

1 Early Diagnosis of Myocardial Infarction in Patients with a History of 2 Coronary Artery Bypass Grafting

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69 **Abbreviations**

70 AMI – Acute myocardial infarction

71 CAD – Coronary artery disease

72 CABG – Coronary artery bypass grafting

73 hs-cTn – High-sensitivity cardiac troponin

74 MI – Myocardial infarction

75 NSTEMI – Non-ST-segment elevation myocardial infarction

76 PCI – Percutaneous coronary intervention

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79 Prompt identification of acute myocardial infarction (AMI) may be particularly challenging in
80 patients with prior coronary artery bypass grafting (CABG). The impact of prior CABG on the
81 diagnostic performance of high-sensitivity cardiac troponin (hs-cTnT/I) concentrations and the
82 European Society of Cardiology (ESC) 0/1h-algorithms is unknown.

83 To address this major gap in knowledge, we performed a secondary analysis from a prospective
84 international multicentre study enrolling adult patients presenting to the emergency department
85 with symptoms suggestive of AMI (ClinicalTrials.gov registry, NCT00470587).(1) Patients on
86 chronic dialysis, an unknown diagnosis after final adjudication and at least one elevated hs-
87 cTnT level possibly indicating AMI, as well as patients with chest pain onset or peak >12 hours
88 before presentation were excluded. According to the intended use, patients with ST-segment
89 elevation myocardial infarction (STEMI) were excluded when analyzing the diagnostic
90 performance of the ESC 0/1h-algorithms.(2,3) Final diagnoses were adjudicated by two
91 independent cardiologists applying the fourth universal definition of AMI using all available
92 medical records, cardiac imaging information, as well as study-specific assessments.(4)

93 Overall, 4015 patients were prospectively enrolled and eligible for the analysis of AMI
94 prevalence. Of these, 3860 patients qualified for the analysis of the diagnostic performance of
95 hs-cTnT/I concentrations, and 3054 patients for analysis of the hs-cTnT ESC 0/1h-algorithm.

96 Patients with prior CABG were older, more often men, more often had prior AMI and known
97 peripheral vascular disease, prior percutaneous coronary intervention, and known
98 cardiovascular risk factors. The prevalence of AMI was significantly higher in patients with
99 previous CABG (35% versus 18%; $p<0.001$). Patients with prior CABG had significantly
100 higher concentrations of hs-cTnT/I at presentation compared to patients without previous
101 CABG (e.g. hs-cTnT median (IQR) 19 (11, 42) ng/L versus 8 (4, 19) ng/L, $p<0.001$), which
102 was exclusively due to higher concentrations in patients with final diagnoses other than AMI

103 including heart failure and rhythm disorders (e.g. hs-cTnT median (IQR) 13 (9, 23) versus 6 (4,
104 11) ng/L; $p < 0.001$). Patients with AMI had much higher hs-cTnT/I concentrations as compared
105 to those with other final diagnoses, irrespective of prior CABG. The size of the index AMI as
106 quantified by peak local cTnT/I concentrations and peak study-specific hs-cTnT/I
107 concentrations was smaller in patients with prior CABG as compared to those without prior
108 CABG (e.g. hs-cTnT/99th percentile median (IQR) ratio 5.2 (2.6, 13.6) versus 7.4 (3.2, 20.9),
109 $p = 0.006$), which might possibly be related to the increased collateral flow provided by the
110 bypass grafts.

111 The diagnostic accuracy of hs-cTnT/I concentrations at presentation was high in patients with
112 prior CABG, but significantly lower compared to patients without prior CABG (hs-cTnT: AUC
113 0.87 [95%CI 0.82-0.91] versus AUC 0.94 [95%CI 0.93-0.95], $p = 0.001$; hs-cTnI: AUC 0.85
114 [95%CI 0.81-0.89] versus AUC 0.94 [95%CI 0.93-0.95]; $p < 0.001$). In patients with prior
115 CABG, the ESC hs-cTnT 0/1h-algorithm maintained very high negative predictive value (100
116 (94.6-100%)) and high positive predictive value (90.6 (81.0-95.6%)), but had lower efficacy
117 with more patients remaining in the observe zone (50% versus 21% compared to patients
118 without prior CABG; $p < 0.001$). Given the high percentage of patients with prior CABG
119 remaining in the observe zone, it is important to highlight the critical importance of detailed
120 clinical assessment, hs-cTn re-sampling at 3h, transthoracic echocardiography, and often also
121 coronary angiography in this subgroup of patients.

122 In conclusion, history of CABG substantially impacts on AMI incidence and the diagnostic
123 accuracy of hs-cTnT/I, while the safety of the hs-cTnT ESC 0/1h-algorithm remains very high.

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138 Figure Legend

139 **Figure 1. Diagnostic performance of hs-cTn and the ESC hs-cTnT 0/1h-algorithm**

140 Diagnostic accuracy of hs-cTnT/I concentrations at presentation for the diagnosis of AMI
141 according to the presence or absence of prior CABG (A). Diagnostic performance of the ESC
142 hs-cTnT 0/1h-algorithm in patients with prior CABG (B).

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144 NSTEMI – Non-ST-elevation myocardial infarction

145 Sens. – Sensitivity

146 Spec. – Specificity

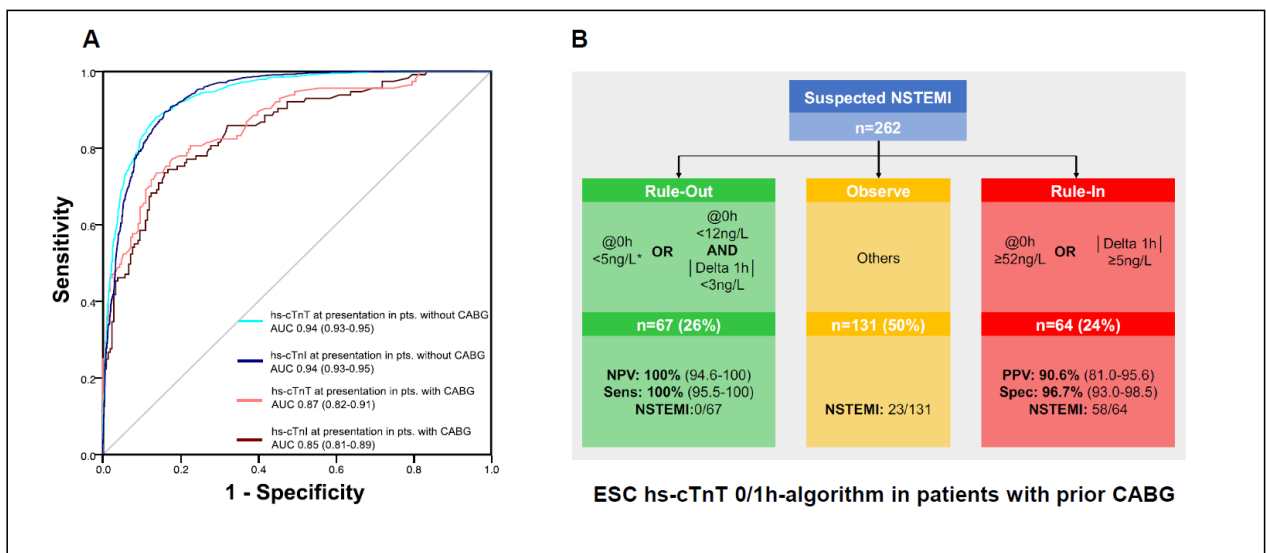
147 NPV – negative predictive value,

148 PPV – positive predictive value,

149 hs-cTnT/I – high-sensitivity cardiac troponin T/I

150 * if chest pain onset >3h

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