Development and validation of an artificial neural network algorithm to predict mortality and admission to hospital for heart failure after myocardial infarction: a nationwide population-based study

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Summary

Background Patients have an estimated mortality of 15–20% within the first year following myocardial infarction and one in four patients who survive myocardial infarction will develop heart failure, severely reducing quality of life and increasing the risk of long-term mortality. We aimed to establish the accuracy of an artificial neural network (ANN) algorithm in predicting 1-year mortality and admission to hospital for heart failure after myocardial infarction.

Methods In this nationwide population-based study, we used data for all patients admitted to hospital for myocardial infarction and discharged alive from a coronary care unit in Sweden (n=139 288) between Jan 1, 2008, and April 1, 2017, from the Swedish Web system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDHEART) nationwide registry; these patients were randomly divided into training (80%) and testing (20%) datasets. We developed an ANN using 21 variables (including age, sex, medical history, previous medications, in-hospital characteristics, and discharge medications) associated with the outcomes of interest with a back-propagation algorithm in the training dataset and tested it in the testing dataset. The ANN algorithm was then validated in patients with incident myocardial infarction enrolled in the Western Denmark Heart Registry (external validation cohort) between Jan 1, 2008, and Dec 31, 2016. The predictive ability of the model was evaluated using area under the receiver operating characteristic curve (AUROC) and Youden’s index was established as a means of identifying an empirical dichotomous cutoff, allowing further evaluation of model performance.

Findings 139 288 patients who were admitted to hospital for myocardial infarction in the SWEDHEART registry were randomly divided into a training dataset of 111 558 (80%) patients and a testing dataset of 27 730 (20%) patients. 30 971 patients with myocardial infarction who were enrolled in the Western Denmark Heart Registry were included in the external validation cohort. A first event, either all-cause mortality or admission to hospital for heart failure 1 year after myocardial infarction, occurred in 32 308 (23.2%) patients in the testing and training cohorts only. For 1-year all-cause mortality, the ANN had an AUROC of 0.85 (95% CI 0.84–0.85) in the testing dataset and 0.84 (0.83–0.84) in the external validation cohort. The AUROC for admission to hospital for heart failure within 1 year was 0.82 (0.81–0.82) in the testing dataset and 0.78 (0.77–0.79) in the external validation dataset. With an empirical cutoff the ANN algorithm correctly classified 73%–6% of patients with regard to all-cause mortality and 61%–5% of patients with regard to admission to hospital for heart failure in the external validation cohort, ruling out adverse outcomes with 97%–98% probability in the external validation cohort.

Interpretation Identifying patients at a high risk of developing heart failure or death after myocardial infarction could result in tailored therapies and monitoring by the allocation of resources to those at greatest risk.

Funding The Swedish Heart and Lung Foundation, Swedish Scientific Research Council, Swedish Foundation for Strategic Research, Knut and Alice Wallenberg Foundation, ALF Agreement on Medical Education and Research, Skane University Hospital, The Bundy Academy, the Mårta Winkler Foundation, the Anna-Lisa and Sven-Eric Lundgren Foundation for Medical Research.

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Introduction Patients have an estimated mortality of 15–20% within the first year after myocardial infarction and one in four patients who survive myocardial infarction will develop heart failure, a condition that severely reduces quality of life and increases the risk of long-term mortality.1,2 Prediction of outcomes after myocardial infarction is therefore of great interest to physicians. Early recognition of patients at high risk of adverse outcomes could save lives during hospitalisation and improve long-term outcomes through tailored therapies and shifting of health-care resources to those in need.
Use of artificial intelligence has grown exponentially due to improved computer hardware and the availability of high-dimensional data. To date, artificial intelligence algorithms have shown potential across several areas of medicine, including radiology, ophthalmology, dermatology, and psychiatry. For example, in cardiology, machine learning algorithms that combine clinical and imaging variables from coronary CT angiography predicted 5-year all-cause mortality in patients with stable coronary artery disease better than did clinical metrics alone.

The Swedish Web system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDHEART) registry collects data for all patients admitted to hospital for myocardial infarction in Sweden and is an optimal tool for undertaking real-world, population-based evaluations of health care. We aimed to use data from the SWEDHEART registry to establish whether artificial intelligence algorithms can be used to predict all-cause mortality and admission to hospital for heart failure within 1 year after myocardial infarction and to validate the model using data from the Western Denmark Heart Registry (WDHR).

Methods

Study design and populations
In this population-based study, we used data from the nationwide SWEDHEART registry to train and test an artificial neural network (ANN) algorithm to predict all-cause mortality and admission to hospital for heart failure within 1 year after myocardial infarction. We validated the model on data for incident myocardial infarction from the WDHR.

The SWEDHEART registry collects information pertaining to all incident myocardial infarctions in patients admitted to all coronary care units in Sweden, and has been described previously. All patients with signs of an acute coronary syndrome admitted to a coronary care unit or other specialised facility are enrolled prospectively in the registry, which records information including sex, age, body-mass index, smoking status, electrocardiograph findings, and the results of previous examinations, as well as interventions, complications, laboratory findings, discharge medications, and diagnoses. Data are collected with a three-part form that is filled in by the treating physician at admission, during hospital stay, and at discharge, and uploaded electronically to the registry holder, Uppsala Clinical Research Centre, from where they can be extracted. We included all patients who were admitted to hospital for myocardial infarction in Sweden between Jan 1, 2008, and April 1, 2017, and who were discharged alive from a coronary care unit. The final diagnosis of myocardial infarction was made by the treating physician at time of discharge according to the fourth universal definition of myocardial infarction. We linked the SWEDHEART registry to the Swedish National Population Registry and National Patient Registry to obtain information about all-cause mortality and admissions to hospital for heart failure. Eligible patients were included who had a myocardial infarction during the study period and patients with a previous diagnosis of heart failure were not excluded. Survival time was...
Patients with myocardial infarction enrolled between Jan 1, 2008, and Dec 31, 2016, in the WDHR were used as an external validation cohort. The WDHR enrolls all patients with an incident myocardial infarction who undergo angiography in western Denmark, covering nearly 60% of the total Danish population. The registry has been described previously and prospectively collects data with an approximated completeness of 98% of myocardial infarctions in western Denmark. The Danish Civil Registration System and the Danish National Patient Registry were used to collect information about all-cause mortality and admission to hospital for heart failure, and the Danish Prescription Registry was used to obtain information on medical treatment.

The study adheres to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) and Standards for Reporting Diagnostic accuracy studies statements, and ethics approval was provided by the Regional Ethical Review Board in Lund. As the registries used are national quality registries with the purpose of health-care improvement, informed consent is not required according to Swedish and Danish law but participants are informed about registration and have the right to deny partaking at any time.

Algorithm development and outcomes
A multi-layered ANN with back-propagation algorithm was trained to predict all-cause mortality and admission to hospital for heart failure within 1 year after myocardial infarction in the training dataset. ANN algorithms attempt to mimic the architecture of the human brain to perform tasks such as pattern recognition and prediction by interconnected artificial neural nodes organised into an input layer receiving data, multiple hidden layers, and an outcome layer. Each node might have multiple input and output connections. Back-propagation allows the model to self-learn. To create an algorithm that could be validated outside the SWEDHEART registry and adhere to the TRIPOD statement, we limited the model to predictor variables that can be found in all other registries. The simplified model was built using a set of 21 variables commonly associated with the outcomes (primarily 1-year mortality). These variables were selected a priori (selected because of clinical experience and a known association with the outcome) and included age, sex, medical history, previous medications, in-hospital characteristics, left ventricular ejection fraction, and discharge medications (table 1). An extended model not restricted to variables found in other registries was developed to estimate the extent to which the ANN can predict outcomes. The extended model had access to 84 variables to predict the outcomes of interest; these variables are presented in the appendix (p 2). The same set of variables (21 variables in the simplified model and 84 variables in the extended model) was used to predict death and admission to hospital for heart failure, but the models were trained separately. The algorithms were tweaked to optimise their precision by increasing the number of hidden layers and training iterations until no improvements were made. There was no improvement in the predictions after ten iterations for any model, and all final models used ten hidden layers. The developer (MAM) of the ANN had no access to the data for the external validation cohort. After training and testing the model, the neural network was saved and transferred to Denmark. The algorithm was uploaded into a central data

| Age (years) | Men | Women |
|------------|-----|-------|
| 71.0 (62.0–80.0) | 17.98 (64.8%) | 10.07 (32.5%) |

| Medical history | Hypertension | Diabetic | Chronic heart failure | History of myocardial infarction | Stroke |
|----------------|-------------|----------|----------------------|-------------------------------|--------|
| 56.08 (50.3%) | 13.94 (50.5%) | 16.36 (52.8%) | 3.47 (3.6%) | 2491 (9.5%) |

| Past medications | Aspirin | ß blockers | ACE-I or ARB | Antidiabetics | Lipid-lowering agents |
|------------------|--------|-----------|-------------|--------------|----------------------|
| 38.11 (34.2%) | 39.26 (35.6%) | 39.73 (35.6%) | 19.65 (17.6%) | 32.15 (28.8%) |

| In-hospital characteristics | STEMI | NSTEMI | Coronary angiography | Heart rate (bpm) | Systolic blood pressure (mm Hg) |
|-----------------------------|-------|-------|----------------------|-----------------|-------------------------------|
| 36.89 (33.1%) | 74.66 (66.9%) | 89.04 (79.8%) | 79 (67–92) | 149 (130–167) |

| Creatinine (µmol/L) | 83 (69–100) | 82 (69–100) | 81 (69–97) |

| Ejection fraction | ≥50% | 40–49% | 30–39% | <30% | Unknown |
|-------------------|------|-------|-------|------|--------|
| 51.88 (46.5%) | 19.07 (17.1%) | 11.74 (10.5%) | 4.86 (4.4%) | 23.99 (21.5%) |

| Discharge medications | PCI inhibitor | ß blockers | ACE-I or ARB |
|-----------------------|-------------|----------|-------------|
| 90.33 (81.0%) | 98.42 (88.3%) | 85.98 (77.1%) |

Data are n (%) or median (IQR), unless otherwise specified. ACE-I=angiotensin converting enzyme inhibitor. ARB=angiotensin receptor blocker. bpm=beats per min. NSTEMI=non-ST-elevation myocardial infarction. STEMI=ST-elevation myocardial infarction. *Mean (SD).
system with access to data for the WDHR cohort, where it was used to predict outcomes. Neither registry, either complete or in part, was transferred across countries.

In addition to predicting the two prespecified outcomes, we conducted a prespecified analysis that aimed to characterise the differences between patient subgroups in which the machine learning algorithms provided correctly predicted outcomes and those with incorrectly predicted outcomes. We also assessed the performance of the artificial intelligence algorithms for the prediction of the outcomes of interest relative to the established Global Registry of Acute Coronary Events (GRACE) risk score. Using the same set of variables included in the ANN, we also did post-hoc analyses testing other artificial intelligence methods for exploratory purposes (gradient boosting, random forest, and logistic regression).

**Figure 1: Performance of the simplified model**

AUROC for both outcomes of interest (1-year all-cause mortality and admission to hospital for heart failure after myocardial infarction) in the training, testing, and validation cohorts. The artificial neural network was trained on 111,536 patients, tested on 27,730 patients, and validated on 30,971 patients. AUROC=area under the receiver operating characteristic curve. SWEDEHEART=Swedish Web system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies.

**Table 2:** Metrics for assessment of predictive accuracy of the artificial neural network for prediction of mortality and admission to hospital for heart failure within the first year after myocardial infarction
Statistical analysis
Several pre-processing techniques were used to prepare the data for the machine learning algorithms. A one-hot-encoding transformation classifying missing values as a separate categorical value (a method commonly used in machine learning models) was used for all categorical variables in the dataset. Continuous variables with missing values were imputed using age-matched and sex-matched means. The rates of missing values are presented in the appendix (p 6). An exploratory analysis was performed, training the artificial intelligence model on individuals with complete case data on left ventricular function by excluding patients with missing data. The area under the receiver operating characteristic curve (AUROC) was used to evaluate predictive ability (concordance index) with a 95% CI calculated using the DeLong method. Youden’s index was established for both outcome measures (1-year mortality and admission to hospital for heart failure after myocardial infarction) as a method of empirical identification of the optimal dichotomous cutoff to assess sensitivity, specificity, positive predictive value, and negative predictive value. Positive and negative likelihood ratios were used as a method of estimating the predictive value of the models. Calibration plots of the observed versus predicted event rate for each decile of risk predicted were used as a secondary means of assessing the models. A two-sided p value less than 0·05 was considered significant. The ANN model was fit using the Brain module in Stata (version 16.0) and gradient boosting, and random forest were fit using the Stata module Pylearn, built on the Python library scikit-learn (Stata version 16.0 and Python 3.6).

Role of the funding source
The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results
139 288 patients who were admitted to hospital for myocardial infarction between Jan 1, 2008, and April 1, 2017, in the SWEDHEART registry were included. The median age was 71 years (IQR 62–80) and 35% were women (table 1). Approximately 35% of patients were receiving aspirin and β-blocker therapy before admission to hospital (table 1). At the time of discharge, 36 897 (33·1%) patients were diagnosed with ST-elevation myocardial infarction (STEMI) and the remaining patients were diagnosed with non-STEMI (NSTEMI). 79·8% of patients in the training dataset and 80·2% of patients in the testing dataset underwent coronary angiography.

30 971 patients with myocardial infarction who were enrolled in the WDHR between Jan 1, 2008, and Dec 31, 2016, were included in the external validation cohort. Patients in the validation cohort were younger than those in the training or testing cohorts, with a median age of 66·0 years (IQR 56·0–75·0), and 14 348 patients (46·3%) were diagnosed with STEMI. Patients in the validation cohort also had lower rates of diabetes, chronic heart failure, and a history of myocardial infarction and stroke, and higher rates of lipid-lowering agent and antidiabetic agent use on admission than did the training or testing cohorts. Median creatinine concentrations were similar between cohorts (table 1). Rates of angiotensin converting enzyme inhibitor, angiotensin receptor blocker therapy, and β-blocker use were lower at discharge in the validation cohort than in the training or testing cohorts (table 1).

A first event, either death or admission to hospital for heart failure, occurred in 32 308 (23·2%) patients within the first year after myocardial infarction in the training cohort.
and testing cohorts combined. The Kaplan-Meier event rate was 13 407 (9.6%) for 1-year all-cause mortality and 20 341 (14.6%) for admission to hospital for heart failure. The corresponding Kaplan-Meier event rates in the external validation cohort were 2724 (8.8%) for 1-year all-cause mortality and 1300 (4.2%) for admission to hospital for heart failure.

The SWEDEHEART registry cohort was randomly divided into a training dataset of 111 558 patients and a testing dataset of 27 730. AUROC area under the receiver operating characteristic curve. NLR=negative likelihood ratio. NPV=negative predictive value. PLR=positive likelihood ratio. PPV=positive predictive value.

The extended ANN model using 84 variables had an AUROC of 0.87 (0.86–0.88) for all-cause mortality in both the training and testing datasets, with the optimal cutoff correctly classifying 21 379 (77.1%) of 27 730 patients. For admission to hospital for heart failure, the extended model had an AUROC of 0.84 (0.84–0.85) in both the training and testing datasets, correctly classifying 20 761 (74.9%) of 27 730 patients (figure 3, appendix p 9).

The ANN had higher discriminatory values for both outcome measures than that obtained with the GRACE risk score (appendix p 10), which had an AUROC of 0.77 (0.76–0.78) for all-cause mortality in the testing dataset and 0.78 (0.77–0.80) in the validation dataset, yielding 67.8–69.3% correct predictions. For admission to hospital for heart failure, the GRACE risk score had an AUROC of 0.71 (0.70–0.72) in the testing dataset and 0.67 (0.65–0.69) in the validation dataset, resulting in 55.5–65.0% correct predictions. The exploratory analysis on individuals with complete case data on left ventricular function did not improve these predictions (appendix p 11).

Patients in the testing dataset who were incorrectly classified (in the prespecified analysis as false positive or false negative) were older, more often women, and presented more frequently with NSTEMI than those who were correctly classified (true positive or true negative; table 3). Those incorrectly classified also had more comorbidities such as diabetes, history of myocardial infarction, and higher creatinine values than did those who were correctly classified (table 3). The largest difference between correctly and incorrectly classified patients was observed for angiography during admission to hospital, with significantly lower rates of angiography performed in the incorrectly classified group. A significantly larger proportion of incorrectly classified patients had unknown left ventricular ejection fraction than did correctly predicted patients (table 3). Medication burden was higher at admission and lower at discharge in patients with an incorrect prediction; these patients were less often discharged with potent antiplatelet agents than were correctly classified patients. Although the proportion of patients discharged with angiotensin converting enzyme inhibitors or angiotensin receptor blockers did not differ notably between patients with and without a correct prediction with respect to admission to hospital for heart failure, patients who had an incorrect prediction with respect to all-cause mortality were less often prescribed this medication group at discharge (table 3). Patient characteristics for individuals classified as true positive, true negative, false positive, and false negative are presented in the appendix (pp 12–17). Further analyses showed that patients classified as true positive and false
positive were older, had a higher comorbidity burden, and were more likely to have an ejection fraction of less than 30% than were patients classified as true negative or false negative (appendix pp 12–17). Only 512 (1·8%) patients were classified as false negative for prediction of all-cause mortality and 865 (3·1%) for prediction of admission to hospital for heart failure.

Results of the post-hoc analyses testing other artificial intelligence methods showed an AUC of 0·83–0·86 for all-cause death and 0·77–0·83 for admission to hospital for heart failure. These results are presented and discussed in the appendix (p 8).

Discussion
In this population-based study, we trained an ANN on more than 130 000 patients with myocardial infarction from a Swedish nationwide registry to predict all-cause mortality and admission to hospital for heart failure within the first year after myocardial infarction. The model identified nearly 75% of all individuals alive and 60% of patients free from admission to hospital with heart failure after 1 year, with a correct negative prediction in 97·1% of cases for mortality and in 98·7% of cases for admission to hospital for heart failure in an external validation dataset of more than 30 000 patients with myocardial infarction in Denmark. The algorithm also predicts outcomes more accurately than the GRACE risk score. However, the accuracy of the ANN used was reduced for older patients, women, patients with comorbidities, and conservatively treated patients who did not undergo coronary angiography.

Current international guidelines for myocardial infarction recommend the use of clinical risk scores together with the assessment of the severity of coronary artery disease, echocardiographic evaluation of left ventricular function, assessment of metabolic profile, assessment of renal function, and consideration of comorbidities to estimate the risk of adverse events.12 However, the recommended risk scores originate from before the widespread use of mechanical reperfusion and potent antithrombotic and antiplatelet agents, limiting their predictive values in the contemporary era. Artificial intelligence algorithms have a promising future role in predicting the outcomes of various medical conditions because they allow for the identification of non-linear predictive algorithms in nationwide registries and electronic health record systems could alert clinicians at patient discharge to patients at high risk of adverse events, but the ability of the ANN to predict admission to hospital for heart failure is also of clinical value. Accurate prediction of subsequent heart failure might allow the identification of patients who are more likely to benefit from intensive infarction, which is more frequent in older individuals or individuals more susceptible to adverse events, but the ability of the ANN to predict admission to hospital for heart failure is also of clinical value. Accurate prediction of subsequent heart failure might allow the identification of patients who are more likely to benefit from intensive
articles.

The success of a predictive model relies on its external validity, which requires the same set of variables to be recorded with a similar degree of quality in an external validation cohort. This requirement can be a major challenge with advanced models that use many variables. We approached this challenge by developing two algorithms, a simplified model restricted to common clinical variables and an extended model unrestricted by the availability of variables in other registries. Developing the extended model was important because it granted the model access to substantially more clinical data to minimise human bias and maximise computational power. The extended model showed a moderately higher AUROC than the simplified model (0.87 vs 0.85 for mortality; and 0.84 vs 0.82 for admission to hospital for heart failure) despite including four times the number of variables, reflecting the difficulty in improving outcome prediction after myocardial infarction. A few articles have assessed the potential of artificial intelligence in predicting death after myocardial infarction. Most were limited by a small sample size or absence of an external validation cohort and no attempts to use artificial intelligence to predict admission to hospital for heart failure have been done. Studies predicting death have shown similar results to those obtained in our study (AUROC 0.85–0.87) regardless of the artificial intelligence method used, further highlighting the difficulty of the task. Among artificial intelligence studies for the prediction of outcomes after myocardial infarction, ours is, to our knowledge, the largest conducted in a real-world setting, the first to predict admission to hospital for heart failure, and is the only one in which machine learning algorithms have been validated in an external dataset from a different country with all-comer patients.

The external validity of the ANN for prediction of admission to hospital for heart failure was only moderate (AUROC 0.78 in the validation cohort vs 0.82 in the training and testing cohorts), highlighting the importance of validation in independent samples. Although the model was generally well calibrated in the testing data, it was less so in the external validation dataset. Patients in the external validation cohort were younger, had more coronary angiography and invasive treatment, and had fewer comorbidities than patients in the training and testing cohorts, which could affect model calibrations and predictions.Baseline differences might also account for the difference in the incidence of heart failure between populations (4.2% in the external validation dataset vs 14.6% in the training and testing datasets) as the incidence of heart failure increases with age. This difference might also have contributed to the moderate external validity of the heart failure algorithm. This hypothesis is supported by the high external validity for the prediction of all-cause mortality, for which event rates did not differ significantly between the two populations (9.6% in the testing and training cohorts vs 8.8% in the validation cohort).

Older patients and those with more comorbidities more often had an incorrectly predicted outcome, as did patients who did not undergo coronary angiography, all of which are considered high-risk clinical characteristics. Inclusion of heterogeneous populations might therefore increase the errors of these algorithms. Minimising diversity by creating prediction models in more homogenous populations could result in improved predictions by reducing data noise; however, this would reduce the external validity, particularly if external cohorts are more heterogenous. Finally, large observational studies have shown that high-risk patients have the most to benefit from, but are less likely to receive, guideline-recommended treatment, an occurrence termed the risk–treatment paradox. Randomised controlled trials testing whether the objective assessment of risk after myocardial infarction improves clinical outcomes after STEMI by increasing adherence to guideline recommendations are ongoing.

The results of these studies might be of value in expanding adherence to these algorithms and guidelines. Future studies should put these algorithms in the context of other risk stratification tools available in clinical practice. Studies comparing the objective risk after myocardial infarction to that predicted by an experienced clinician would be of interest.

This study has several limitations. Admission to hospital for heart failure in the external validation cohort (WDHR) has not been specifically validated in the Danish National Patient Registry and results should therefore be interpreted cautiously. The model predicting admission to hospital for heart failure might be improved by the addition of the heart failure biomarker N-terminal pro-B-type natriuretic peptide, which is not routinely measured in the SWEDHEART registry. Various different artificial intelligence techniques, with different advantages and disadvantages, might have performed differently in our study. However, the exploratory analyses using alternative artificial intelligence techniques indicated no major benefit of other techniques over the implemented ANN model. We imputed missing values in continuous variables with age-matched and sex-matched means and missing data in categorical variables were treated as a separate category. This method has several benefits, such as the prevention of data loss and simple implementation, but also results in the addition of new features that can theoretically alter model performance. Whether other methods of handling missing data (eg, multiple
imputation by chained equation) would have improved model performance or calibration is unknown. The artificial intelligence model included some variables influenced by clinical judgement such as referral to coronary angiography and therefore cannot be considered entirely objective. However, these variables contain important prognostic information, and exclusion might reduce the predictive value of the model. Finally, data on race or ethnicity are not collected in the SWEDEHEART registry, and therefore could not be included in the algorithm, which could influence predictions.

In conclusion, in this nationwide, population-based study, with external validation in a neighbouring country, an ANN was able to accurately identify individuals who were alive and had not been admitted to hospital for heart failure within the first year after myocardial infarction.

Contributors
All authors fulfil the International Committee of Medical Journal Editors Criteria for Authorship. All authors contributed to the design of the study. MAM, DE, SK, TJ, TB, JS, SJ, and RR had access to the raw derivation data and KKWO and MM had access to the raw validation dataset. Registry data could not be transferred between countries due to restrictions, but MAM and KKWO had access to and verified all data after extraction. All authors had access to the data presented in the manuscript. MAM wrote the ANN algorithm and did all statistical analyses. KKWO was responsible for external validation and all analyses related to it. MAM and KKWO verified the results of both datasets. MAM drafted the manuscript and KKWO, SK, CPG, RR, TJ, TB, JS, SJ, BL, MM, and DE interpreted the data and results, and intellectually and critically revised the manuscript and approved its final form. MAM and DE were responsible for the decision to submit the manuscript for publication.

Declaration of interests
We declare no competing interests.

Data sharing
The datasets used to train and validate the ANN are legally restricted because of Swedish and Danish patient privacy and secrecy laws and are therefore not publicly available. The ANN algorithms that were trained in this study are publicly available in the appendix (brm files) together with instructions on how to use them (appendix p 18 and .do file).

Acknowledgments
We thank the staff of all coronary care units in Sweden and western Denmark for their help and cooperation with providing extensive data to the SWEDEHEART registry and WDH. This work was supported by The Swedish Heart and Lung Foundation (DE), Swedish Scientific Research Council (DE), SSF (TOTAL-AMI) (DE), Knut and Alice Wallenberg Foundation (DE), ALF (DE), Skane University Hospital funds (DE), The Bundy Academy (MAM), The Maëra Winkler Foundation (MAM), and the Anna-Lisa and Sven-Eric Lundgren Foundation for Medical Research (MAM).

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