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Citation for published version:

Cooper, JG, Donaldson, LA, Coutts, AJ, Body, R & Mills, NL 2024, 'Pre-hospital T-MACS and HEART scores in the prediction of myocardial infarction: a prospective evaluation ', *Emergency Medicine Journal*.
<https://doi.org/10.1136/emmermed-2023-213639>

Digital Object Identifier (DOI):

[10.1136/emmermed-2023-213639](https://doi.org/10.1136/emmermed-2023-213639)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Emergency Medicine Journal

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**Pre-hospital T-MACS and HEART scores in the prediction
of myocardial infarction – a prospective evaluation**

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FUNDING AND DECLARATIONS

The study was supported financially by the Digital Health & Care Institute (DHI) (Reference DHI/MCADAM), Scotland and by the NHS Grampian Endowment Fund (Grant Number N0042903) and the University of Aberdeen contributed to the design and administration of the study. The funders had no role in study design, data collection, or interpretation, or the writing of the report. JGC was supported by a National Research Scotland Clinical Research Fellowship. NLM is supported by the British Heart Foundation through a Chair Award, Programme Grant, and Research Excellence Award (CH/F/21/90010, RG/20/10/34966, RE/18/5/34216).

COMPETING INTEREST STATEMENT

RB has undertaken consultancy with Roche, Abbott, Siemens, Beckman Coulter, Radiometer, Aptamer Group, and Lumira Dx, has recent research grants with Abbott Point of Care and Siemens and has conducted research involving donation of reagents by Roche, all unrelated to this work. NLM has received research grants to the University of Edinburgh, and honoraria or consultancy from Abbott Diagnostics, Roche Diagnostics, Siemens Healthineers, and LumiraDx that are unrelated to this work. None of the other authors have any competing interests to declare.

ACKNOWLEDGMENTS

We are particularly indebted to the following people Professor James Ferguson, Ms Kim Black, Ms Kate Livock, Ms Judith Horrill, Dr Elaine Davidson, Dr Neil Scott, Professor Amanda Lee, Dr Takeshi Fujisawa, Dr Kuan Ken Lee and Dr Anoop Shah for their considerable help in the delivery of this project. We would also like to acknowledge the invaluable contribution of all the participating Scottish Ambulance Service (SAS) paramedics and technicians as well as the support of the regional and national SAS managerial structures. We are also thankful for the involvement of numerous medical, nursing, reception and portering staff within the Emergency Department of Aberdeen Royal Infirmary and the assistance of Gary Robinson, Chaloner Chute and Susan Scotland from the DHI.

ETHICAL STATEMENT

This study was approved by the National Ethics Committee (REC 14/NS/1037), registered in the Research Registry (UIN 2671), and was conducted in accordance with the Declaration of Helsinki.

49 CONTRIBUTORSHIP STATEMENT

50 JGC and RB conceived the study and its design. JGC, LAD and AJC acquired the data. JGC
51 performed the analysis. JGC, RB and NLM interpreted the data. JGC, RB and NLM drafted the
52 manuscript. All authors reviewed the manuscript critically for intellectually important content and
53 provided their final approval of the version to be submitted. All authors are accountable for the work.
54 JGC is the guarantor.

55 PRESENTATION

56 These results have not been presented

57

58 DATA SHARING STATEMENT

59 No additional data available

60

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65 **Word Count** **599** (600)

66 **Figures and Tables** **2** (2)

67 **References** **6** (6)

68

69 Chest pain suspicious for an acute myocardial infarction (MI) is a common reason for
70 emergency ambulance contact. Most patients have a non-diagnostic electrocardiogram and
71 transport to hospital for troponin testing is the rule. In the Emergency Department (ED), tools
72 such as the T-MACS decision aid (1) and the HEART score (2) are used to identify those at
73 low-risk of MI and consideration of early discharge. Recently, the HE-MACS decision aid
74 (3) and the HEAR score (4) have been developed, aiming to identify low-risk patients
75 without troponin testing. We previously demonstrated the feasibility of paramedics using the
76 HEAR and HEART score (5,6), but performance did not enable safe rule-out of MI in this
77 setting. Whether the T-MACS or HE-MACS scores would perform better and enable
78 paramedics to manage low-risk patients without hospital transfer is uncertain.

79 The Ambulance Cardiac Chest pain Evaluation in Scotland Study (ACCESS) was performed
80 in northeast Scotland (5). Patients with chest pain suspicious for MI were approached by
81 study-trained paramedics. A subset of the study population provided contemporaneous pre-
82 hospital data for HE-MACS, HEAR and HEART and T-MACS (Supplementary Material)
83 scores and had blood drawn for later testing with the Abbott ARCHITECT_{STAT} high
84 sensitivity cardiac troponin I assay. This assay has a limit of detection of 2 ng/L (LOD), an
85 optimised rule-out threshold of 5 ng/L and sex-specific 99th percentile upper reference limits
86 (URL) of 16 ng/L (women) and 34 ng/L (men).

87 Patients were followed up for type 1, type 4b or type 4c MI or cardiac death at 30-days. All
88 patients with myocardial injury and all deaths were independently adjudicated by two
89 cardiologists as previously described (5). We calculated the sensitivity, specificity, negative
90 predictive value (NPV), and positive predictive value (PPV) with 95% confidence intervals
91 (CI) for score thresholds that defined low-risk: HEAR ≤ 1 , HEART, and modified HEART
92 (troponin component 0 if $< \text{LOD}$, 1 if between LOD and URL, 2 if $> \text{URL}$) ≤ 3 , and the very-
93 low-risk (VLR) threshold for HE-MACS and T-MACS.

94 Of 261 eligible patients, 247 (mean 66 [standard deviation 16] years, 44% women) had
95 complete data for all scores, of whom 40 (16%) had a MI or cardiac death at 30-days (Figure
96 1) (Tables S1 and S2). Both the HEAR score ≤ 1 and HE-MACS VLR outcome had 100%
97 (95% CI 91.2 to 100%) sensitivity, but only identified 4% of patients as low-risk. A HEART
98 score ≤ 3 identified 26% of patients as low-risk with a sensitivity of 92.5% (95% CI 80.1 to
99 97.4%) and NPV of 95.3% (95% CI 87.1 to 95.3%). A modified HEART score ≤ 3 identified
100 fewer patients as low-risk (16%), but with a sensitivity and NPV of 100%. Similarly, T-
101 MACS identified 20% of patients as very low-risk with a sensitivity and NPV of 100%
102 (Table 1).

103 In patients with chest pain in the pre-hospital setting, our findings demonstrate that
104 paramedics may be able to use the T-MACS decision aid and a modified HEART score ≤ 3 to
105 recognise 1 in 5 patients as low-risk of MI or cardiac death with excellent sensitivity and
106 NPV. Strategies not involving troponin testing are clearly attractive, but only identified 1 in
107 25 patients as low-risk, something that may hinder adoption of those methods into practice.
108 We acknowledge that incorporation of a core laboratory performed cardiac troponin test into
109 pre-hospital clinical assessment is theoretical. However, our results are very similar to those
110 described in a recent multicentre diagnostic study (7) and provide some external validation to
111 these findings. The T-MACS decision aid and modified HEART score are promising tools to
112 evaluate further in the pre-hospital setting, ideally using a high-sensitivity troponin test at the
113 point of care.

114

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132

133 FIGURES and TABLES

134

135 *Figure 1.* Patient Flow Chart

136

137 **Table 1.** Rule-out performance of low-risk strategies for myocardial infarction or cardiac death at 30-days.

| Rule-out | Proportion low-risk | Myocardial Infarction or Cardiac Death at 30 days | | No Myocardial Infarction or Cardiac Death at 30 days | | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) |
|-------------------------|---------------------|---|----------|--|----------|----------------------|----------------------|-------------------|-------------------|
| | | Not low-risk | Low-risk | Not low-risk | Low-risk | | | | |
| HE-MACS VLR | 9 (4%) | 40 | 0 | 198 | 9 | 100% (91.2-100) | 4.3% (2.3-8.1) | 16.8% (12.6-22.1) | 100% (70.1-100) |
| T-MACS VLR | 50 (20%) | 40 | 0 | 157 | 50 | 100% (91.2-100) | 24.2% (18.8-30.4) | 20.3% (15.3-26.5) | 100% (92.9-100) |
| HEAR ≤ 1 | 11 (4%) | 40 | 0 | 196 | 11 | 100% (91.2-100) | 5.3% (3.0-9.3) | 16.9% (12.7-22.3) | 100% (74.1-100) |
| HEAR ≤ 3 | 69 (28%) | 35 | 5 | 143 | 64 | 87.5% (73.9-94.5) | 30.9% (25.0-37.5) | 19.7% (14.5-26.1) | 92.8% (84.1-96.9) |
| HEART ≤ 3 | 64 (26%) | 37 | 3 | 146 | 61 | 92.5% (80.1-97.4) | 29.5% (23.7-36.0) | 20.2% (15.0-26.6) | 95.3% (87.1-98.4) |
| Modified HEART ≤ 3 | 39 (16%) | 40 | 0 | 168 | 39 | 100% (91.2-100) | 18.8% (14.1-24.7) | 19.2% (14.5-25.1) | 100% (91.0-100) |

138 Abbreviations: CI = confidence interval; HE-MACS = history and electrocardiogram only – Manchester acute coronary syndromes decision aid; LR = likelihood ratio; NPV =
 139 negative predictive value; PPV = positive predictive value; T-MACS = troponin only – Manchester acute coronary syndromes decision aid; VLR = very low risk.
 140