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Clinical decision support using machine learning and cardiac troponin for the diagnosis of myocardial infarction

Martin P Than, MD,[1] John W Pickering PhD,[1,2] Johannes Mair, MD,[3]
Nicholas L. Mills, MBChB, PhD[4,5] on behalf of the Study Group on Biomarkers of the Association for Acute CardioVascular Care of the ESC

[1] Emergency Department, Christchurch Hospital, Christchurch, New Zealand
[2] Christchurch Heart Institute, Department of Medicine, University of Otago, Christchurch, New Zealand
[3] Department of Internal Medicine III - Cardiology and Angiology, Innsbruck Medical University, Innsbruck, Austria
[4] BHF Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, United Kingdom
[5] Usher Institute, University of Edinburgh, Edinburgh, United Kingdom

Corresponding author:
Dr Martin Than
Emergency Department
Christchurch Hospital
2 Riccarton Avenue
Christchurch 8014
New Zealand
Email address: martin@thanstedman.onmicrosoft.com

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Current assessment of chest pain and possible myocardial infarction is based on cardiac troponin (cTn) measurement, electrocardiogram (ECG) and either structured or subjective risk assessment. Pathway performance varies with patient age, sex, and ethnicity, and the time of blood sampling from symptom onset and between samples. This heterogeneity is not accounted for in strategies using fixed cTn thresholds for all patients or in those that categorise patients into two to four risk groups. This compartmentalisation at best crudely recognises risk differences due to demographics or small variation in cTn results or timing. It requires considerable clinical experience for the human brain to accurately weigh all of these factors when decision-making. Machine learning (ML) is a quantitative and reproducible way to combine multiple variables to improve predictive accuracy.

There are multiple ML methodologies available of which most are variations of statistical regression modelling. Generally, they allow for individualised risk assessment by combining variables, both quantitative and categorical. They account for non-linear complex interactions between variables. ML can also incorporate temporal variation such as the rate of change in troponin concentration. This is important because contemporary pathways rely on fixed absolute or relative change in cTn thresholds, which require consistency in the timing of blood sampling and is not always possible in a busy Emergency Department. In contrast, ML can account for variation in the time intervals between blood draws.

Three ML approaches that estimate the probability of myocardial infarction in the Emergency Department have been derived and validated: MI[3] (Myocardial-Ischaemic-Injury-Index), CODE-

ACS (Collaboration for the Diagnosis and Evaluation of Acute Coronary Syndrome), and ARTEMIS (ARTificial intelligencE in suspected Myocardial Infarction Study).[1-3] MI[3] incorporates age, sex and paired cTnI measurements over 1-3 hours. A low MI[3] score identified 69.5% of patients as low probability after serial testing with a negative predictive value (NPV) of 99.7% and sensitivity of 97.8%.[1] A high MI[3] score identified 10.6% of patients as high probability, with a positive predictive value (PPV) of 71.7% and specificity of 96.7%. The MI[3] score performed better than a conventional 0/3-hour cTn pathway using the 99th percentile. CoDE-ACS can be calculated using a single cTn measurement and incorporates additional variables including age, sex, comorbidities, previous ischemic heart disease, chest pain, time from symptom onset, ECG, blood pressure, and pulse rate.[2] Following a single cTn measurement, a low CoDE-ACS score identified twice as many patients as low-probability as a low cTn threshold (61% *versus* 27%) with a similar NPV (99.6% *versus* 99.7%) and sensitivity of (98.3% *versus* 97.9%). A high CoDE-ACS score was superior to the use of sex-specific 99th percentile with PPVs of 85.1% and 63.6%, respectively. CoDE-ACS with a single or serial cTn measurement was more effective than current guideline recommended pathways.[3] ARTEMIS was trained using multiple assays and combines age, sex, symptom onset time, ECG, and several other cardiovascular risk factors with cTn.[4] The probability of myocardial infarction was calculated with high accuracy, achieving a PPV >70% for all but one assay.

A good clinical decision aid is easy to use, fits well within the clinician's workflow, and saves time. Unfortunately, user interface, and consequently experience, are often poor. Key history and presentation variables are needed for accurate prediction and should be, but rarely are, incorporated into the medical record. Wayfind is an example of such a decision support tool.[5] It provides numerical and visual depiction using an icon array of probabilities calculated using local pathways. Depending on local acceptability and resource availability, it can provide specific patient management guidance tailored to the institution. Workload is reduced by providing direct links to further tasks (e.g. ordering further tests, or printing information for a patient). Importantly, the tool will output an easy-to-read medical record, which makes the patient management decision less burdensome.

Ideally ML algorithms would undergo verification, particularly calibration, in each hospital before implementation.[6] This will be challenging for most hospitals, but decision support tools that collect the relevant data could achieve this if data are linked to clinical outcomes. This is the basis of a learning health care system that can evolve in time, accounting for changing demographics of patients, which has major potential to improve both effectiveness and safety of decision making for patients with possible myocardial infarction.

Declarations of Interest

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Wayfind Health. MPT has received research support and honoraria from Abbott Diagnostics, Beckman Coulter, Ortho-Quidel, Radiometer, Roche Diagnostics and Siemens Healthineers.

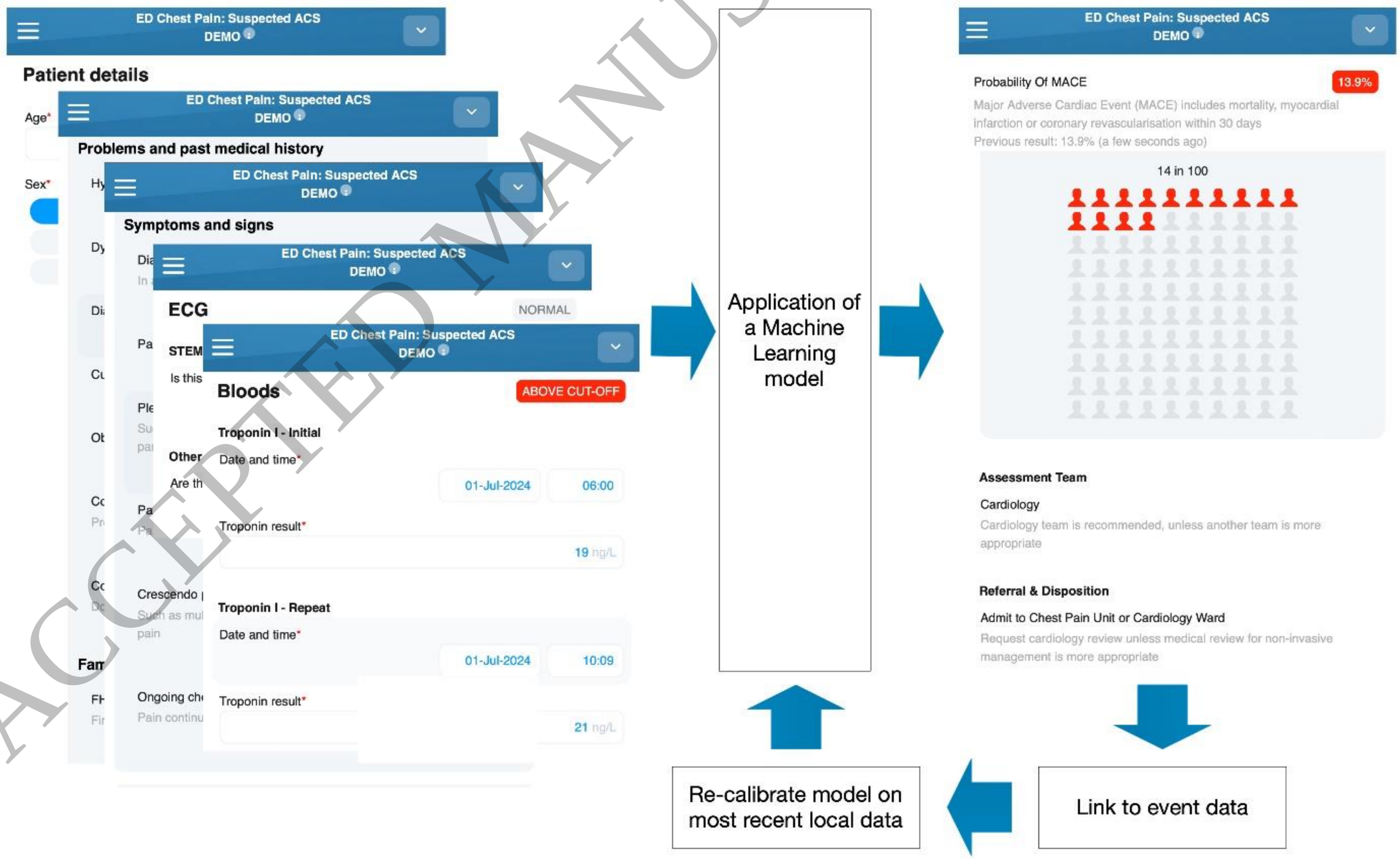
Figure legend

Figure 1. Illustration of the retraining of machine learning models to support clinical decisions in patients with possible myocardial infarction

Visual representation depicts sequential data capture of key variables in the assessment of a patient with possible myocardial infarction. Overlapping windows depict user-interfaces for patient demographics, presenting problem and past medical history, symptoms and signs, the electrocardiogram and cardiac troponin results. A machine learning algorithm estimates diagnostic probabilities in the background and presents an individualised probability of myocardial infarction both numerically and visually (using an icon array display). Recommended actions for the clinician are given based on this probability. Once risk predictions are linked to data on patient outcomes, the model can be re-calibrated to improve accuracy. The combination of routine high-fidelity data capture matched to prediction, outcomes and re-calibration allows for the creation of a learning healthcare system.

Images from Wayfind.Health, used with permission.

Figure 1.


ED Chest Pain: Suspected ACS
DEMO
Patient details
Age*
Sex*
Problems and past medical history
Symptoms and signs
ECG
NORMAL
Bloods
ABOVE CUT-OFF
Troponin I - Initial
Date and time*
01-Jul-2024
06:00
Troponin result*
19 ng/L
Troponin I - Repeat
Date and time*
01-Jul-2024
10:09
Troponin result*
21 ng/L
Crescendo
Ongoing ch
Pain continu
Application of a Machine Learning model
Probability Of MACE
13.9%
Major Adverse Cardiac Event (MACE) includes mortality, myocardial infarction or coronary revascularisation within 30 days
Previous result: 13.9% (a few seconds ago)
14 in 100
Assessment Team
Cardiology
Cardiology team is recommended, unless another team is more appropriate
Referral & Disposition
Admit to Chest Pain Unit or Cardiology Ward
Request cardiology review unless medical review for non-invasive management is more appropriate
Link to event data
Re-calibrate model on most recent local data

References

1. Than MP, Pickering JW, Sandoval Y, Shah ASV, Tsanas A, Apple FS, et al.; MI[3] Collaborative. Machine Learning to Predict the Likelihood of Acute Myocardial Infarction. *Circulation.* 2019;140(11):899-909.
2. Doudesis D, Lee KK, Boeddinghaus J, Bularga A, Ferry AV, Tuck C, et al.; CoDE-ACS Investigators. Machine learning for diagnosis of myocardial infarction using cardiac troponin concentrations. *Nat Med.* 2023;29(5):1201-1210.
3. Boeddinghaus J, Doudesis D, Lopez-Ayala P, Lee KK, Koechlin L, Wildi K, et al.; CoDE-ACS and APACE Investigators. Machine Learning for Myocardial Infarction Compared With Guideline-Recommended Diagnostic Pathways. *Circulation.* 2024;149(14):1090-1101.
4. Neumann JT, Twerenbold R, Ojeda F, Aldous SJ, Allen BR, Apple FS, et al; ARTEMIS study group. Personalized diagnosis in suspected myocardial infarction. *Clin Res Cardiol.* 2023;112(9):1288-1301.
5. Wayfind: a decision support tool for health professionals. https://wayfind.health/ (accessed July 1st 2024)
6. Doudesis D, Lee KK, Yang J, Wereski R, Shah ASV, Tsanas A, et al.; High-STEACS Investigators. Validation of the myocardial-ischaemic-injury-index machine learning algorithm to guide the diagnosis of myocardial infarction in a heterogenous population: a prespecified exploratory analysis. *Lancet Digit Health.* 2022;4(5):e300-e308.