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Clinical paper

Prearrest prediction of favourable neurological survival following in-hospital cardiac arrest: The Prediction of outcome for In-Hospital Cardiac Arrest (PIHCA) score

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Abstract

Background: A prearrest prediction tool can aid clinicians in consolidating objective findings with clinical judgement and in balance with the values of the patient be a part of the decision process for do-not-attempt-resuscitation (DNAR) orders. A previous prearrest prediction tool for in-hospital cardiac arrest (IHCA) have not performed satisfactory in external validation in a Swedish cohort. Therefore our aim was to develop a prediction model for the Swedish setting.

Methods: Model development was based on previous external validation of The Good Outcome Following Attempted Resuscitation (GO-FAR) score, with 717 adult IHCAs. It included redefinition and reduction of predictors, and addition of chronic comorbidity, to create a full model of 9 predictors. Outcome was favourable neurological survival defined as Cerebral Performance Category score 1–2 at discharge. The likelihood of favourable neurological survival was categorised into very low (<1%), low (1–3%) and above low (>3%).

Results: We called the model the Prediction of outcome for In-Hospital Cardiac Arrest (PIHCA) score. The AUROC was 0.808 (95% CI 0.807–0.810) and calibration was satisfactory. With a cutoff of 3% likelihood of favourable neurological survival sensitivity was 99.4% and specificity 8.4%. Although specificity was limited, predictive value for classification into ≤3% likelihood of favorable neurological survival was high (97.4%) and false classification into ≤3% likelihood of favourable neurological survival was low (0.6%).

Conclusion: The PIHCA score has the potential to be used as an objective tool in prearrest prediction of outcome after IHCA, as part of the decision process for a DNAR order.

Keywords: In-hospital cardiac arrest, Heart arrest, Cardiopulmonary resuscitation, Prognosis, Clinical decision-making, Medical futility, Models-Statistical

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Introduction

The estimated incidence of IHCA is 1.6 to 4 events per 1000 hospital admissions, with survival to hospital discharge in the range of 18–29%.[1–4] However, the majority of patients who die in-hospital do not undergo cardiopulmonary resuscitation (CPR), and resuscitation is initiated in 4–12% of in-hospital deaths.[2,5–8] The ethics of resuscitation are based upon the traditional ethical principles of autonomy, beneficence, non-maleficence and justice. A do-not-attempt-resuscitation (DNAR) order may be issued when it is against the expressed wishes of the patient to receive CPR, or when CPR is considered medically futile; that is when the chances of good quality survival are minimal.[9–11] Physicians must comprehend the individual patient's prognostic predictors to assess the chance of good quality survival and balance against the patient's values and goals of care in order to make a decision regarding a DNAR order that will be beneficial. Hence, there is need for a prearrest prediction tool that can supply objective prognostic information, to be used in conjunction with clinical judgement in the decision process regarding DNAR orders. The Good Outcome Following Attempted Resuscitation (GO-FAR) score[12] is a prearrest prediction tool for neurologically intact survival after IHCA that was published in 2013. External validation of the GO-FAR score in Sweden has shown good discrimination in two external validation studies.[13,14] However, in one of the studies, the model showed poor calibration with systematic underestimation of neurologically intact survival indicating limited applicability in the Swedish setting.[14] There are different ways of approaching model update.[15] Rather than recalibration of the GO-FAR score, we chose development of a new model based on the GO-FAR score, using the results and cohort from the external validation.[14] This enabled us to use the strengths of development of the GO-FAR score in producing strong predictors, while keeping up with temporal changes, differing local circumstances regarding clinical feasibility of predictors and addition of a more recently identified predictor (chronic comorbidity). Through this, information could be retained and the prediction model optimised regarding predictive ability and clinical applicability.[15] The aim of this study was to produce a prearrest prediction model for the Swedish setting, that can prognosticate and with a high predictive value identify patients with a minimal chance of good quality survival after IHCA, to be used in conjunction with clinical judgement and in balance with the patients' values and goals of care in the decision process for DNAR orders.

Methods

The GO-FAR score

The design of the GO-FAR score was used to guide development of the new model.[12] It was developed from a cohort of 51 240 index episodes of IHCA in adults from 366 hospitals participating in the Get With The Guidelines-Resuscitation registry[16] 2007–2009 in the United States.[12] The outcome of the GO-FAR score is neurologically intact survival defined as a Cerebral Performance Category (CPC) score[17] of 1 at discharge (CPC 1: alert, able to work and lead a normal life, may have minor psychologic or neurologic deficits). Prearrest predictors were selected based on a previous meta-analysis[18] and clinical significance. The final set of variables were identified statistically, resulting in a model of 13 predictors (eTable 1). The likelihood of neurologically intact survival was categorised into risk groups based on definitions of futility as very low (<1%), low (1–3%), average (>3 to 15%) and above average (>15%). The area under the receiver operating curve (AUROC) was 0.78, and testing for calibration and classification accuracy was satisfactory.

Study design and population for the model development

The sample for this model development was the same population-based retrospective cohort as for the external validation performed in 2018.[14] The cohort consisted of 717 index episodes of adult IHCAs in 6 out of 7 hospitals in Stockholm County (2.3 million inhabitants) 2013–2014 identified through the Swedish Cardiopulmonary Resuscitation Registry (SCRR).[2,19] The study was approved by the regional Ethical Review Board in Stockholm, Sweden (2013/1959-31/4, 2014/2064-32, 2015/2157-32). All IHCA survivors were asked for informed consent and agreed to participate in SCRR and on-going studies based upon it.

Predictors in the new model

Table 1 contains detailed information on the definitions of the predictors and basis for reduction in the new model. Chronic comorbidity, assessed as the validated and updated Charlson Comorbidity Index[20,21] (CCI) (eTable 2), was added as a predictor variable as it has emerged as an independent predictor of outcome for IHCA.[22–25] The CCI was added as a continuous variable, identified through linkage with the National Patient Register from 2005 until the date of IHCA.[26] Major trauma and stroke were excluded based on low prevalence in conjunction with reasons associated with clinical practice. Admission from a skilled nursing facility was excluded due to a significant difference in social structures, reducing its significance as a predictor. Metastatic or hematologic cancer and hepatic insufficiency were excluded since they are included in the CCI.

In order to keep up with temporal changes, the predictor sepsis was updated to current guideline definitions.[27] Redefinition of renal failure was made based upon separation of chronic and acute state, since chronic renal failure is included in the CCI. The timeframe for defining hypotension and respiratory insufficiency was increased from 4 to 12 h, in order to reduce missing data but with preserved validity. Data for redefinition of predictors were obtained from manual review of the electronic patient records by an Internal and Emergency Medicine consultant (EP) in the same manner as for the external validation publication.[14] The outcome was blinded to the reviewer.

Outcome

The outcome of the GO-FAR score is CPC 1 at discharge. For the new model the outcome was changed to CPC[17] 1 and 2 at discharge (CPC 2: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment. May have hemiplegia, seizures, ataxia, dysarthria, or permanent memory or mental changes) and called favourable neurological survival. The reason for this change was that by convention CPC 1 and 2 are regarded as a good outcome, as they reflect independency of life, and are recommended as the outcome by the Utstein template.[28,29] Poor outcome was defined as deceased or CPC > 2.

Table 1 – Definitions, addition and reduction of predictor variables for the new model based on the Good Outcome Following Attempted Resuscitation (GO-FAR) score[12] and external validation study.[14]

Variable	Definition/reason for reduction
Definition unchanged	
Medical non-cardiac admission	Admission with medical non-cardiac condition[a]. Binary variable
Pneumonia	Documented diagnosis of active pneumonia, in which antibiotic therapy has not yet been started or is still ongoing. Binary variable
Definition revised	
Neurologically intact at admission	GCS 15 according to the definition in the external validation study.[14] Binary variable
Hypotension	Evidence of hypotension extended from within 4 to within 12 h of the event, defined as any of the following: SBP $<$ 90 or MAP $<$ 60 mmHg; vasopressor or inotropic requirement after volume expansion (except for dopamine $\leq$3 μg/kg/min); or intra-aortic balloon pump. Binary variable
Respiratory insufficiency	Evidence of acute or chronic respiratory insufficiency extended from within 4 to within 12 h of the event, defined as any of the following: PaO_2/FiO_2 ratio $<$ 300, PaO_2 $<$ 60 mmHg, or SaO_2 $<$ 90% (without preexisting cyanotic heart disease); $PaCO_2$, $ETCO_2$, or $TcCO_2$ $>$ 50 mmHg; spontaneous respiratory rate $>$ 40/min or $<$ 5/min; requirement for noninvasive ventilation; or requirement for ventilation via invasive airway. Binary variable
Acute kidney injury	Evidence of AKI defined as an absolute increase in serum CR by $\geq$26.5 μmol/l within 48 h or an increase in serum CR to $\geq$1.5-fold baseline within previous 7 days. Baseline serum CR is defined as the median of CR values two years preceding the CA (maximum 50 observations). Cases without history of chronic kidney failure and unknown baseline kidney function was assumed to have a baseline estimated glomerular filtration rate of 75 ml/min/1.73m^2 according to CKD-EPI.[38] Binary variable
Sepsis	Evidence of sepsis as life-threatening organ dysfunction due to a dysregulated host response to infection defined as at least 2 out of 3 of the clinical criteria qSOFA[27]: respiratory rate$\geq$22/min, altered mentation (GCS $<$ 15), or SBP $\leq$ 100 mmHg during the admission preceding the CA. Binary variable
Age, y	Changed from categorical to continuous variable
Predictor addition	
Chronic comorbidity	According to CCI.[20,21] Continuous variable
Predictor reduction	
Metastatic or hematologic cancer	Chronic condition already included in CCI
Acute stroke	Low prevalence in the external validation cohort (2.9%).[14] Also contributing to the reduction was that in clinical practice prearrest assessment of outcome in case of a cardiac arrest for this group of patients is multi-factorial and influenced by the clinical effect of the stroke in conjunction with patient factors that are not captured by a more general prediction model
Major trauma	Low prevalence in the external validation cohort (2.2%).[14] Also contributing to the reduction was that in clinical practice prearrest assessment of outcome in case of a cardiac arrest for trauma-patients is multi-factorial and influenced by the severity of the trauma in conjunction with other patient related factors that are not captured by a more general prediction model
Hepatic insufficiency	Chronic liver disease included in CCI both as mild and moderate/severe liver disease. According to our knowledge the most important and prevalent acute liver disease states that influence mortality are based on an underlying chronic liver disease (acute liver failure without underlying liver disease is rare[39]), with for example decompensation of chronic liver disease, hepato-renal syndrome, acute-on-chronic liver failure. The definition of hepatic insufficiency in the GO-FAR score (evidence of hepatic insufficiency within 24 h of the event, defined by total bilirubin$>$ 34 μmol/l and (AST $>$ 2 times the upper limit of normal or cirrhosis) is non-specific for these conditions and include other hepatocellular damage, for example gallstone, pancreatitis, bile-duct/hepatic malignancies. The prevalence of all underlying causes for hepatic insufficiency according to the GO-FAR definition was only 4% in the validation cohort.[14] In our opinion CCI will capture the underlying increased risk of poor outcome with chronic liver disease and liver associated malignancies. The predictor hepatic insufficiency was therefore excluded
Admission from skilled nursing facility	The prevalence of the predictor in the external validation cohort was only 6.1% as compared to 26% in the GO-FAR cohort.[12,14] In Sweden home help services are well developed while living in skilled nursing facilities is less widespread. In 2012 9% of the population 65 years and older and 24% of 80 years and older in ordinary housing were granted home help services, 5% of the population 65 years and older and 14% of 80 years and older lived permanently in special forms of housing.[40] The extent of help service granted could complement admission from skilled nursing facility, however there is no access to this information through the electronic patient record or any other registry. Thus, admission from nursing facility is not a clinically feasible predictor in our setting and was therefore excluded

Abbreviations: GCS, Glasgow coma scale; SBP, systolic blood pressure; MAP, mean arterial pressure; PaO_2, arterial partial pressure of oxygen; FiO_2, fraction of inspired oxygen; SaO_2, arterial oxygen saturation; $PaCO_2$, arterial partial pressure of carbon dioxide; $ETCO_2$, end-tidal carbon dioxide pressure; $TcCO_2$, transcutaneous carbon dioxide pressure; AKI, acute kidney injury; CR, creatinine; CA, cardiac arrest; CKD-EPI, chronic kidney disease epidemiology collaboration; qSOFA, quick sequential (sepsis-related) organ failure assessment; CCI, Charlson Comorbidity Index; AST, aspartate aminotransferase.
[a] According to the Get With The Guidelines-Resuscitation registry.[16]

Risk group categorisation

Quantitative futility refers to the situation where treatment is unlikely to benefit the patient, that is, that the chances of good outcome are minimal.[10,30] Although there is no objective and valid criterion, quantitative futility has been proposed to be defined as a likelihood of good outcome of less than 1% or less than 3%.[30] According to this, the likelihood of favourable neurological survival was categorised into:

very low likelihood (<1%), low likelihood (1–3%) and above low likelihood (>3%). We combined the risk groups average (>3 to 15%) and above average (>15%) into one risk group above low likelihood (>3%). This was made because risk group categorisation reflects upon the definition of futility, and further risk group categorisation above 3% would not aid in clinical guidance as how to relate to futility.

Statistical analyses

Chi-squared was used to compare binary variables, Wald tests to compare categorical variables, logistic regression with bootstrap and the Mann–Whitney test to compare continuous variables. Significance tests were two-sided with a significance level of 0.05.

Model development was performed on complete case data. In the first stage a full model was developed with logistic regression containing 9 predictors: neurologically intact at admission, sepsis, pneumonia, hypotension, respiratory insufficiency, medical non-cardiac admission, acute kidney injury, CCI and age. Non-linearity was explored for the continuous variables age and CCI. Based on clinical reasoning and findings from previous studies[12] the interaction terms age × CCI, sepsis × hypotension, sepsis × respiratory insufficiency and hypotension × respiratory insufficiency were explored. The risk of over-optimism was quantified with 1000-bootstrap validation.[15] Quantification of the over-optimism is a way to assess what predictive performance to expect in external validation of the prediction model in a different population. In the second stage, the full model was recalibrated based on the assessment of the over-optimism. The recalibrated model's performance was quantified in internal validation by assessing discrimination, calibration and classification through 1000-bootstrap sampling. Discrimination is the models ability to discriminate between those with good outcome from those with adverse outcome and was assessed by estimating the AUROC with confidence intervals calculated based on 1000-bootstrap sampling. Calibration refers to the agreement between predicted probabilities and observed frequencies, how close predictions are to the actual outcome. This was evaluated in a calibration

Table 2 – Demographics and predictors for the cohort of in-hospital cardiac arrests in Stockholm County 2013-2014.

	Complete case Total number 628 (87.6%)	Missing data[a] Total number 89 (12.4%)	P-value[b]
Survival with CPC 1–2, No. (%)	174 (27.7)	7 (7.9)	<0.001
Characteristic			
Demographics			
Age, mean (SD) y	72 (13.7)	72 (15.8)	0.84
Male sex, No. (%)	391 (62.3)	53 (59.6)	0.62
Cardiac arrest characteristics			
Initial rhythm, No. (%)			
VF and pulseless VT	117 (23.3)	10 (13.9)	0.10[c]
PEA	154 (30.7)	20 (27.8)	
Asystole	231 (46)	42 (58.3)	
Missing	126 (25.1)	17 (23.6)	
Hospital location, No. (%)			
Coronary care unit	79 (12.6)	5 (5.6)	<0.001[c]
Catheterization lab	45 (7.2)	3 (3.4)	
Intensive care unit	67 (10.7)	1 (1.1)	
Operating theatre	19 (3)	0	
Emergency department	44 (7)	7 (7.9)	
General ward	335 (53.3)	69 (77.5)	
Outpatient clinic, radiology, lab	27 (4.3)	3 (3.4)	
Other	12 (1.9)	1 (1.1)	
Predictors, No. (%)			
Neurologically intact at admission[d]	505 (80.4)	67 (75.3)	0.26
Sepsis	81 (12.9)	6 (6.7)	0.10
Pneumonia	87 (13.9)	13 (14.6)	0.85
Hypotension	137 (21.8)	11 (26.8)	0.45
Respiratory insufficiency	307 (48.9)	21 (56.8)	0.35
Medical non-cardiac admission	272 (43.3)	47 (52.8)	0.09
Acute Kidney Injury	211 (33.6)	16 (29.1)	0.50
CCI, mean (SD),	2.25 (2.45)	2.17 (2.27)	0.74
Median [IQR]	2 [0;3]	2 [0;3]	0.84
Range	0,14	0,14	

Abbreviations: CPC, cerebral performance category score; VF, ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity; lab, laboratory; CCI, Charlson Comorbidity Index.

[a] Missing occurred in the predictors hypotension (48 patients), respiratory insufficiency (52 patients) and acute kidney injury (34 patients).

[b] P-values contrast complete case with missing data assessed with the chi-squared test for binary variables, Wald test for categorical variables, linear regression with bootstrap and the Mann-Whitney test for continuous variables.

[c] Global P-value.

[d] Glasgow coma scale (GCS) 15.

Table 3 – Predictors included in the multivariable model for in-hospital cardiac arrests in Stockholm county 2013-2014.

Predictors	OR full model (95% CI)	β coefficient full model (95% CI)	Recalibrated score points PIHCA score
Neurologically intact at admission	1.61 (0.88–2.95)	0.48 (−0.13 to 1.08)	0.42
Sepsis	0.56 (0.22–1.45)	−0.57 (−1.52 to 0.37)	−0.50
Pneumonia	0.52 (0.23–1.16)	−0.65 (−1.45 to 0.15)	−0.57
Hypotension	0.45 (0.25–0.81)	−0.80 (−1.38 to −0.21)	−0.69
Respiratory insufficiency	0.44 (0.28–0.68)	−0.83 (−1.27 to −0.39)	−0.72
Medical non-cardiac admission	0.41 (0.25–0.66)	−0.90 (−1.39 to −0.41)	−0.78
Acute Kidney Injury	0.37 (0.23–0.62)	−0.98 (−1.49 to −0.48)	−0.85
CCI	0.88 (0.80–0.97)	−0.12 (−0.22 to −0.03)	−0.11
Age spline 1[a]	1.01 (0.95–1.07)	0.01 (−0.05 to 0.07)	0.01
Age spline 2[a]	0.94 (0.89–1.00)	−0.06 (−0.12 to 0.00)	−0.05
Constant		0.97 (−1.68 to 3.62)	0.74
AUROC (95% CI)		0.808 (0.769 to 0.848)	0.808 (0.807 to 0.810)

Abbreviations: PIHCA score, the Prediction of outcome for In-Hospital Cardiac Arrest score; CCI, Charlson Comorbidity Index; AUROC, area under the receiver operating curve.
[a] Natural cubic splines was used with one internal knot placed at 55 years and two knots placed outside the observed age range.

plot (see eSupplement 1). Classification accuracy was assessed through risk group categorisation. Analyses were performed using Stata 13 and 15.1 for Windows (Stata Corp., College Station, TX).

Results

For the cohort of 717 patients, mean age was 72 years, 30-day survival was 27.5% and favourable neurological survival at discharge was 25.2%. Data was complete for 628 cases (87.6%) with missing in the variables hypotension (6.7%), respiratory insufficiency (7.3%) and acute kidney injury (4.7%) (Table 2). Only complete case data was included in the regression model for the prediction model. A checklist for model development[15] is presented in eTable 3 and predictors according to favourable neurological survival versus poor outcome are presented in eTable 4.

The distribution of age proved to be non-linear and was modelled with natural cubic splines (Table 3). We found one significant interaction between respiratory insufficiency and hypotension. After controlling for multiple comparisons we postulate that the significance is a type 1 error, and that inclusion would not add to the predictive ability of the model. Hence, the full model included 9 predictors, with β coefficients as presented in Table 3. The full model had an AUROC of 0.808 (95% CI 0.769 to 0.848) and over-optimism was limited (eTable 5). Still, in order to optimise performance in future external validation, the full model was recalibrated using the bootstrap validation derived intercept of −0.10 (95% CI −0.12 to −0.09) and calibration slope of 0.87 (95% CI 0.85 to 0.88). The β coefficients for the recalibrated model are presented in Table 3, and were used as score points for the new model that we call the Prediction of outcome for In-Hospital Cardiac Arrest (PIHCA) score.

In internal validation the AUROC of the PIHCA score was 0.808 (95% CI 0.807 to 0.810). The calibration plot for the PIHCA score is shown in Fig. 1, and shows evidence of good calibration with predictions near the dotted line that indicates perfect calibration.

The risk group categorisation into very low (<1%) likelihood of favourable neurological survival could not be estimated with the sample size of this study. Classification measures with risk group categorisation into very low/low likelihood of favourable neurological survival (≤3%) and above low likelihood (>3%) are shown in Table 4. Sensitivity, that is the probability of true favourable neurological survival to be classified into >3% likelihood of favourable neurological survival, was 99.4%. Specificity, that is the probability of true poor outcome to be classified into ≤3% likelihood of favourable neurological survival, was 8.4%. The positive predictive value of classification into >3% likelihood of favourable neurological survival was 29.4%, whereas the negative predictive value of classification into ≤3% likelihood of favourable neurological survival was 97.4%. False classification into ≤3% likelihood of favourable neurological survival was 0.6%.

Discussion

We have produced a prearrest prediction model for favourable neurological survival after IHCA called the PIHCA score. According to the ethical principle of autonomy, the patient has the right to be informed and to participate in health care decisions, including decisions regarding DNAR orders.[9–11] Previous studies have shown that prognostic information influences patient wishes regarding CPR preferences,[31,32] and that it is difficult for medical personnel to accurately predict outcome after cardiac arrest.[33] The decision process for a DNAR order is complex and the PIHCA score could have potential to be used as a complement for the clinician in comprehending the patient's prognostic predictors supplying an aid in producing an objective assessment of outcome after IHCA. However, several steps have to be taken before considering taking it into clinical practice. The performance of the PIHCA score must be scrutinised in external validation. Further, the clinical application has to be investigated retro- and prospectively in non-selected populations, exploring the value for clinicians as well as for patients so that guidance in how to use the score can be established. Presentation of this prediction tool is merely one of the first steps in the effort to support health care providers in the complex decision process regarding DNAR orders.

The model showed good discrimination and the calibration plot showed a good match between observed and predicted outcomes. In deviating from this, in the low range of favourable neurological survival, the PIHCA score somewhat overestimates the outcome. The clinical relevance is that it is in this range that a DNAR order might be an option, and in issuing a DNAR order, the patient might be deprived of lifesaving treatment with CPR. Further, the high predictive value of

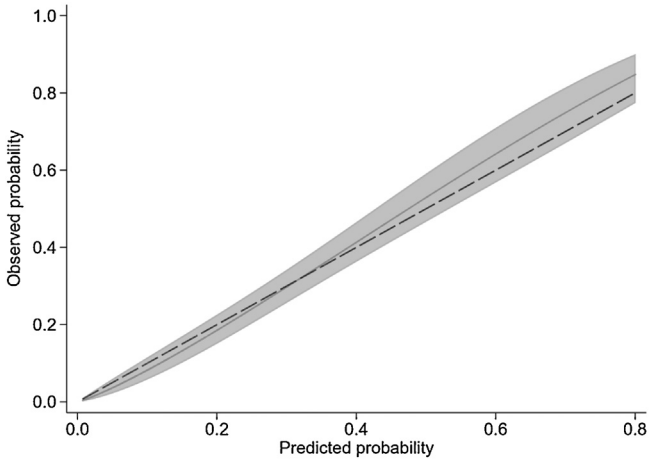

Fig. 1 – Calibration plot for the Prediction of outcome for In-Hospital Cardiac Arrest (PIHCA) score. The dotted line indicates the ideal calibration plot, with perfect match between predictions and observed outcomes.

Table 4 – Model performance of the Prediction of outcome for In-Hospital Cardiac Arrest (PIHCA) score with risk-group categorisation into very low/low (≤3%) and above low (>3%) probability of favourable neurological survival.

	True		
Classified into risk groups	Favourable neurological survival[a]	Poor outcome[b]	Total
Above low (>3%) "positive"	173	416	589
Very low/low (≤ 3%) "negative"	1	38	39
Total	174	454	628
Sensitivity 173/174 = 99.43%			
Specificity 38/454 = 8.37%			
Positive predictive value 173/589 = 29.37%			
Negative predictive value 38/39 = 97.44%			
False positive rate for true poor outcome 416/454 = 91.63%			
False negative rate for true favourable neurological survival 1/174 = 0.57%			
False positive rate for classified positive 416/589 = 70.63%			
False negative rate for classified negative 1/39 = 2.56%			

[a] Survival with Cerebral Performance Category (CPC) score 1–2.
[b] Deceased or survival with CPC > 2.

classification into very low/low likelihood of favourable neurological survival (97.4%), and the low false classification into this risk group (0.6%) indicate that if, through using the PIHCA score, a patient is assigned to the very low/low risk group, there is a low probability of favourable outcome and that a DNAR order can be considered without the patient being disadvantaged. However, the cutoffs were chosen based on the theoretical proposition of quantitative medical futility.[30] It is important to bear in mind that there is no valid cutoff for quantitative futility,[34] and that qualitative futility, that is the capacity of the patient to appreciate the benefits of treatment,[30] has to be taken into consideration as well. The PIHCA score could serve as an aid in producing an objective assessment of outcome for IHCA, but does not replace full comprehension of all contributing factors that have to be taken into consideration.

This model development was performed as previous external validations of the GO-FAR score showed good discrimination (AUROC 0.85 Ohlson et al.[13] and AUROC 0.82 Piscator et al.[14]), but unsatisfactory calibration, with systematic underestimation of good outcome.[14] Several factors likely contribute to this, one of which may be a different use of DNAR orders in Sweden as compared to the original cohort.[2,8,35] The unsatisfactory calibration supported the need to customise the model for the Swedish setting. We chose to produce a new model based on the GO-FAR score, taking advantage of the model's robust selection process for strong predictors of outcome after IHCA. Another option would have been to retain the GO-FAR score and shift the cutoffs for what defines a poor outcome. This however, would not have given us the opportunity to adapt the model to temporal changes and local conditions, nor add chronic comorbidity as a predictor. Chronic comorbidity has emerged as an independent predictor of outcome for IHCA,[22–25] and according to our clinical experience, with support from a few published studies, chronic comorbidity is part of the predictive assessment for decisions regarding DNAR orders.[6,36] The AUROC for the GO-FAR score in this cohort was slightly higher than for the PIHCA score (0.82[14] vs 0.808). However, this was outweighed by the higher performance in calibration for the PIHCA score. We chose to change the outcome because although survival with CPC 1 is regarded as neurologically intact survival, it does not take into consideration outcomes that include independency of life, which can be considered favourable and is defined as such by the Utstein template.[28,29] As to the best of our knowledge, there is no evidence supporting a different association between the predictors and the outcome including CPC 2.

Some of the predictors were not significant in the logistic regression for the full model in our data set (Table 3), but since there were no signs of over-optimism, these predictors were kept in the model.

Our study had several limitations. Our cohort consisted of patients who underwent CPR, without a previous DNAR order. This selection process could create a systematic bias. Ideally prearrest prediction scores should be derived and tested in a non-selected population of patients receiving CPR after a cardiac arrest and expected or unexpected cessation of circulation. Unfortunately, such a population is not available. The validity of the PIHCA score will have to be scrutinised retro- and prospectively, in larger and non-selected populations. Also, as mentioned previously, this publication does not include guidance on the clinical use of the PIHCA score and further research is warranted to set the context in how to use the score in clinical practice. Missingness in the study was 12.4%. However, this proportion was considered acceptable, not too extensive to introduce large biases. Also, the SCRR does not include information about race/ethnicity, a factor known to be associated with outcome after IHCA.[35,37] Further, risk group categorisation into $\leq$1% likelihood of favourable neurological survival could not be assessed due to few outcomes in this risk group. The limited sample size of this cohort related to first being intended to be used for external validation of the GO-FAR score. Although calibration was satisfactory, the cutoff of 3% for risk group categorisation resulted in a specificity of only 8.4%. This means that the ability of the PIHCA score to classify patients into $\leq$3% probability of favourable neurological survival is limited. This is outweighed by the high predictive value (97.4%), and low false classification (0.6%) into this risk group. Again, there is no replacement of the clinician's assessment of the complete picture of the patient, weighing the ethical principles of autonomy, beneficence, non-maleficence and justice.

As with all prediction models, generalisability of the PIHCA score will depend on the case-mix where it is used, and the predictive performance will depend on similarity of the distribution of predictors, clinical setting and outcome. The PIHCA score was developed for the Swedish setting and generalisability will be restricted by this.

To simplify the validation of the PIHCA score, an online calculator is under development.

Conclusion

The prediction model PIHCA score has the potential to be used as an objective tool in prearrest prediction of outcome after IHCA, as part of the decision process for a DNAR order in Sweden. External validation will have to assess model performance, and further research is needed to establish guidance in the clinical use of the prediction tool.

Conflicts of interest

ME was the original developer of the GO-FAR score, no other disclosures for all other authors.

Contributorship

All authors of this manuscript have directly participated in the planning, execution, and analyses of the study. All authors have read and approved the final version of the submitted manuscript. There are no directly related manuscripts or abstracts, published or unpublished, by any of the authors of this paper.

Detailed author contribution	EP	KG	SF	MB	ME	JH	TD
Study concept and design	X	X	X	X	X	X	X
Acquisition of data	X						X
Analysis and interpretation of data	X	X	X	X			X
Drafting of the manuscript	X	X	X				X
Critical revision of the manuscript for important intellectual content	X	X	X	X	X	X	X
Statistical analyses	X			X			X
Obtained funding	X						X
Administrative, technical, or material support							X
Study supervision		X	X			X	X

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.08.010.

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