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Original Article

Validation of the CREST score for predicting circulatory-aetiology death in out-of-hospital cardiac arrest without STEMI

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Abstract: Aims: The CREST tool was recently developed to stratify the risk of circulatory-aetiology death (CED) in out-of-hospital cardiac arrest (OHCA) patients without ST-elevation myocardial infarction (STEMI). We aimed to validate the CREST score using an external cohort and determine whether it could be improved by the addition of serum lactate on admission. Methods: The study involved the retrospective analysis of consecutive patients admitted to a single tertiary centre with OHCA of presumed cardiac origin over a 51-month period. The CREST score was calculated by attributing points to the following variables: Coronary artery disease (CAD), non-shockable Rhythm, Ejection fraction <30%, cardiogenic Shock at presentation and ischaemic Time ≥25 minutes. The primary endpoint was CED vs neurological aetiology death (NED) or survival. Results: Of 500 patients admitted with OHCA, 211 did not meet criteria for STEMI and were included. 115 patients died in hospital (71 NED, 44 CED). When analysed individually, CED was associated with all CREST variables other than a previous diagnosis of CAD. The CREST score accurately predicted CED with excellent discrimination (C-statistic 0.880, 95% CI 0.813-0.946) and calibration (Hosmer and Lemeshow P=0.948). Although an admission lactate ≥7 mmol/L also predicted CED, its addition to the CREST score (the C-AREST score) did not significantly improve the predictive ability (CS 0.885, 0.815-0.954, HS P=0.942, X^2 difference in -2 log likelihood =0.326, P=0.850). Conclusion: Our study is the first to independently validate the CREST score for predicting CED in patients presenting with OHCA without STEMI. Addition of lactate on admission did not improve its predictive ability.

Keywords: Out-of-hospital cardiac arrest, coronary angiography, predictive scoring systems

Introduction

Out-of-hospital cardiac arrest (OHCA) is a major cause of global mortality and coronary artery disease (CAD) is the leading cause, with clinically significant CAD occurring in 70% of patients [1, 2]. Treatment decisions can be challenging, but urgent coronary angiography and, if appropriate, percutaneous coronary intervention (PCI) have been shown to increase survival in observational studies [3, 4]. Current guidelines recommend a primary PCI strategy is followed in resuscitated OHCA patients with ST-elevation myocardial infarction (STEMI) and that it is considered in those with other ECG patterns if there is a suspicion of myocardial ischaemia and no obvious non-cardiac cause [5, 6]. However, the benefits of urgent coronary angiography in patients without ST-elevation remain uncertain. Indeed, the recent COACT trial reported no significant difference in 90-day mortality amongst patients without ST-elevation who were randomised to either undergo immediate or delayed coronary angiography [7]. The major risk factors associated with a an OHCA in those with STEMI include younger age,

fewer conventional cardiovascular risk factors, an larger territory of infarction and delays in the arrival of the emergency medical services (EMS) [8]. It is thought that these risk factors are similar in OHCA cases without STEMI as well.

Around 60% of deaths in patients resuscitated from OHCA are thought to be neurological-aetiology deaths (NED) [9]. Although the early prediction of the severity of neurological injury in patients resuscitated from OHCA is difficult, several recently developed assays have been shown to be far more specific than traditional techniques [10, 11]. Risk scores have also been developed and validated to predict poor neurological outcome [12]. Predicting neurological outcome early post-resuscitation, especially in patients without STEMI, aids decisions on whether to withhold invasive coronary angiography and mechanical circulatory support (MCS) and whether to offer neuro-protective therapies, such as therapeutic temperature management (TTM) [13].

Conversely, few tools exist to predict patients at a high risk of circulatory-aetiology deaths (CED), which includes death from refractory cardiac arrests, worsening circulatory shock or refractory arrhythmias. Such tools could be combined with the methods designed to predict the severity of neurological injury to further guide management strategies by balancing the competing risks of CED and NED. The CREST tool was recently developed to stratify risk of CED in patients without STEMI and includes: CAD, non-shockable Rhythm, Ejection fraction (EF) <30%, cardiogenic Shock at presentation and ischaemic Time ≥25 minutes [14]. This tool has yet to be externally validated. Additionally, others have suggested that the addition of biochemical parameters such as lactate or pH on admission may enhance the predictive ability of this score [15, 16]. Indeed, the American College of Cardiology (ACC) have recommended the incorporation of an admission lactate ≥7 mmol/L in assessing whether to offer invasive coronary angiography to patients resuscitated from OHCA without STEMI [17]. However, these measures have also been shown to be poor differentiators of CED and NED and instead predict overall mortality [18].

The aims of this study were to independently validate the CREST score for prediction of CED in patients resuscitated from OHCA without STEMI and to assess whether the addition of admission lactate improved its predictive ability.

Methods

Patient inclusion and study design

The patient population was derived from a prospectively collected database of all OHCA patients who achieved return of spontaneous circulation (ROSC) and were admitted to a single cardiac centre between June 2014 and September 2018. 500 consecutive patients were admitted to our unit with a resuscitated OHCA over this period, of which 211 (42.2%) were not diagnosed with STEMI and were included in the study cohort. ROSC was defined as signs of spontaneous cardiac contractility lasting for greater than or equal to 20 minutes at any point (including prior to or after hospital arrival), in line with previously accepted definitions [19]. Resuscitated OHCA patients were streamed to the centre by the emergency services if no obvious non-cardiac cause was present and they were within a defined geographic area; patients who did not meet these criteria were streamed to the nearest secondary care unit. On arrival, it was at the discretion of the lead clinician as to whether urgent coronary angiography was appropriate, based on the suspected likelihood of identifying an acute coronary lesion, medical co-morbidities and the likely prognosis. Patients with repeated arrests on arrival did not undergo coronary angiography until stable ROSC was achieved. No risk scores were used to stratify patients at the centre; all patients instead underwent routine assessment including arterial or venous blood gas, laboratory bloods, bedside echocardiography and clinical assessment to inform the above decisions. Patients were followed up until discharge or in-hospital death.

Data collection

Clinical data was collected in an Utstein-structured manner and entered into the local British Cardiac Intervention Society (BCIS) database and the Myocardial Infarction National Audit Project (MINAP) database, along with procedural data. As such, no formal ethical approval was required. All fields were checked/validated to ensure accurate data entry.

Patient information collected included demographic profile, risk factors for atherosclerosis and the presence of cardiogenic shock, which was defined as persistent hypotension (≥30 minutes of systolic blood pressure ≤90 mmHg) with clinical evidence of hypoperfusion or requiring inotropes or MCS to maintain a systolic blood pressure >90 mmHg, in line with the definition supported by the ACC [20]. Arrest-related characteristics included the initial underlying cardiac rhythm (ventricular fibrillation, ventricular tachycardia, pulseless electrical activity or asystole) as documented by the EMS, as the first rhythm on their arrival at the scene after attaching a cardiac monitor, whether the arrest was witnessed by bystander or EMS, whether bystander cardiopulmonary resuscitation (CPR) was administered and the time from arrest to ROSC (the ischaemic time). The ischaemic time was estimated from a combination of EMS documentation and call-out times. The presence or absence of ST-elevation was determined by use of a 12-lead ECG as soon as ROSC was achieved and CPR had stopped, either by EMS or by hospital staff, and all ECGs were reviewed by the lead clinician on arrival to the hospital. ST-elevation in two contiguous ECG leads of ≥2 mm in the chest leads or ≥1 mm in the limb leads was considered positive. Admission lactate was taken as the lactate on the first arterial or venous blood gas on arrival to hospital.

Outcomes

Patients who died were prospectively classified as either CED or NED when data was entered into the databases. Patients were split into two groups for comparison: those that died from CED and those that either survived or died from NED. CED was defined as death from refractory or recurrent cardiac arrests with failed resuscitation, refractory circulatory shock with multi-organ dysfunction, refractory arrhythmias or other major non-cerebral vascular events. NED was defined as death from major cerebral vascular events, refractory status epilepticus or from withdrawing or withholding circulatory and respiratory support due to either failure to show neurological recovery on sedation hold after 72 hours post-resuscitation or from being determined to have a poor neurological prognosis on imaging and electroencephalographic (EEG) assessment.

Validation and modification of the CREST score

The CREST tool was recently developed to stratify risk of CED in patients without STEMI and includes: CAD, non-shockable Rhythm, Ejection fraction (EF) <30%, cardiogenic Shock at presentation and ischaemic Time ≥25 minutes [14]. Only patients with data regarding all of the CREST variables were included in the multivariable analysis. Patients with any missing data were excluded from the analysis. Scores were totalled with each factor given one point and analysed with respect to CED. Patients with data on admission lactate were also analysed to determine whether the addition of this factor improved the prediction of mortality.

Statistics

IBM SPSS Statistics Grad Pack Version 24 (Chicago, IL, USA) was used to analyse data. Binary data was analysed using the Chi Squared test for proportions and continuous data was analysed using the Mann-Whitney U test. Continuous data was reported as median ± interquartile range (IQR). Results $P<0.05$ were considered statistically significant.

Individual components of the CREST scores were analysed independently and then again using binary logistic regression in a multivariable model with adjustment of the following factors: age, ethnicity, gender, other medical comorbidities and arrest-related characteristics. Results were reported as odds ratio (OR) ±95% confidence interval (CI). Each criterion was given one point and scores were totalled. Models were developed and interrogated by analysis of the receiver operator curve (ROC) with respect to both discrimination (denoted by C-statistic and presented with 95% CI) and calibration (denoted by the Hosmer and Lemeshow *P* value). The CREST score was then modified by addition of an admission lactate of ≥7 mmol/L, given the value placed on this particular criteria by international guidelines and this was termed the 'C-AREST' score [16]. The CREST and C-AREST models were compared by the X^2 difference in -2 log likelihood.

Results

500 consecutive patients were admitted to our unit with a resuscitated OHCA over a 51-month period, of which 211 (42.2%) were not diag-

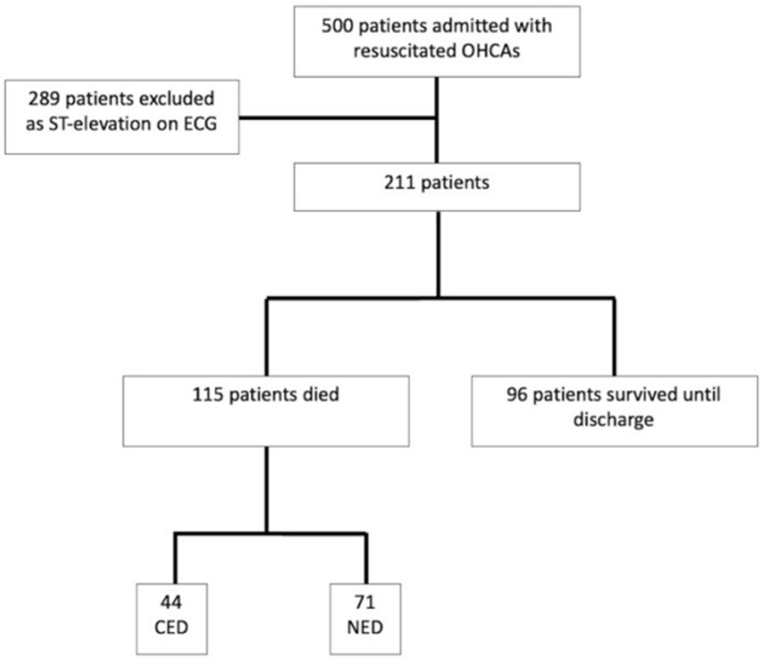

Figure 1. Patient flowchart denoting those who survived and those who suffered circulatory-aetiology death (CED) or neurological-aetiology death (NED); STEMI, ST-elevation myocardial infarction.

nosed with STEMI and were included in the study cohort (**Figure 1**). The median age was 62.0 (IQR 51.0-75.0) years and 160 (75.8%) patients were male. 93 (44.1%) were diagnosed with non-ST elevation ACS and 118 (55.9%) had other causes identified or suspected, including arrhythmias (n=24), structural heart disease (n=24), other vascular events (n=3), pulmonary embolism (n=9), respiratory disease (n=5), intracranial events (n=4) and in 49 cases, no cause was identified. 115 (54.5%) patients died in hospital, of which 71 (61.7%) died from NED and 44 (38.3%) from CED. 96 patients survived to discharge from hospital. 137 (64.9%) patients underwent urgent coronary angiography and 41 (19.4%) had PCI.

CED was associated with (**Table 1**): an older age, a previous diagnosis of heart failure or CABG but not with gender, ethnicity or other medical comorbidities. Additionally, CED was associated with a lower admission systolic blood pressure and a lower chance of obtaining out-of-hospital ROSC. Patients were also more likely to have non-STE ACS as the diagnosis, but were less likely to have undergone a coronary angiogram. There was no difference in the number of patients undergoing PCI. Patients suffering CED had a shorter LOS.

Validation of the CREST score

When analysed with respect to the CREST variables using univariate analysis (**Table 1**), CED was associated with (CED vs either NED or survival): a non-shockable rhythm (47.7% vs 29.9%, P=0.026), an EF<30% (93.0% vs 29.7%, P=0.0001), cardiogenic shock (93.2% vs 43.7%, P=0.0001) and an ischaemic time ≥25 minutes (90.7% vs 34.7%, P=0.0001), but not with a previous diagnosis of CAD (31.8% vs 23.4%, P=0.249). When analysed with binary logistic regression in the multivariable model, only EF<30% (OR 37.5, 95% CI 7.0-200, P=0.0001), cardiogenic shock (OR 54.2, 4.3-675.3, P=0.002), and ischaemic time ≥25 minutes (OR 11.0, 2.1-57.5, P=0.004), remained significant, whilst CAD (OR 1.6, 0.3-7.7, P=0.576) and a non-shockable rhythm (OR 1.1, 0.2-4.8, P=0.941) were not.

Each factor on the CREST score was allocated one point and increasing CREST scores were associated with an increasing risk of CED (**Figure 2**); only patients with data regarding all variables included in analysis (represented as number with CED/n, %): 0 (0/36, 0%), 1 (0/39, 0%), 2 (5/39, 12.8%), 3 (13/43, 30.2%), 4 (20/28, 71.4%), 5 (5/6, 83.3%). 20 patients had incomplete data, of which 1 (5.0%) suffered CED. When the ROC was interrogated, the CREST score accurately predicted CED with excellent discrimination (C-statistic 0.880, 95% CI 0.813-0.946) and calibration (Hosmer and Lemeshow P=0.948).

Biochemical variables and modification of the CREST score

CED was found to be associated with the following biochemical variables on admission (**Table 1**): a higher lactate and a lactate ≥7 mmol/L, a lower bicarbonate and a lower pH. When analysed alone, the predictive ability of an admis-

Table 1. Comparing patients who suffered circulatory-aetiology death (CED) with those who either survived or suffered neurological-aetiology death (NED) in terms of baseline demographic and medical characteristics, arrest-related details and the management performed (CAD, coronary artery disease

	Data available (total n=211)	Circulatory-aetiology death (n=44)	Neurological-aetiology death or survival (n=167)	P
Male gender (%)	211	32 (72.7)	128 (76.6)	0.589
Age, y (IQR)	211	71.5 (46.5-81.5)	61.5 (54.5-73.0)	**0.021**
Ethnicity (%)				
Caucasian	177	22 (61.1)	85 (60.3)	0.928
Black	177	2 (5.6)	18 (12.8)	0.223
Asian	177	9 (25.0)	29 (20.6)	0.563
Mixed/other	177	3 (8.3)	9 (6.4)	0.678
Past medical history/atherosclerotic risk factors (%)				
Hypertension	170	16 (51.6)	72 (51.8)	0.985
Hypercholesterolaemia	169	12 (38.7)	50 (36.2)	0.796
Smoking history	104	6 (50.0)	56 (60.9)	0.470
Diabetes (any)	174	12 (36.4)	41 (29.1)	0.413
Previous PCI	170	5 (16.1)	22 (15.8)	0.967
Previous CABG	171	8 (24.2)	11 (8.0)	**0.008**
FH CAD	131	1 (4.5)	20 (18.3)	0.107
PVD	164	2 (6.7)	7 (5.2)	0.754
CVD	167	4 (13.3)	12 (8.8)	0.441
Airway disease	170	6 (19.4)	18 (12.9)	0.354
CKD	170	5 (16.1)	14 (10.1)	0.333
CHF	168	7 (21.9)	12 (8.8)	**0.036**
Arrest-related details				
Arrest after EMS arrival (%)	211	8 (18.2)	18 (10.8)	0.184
Bystander CPR (%)	211	26 (59.1)	110 (65.9)	0.403
OH ROSC (%)	208	19 (44.2)	154 (93.3)	**0.0001**
Chest pain prior to arrest (%)	104	9 (29.0)	15 (20.5)	0.348
Time without CPR, min (IQR)	182	0 (0-5.3)	0 (0-5.0)	0.546
Number of shocks delivered (IQR)	202	2 (0-7)	2 (0-4)	0.851
Admission systolic blood pressure, mmHg (IQR)	164	110 (53-124)	115 (90-132)	**0.046**
Admission HR (IQR)	163	80 (46-96)	88 (74-100)	0.958
CREST variables (%)				
CAD	211	14 (31.8)	39 (23.4)	0.249
Rhythm non-shockable	211	21 (47.7)	50 (29.9)	**0.026**
EF<30%	191	40 (93.0)	44 (29.7)	**0.0001**
Cardiogenic Shock	211	41 (93.2)	73 (43.7)	**0.0001**
Ischaemic Time ≥25 mins	210	39 (90.7)	58 (34.7)	**0.0001**
Biochemical variables				
Admission pH (IQR)	133	7.08 (6.86-7.36)	7.29 (7.17-7.34)	**0.0001**
Admission base excess (IQR)	117	-10.9 (-14.0–4.1)	-4.2 (-8.9–1.8)	**0.0001**
Admission bicarbonate, mmol/L (IQR)	88	14.6 (8.9-20.9)	20.4 (16.9-21.7)	**0.0001**
Admission lactate, mmol/l (IQR)	123	5.9 (2.2-8.8)	3.4 (2.2-7.7)	**0.0001**
Admission lactate ≥7 mmol/L (%)	123	22 (75.9)	36 (38.3)	**0.0001**
Serum potassium, mmol/L (IQR)	105	4.1 (3.8-4.4)	4.2 (3.5-4.6)	0.097
Diagnosis (%)				
Non-STE ACS	211	26 (59.1)	67 (40.1)	**0.024**
Management				
Angiogram (%)	211	12 (27.3)	125 (74.9)	**0.0001**
PCI (%)	211	8 (18.2)	33 (19.8)	0.814
LOS, days (IQR)	211	1 (0-4)	8 (6-14)	**0.0001**

MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; FH, family history; PVD, peripheral vascular disease; CVD, cerebrovascular disease; CKD, chronic kidney disease; CHF, congestive heart failure; EMS, emergency medical service; CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; EF, ejection fraction; STEMI, ST-elevation myocardial infarction; ACS, acute coronary syndrome; LOS, length of stay. P<0.05 taken as significant (bold).

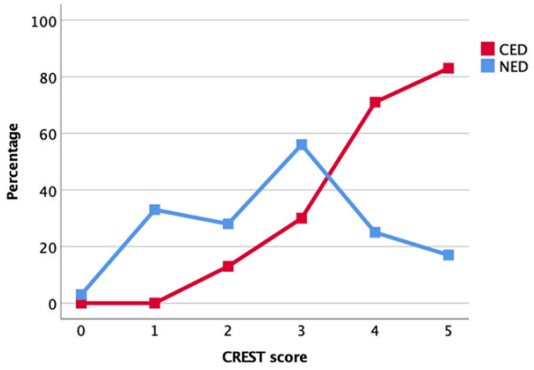

Figure 2. The association of the CREST score with circulatory-aetiology death (CED) and neurological-aetiology death (NED) in out-of-hospital cardiac arrest patients without STEMI. CREST consists of existing Coronary artery disease, non-shockable Rhythm, Ejection fraction <30%, cardiogenic Shock on admission, ischaemic Time ≥25 minutes (all one point). Only patients with data regarding all variables included in analysis; 0 (n=36), 1 (n=39), 2 (n=39), 3 (n=43), 4 (n=28), 5 (n=6).

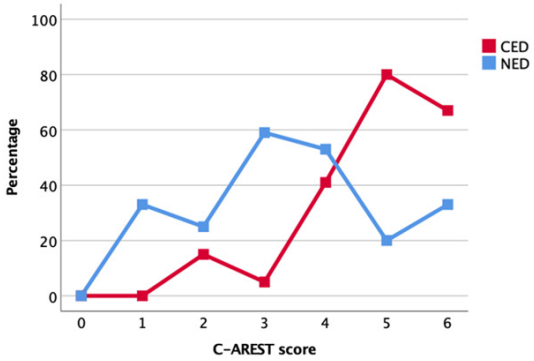

Figure 3. The association of the modified CREST score (C-AREST score) with circulatory-aetiology death (CED) and neurological-aetiology death (NED) in out-of-hospital cardiac arrest patients without STEMI. C-AREST consists of existing Coronary artery disease, admission Lactate ≥7 mmol/L, non-shockable Rhythm, Ejection fraction <30%, cardiogenic Shock, ischaemic Time ≥25 minutes (all one point). Only patients with data regarding all variables included in analysis; 0 (n=12), 1 (n=18), 2 (n=20), 3 (n=22), 4 (n=17), 5 (n=20), 6 (n=3).

sion lactate ≥7 mmol/L was inferior to the CREST score (C-statistic 0.688, 0.580-0.796, X^2 difference in -2 log likelihood CREST vs lactate =18.3, P<0.0001). Admission lactate ≥7 mmol/L was added to the CREST score as a sixth parameter also worth one point (the C-AREST score). Increasing C-AREST scores were also associated with an increasing chance of CED (**Figure 3**); only patients with data regarding all variables included in analysis: 0 (0/12, 0%), 1 (0/18, 0%), 2 (3/20, 15.0%), 3 (1/22, 4.5%), 4 (7/17, 41.2%), 5 (16/20, 80.0%), 6 (2/3, 66.7%). 99 patients had incomplete data, of which 15 (15.2%) suffered CED. When the ROC was analysed, the C-AREST score accurately predicted the risk of CED (C-statistic 0.885, 0.815-0.954, Hosmer and Lemeshow P=0.942). However, when models were compared, the C-AREST score was not significantly better than the CREST score in predicting CED (X^2 difference in -2 log likelihood =0.326, P=0.850).

Discussion

The CREST score accurately predicted the risk of CED in OHCA patients without STEMI. CED was associated with all of the individual components of the CREST model other than existing CAD. Additionally, CED was strongly associated with biochemical variables, including lactate and pH on admission, although addition of an admission lactate ≥7 mmol/L to the model (the C-AREST) score did not significantly improve its predictive ability.

OHCA remains a major health burden with a largely unchanged overall mortality in decades [21]. The traditional focus has been on the pre-hospital links in the chain or survival, but attention has been increasingly directed at in-hospital post-resuscitation care [22, 23]. CAD is known to be a major cause of OHCA and correspondingly, international guidelines clearly recommend a primary PCI strategy in patients resuscitated from an OHCA with STEMI [5]. However, the early in-hospital management of resuscitated OHCA patients without STEMI is less clear [6].

Whilst the majority of deaths from resuscitated OHCA are due to NED, as many as one third occur due to CED [9, 24, 25]. The ability to rapidly determine which patients are at higher risk of severe neurological injury compared to those more likely to suffer critical circulatory dysfunction may allow for more appropriate triage of post-resuscitation interventions to each group. This is especially the case in patients without STEMI, where early decisions are less evidence-based and more dependent on individual clinical assessment. For example, in addition to standard neuro-protective mea-

sures, such as control of cerebral perfusion, seizure management and maintaining normoglycaemia, TTM is now recommended for all resuscitated OHCA patients who remain comatosed to improve neurological recovery [6, 26]. Although initial evidence suggested a greater degree of benefit in patients with shockable rhythms, subsequent work has demonstrated similar benefit in those with non-shockable rhythms as well [27-29]. Nonetheless, subanalyses of trials investigating TTM indicate that lower temperature targets are associated with a reduced cardiac index, higher serum lactate and higher vasopressor requirements, compared to more conservative targets [30-32]. Although these effects seem to primarily be mediated by a reduced heart rate, rather than stroke index, TTM may have the potential for worsening circulatory function in patients with more severe cardiogenic shock post-OHCA [33]. Furthermore, the degree of benefit from TTM may be diminished in patients with the longest ischaemic times [34]. These results suggest that patients at particularly high risk of CED, rather than NED, are least likely to benefit from TTM.

Conversely, deciding whether to offer interventions designed to support impaired circulatory function is controversial in resuscitated OHCA patients without STEMI. Although current guidelines suggest that early angiography should be at least considered in this cohort, recent trials have shown conflicting results, casting significant doubt on its benefit [7, 35]. Furthermore, in the COACT trial, patients randomised to receive early coronary angiography had a corresponding delay in achieving their therapeutic temperature targets, indicating that it may be associated with harm in patients who are particularly susceptible to neurological injury [7]. In contrast, specific sub-groups of OHCA patients without STEMI may be more likely to benefit from early coronary angiography. In resuscitated OHCA patients with cardiogenic shock, worse shock severity has been associated with a greater beneficial effect of early coronary angiography [36]. Additionally, observational studies suggest that clinicians naturally incorporate factors such as cardiogenic shock, prognosis, initial rhythm and the presence of previous CAD when deciding whether to offer coronary angiography to patients without STEMI [37, 38]. With respect to MCS, recent work suggests that specific cohorts of patients are more likely to benefit from veno-arterial ECMO, although these results are somewhat confounded by the selection of such patients for this therapy [39, 40].

Predicting whether an individual patient is likely to suffer CED or NED is difficult in the early post-resuscitation period, not least because traditionally accepted examination findings suggesting a poor neurological outcome, such as absent brainstem reflexes, have an unacceptably high false positive rate within the first 72 hours [11]. Nonetheless, more recently developed biochemical, electroencephalographic and imaging-based techniques have been shown to be much better prognosticators for NED [10]. With the advent of novel techniques and also possibly algorithms that combine information from these assays, accurate prediction of NED is likely to be possible in the near future [41, 42]. Equivalently, the CREST score was developed to identify patients instead at a high risk of CED [14]. Our results support the use of the CREST score in helping to balance the competing risks of CED and NED. We also examined the use of biochemical parameters to predict CED, including a lactate ≥7 mmol/L, as has been suggested by the ACC [17]. Although an admission lactate ≥7 mmol/L was a strong predictor of CED, it was not superior to the CREST score, nor did it significantly improve its predictive ability. These parameters may instead be better predictors of overall mortality in this cohort [43, 44].

Regarding the individual components of the CREST score, it is interesting that we found all components, other than the presence of existing CAD, to be associated with CED, in contrast to the derivation study [14]. Although we found that OHCA patients diagnosed with ACS were more likely to suffer CED, the relationship between existing *diagnosed* CAD and the cause of OHCA is conceivably more complex. Such patients are likely to be well managed and followed up in the community [36]. Indeed, others have found existing CAD to be associated with a reduced risk of finding a treatable lesion on angiography after OHCA [45]. Correspondingly, we did not find any difference in the rate of PCI between patients suffering CED and those surviving or dying from NED.

When applied to our cohort, we found the CREST score to have a stronger C-statistic com-

pared to the original cohort [14]. This might, in part, be due to the fact that our cohort was from a single centre where protocols are streamlined and patients are likely to be managed in a similar way, compared to the multinational cohort analysed by Bascom and colleagues. Additionally, our definition of ROSC was more liberal, including all patients with ROSC for greater than 20 minutes, compared to those surviving long enough for ICU admission. This decision was chosen to improve the applicability of the CREST tool to all patients arriving in the emergency department, rather than selecting only those well enough to survive to ICU admission, after urgent angiography is usually performed [14]. This may have had the effect of including more patients with higher CREST scores, who had more severe cardiogenic shock and refractory arrhythmias. Nonetheless, we found a similar ratio of patients died from CED, suggesting a high degree of comparability.

Our study is limited by its retrospective nature, which is not how the CREST score was designed to be applied. Additionally, even though the cause of death was determined prospectively, there remains a possibility for observer bias. This was reduced as much as possible as investigators were trained to strictly assign causes of death based on the above definitions for each outcome. Finally, it also relies on there being measures designed to rapidly neuroprognosticate patients to allow for comparison of the competing risks of CED and NED.

Our study is the first to independently validate the CREST score to stratify the risk of CED in patients presenting with OHCA without STEMI. It may be used by clinicians, along with individualised clinical assessment, to help objectively prognosticate and to guide the use of interventions such as early angiography and MCS in this cohort. Further work should aim to apply the CREST score in a prospective manner on arrival to hospital and possibly combine it with methods to predict neurological injury.

Disclosure of conflict of interest

None.

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