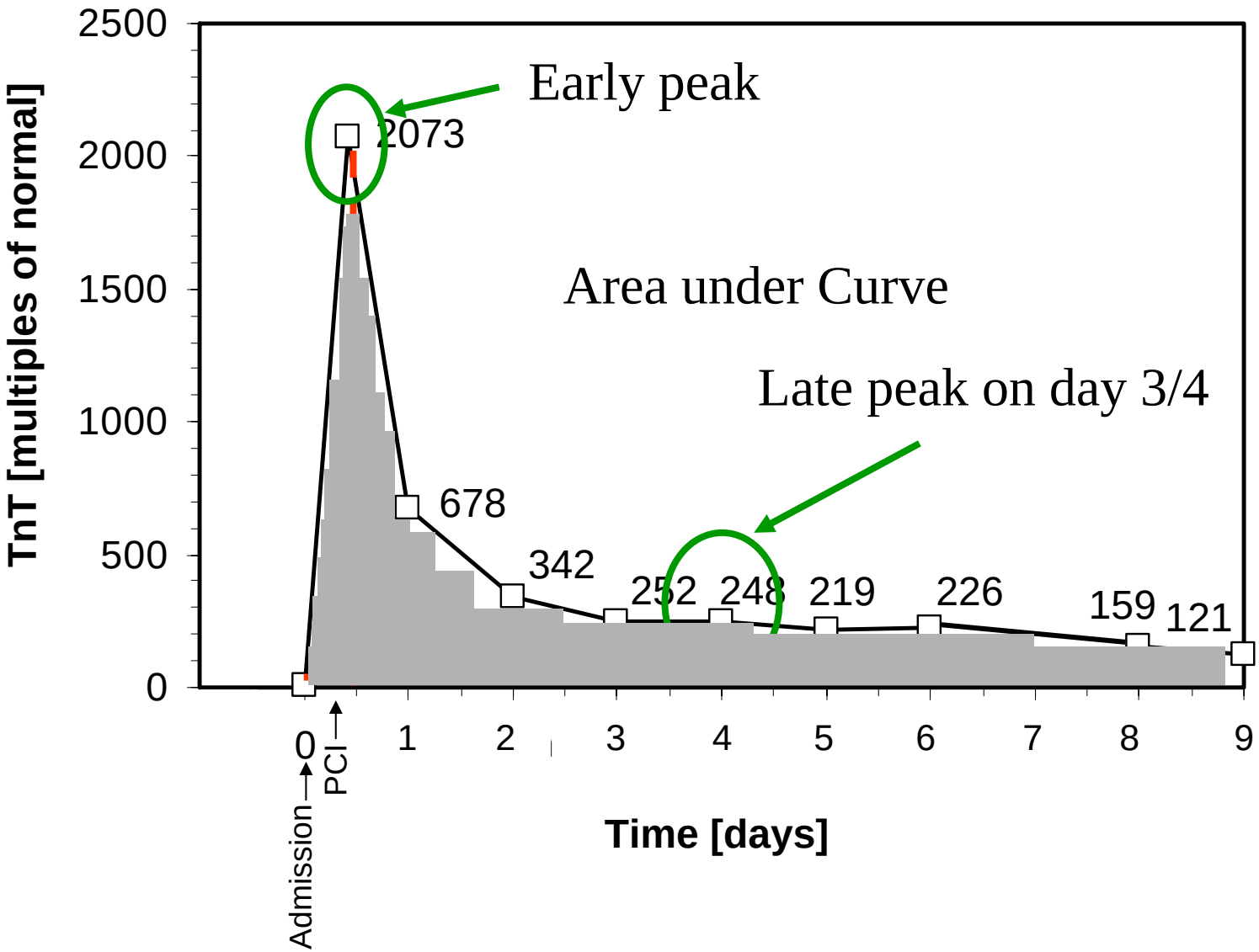
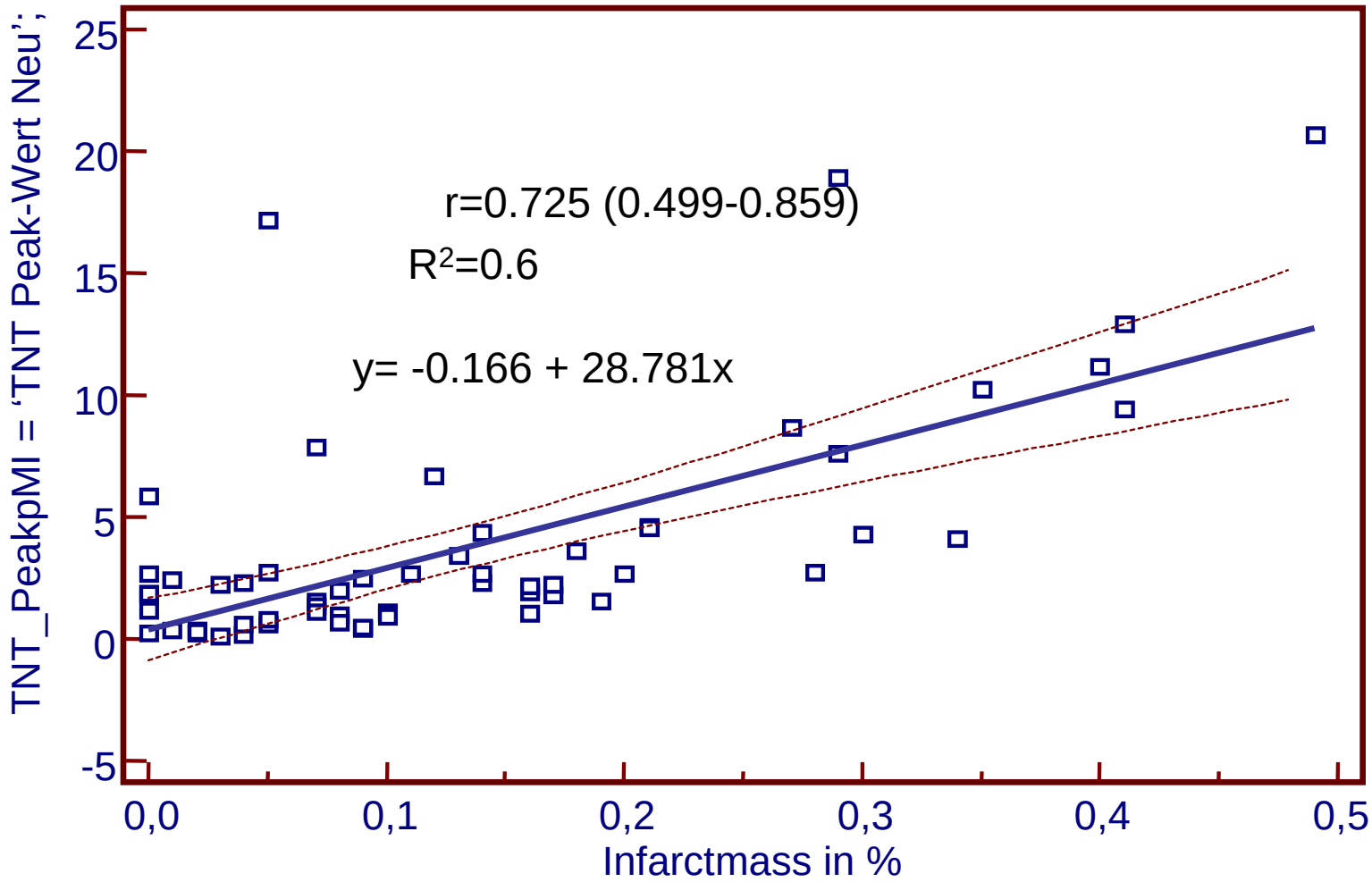
MRI – Late Hyperenhancement for Infarct Sizing

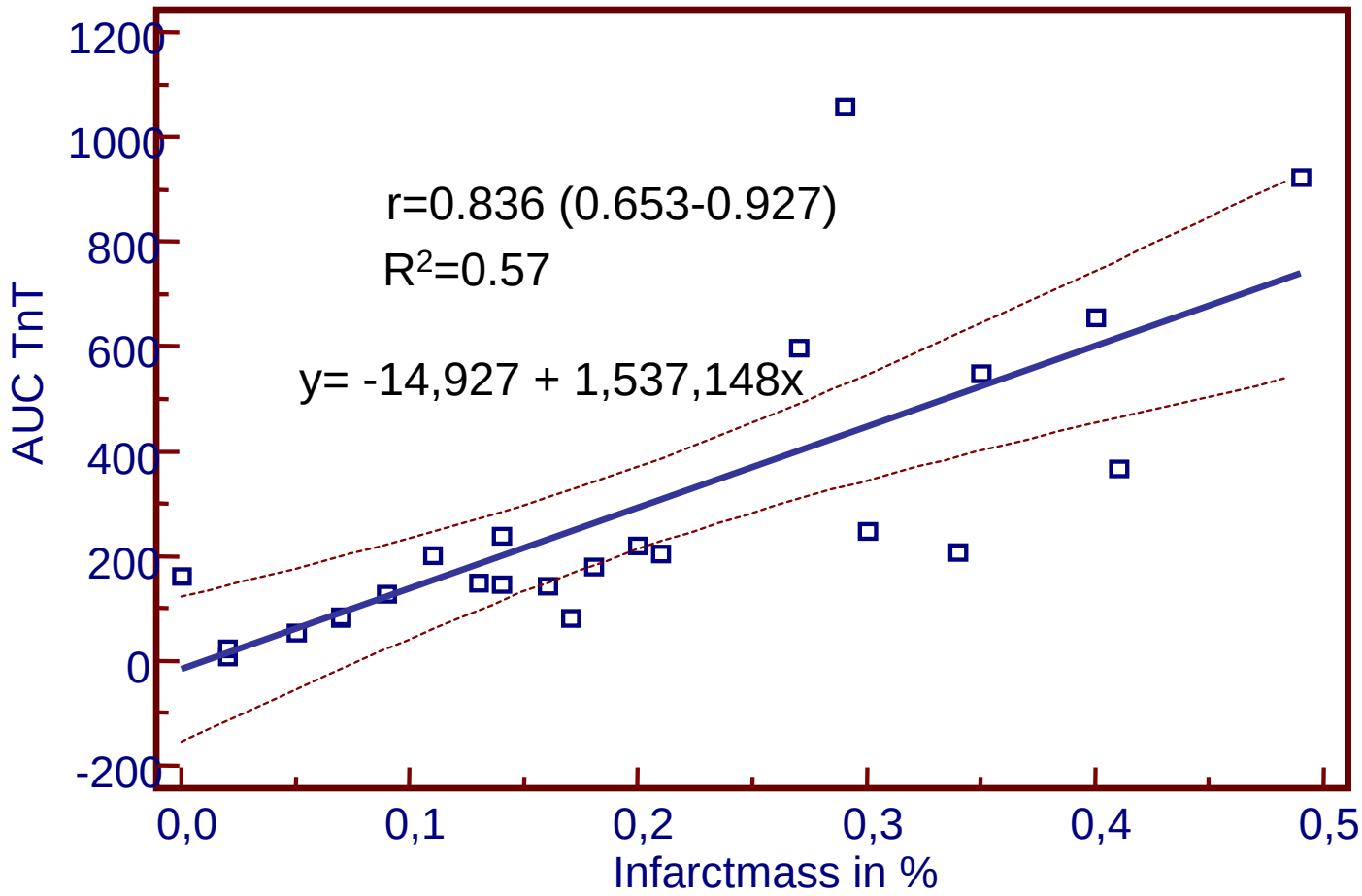



Early peak
2073
Area under Curve
Late peak on day 3/4
678
342
252
248
219
226
159
121
TnT [multiples of normal]
2500
2000
1500
1000
500
0
0
1
2
3
4
5
6
7
8
9
Admission
PCI
Time [days]

Methods for Infarct Sizing – Peak cTnT

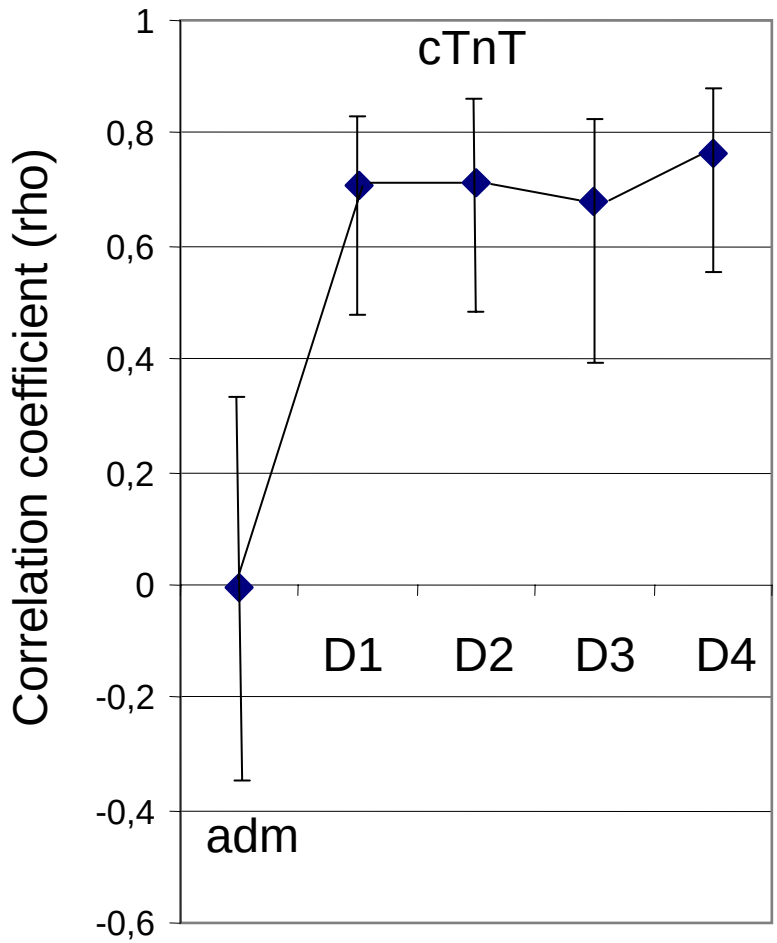


Methods for Infarct Sizing – AUC cTnT



Infarct Sizing in STEMI

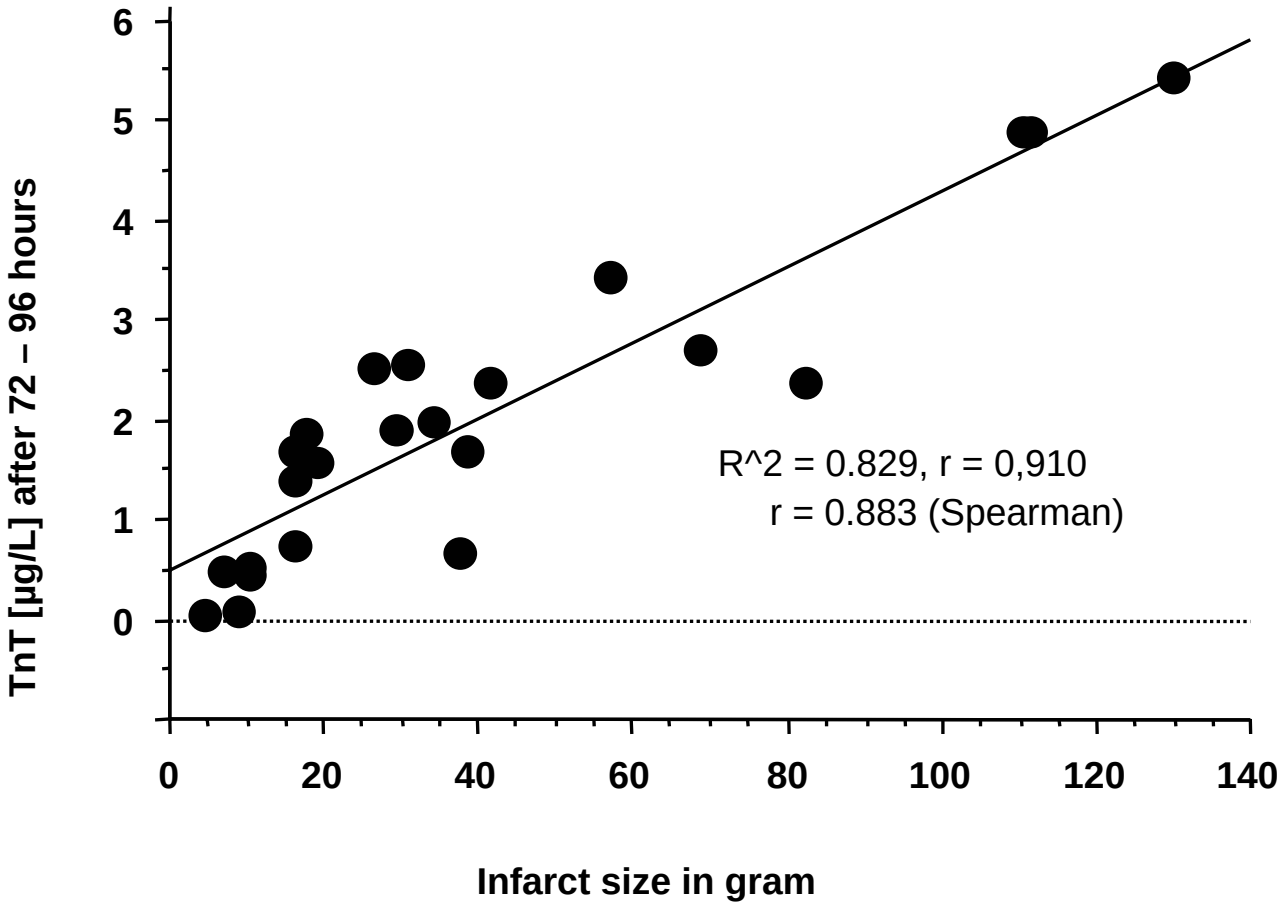
Optimal Single-Time-Point Measurement



N=32

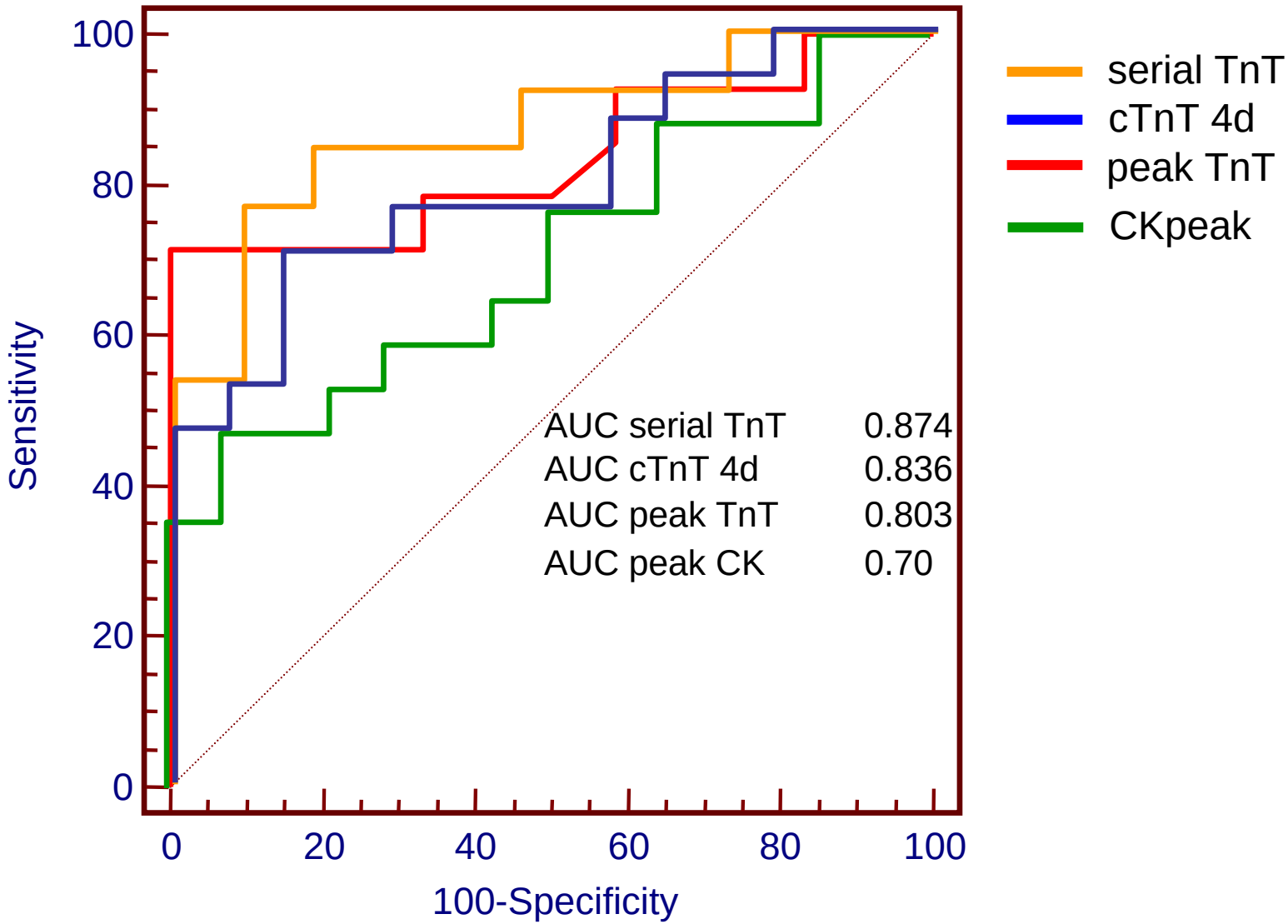
Giannitsis E, et al (submitted)

Methods for Infarct Sizing – cTnT on D4



Comparison of Methods

Relative infarct size > median



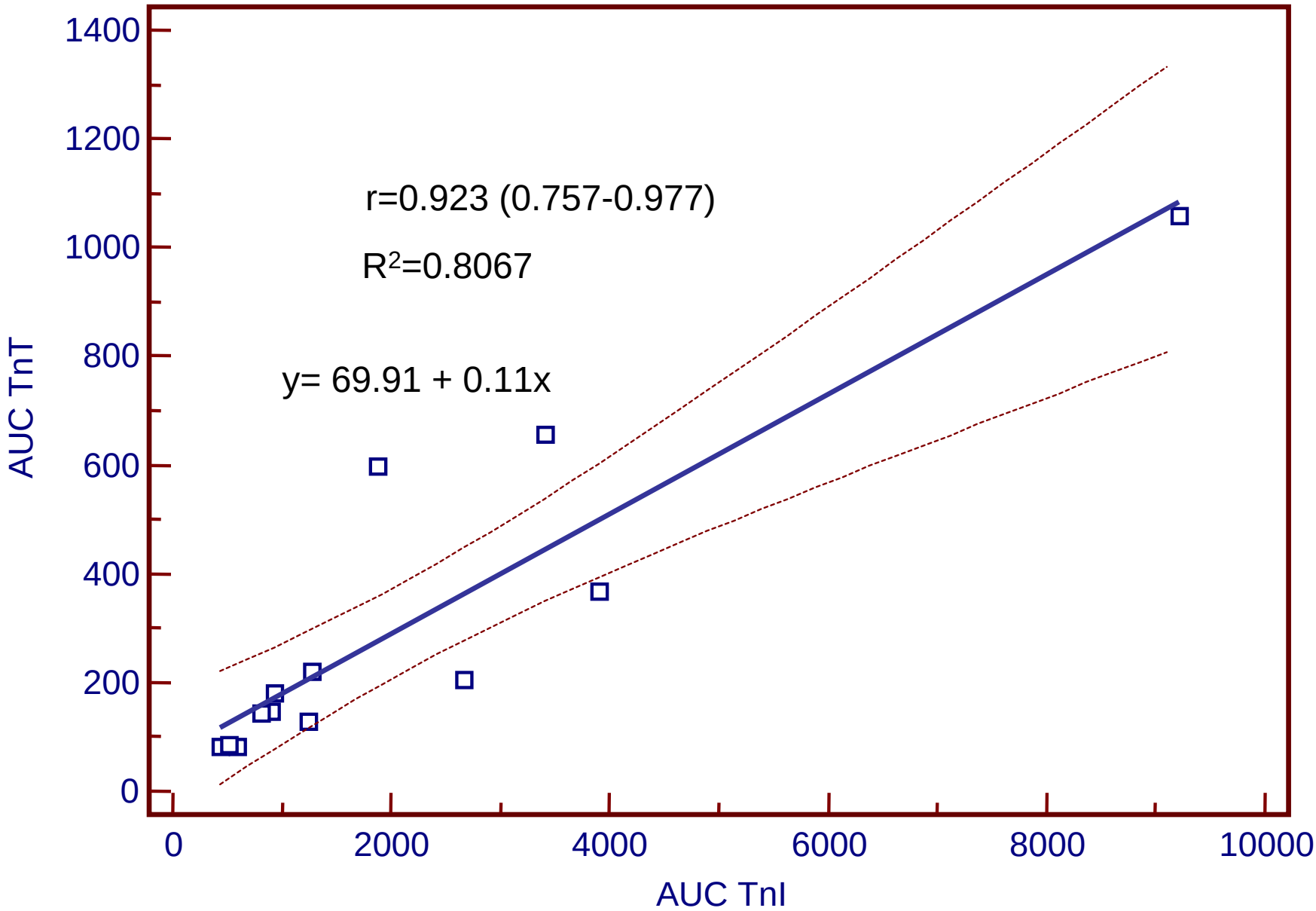
Summary

- There are several less well acknowledged indications for troponin testing beyond diagnosis in STEMI

- Well established
  - Admission troponin for risk stratification
  - Assessment of Reperfusion Success after Thrombolysis

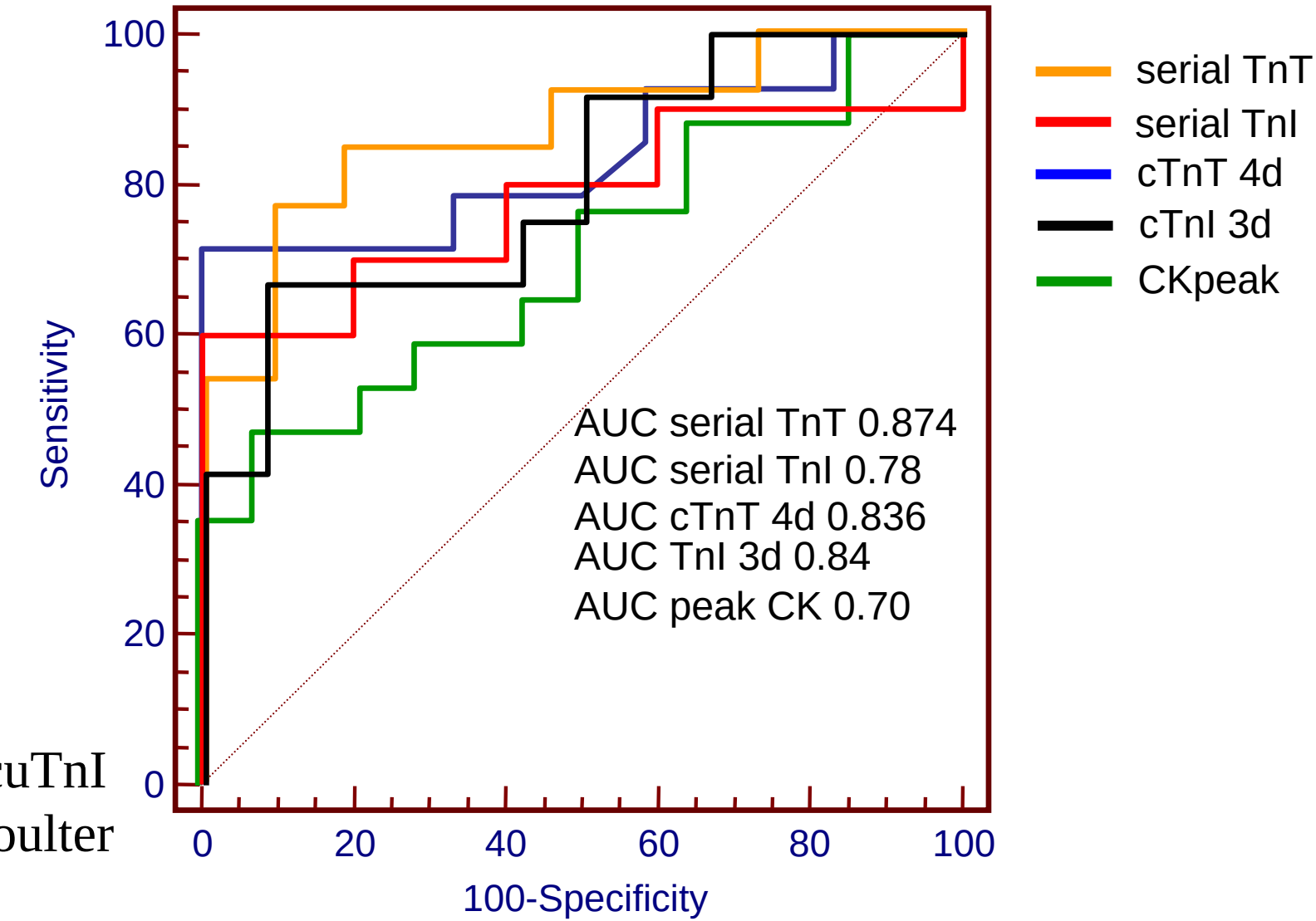
- Still Investigational, but promising
  - Assessment of microvascular reperfusion after pPCI
  - Monitoring of therapy with GP Inhibitors
  - Infarct Sizing

Comparison of cTnT and cTnI



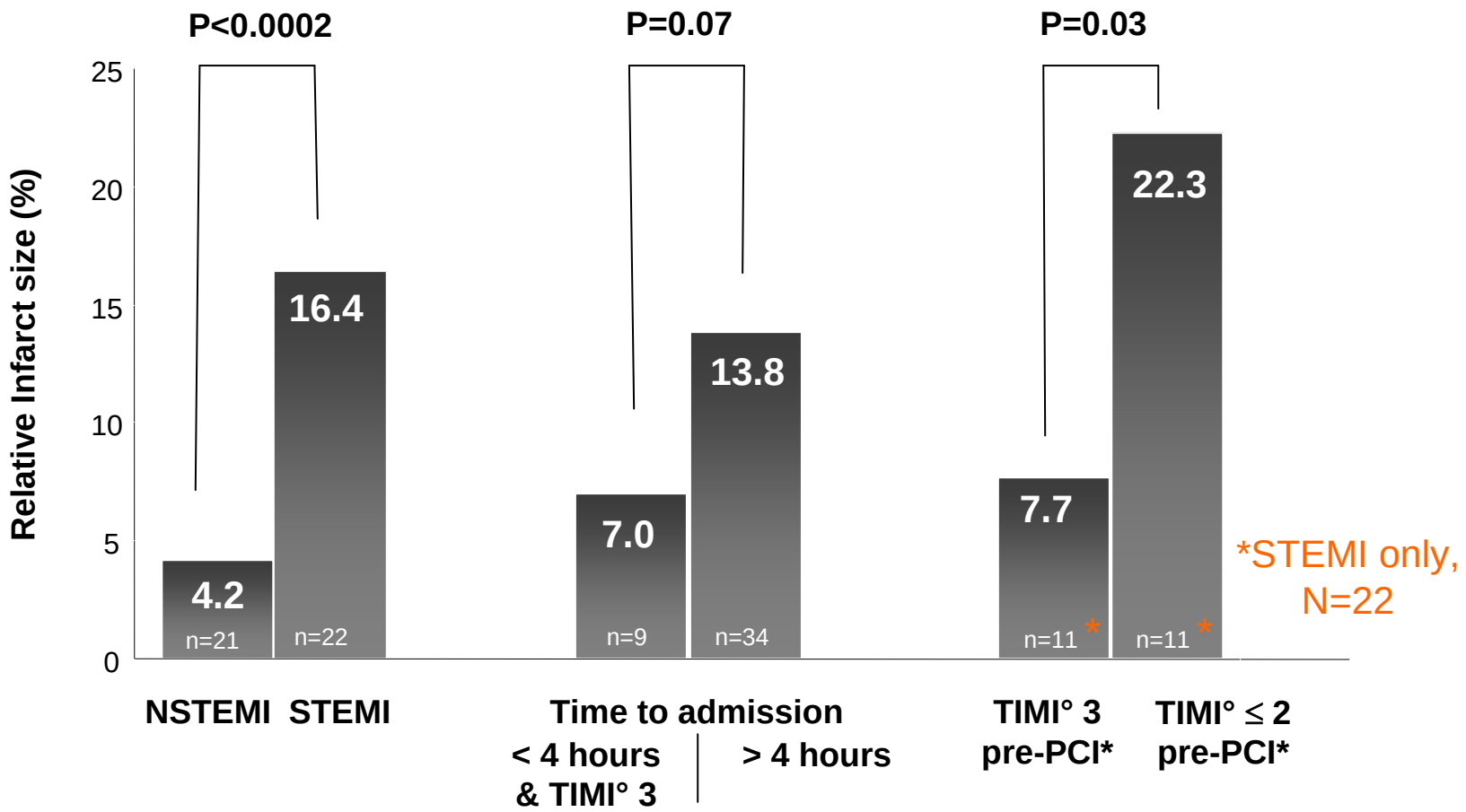
Comparison of Methods

Relative infarct size > median



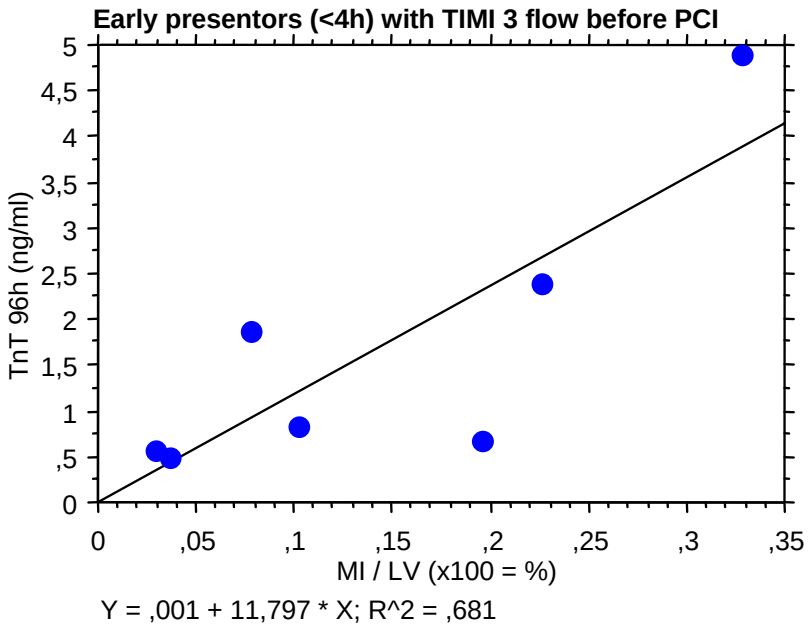
Access AccuTnI
BeckmanCoulter

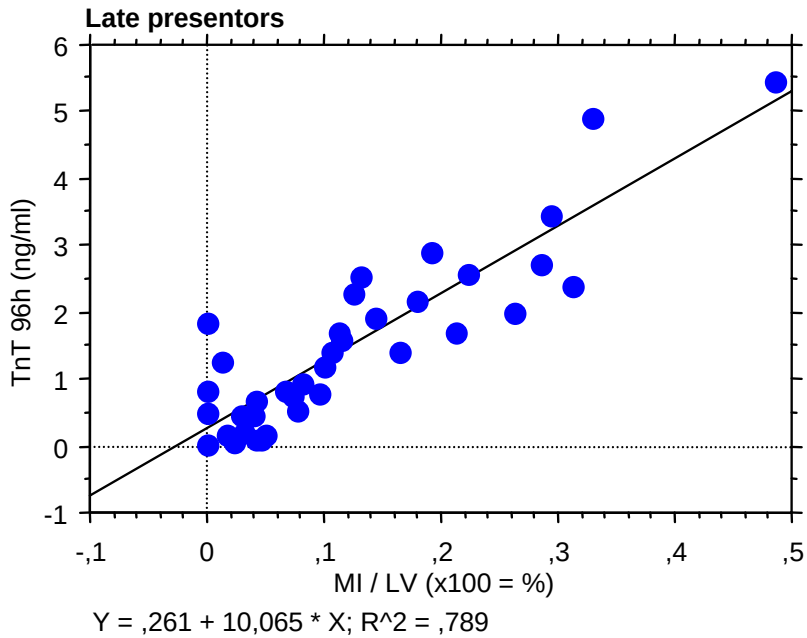
Relative Infarct Size



Early (<4h) presentors with spontaneous reperfusion (TIMI 3 pre-intervention) versus late (>4h) presentors:

Relative infarct size in % of LV





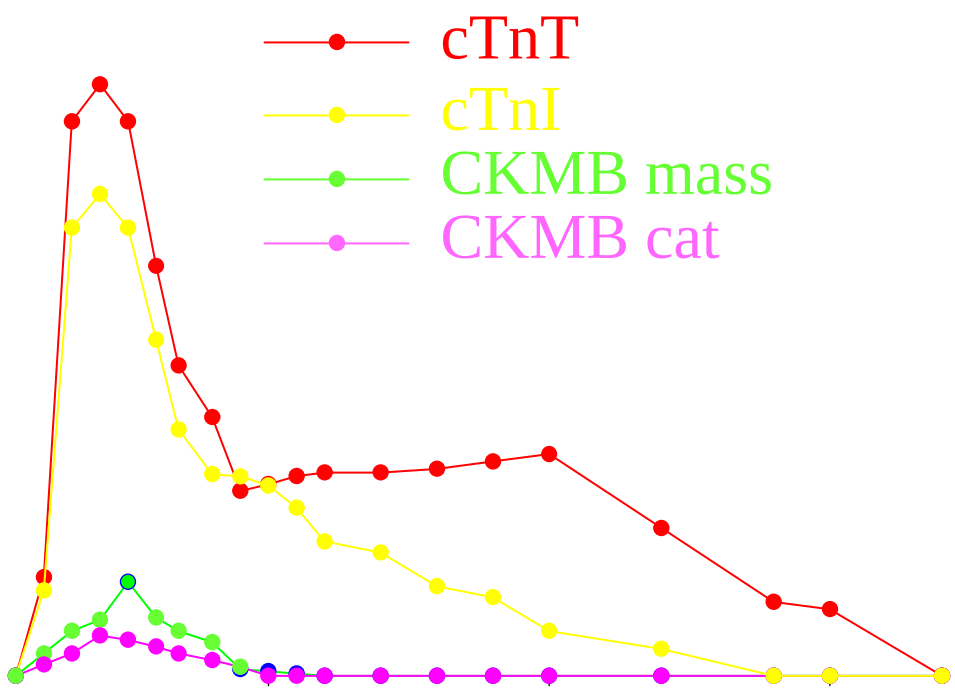
R = 0,825; p= 0,0223

R = 0,888; p<0,0001

Spearman: r = 0,821; p=0,0442

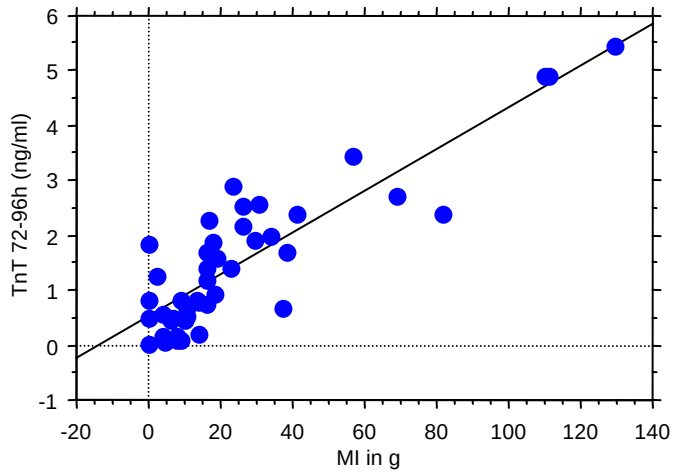
Spearman: r = 0,825; p<0,0001

Release of Cardiac Markers in AMI



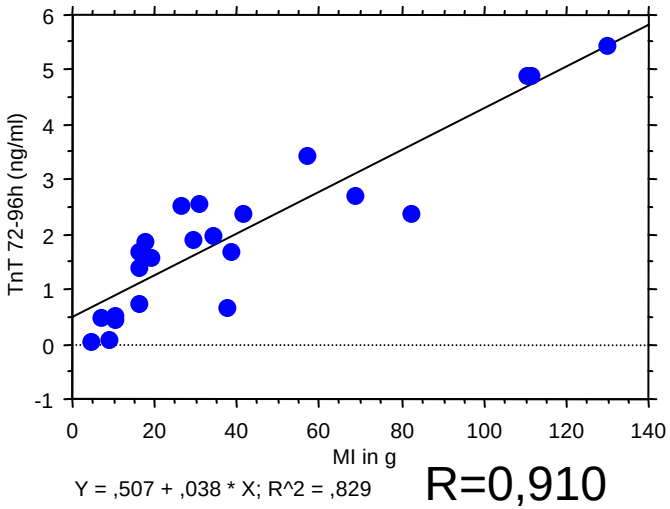
MRI-cTnT Pilot

N=44



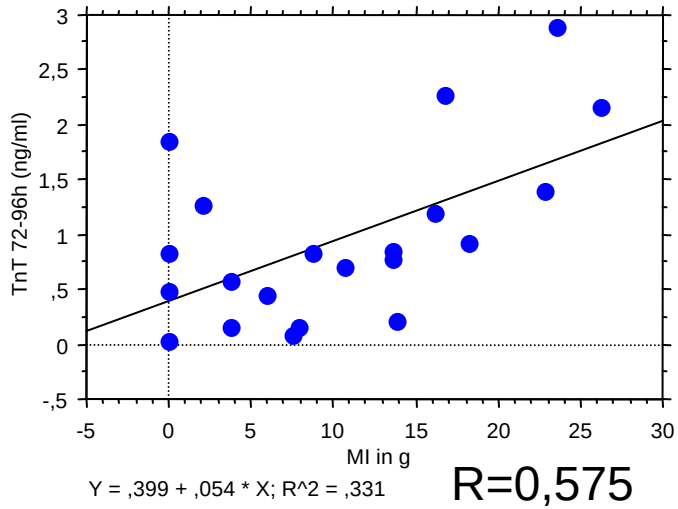
R=0,878

STEMI



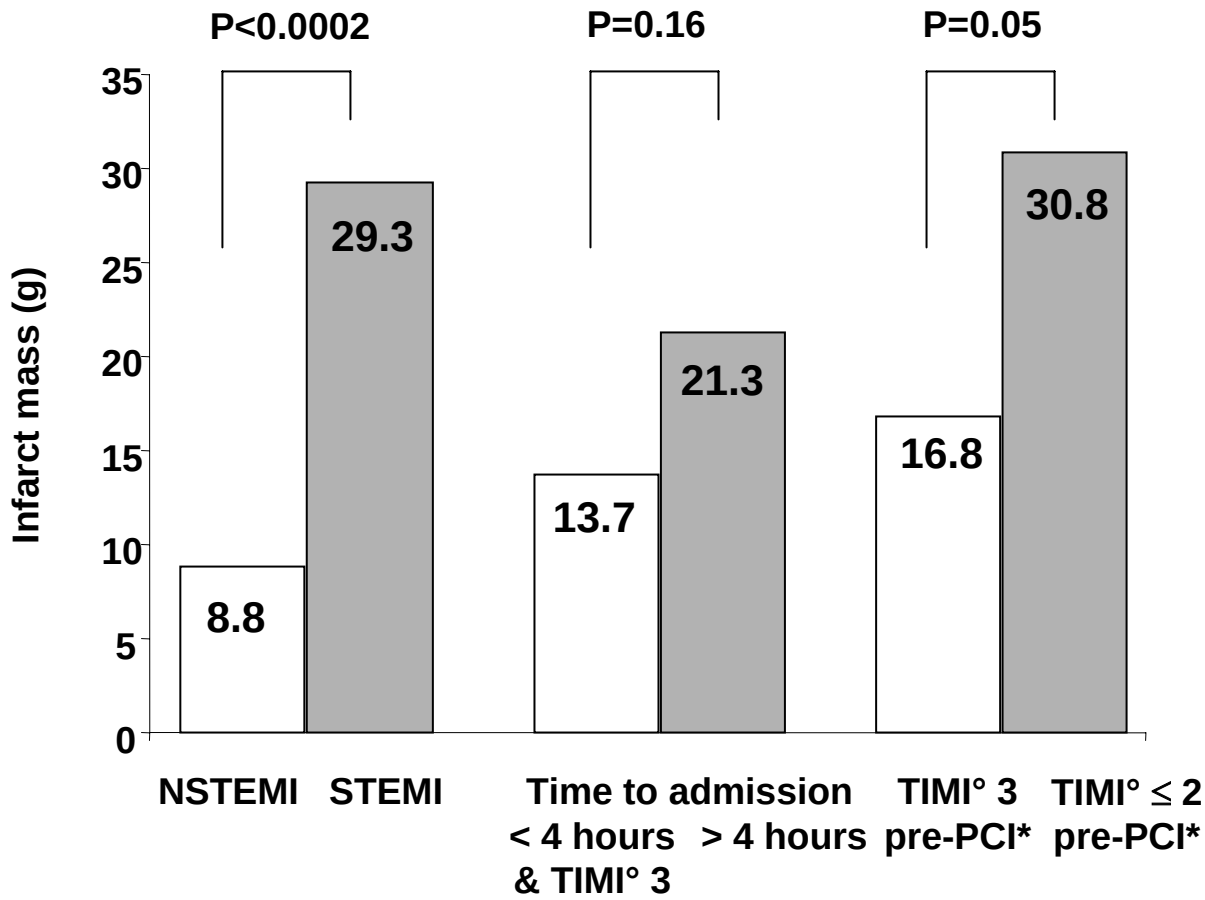
R=0,910

NSTEMI



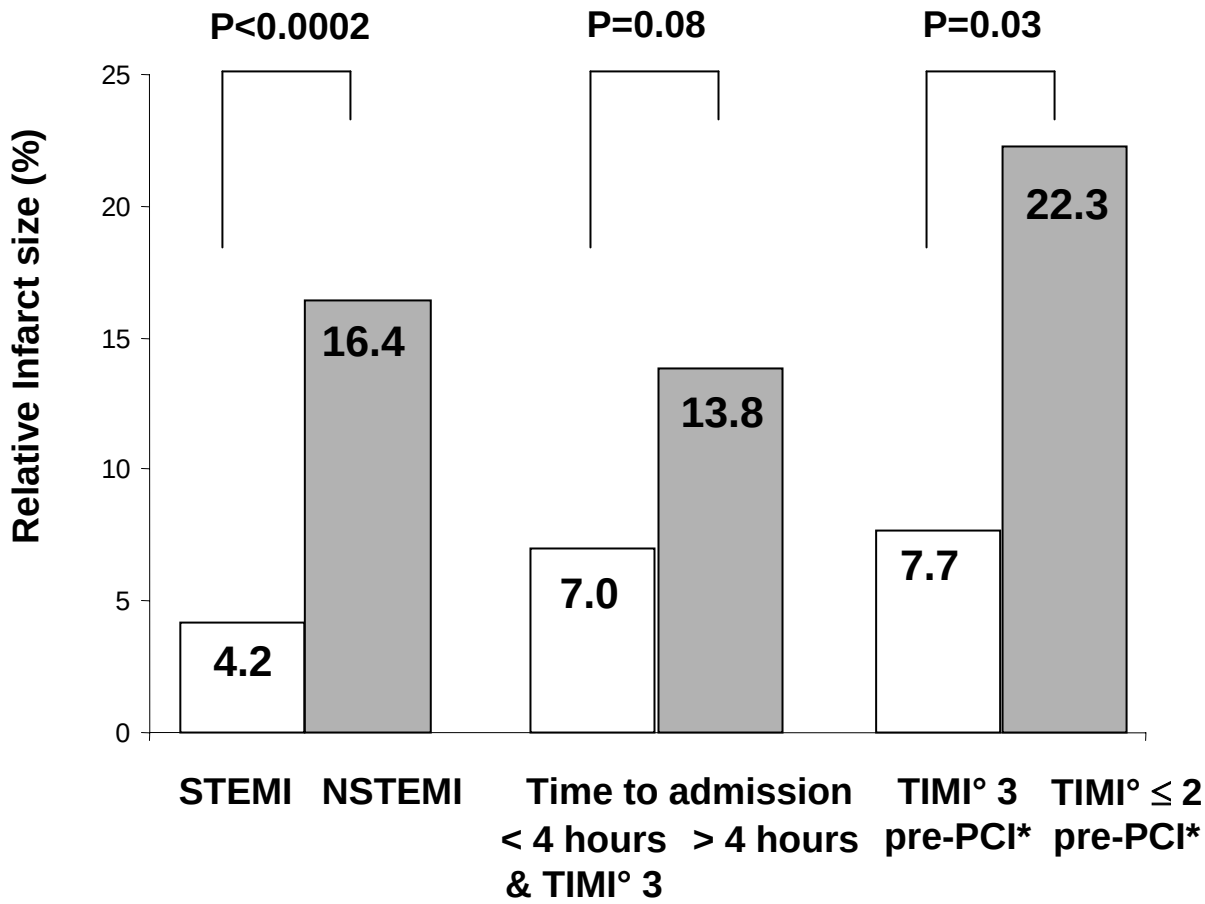
R=0,575

CE-MRI for Infarct Sizing

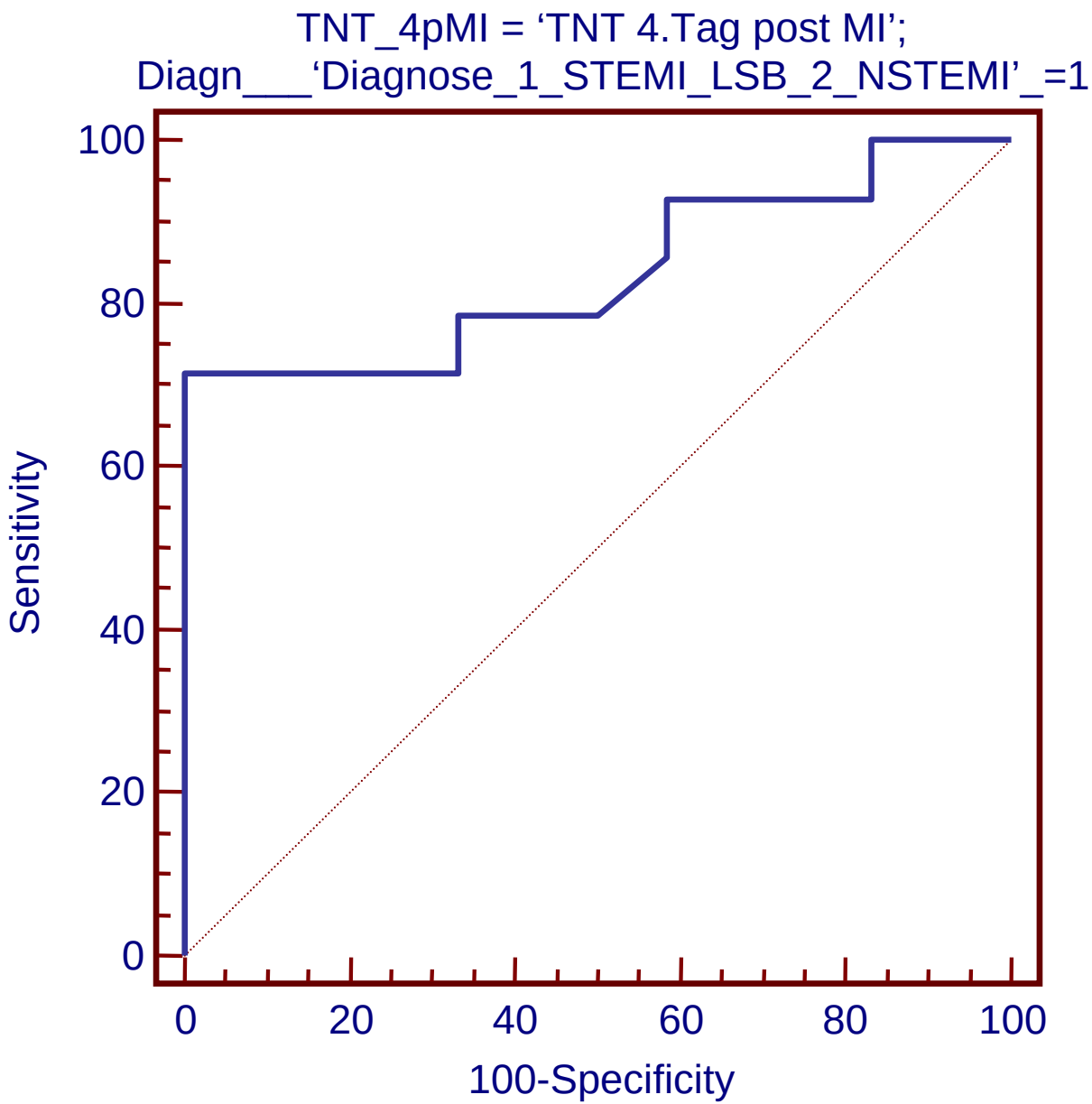


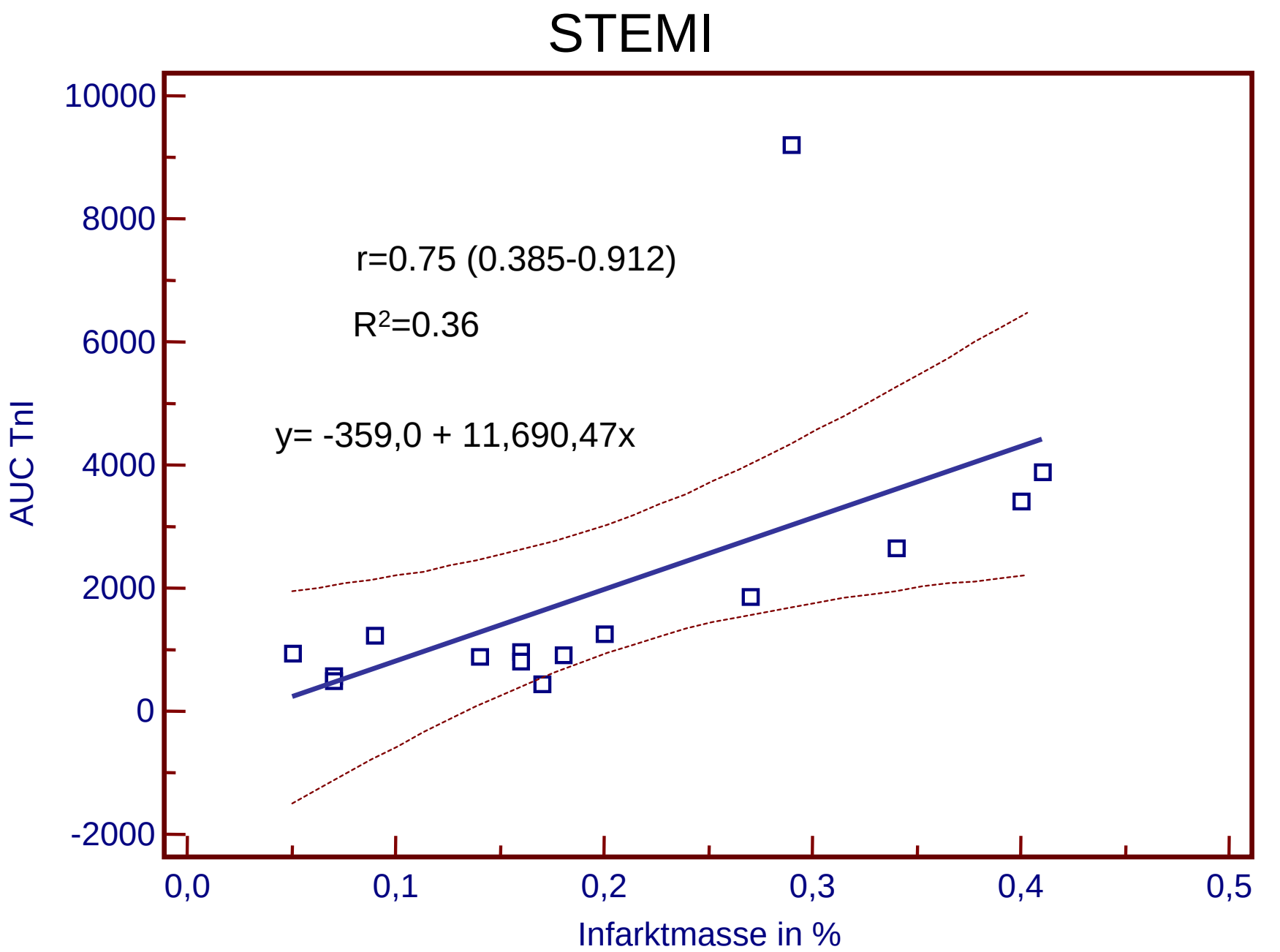
*STEMI only, N=23

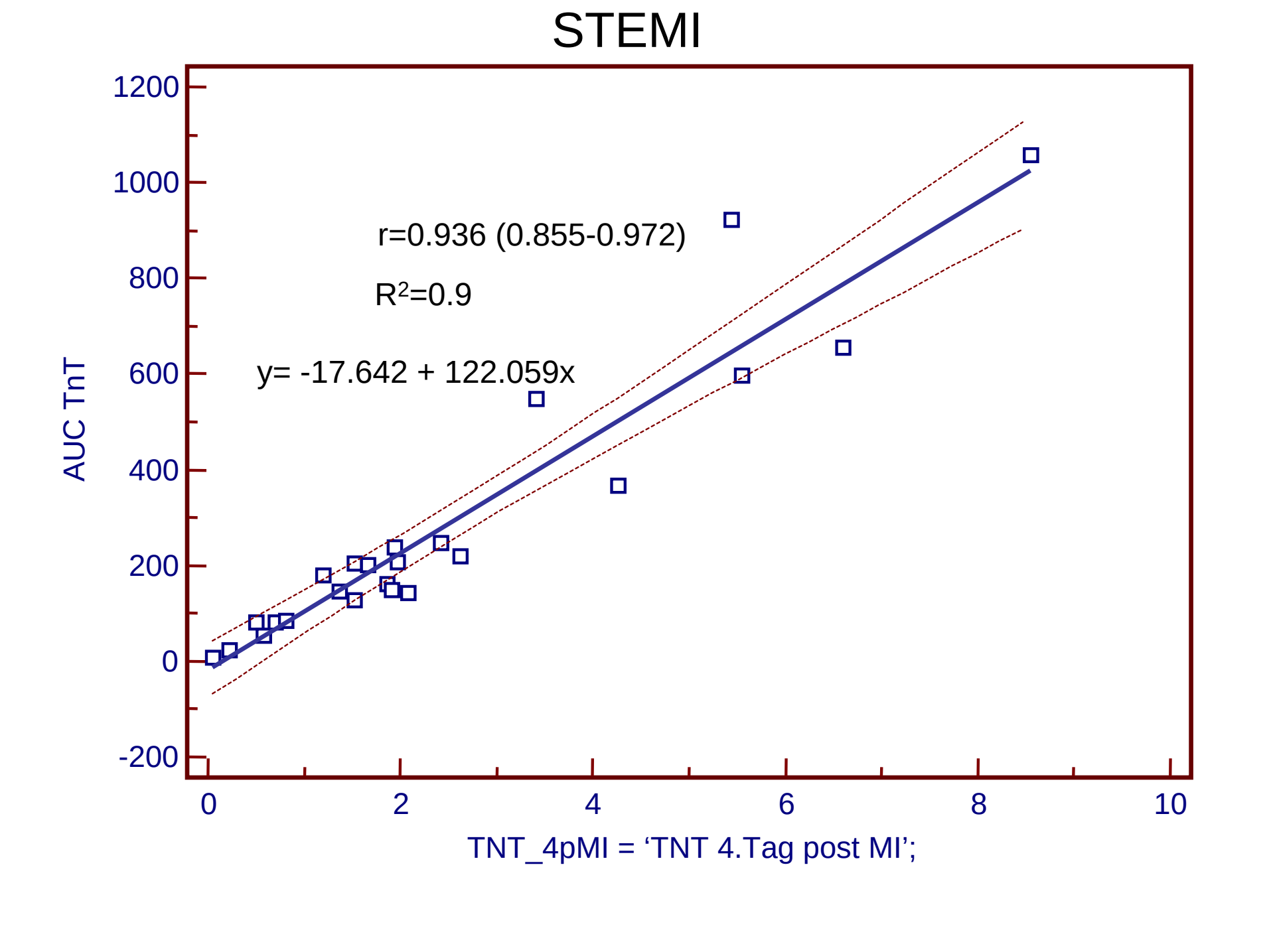
CE-MRI for Infarct Sizing

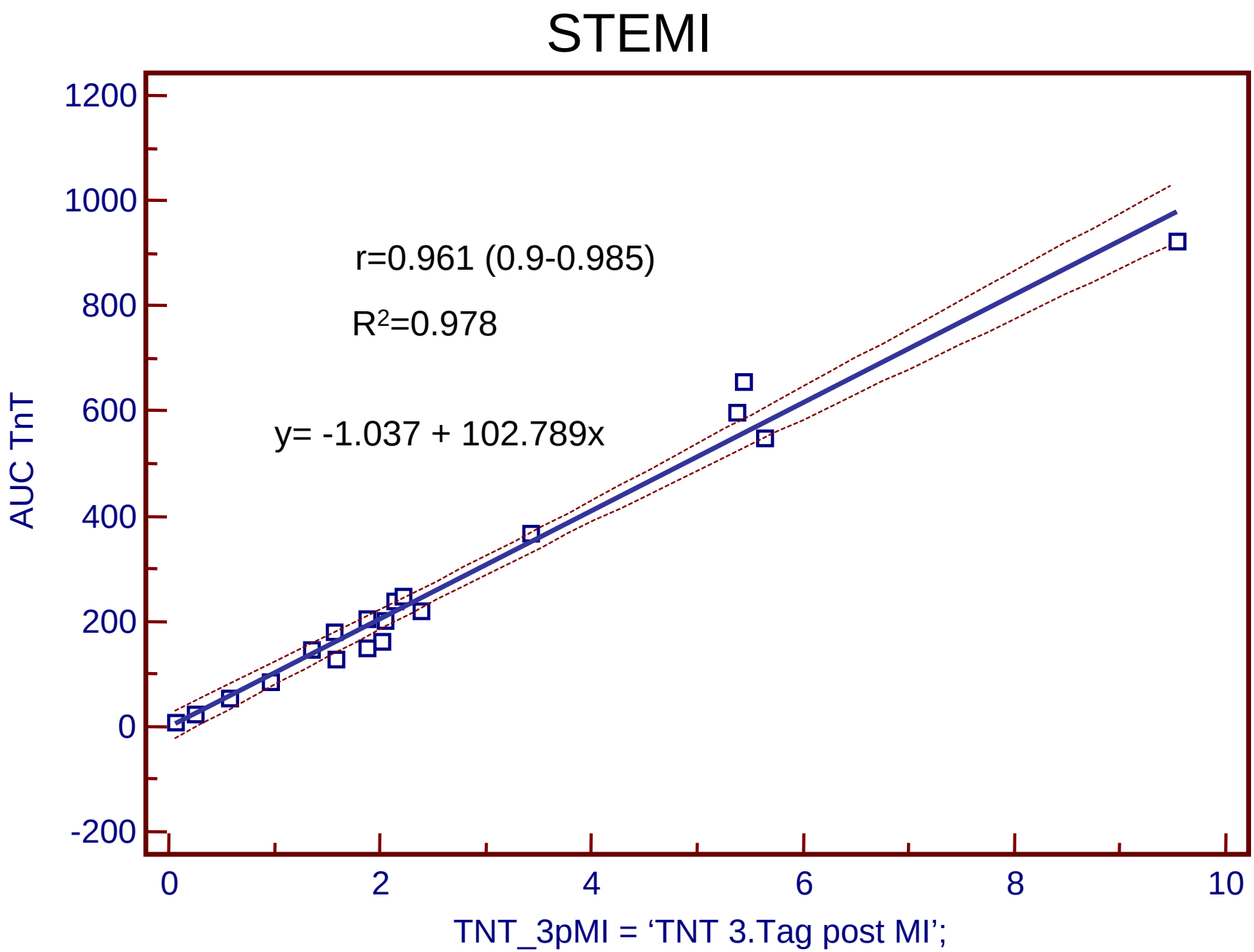


*STEMI only, N=23

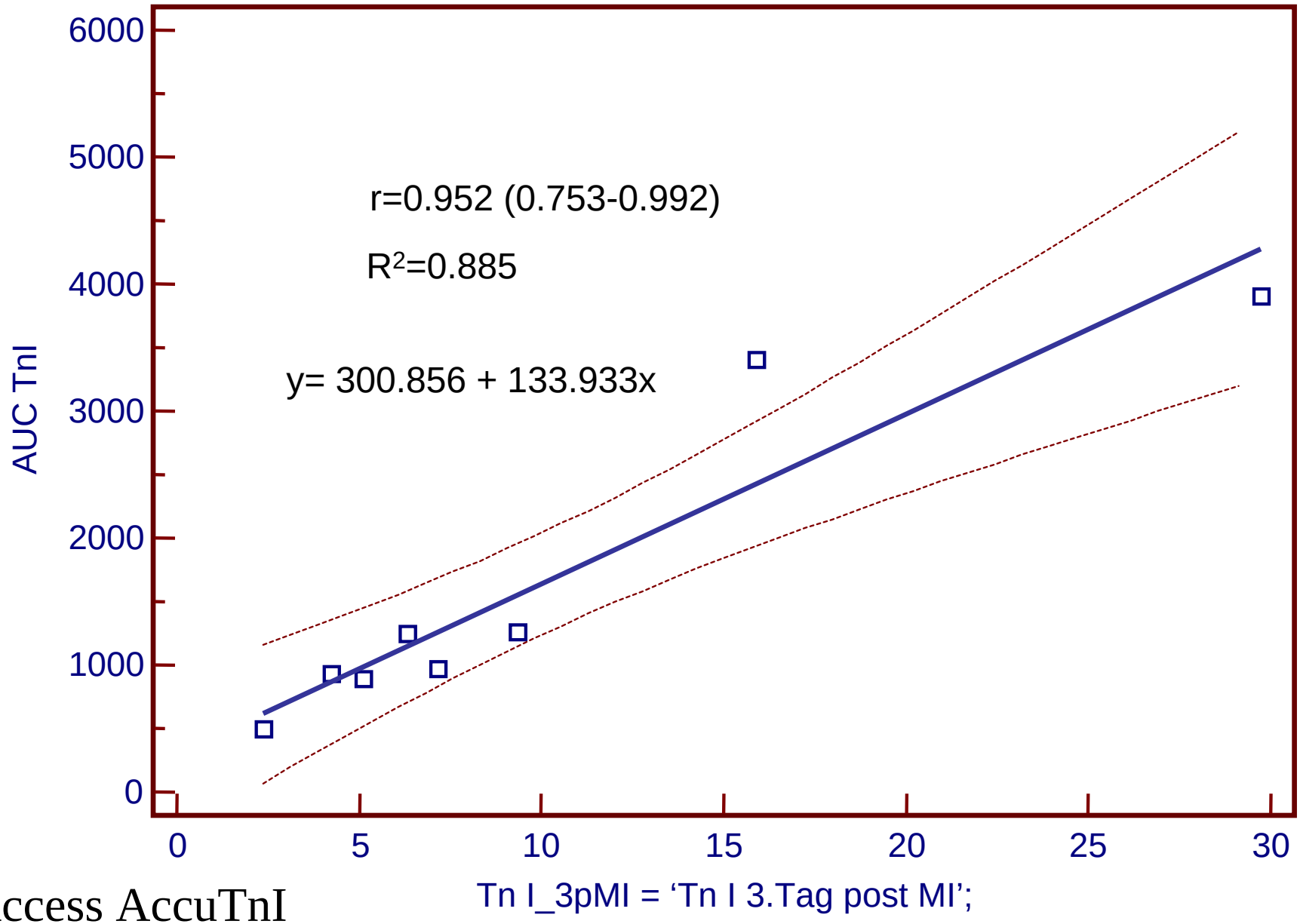

TNT_4pMI = 'TNT 4.Tag post MI';
Diagn___'Diagnose_1_STEMI_LSB_2_NSTEMI'_=1
Sensitivity
100
80
60
40
20
0
0
20
40
60
80
100
100-Specificity


STEMI
10000
8000
6000
4000
2000
0
-2000
AUC TnI
r=0.75 (0.385-0.912)
R2=0.36
y= -359,0 + 11,690,47x
0,0
0,1
0,2
0,3
0,4
0,5
Infarktmasse in %

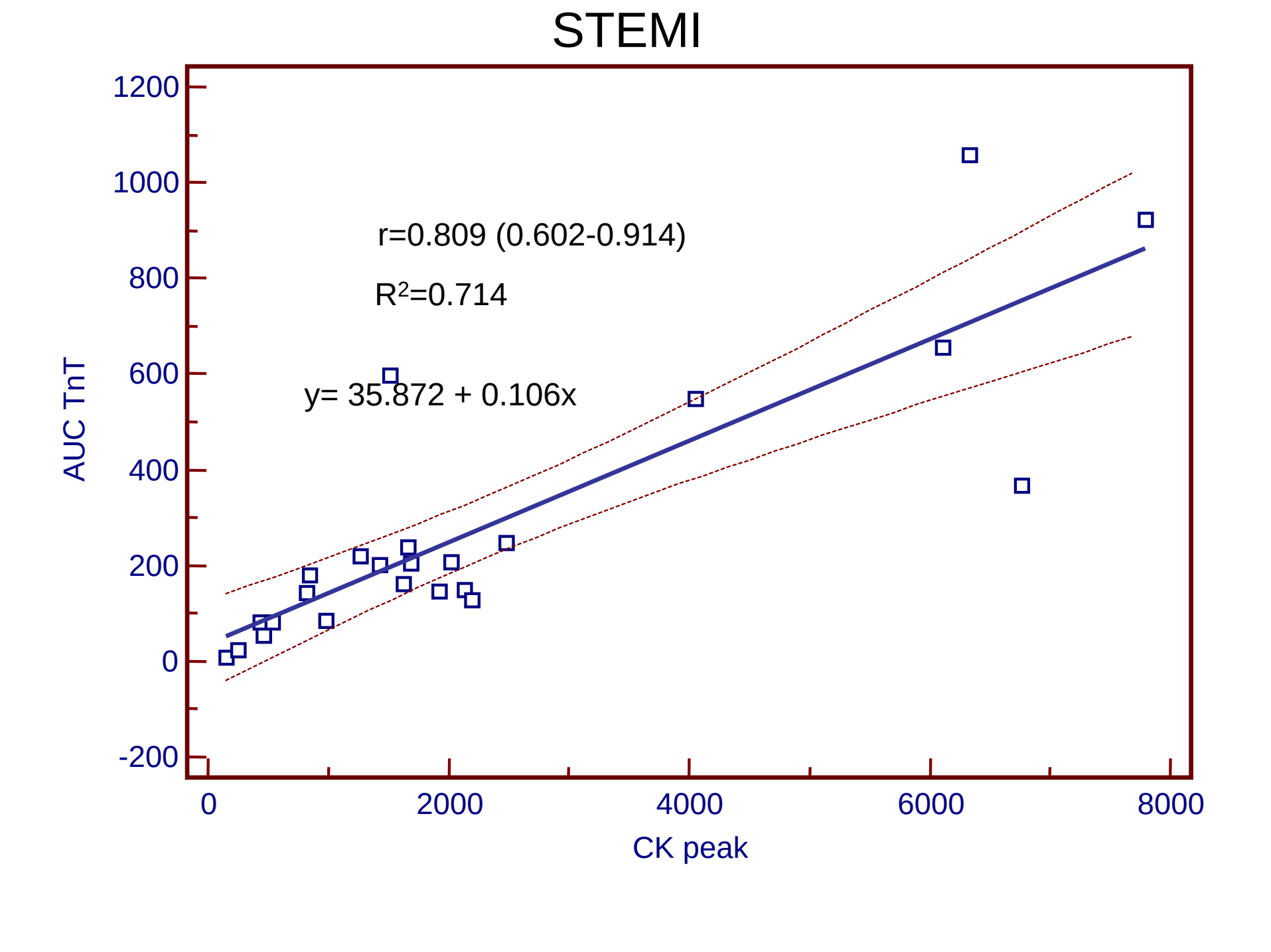

STEMI
1200
1000
800
600
400
200
0
-200
AUC TnT
r=0.936 (0.855-0.972)
R2=0.9
y= -17.642 + 122.059x
0
2
4
6
8
10
TNT_4pMI = 'TNT 4.Tag post MI';


STEMI
1200
1000
800
600
400
200
0
-200
AUC TnT
r=0.961 (0.9-0.985)
R2=0.978
y= -1.037 + 102.789x
0
2
4
6
8
10
TNT_3pMI = 'TNT 3.Tag post MI';

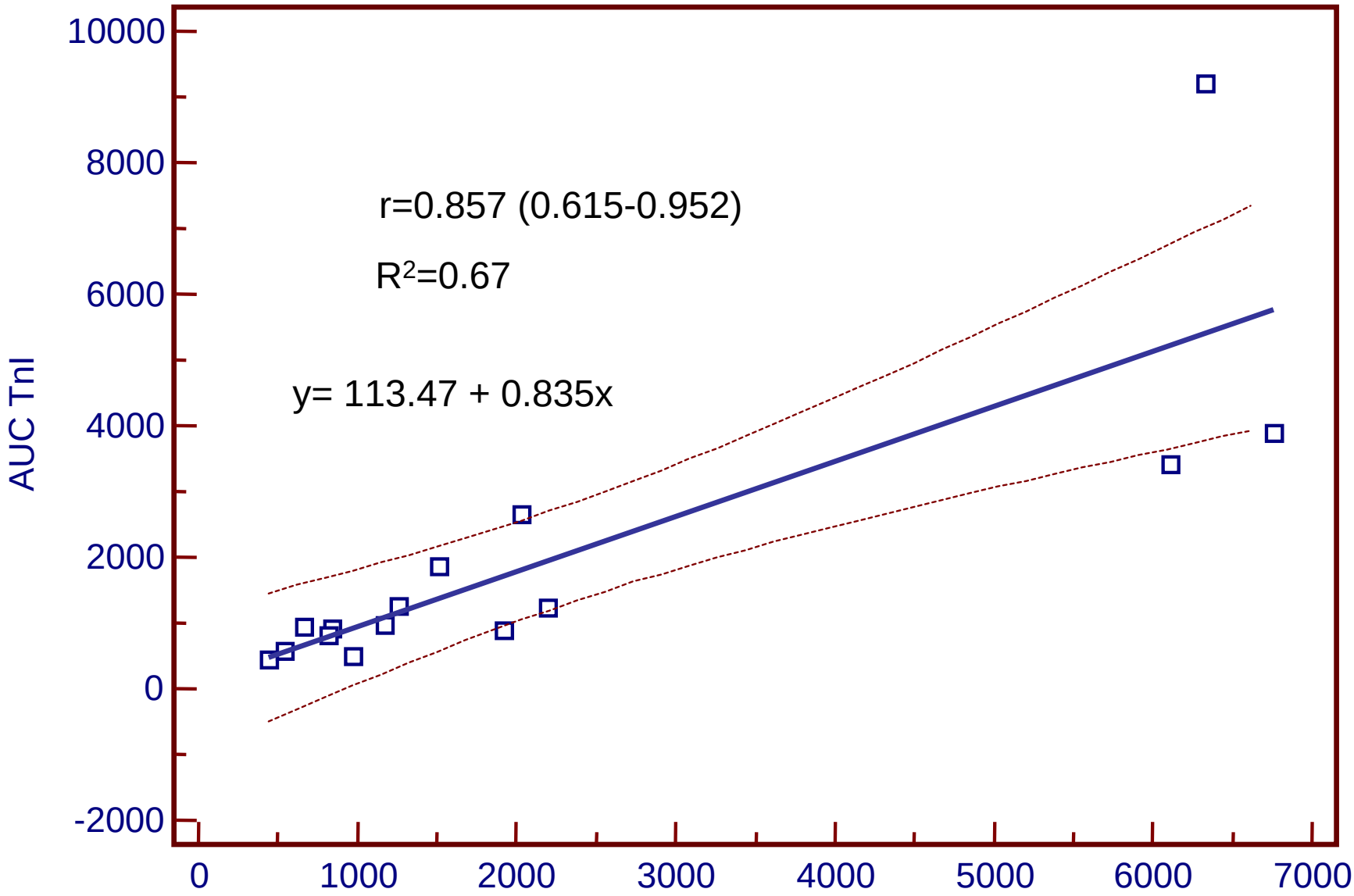
STEMI



Access AccuTnI
BeckmanCoulter

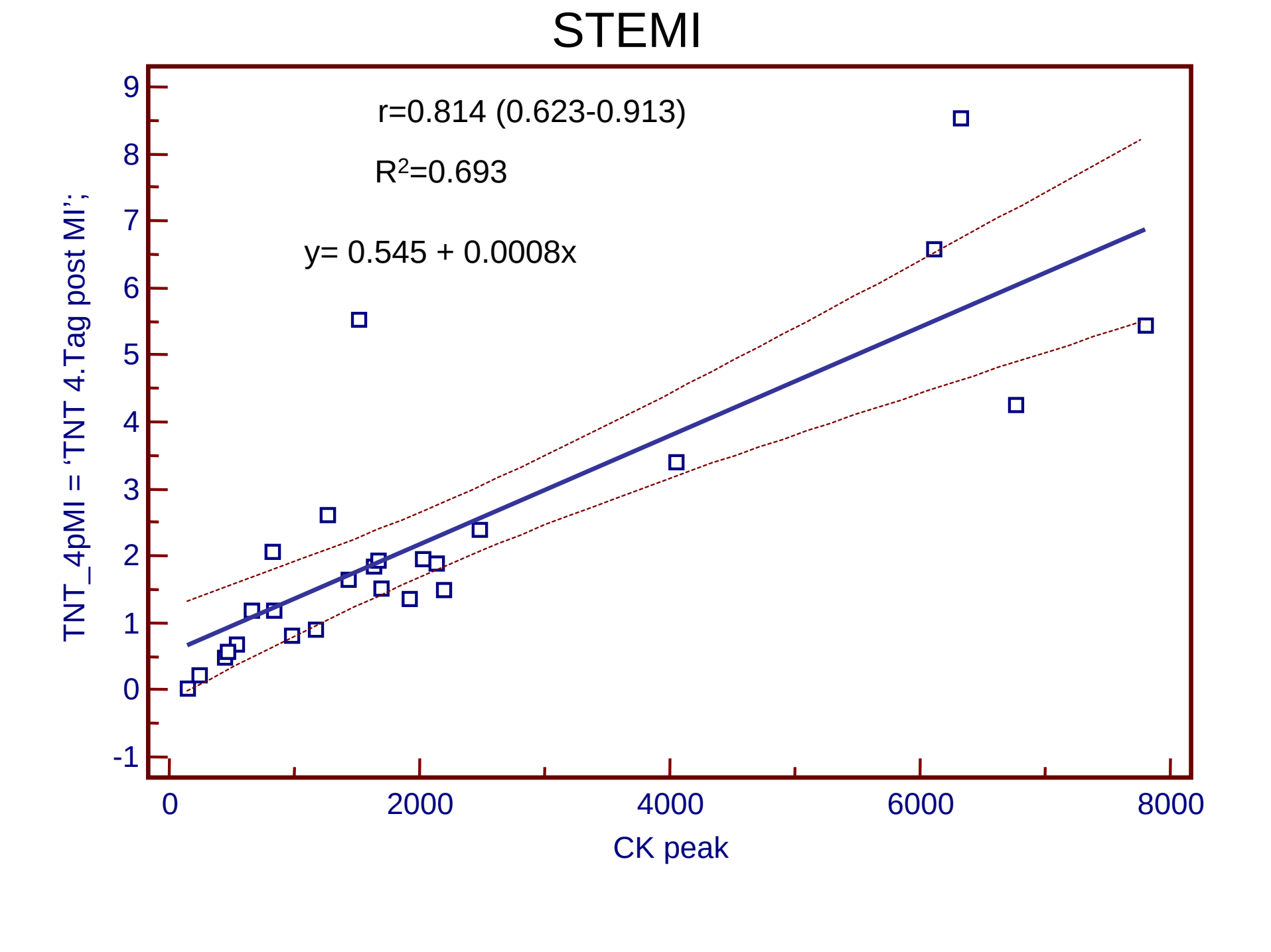

STEMI
1200
1000
800
600
400
200
0
-200
AUC TnT
r=0.809 (0.602-0.914)
R2=0.714
y= 35.872 + 0.106x
0
2000
4000
6000
8000
CK peak

STEMI

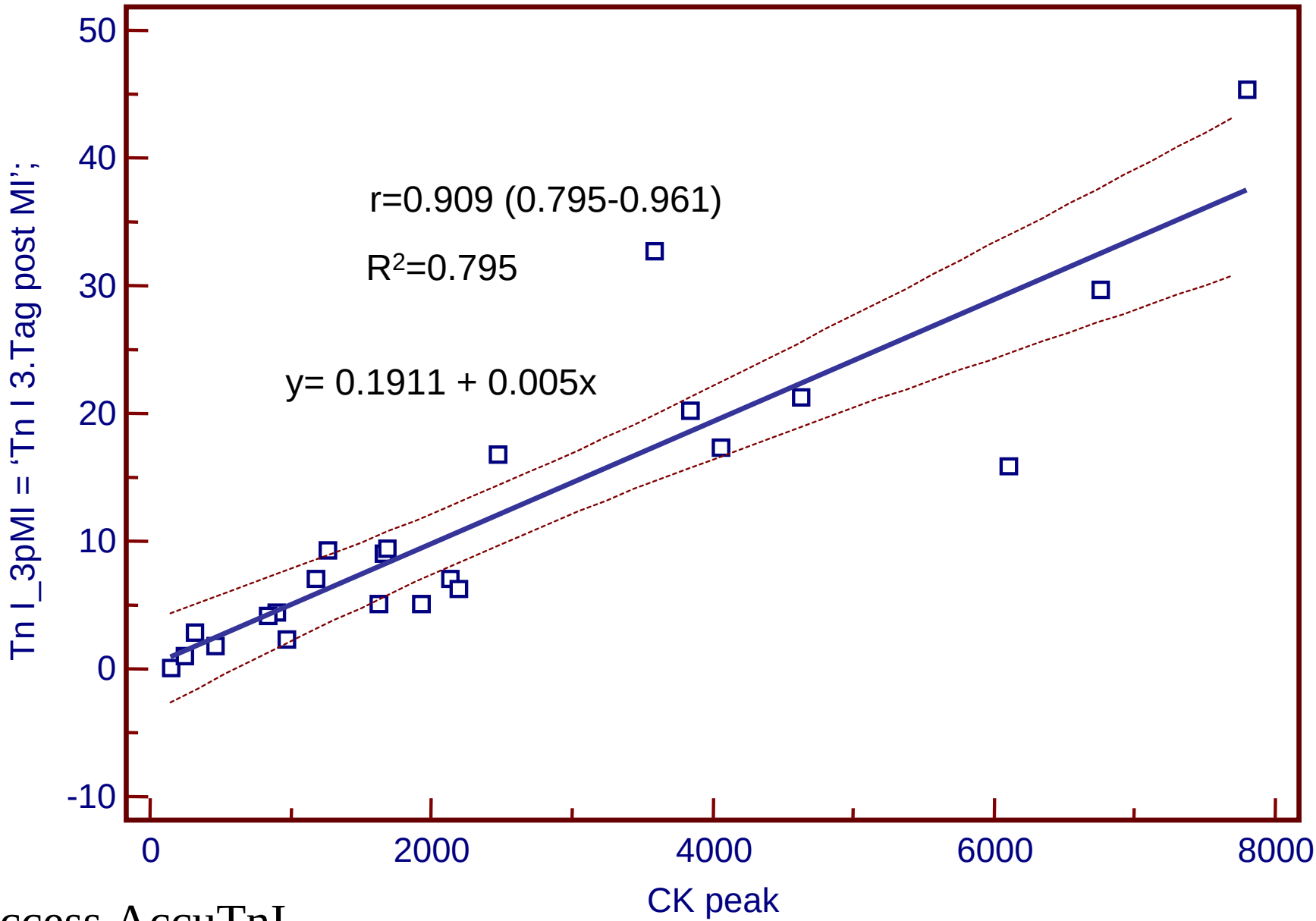


Access AccuTnI
BeckmanCoulter

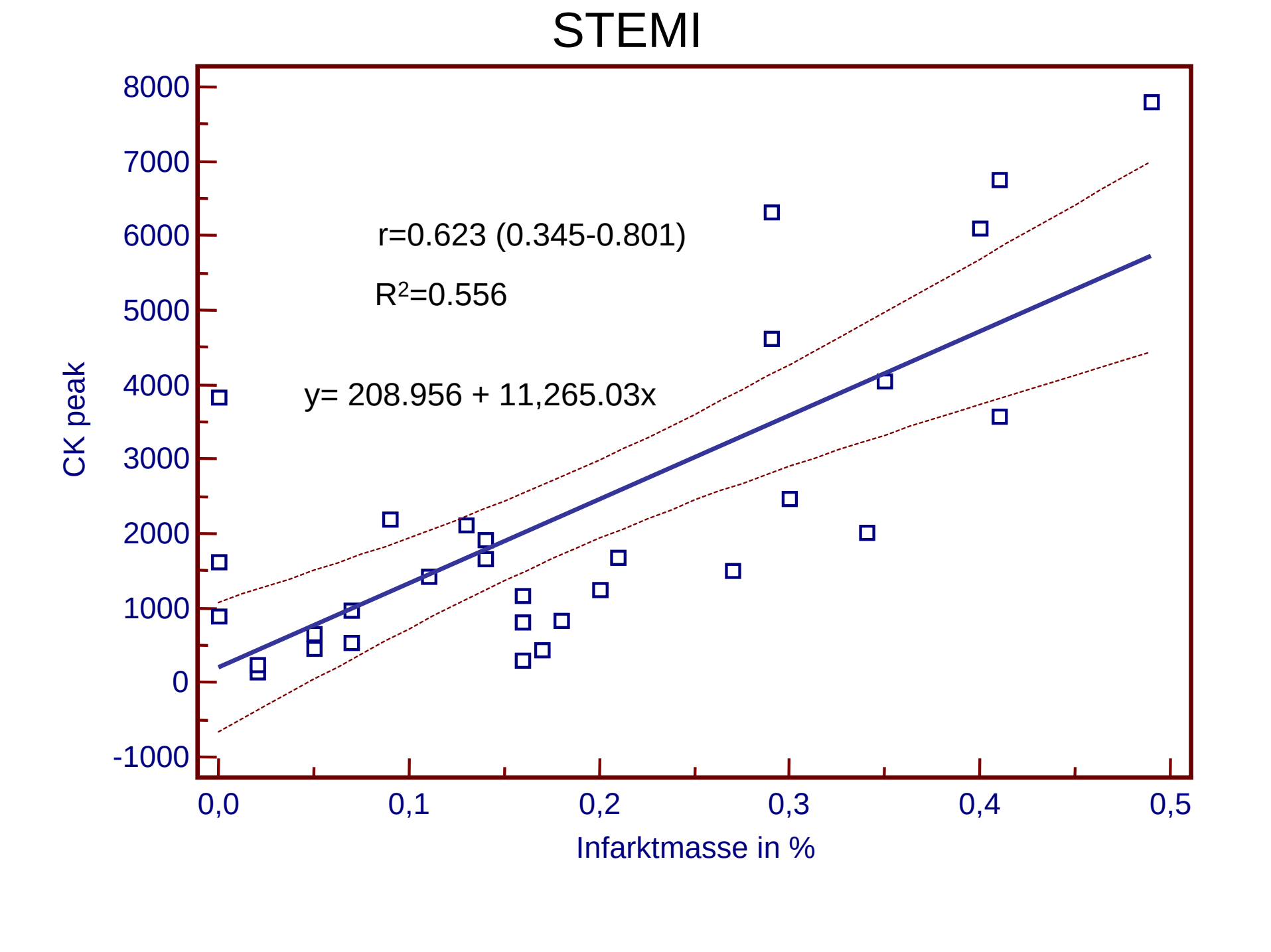
Diagn___'Diagnose_1_STEMI_LSB_2_NSTEMI'_=1


STEMI
r=0.814 (0.623-0.913)
R2=0.693
y= 0.545 + 0.0008x
TNT_4pMI = 'TNT 4.Tag post MI';
CK peak
9
8
7
6
5
4
3
2
1
0
-1
0
2000
4000
6000
8000

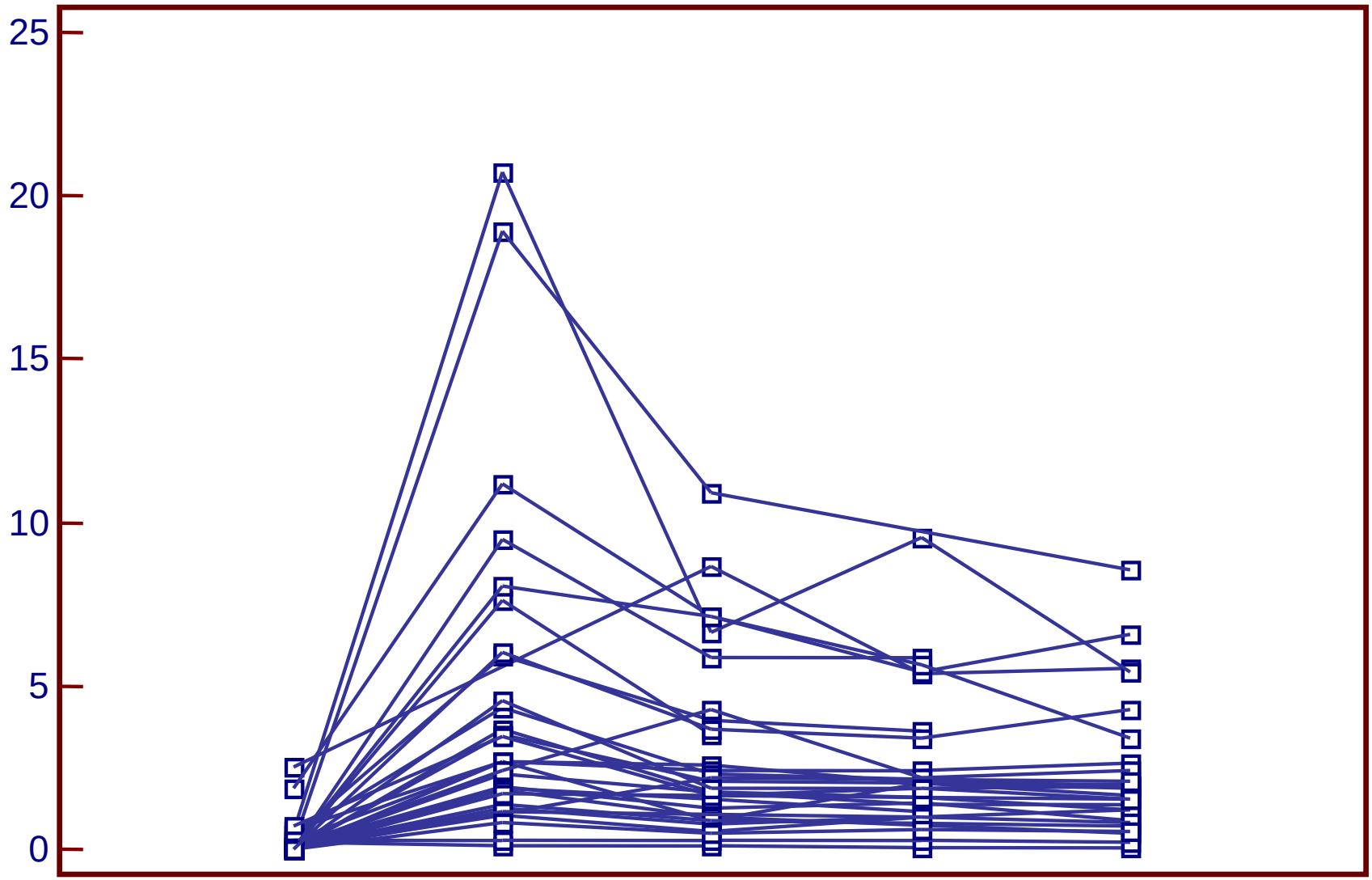
STEMI



Access AccuTnI
BeckmanCoulter

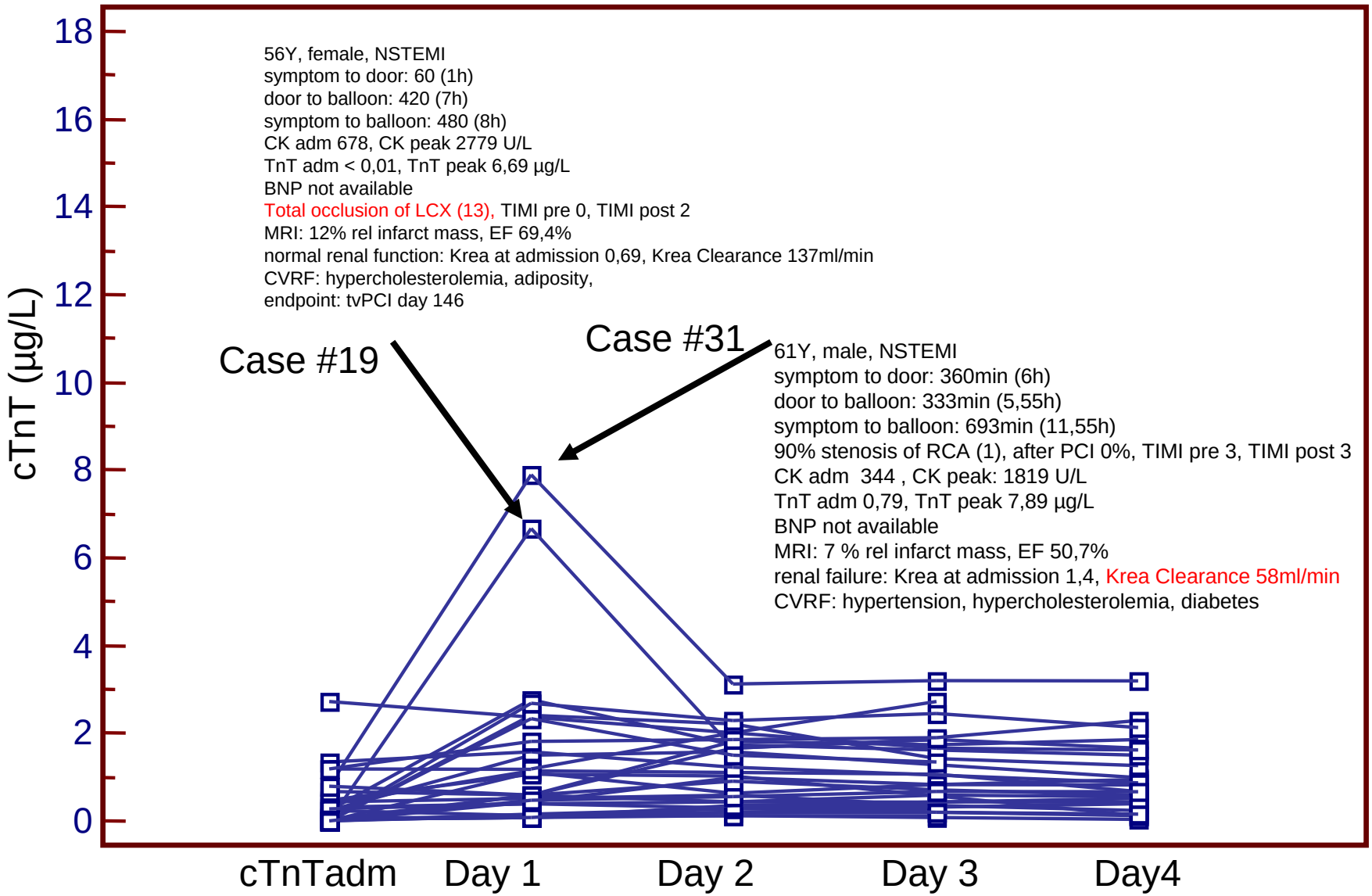

STEMI
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
CK peak
r=0.623 (0.345-0.801)
R²=0.556
y= 208.956 + 11,265.03x
0,0
0,1
0,2
0,3
0,4
0,5
Infarktmasse in %

STEMI

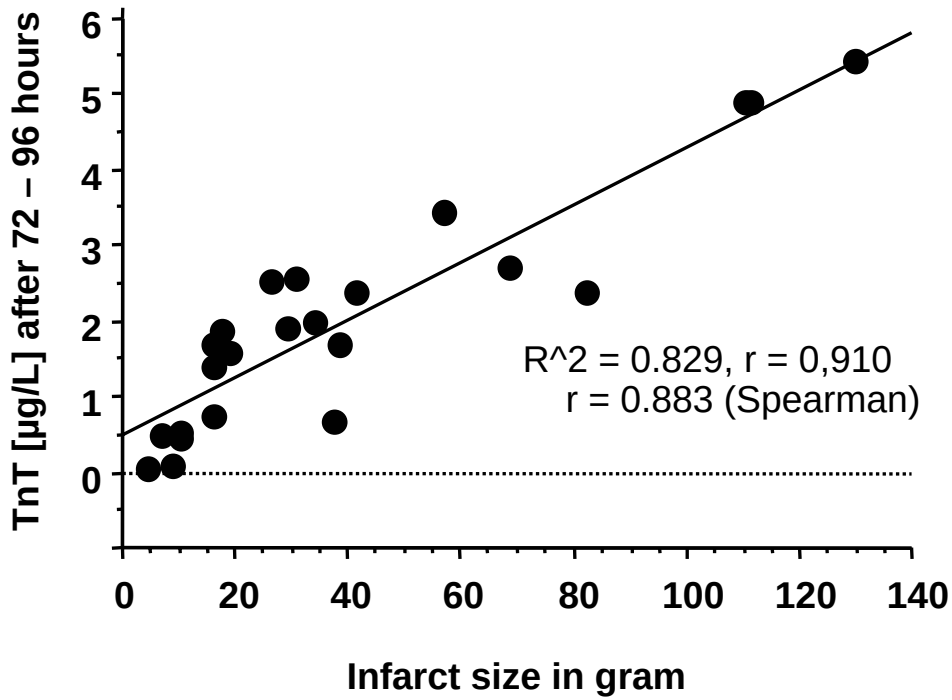


TNT_Auf = ‘TNT Aufnahme mg/dl’; TNT_3pMI = ‘TNT 3.Tag post MI’;

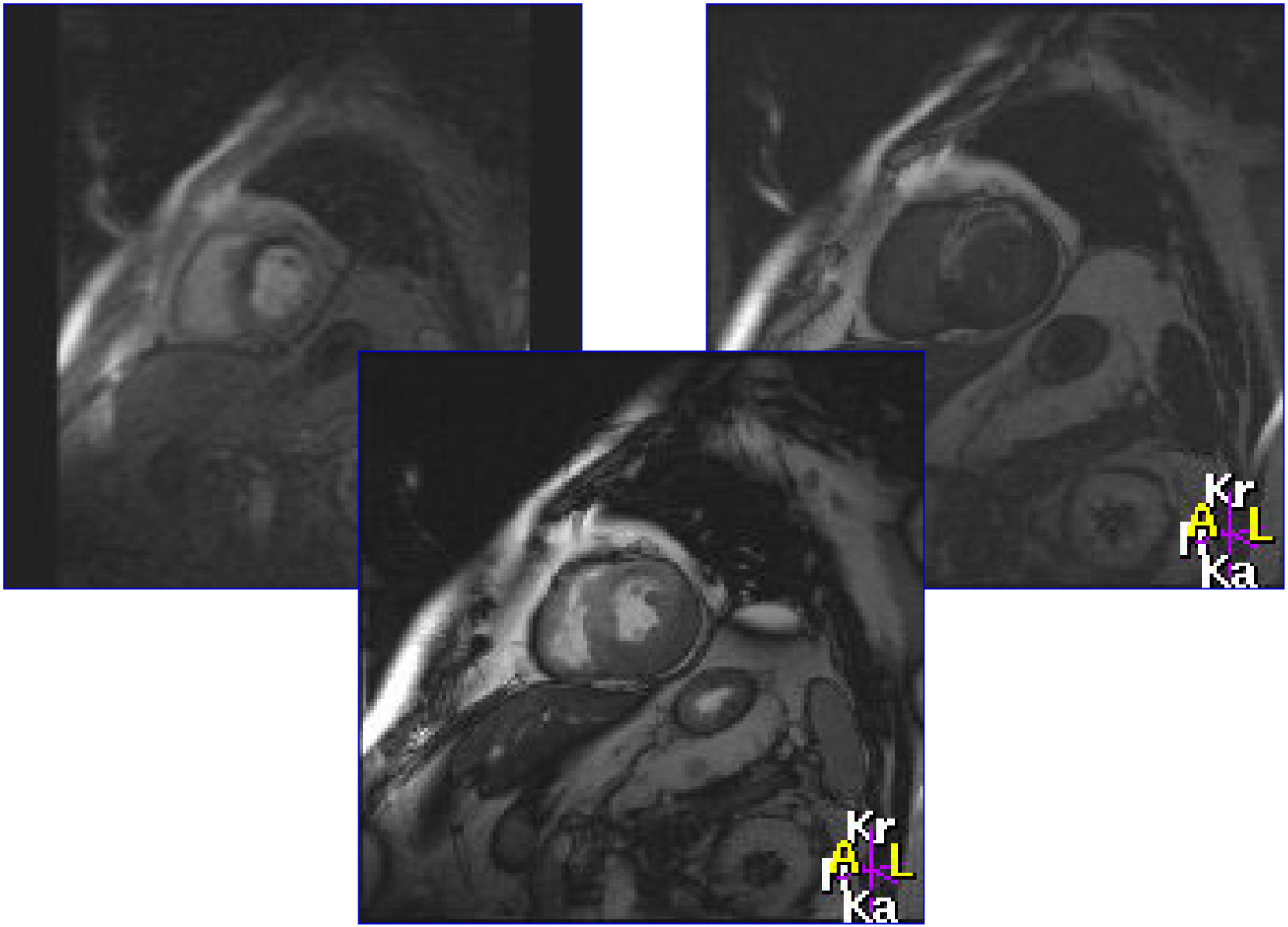
NSTEMI

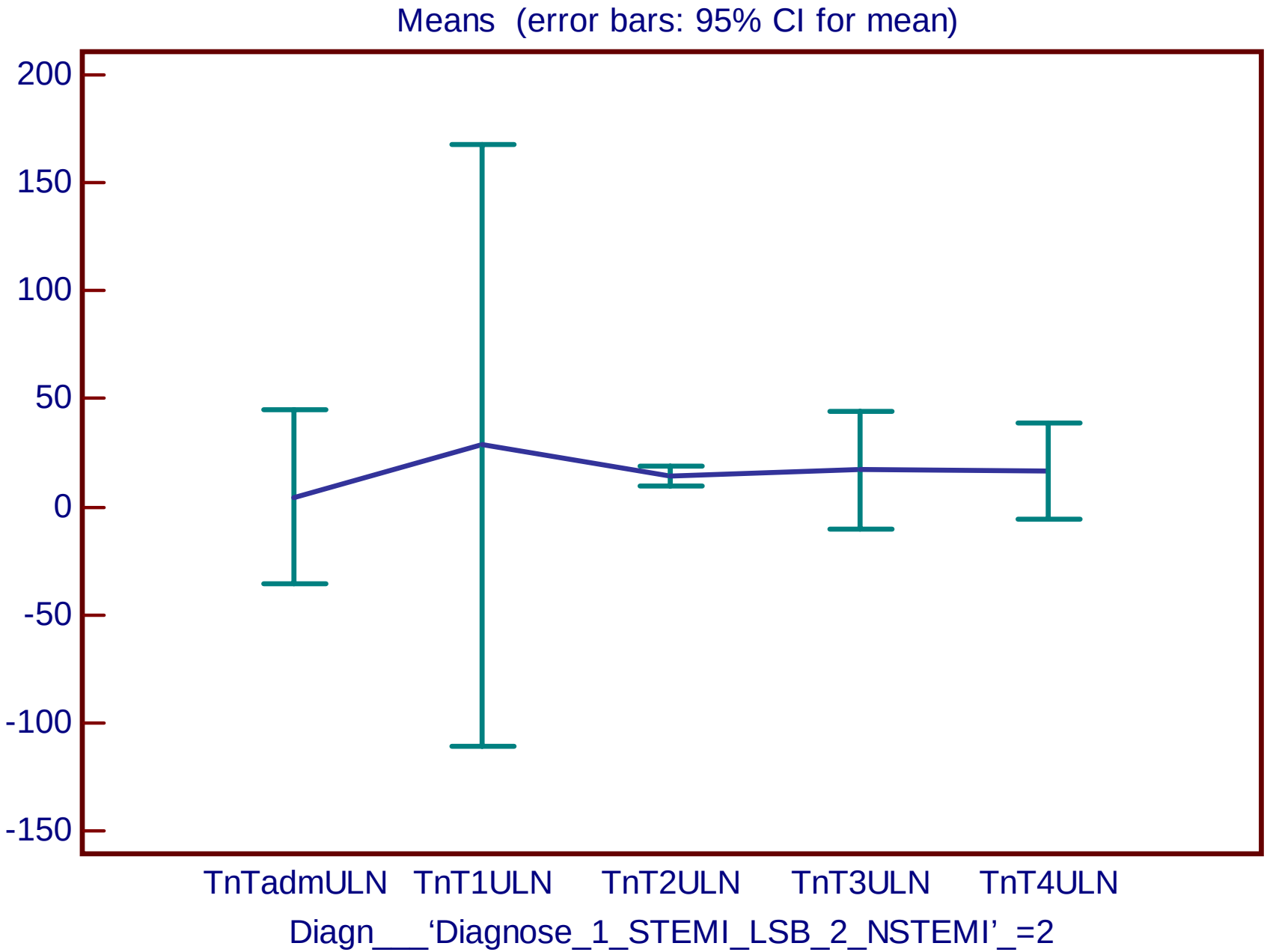

18
16
14
12
10
8
6
4
2
0
cTnT (µg/L)
56Y, female, NSTEMI
symptom to door: 60 (1h)
door to balloon: 420 (7h)
symptom to balloon: 480 (8h)
CK adm 678, CK peak 2779 U/L
TnT adm < 0,01, TnT peak 6,69 µg/L
BNP not available
Total occlusion of LCX (13), TIMI pre 0, TIMI post 2
MRI: 12% rel infarct mass, EF 69,4%
normal renal function: Krea at admission 0,69, Krea Clearance 137ml/min
CVRF: hypercholesterolemia, adiposity,
endpoint: tvPCI day 146
Case #19
Case #31
61Y, male, NSTEMI
symptom to door: 360min (6h)
door to balloon: 333min (5,55h)
symptom to balloon: 693min (11,55h)
90% stenosis of RCA (1), after PCI 0%, TIMI pre 3, TIMI post 3
CK adm 344 , CK peak: 1819 U/L
TnT adm 0,79, TnT peak 7,89 µg/L
BNP not available
MRI: 7 % rel infarct mass, EF 50,7%
renal failure: Krea at admission 1,4, Krea Clearance 58ml/min
CVRF: hypertension, hypercholesterolemia, diabetes
cTnTadm
Day 1
Day 2
Day 3
Day4


Late enhancment


TnT [µg/L] after 72 – 96 hours
6
5
4
3
2
1
0
0
20
40
60
80
100
120
140
Infarct size in gram
R^2 = 0.829, r = 0,910
r = 0.883 (Spearman)

MRT
-Microvascular obstruction-




Means (error bars: 95% CI for mean)
200
150
100
50
0
-50
-100
-150
TnTadmULN
TnT1ULN
TnT2ULN
TnT3ULN
TnT4ULN
Diagn___'Diagnose_1_STEMI_LSB_2_NSTEMI'_=2