Evaluation of the optimal myocardial infarction cutoff for the PATHFAST Troponin I assay of Mitsubishi Kagaku Iatron (MKI)

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Study Purpose

The objective of this study is to generate data for the determination of the optimal diagnostic cutoff for diagnosis of acute myocardial infarction with the PATHFAST Troponin I assay

Patients

Between June 1999 and February 2004, 1908 patients who underwent coronary angiography at the Department of Medicine II of the Johannes Gutenberg-University Mainz or the Bundeswehr Central Hospital Koblenz and who had at least 1 stenosis >30% diagnosed in a major coronary artery were enrolled in the AtheroGene study registry. A detailed description of the design of the AtheroGene

Study has been described in detail elsewhere (1). Briefly, the exclusion criteria were evidence of hemodynamically significant valvular heart disease, surgery, or trauma within the previous month, known cardiomyopathy, known cancer, febrile conditions, or use of oral anticoagulant therapy within the previous 4 weeks. The study was approved by the local ethics committee. Participation was voluntary, and each subject gave written, informed consent.

For ROC-analysis of optimal AMI cutoff of the PATHFAST TnI assay we selected 274 consecutive patients (72 female, median age: 70.0 a, age range: 44-84a; 202 male, median age: 64.5a, age range: 31-85a) of this study group with the following diagnoses:

1. stable angina pectoris (SAP, n=112)
2. non ST-elevation myocardial infarction (NSTEMI, n=52) and
3. ST-elevation myocardial infarction (STEMI, n=84)

In 168 patients a Troponin T value (Roche Diagnostics) was also available for ROC analysis.

Statistical Evaluation was performed in cooperation with the Institute of Medical Biometry, Epidemiology and Informatics of the Johannes Gutenberg-University Mainz. Data were analyzed with Receiver operating curve analysis /ROC).

Results

Data were valuated according to diagnosis (SAP, NSTEMI, STEMI) and time point (time elapsed since onset of pain). The following groups for comparison were used, each with three variations of the time point (all time points, <6 hours and >6 hours):

1. SAP vs. NSTEMI&STEMI and
2. SAP vs. STEMI

For comparison of the Pathfast TnI assay with the Roche Diagnostics TnT assay the same evaluation of data was done with a data set of 168 patients in which both TnI and TnT were available.

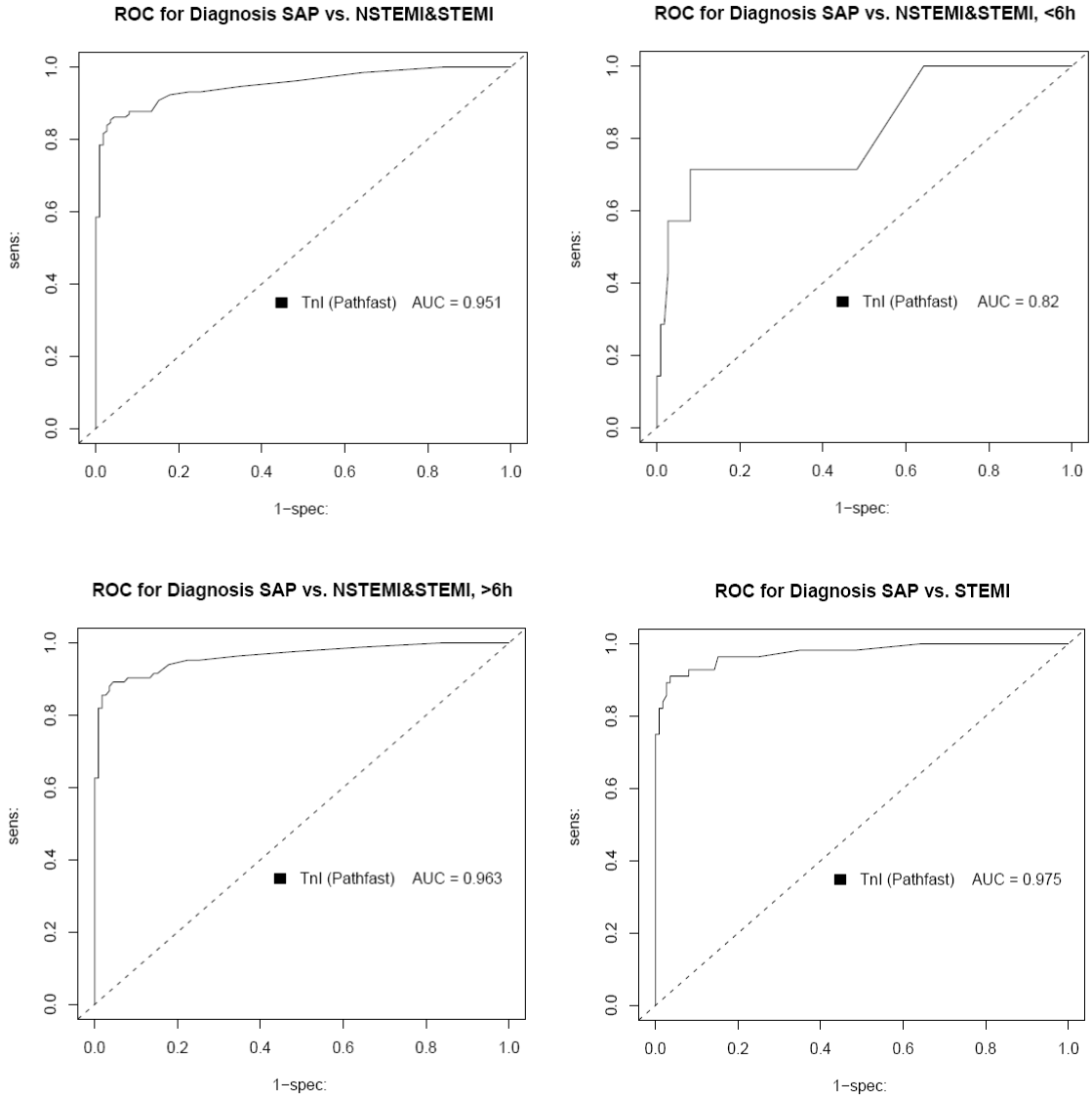
In Table 1 a synopsis of the areas under the curve (AUC) of all data is shown, the corresponding ROC curves are displayed below the table.

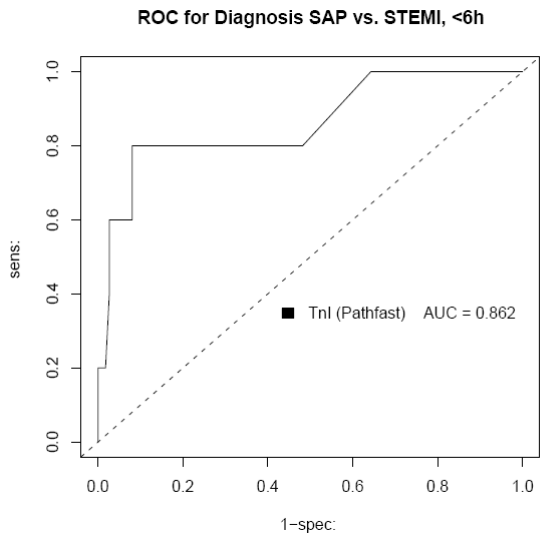
Best diagnostic performance was achieved, as expected, for the diagnosis of STEMI with chest pain for >6h. In comparison to the Roche TnT assay, the Pathfast TnI assay showed slightly higher AUCs at all time points and in all combinations.

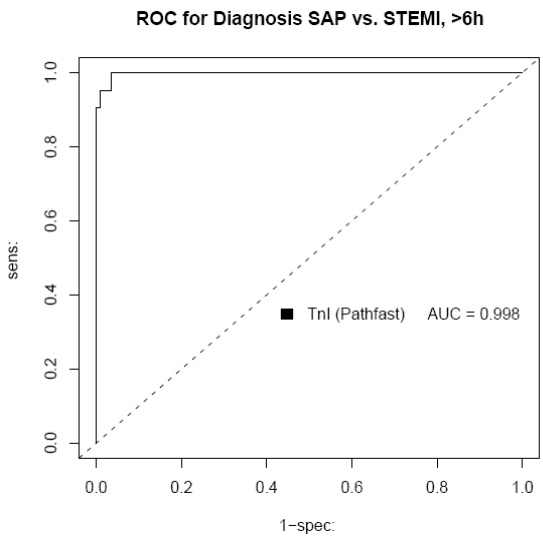
Table 1: Synopsis of ROC-Analysis data

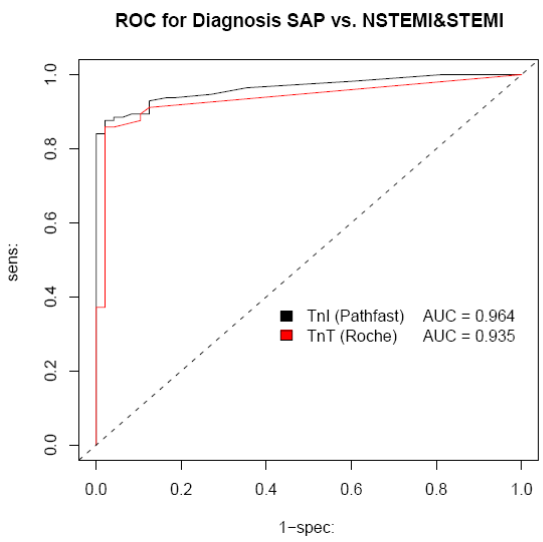
ROC neg	SAP	SAP	SAP	SAP	SAP	SAP	SAP	SAP	SAP	SAP	SAP	SAP
ROC pos	NSTEMI &STEMI	NSTEMI &STEMI	NSTEMI &STEMI	STEMI	STEMI	STEMI	NSTEMI &STEMI	NSTEMI &STEMI	NSTEMI &STEMI	STEMI	STEMI	STEMI
Time points	All	<6h	>6h	All	<6h	>6h	All	<6h	>6h	All	<6h	>6h
N	274						168					
AUC TnI	0.951	0.82	0.963	0.975	0.862	0.998	0.964	0.896	0.973	0.98	0.87	1.0
AUC TnT	-	-	-	-	-	-	0.935	0.86	0.953	0.943	0.854	0.99

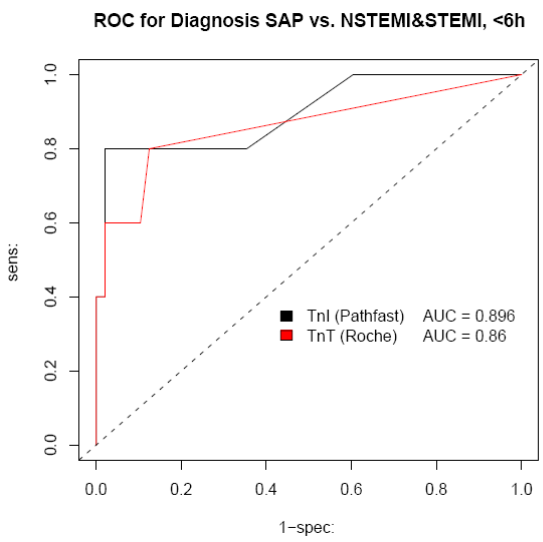
Figure 1a-l: ROC curves

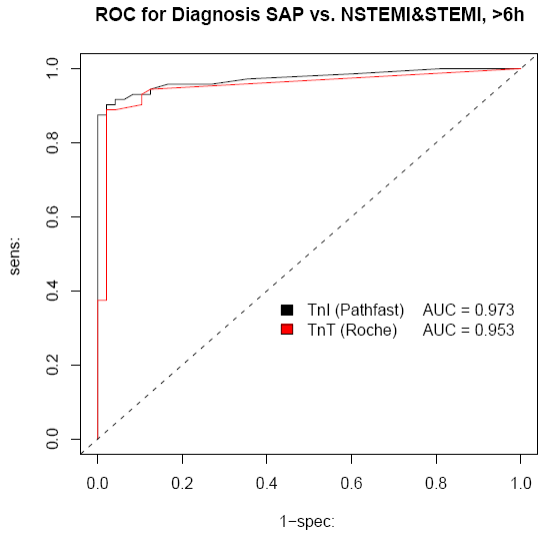


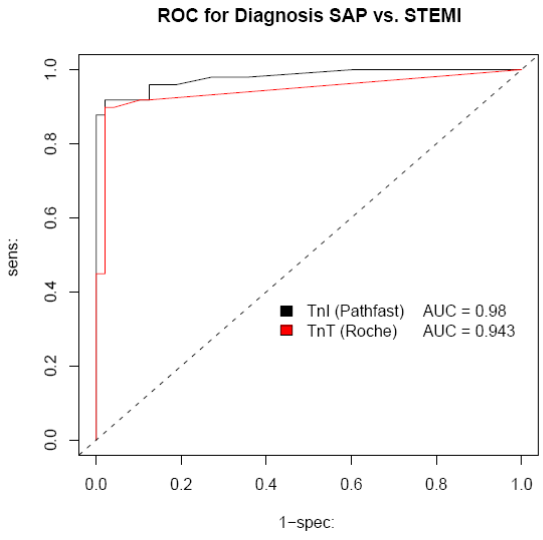

ROC for Diagnosis SAP vs. STEMI, <6h
sens:
1−spec:
TnI (Pathfast) AUC = 0.862

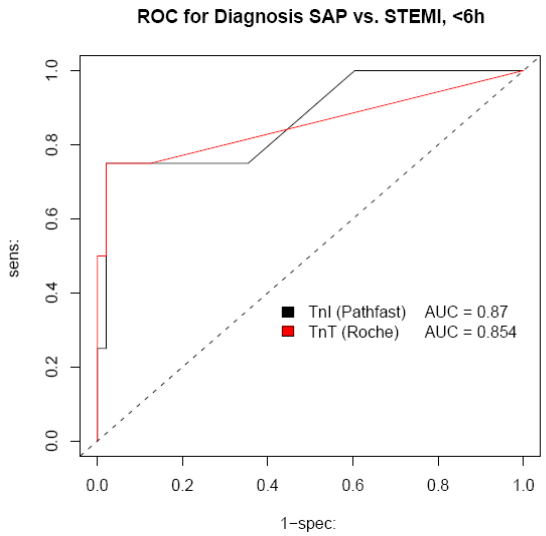

ROC for Diagnosis SAP vs. STEMI, >6h
sens:
1−spec:
TnI (Pathfast) AUC = 0.998

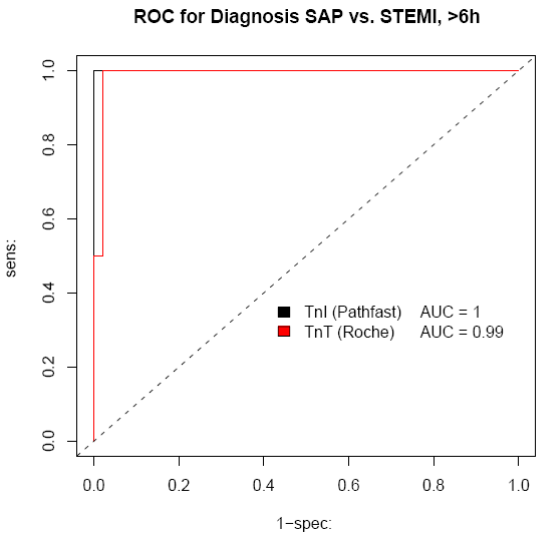

ROC for Diagnosis SAP vs. NSTEMI&STEMI
sens:
1−spec:
TnI (Pathfast) AUC = 0.964
TnT (Roche) AUC = 0.935


ROC for Diagnosis SAP vs. NSTEMI&STEMI, <6h
sens:
1−spec:
TnI (Pathfast) AUC = 0.896
TnT (Roche) AUC = 0.86


ROC for Diagnosis SAP vs. NSTEMI&STEMI, >6h
sens:
1−spec:
TnI (Pathfast) AUC = 0.973
TnT (Roche) AUC = 0.953


ROC for Diagnosis SAP vs. STEMI
sens:
1−spec:
TnI (Pathfast) AUC = 0.98
TnT (Roche) AUC = 0.943





Calculation of optimal cutoff, sensitivity and specificity was done for the Pathfast TnI assay and results are shown in table 2. Cutoffs were selected in two ways: first the cutoff with the highest sum of sensitivity and specificity was selected, in a second approach requested sensitivity was defined as >95% and the corresponding cutoffs and specificity data are displayed.

Table 2: Optimal cutoffs for Pathfast TnI and Roche TnT

PATHFAST Troponin I						
ROC neg	SAP	SAP	SAP	SAP	SAP	SAP
ROC pos	NSTEMI &STEMI	NSTEMI &STEMI	NSTEMI &STEMI	STEMI	STEMI	STEMI
Time points	All	<6h	>6h	All	<6h	>6h
N	274			196		
Highest sum of sensitivity and specificity						
Cutoff (ng/ml)	**0.0205**	0.0145	**0.0195**	**0.0205**	0.0145	**0.0205**
Sens.	**85.4**	71.4	**89.2**	**91.1**	80.0	**100**
Spec.	**96.4**	92.0	**95.5**	**96.4**	92.0	**96.4**
Sensitivity >95%						
Cutoff (ng/ml)	0.0035	-	0.0065	0.0085	0.0025	**0.0205**
Sens.	96.2	-	95.2	96.4	100	**100**
Spec.	51.8	-	77.7	84.8	35.7	**96.4**
ROCHE ELECSYS 2010 Troponin T						
ROC neg	SAP	SAP	SAP	SAP	SAP	SAP
ROC pos	NSTEMI &STEMI	NSTEMI &STEMI	NSTEMI &STEMI	STEMI	STEMI	STEMI
Time points	All	<6h	>6h	All	<6h	>6h
N	172			107		
Highest sum of sensitivity and specificity						
Cutoff (ng/ml)	**0.1**	0.015	**0.095**	**0.13**	-	**0.21**
Sens.	**85.6**	80.0	**88.9**	**89.8**	-	**100**
Spec.	**97.9**	87.5	**97.9**	**97.9**	-	**97.9**
Sensitivity >95%						
Cutoff (ng/ml)	-	-	0.015	-	-	0.21
Sens.	-	-	*94.4*	-	-	100
Spec.	-	-	87.5	-	-	97.9

Conclusion

Either looking for all time points in NSTEMI or only in STEMI patients as well as at time point >6h in both groups a **TnI value of 0.02 ng/ml** is the optimal cutoff for diagnosis of myocardial infarction.

Literature

1. Blankenberg S, Tiret L, Bickel C, Peetz D, Cambien F, Meyer J, Rupprecht HJ. Interleukin-18 is a strong predictor of cardiovascular death in stable and unstable angina. Circulation. 2002;106: 24–30.