DATA SUPPLEMENT

**A novel high-sensitivity cardiac troponin I assay in patients with suspected acute coronary syndrome**

Andrew R Chapman MD, 1 Takeshi Fujisawa PhD, 1 Kuan Ken Lee MD, 1

Jack Andrews MD,1 Atul Anand MD, 1 Dennis Sandeman MSc, 1 Amy V Ferry BSc, 1

Stacey Stewart MN, 1 Lucy Marshall MSc, 1 Fiona E Strachan PhD, 1 Alasdair Gray MD, 2,3

David E Newby MD PhD, 1Anoop SV Shah MD, 1 Nicholas L Mills MD PhD1

*1BHF Centre for Cardiovascular Science, University of Edinburgh, United Kingdom*

*2Department of Emergency Medicine, Royal Infirmary of Edinburgh, United Kingdom*

*3EMERGE Research Group, Royal Infirmary of Edinburgh, United Kingdom*

**Running title:** *Novel high-sensitivity troponin assay in acute coronary syndrome*

**Address for correspondence:**

Dr Andrew R Chapman

BHF/University Centre for Cardiovascular Science

Chancellor’s Building

University of Edinburgh

Edinburgh EH16 4SB

United Kingdom

Phone: +44 131 242 6431

Fax: +44 131 242 6379

E-mail: [a.r.chapman@ed.ac.uk](mailto:a.r.chapman@ed.ac.uk)

Twitter: @chapdoc1

**Supplemental figures and tables: 7**

**Supplemental appendices: 1**

**Figure S1 – Flow diagram with identification of the study population**



**Figure S2 – Diagnostic performance of the HighSTEACS pathway in pre-specified subgroups**

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*Vertical dashed line illustrates central estimate of NPV for the pathway*

**Figure S3 – Diagnostic performance of the ESC 3-hour pathway in pre-specified subgroups**

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*Vertical dashed line illustrates central estimate of NPV for the pathway*

**Figure S4 – Diagnostic performance of the ESC 1-hour pathway in pre-specified subgroups**

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*Vertical dashed line illustrates central estimate of NPV for the pathway*

**Table S1.** Available blood samples and median time of sampling

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Presentation** | **3 hours from presentation** | **6 – 12 hours from presentation** | **1 hour from first sample** |
| **Time from arrival to sample (minutes)**  *Median (IQR)* | 28 (15 – 46) | 176 (146-205) | 416 (246-605) | 65 (60 – 73) |
| **Proportion of patients with samples available**  *% (n)* | 100 (1,920) | 95.3 (1,829) | 51.4 (987) | 21 (406) |
| **Sample rules** | All samples included | All samples included | All samples included | Included if ≥ 30 and ≤90 minutes from time of first sample |

**Table S2.** Diagnostic performance of four rule out pathways using the single diagnostic threshold (>45 ng/L)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Negative predictive value (95% CI) | Sensitivity  (95% CI) | Positive predictive value (95% CI) | Specificity  (95% CI) | Rule out(%) | Observe (%) | Rule in (%) |
| High-STEACS  (n=1,920) | 99.5 (99-99.8) | 97.7 (95.9-99.2) | 38.8 (35.2-42.4) | 73.9 (71.8-76) | 63.6% | NA | 36.4% |
| ESC 0 / 1 hour  algorithm  (n=406) | 99.0 (97.6-99.8) | 92.2 (83.0-99.4) | 77.6 (61.1-90.5) | 98.2 (96.8-99.4) | 64.5% | 28.6% | 6.9% |
| ESC 0 / 3 hour  algorithm  (n=1,920) | 97.8 (96.9-98.5) | 90.1 (86.6-93.5) | 37.4 (33.8-41.1) | 74.5 (72.4-76.6) | 65.2% | NA | 34.8% |

*Diagnostic metrics for the High-STEACS and ESC 0/3 hour algorithm contain all patients (n=1,920)*

*Diagnostic metrics for the ESC 0 / 1 and 0 / 2 algorithm exclude patients in the ‘observe zone’ and correspond to ‘rule out’ (NPV / sensitivity) and rule in (PPV / specificity) zones.*

*ESC – European Society of Cardiology, CI – confidence interval.*

**Table S3.** Diagnostic performance of three rule out pathways for a composite outcome of type 1 or type 2 myocardial infarction or myocardial injury or cardiac death at 30 days.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Negative predictive value (95% CI) | Sensitivity  (95% CI) | Positive  predictive value (95% CI) | Specificity  (95% CI) | Rule out (%) | Observe (%) | Rule in (%) |
| High-STEACS  (n=1,920) | 99.5 (99.0-99.8) | 98,2 (96.9-99.4) | 51.7 (48.0-55.4) | 78.1 (76.1-80.2) | 63.4% | NA | 36.6% |
| ESC 0 / 1 hour  algorithm  (n=406) | 99.0 (97.6-99.8) | 93.8 (86.3-99.6) | 91.4 (79.0-98.5) | 99.3 (98.4-100) | 64.5% | 28.6% | 6.9% |
| ESC 0 / 3 hour  algorithm  (n=1,920) | 97.0 (96.0-97.9) | 89.9 (86.8-92.9) | 49.4 (45.6-53.2) | 78.1 (76.0-80.1) | 65.0% | NA | 35.0% |

*Diagnostic metrics for the High-STEACS and ESC 0/3 hour algorithm contain all patients (n=1,920)*

*Diagnostic metrics for the ESC 0 / 1 and 0 / 2 algorithm exclude patients in the ‘observe zone’ and correspond to ‘rule out’ (NPV / sensitivity) and rule in (PPV / specificity) zones.*

*ESC – European Society of Cardiology, CI – confidence interval.*

**Appendix 1. Additional information on diagnostic adjudication**

Criteria for adjudication of patients with myocardial necrosis

|  |  |
| --- | --- |
| **Type 1 myocardial infarction** | Myocardial necrosis (any cardiac troponin I [cTnI] concentration above the upper reference limit) with rise and or fall in cTnI concentration where serial testing was available AND symptoms OR signs of myocardial ischaemia |
| **Type 2 myocardial infarction** | Myocardial necrosis (any cTnI concentration above the upper reference limit) with rise and or fall in cTnI concentration where serial testing was available AND symptoms OR signs of myocardial ischaemia AND evidence of increased oxygen demand (e.g. tachyarrhythmia, hypertrophy) or reduced supply (e.g. hypotension, hypoxia or anaemia) in context of alternative clinical diagnosis |
| **Myocardial injury** | Myocardial necrosis (any cTnI concentration above the upper reference limit) without symptoms OR signs of myocardial ischaemia in context of alternative clinical diagnosis |

*The process of adjudication was conducted by two cardiologists independently. Both had access to the electronic patient record. The adjudicated diagnosis was reached by evaluating the attending clinicians documentation of the presenting complaint, past medical history, cardiovascular risk factors and clinical examination findings including routine observations (pulse, blood pressure, pulse oximetry, temperature and conscious level). All investigation results undertaken by the attending clinician were available for review, including biochemistry and haematology results, the 12 lead electrocardiogram, echocardiogram, chest X-ray and invasive coronary angiography findings when performed. Both adjudicating cardiologists had access to the final discharge letter documenting the attending clinicians’ final diagnosis.*