Adding stress biomarkers to high sensitivity troponin measurements increases precision and efficacy of rapid rule out protocols for NSTEMI

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Background: NSTEMI may be ruled out in patients presenting with acute chest pain based on low baseline high sensitivity troponin (cTn) at admission. This procedure is limited by a low expected frequency of ruled out non-cardiac chest pain (NCCP) patients.

Purpose: To investigate if stress-induced biomarkers (glucose or copeptin) combined with cTn can increase the rate of NCCP ruled out without an unacceptable increase in incorrectly ruled out NSTEMI.

Method: 971 patients with suspected NSTE-ACS were included. Final diagnosis was adjudicated by two independent cardiologists using clinical data including routine cTnT. Additionally, baseline cTnI, cTnI from Singulex Clarity System (cTnI(sgx)), copeptin and glucose were measured. Diagnostic performance to rule out NSTEMI was compared between the ESC rule out algorithms for cTnT and cTnI(Abbott), a local cTnI(sgx) algorithm and different combinations of cTn with copeptin or glucose

Results: Median age 61 years, 60% male. 13% had NSTEMI, 12% had UAP and 60% NCCP. Distribution of copeptin and glucose concentrations (NSTEMI and NCCP) is shown in figure 1. Copeptin and cTnT produces an algorithm with lower miss rate for NSTEMI, increased rule out rate for NCCP and significantly higher AUC (DeLong test, p value <0.001) compared to the ESC algorithm (Table 1). cTnI(sgx) and copeptin showed higher rule out for NCCP and higher AUC (p value <0.001), however an increased rule out rate for NSTEMIs. Combining cTnI(Abbott) and glucose gave a similar miss rate for NSTEMI as ESC, but increased rule out rate for NCCP and higher AUC (p value <0.001).

Conclusion: Combining cTnT or cTnI(sgx) with copeptin; or cTnI with glucose, improves diagnostic precision and efficacy of rule out protocols for NSTEMI in patients presenting with acute chest pain.

Table 1. Diagnostic performance for ruling out NSTEMI by high sensitivity troponins alone and in combination with different stress induced biomarkers

Algorithm	Rule out rate		Sensitivity	NPV	Specificity	PPV	AUC
	NSTEMI, %	NCCP, %					
cTnT <5 ng/L	1.6	42.6	98.4	99.3	35.0	18.6	0.67
cTnT <7 ng/L and copeptin <9 ng/L	0.8	58.6	99.2	99.8	47.3	22.1	0.73
cTnI (sgx) <2 ng/L	0.8	50.5	99.2	99.7	42.5	20.6	0.71
cTnI (sgx) <4.35 ng/L and copeptin <9 ng/L	2.4	69.8	97.6	99.3	59.7	26.6	0.79
cTnI (Abbott) <2 ng/L	2.4	33.1	97.6	98.7	26.0	16.6	0.62
cTnI (Abbott) <13 ng/L and glucose <5.6 mmol/L	2.4	42.9	97.6	99.0	36.5	18.7	0.67

Figure 1. Median, 10 and 90 percentile for baseline copeptin and glucose concentrations in NSTEMI and NCCP patients

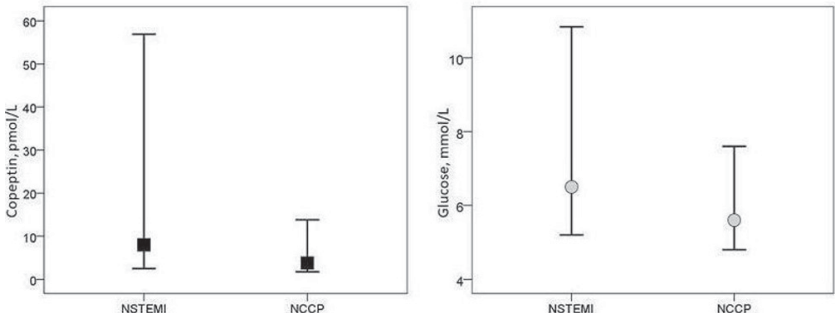

Figure 1