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MIRACLE2 score validation for neuroprognostication after out-of-hospital cardiac arrest: a district general hospital experience

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ABSTRACT

Introduction and objectives Decision-making regarding prognosticating out-of-hospital cardiac arrest (OHCA) remains challenging at the front door. The MIRACLE2 score provides a simple and practical tool for early neuroprognostication to aid decision-making. The study aims to validate the MIRACLE2 score in a district general hospital (DGH).

Material and methods This is a retrospective analysis of the patients with OHCA and return of spontaneous circulation (ROSC) in the community who attended the cardiac catheter laboratory in a DGH between 1 September 2021 and 25 September 2023. Patients with a Glasgow Coma Scale of 15/15 after ROSC were excluded. Medical notes were examined, and the MIRACLE2 score was calculated and correlated with the Cerebral Performance Category (CPC) on discharge and compared with other neuroprognostication risk scores. The primary outcome was poor neurological recovery at hospital discharge, and the secondary outcome included poor neurological recovery at 6 months.

Results A total of 46 patients satisfied the study criteria, of which 43 (93%) were males. The median age was 64; half had a CPC of 0–2 on discharge and at 6 months. The MIRACLE2 score was low (0–2) in 14 patients (30%), intermediate (3–4) in 16 patients (35%) and high (≥5) in 16 patients (35%). The MIRACLE2 score performed well in neuroprognostication as a MIRACLE2 score ≥5 had a positive predictive value of 91%, while a MIRACLE2 score ≤2 had a negative predictive value of 92% for poor neurological outcomes at discharge.

Conclusions The MIRACLE2 score provides an accurate and practical neuroprognostication tool in patients with OHCA of cardiac origin presenting to this DGH.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The MIRACLE2 score is a simple and practical tool validated in tertiary care referral centres to assess neuroprognostication in patients with out-of-hospital cardiac arrest.

WHAT THIS STUDY ADDS

⇒ This study validates the MIRACLE2 score in patients admitted to a heart attack centre within a district general hospital, extending its use beyond tertiary referral centres for neuroprognostication in out-of-hospital cardiac arrest.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study encourages using the MIRACLE2 score as a practical adjunct to clinical judgement in a broader range of healthcare settings, including secondary care facilities (district general hospitals) and tertiary referral care centres, to assess neurological outcomes in patients following an out-of-hospital cardiac arrest.

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains a significant clinical challenge, with an annual incidence of 250 000 globally.[1] In the UK, around 31 000 resuscitation attempts take place annually, with the aetiology being cardiac in origin in almost 85%.[2] According to international consensus, this cohort should be investigated and managed in a heart attack centre (HAC).[3] Early neuroprognostication in these patients is crucial to aid rapid clinical decision-making and identification of poor prognosis, aiming to facilitate appropriate resource allocation and prevent futility. Yet, survival after OHCA remains poor despite therapeutic advances. A recent study demonstrated that OHCA patients' survival to hospital and survival to discharge was 36% and 8%, respectively.[4] Furthermore, of patients admitted to the intensive care unit (ICU) after OHCA, predischarge mortality was almost 50%, with hypoxic brain injury being the leading cause of death.[4 5]

Former studies attempted to develop clinical decision tools to predict the outcome of OHCA, including the Cardiac Arrest Hospital Prognosis Score (CAHP), the target temperature management (TTM) risk score and the OHCA score.[6–8] However, these scores are complex, and their use during emergencies can be challenging. MIRACLE2 was

subsequently developed as a practical risk score designed to predict neurological outcomes, with the advantage of being simple to use in the acute setting comprising seven readily available parameters.[9] It exhibited a better receiver operating characteristic curve (ROC) and area under the curve (AUC) than the previous scores. Many prognostic tools, including the MIRACLE2 score, are developed and validated in the context of tertiary or quaternary referral centres but not in a district general hospital (DGH) setting.[9 10] For example, CAHP was initially validated in 2016 and later externally validated in tertiary care settings.[6 10] However, the complexity and resource requirements for electroencephalogram monitoring needed to conduct CAHP score may not be feasible in DGHs, where such specialised equipment and expertise may not be available.

Moreover, a previous study demonstrated that patients treated at tertiary centres had significantly different outcomes than those treated at DGHs, primarily due to advanced therapeutic interventions and specialised staff availability.[11] These discrepancies highlight the need for local studies to authenticate the effectiveness of the MIRACLE2 in a DGH setting after it has been validated in tertiary and quaternary settings, which is what our study aimed to do.

METHODS

Population

A single-centre retrospective cohort study was conducted at the Royal Derby Hospital (RDH). RDH is a DGH with 24/7 access to invasive coronary angiography (ICA). It has 25 non-specialist ICU beds, two cardiac catheterisation laboratories and no on-site cardiac surgery service. Cardiac catheterisation laboratory online records were screened for OHCA using relevant codes (BCIS, lab3-5, 6.03). All patients over 18 years old with OHCA and return of spontaneous circulation (ROSC) in the community were included between 1 September 2021 and 25 September 2023 (654 days). Patients must either have had ST elevation on the post-ROSC ECG or no ST elevation and absence of non-cardiac causes of the OHCA. The exclusion criteria were patients with comorbidity causing a life expectancy <6 months, in-hospital cardiac arrest, patients with Glasgow Coma Scale (GCS) of 15 on admission, previous severe neurological compromise (Cerebral Performance Category (CPC) of 3–4), confirmed intracranial haemorrhage, mortality prehospital arrival and a non-cardiac cause of OHCA including trauma, suicide, respiratory arrest and substance overdose. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (Supplementary Table 1).[12]

Data source

East Midlands Ambulance Service and emergency department (ED) electronic records were used to obtain prehospital data. The hospital's electronic records collected 12-lead ECGs, transthoracic echocardiograms, baseline blood tests, vital signs, ICA reports and admission details. The total cardiopulmonary resuscitation (CPR) time, including CPR after re-arrest resulting in multiple ROSCs, was described as low-flow time. Early intervention strategy was defined as ICA within the first 24 hours of admission.

Scoring system details

The MIRACLE2 comprises seven variables with a maximum score of 10 points. Higher scores have been shown to predict incrementally higher risk of poor neurological outcomes, defined as CPC 3–5 (severe disability to death). The score components are 1—unwitnessed cardiac arrest (1 point).

1. Initial non-shockable rhythm (one point).
2. Lack of pupillary reactivity at ROSC (one point).
3. Age (≤60 years: 0 points, 60–80 years: 1 point, >80 years: 3 points).
4. Changing rhythms (any two of pulseless electrical activity, asystole or ventricular fibrillation: 1 point).
5. Initial blood pH<7.20 (1 point).
6. Any epinephrine dose given (2 points).

To externally validate the score, we assessed the MIRACLE2 score performance against previously validated scores (OHCA, CAHP and TTM).

1. The OHCA score uses an equation to produce an overall score involving the following factors: zero-flow time, initial rhythm, low-flow time, initial lactate and serum creatinine levels.
2. The CAHP score uses a complex nomogram, resulting in an overall score based on total epinephrine dose, arrest setting, age, initial blood pH, zero-flow time, initial rhythm and low-flow time.
3. The TTM score is similar but more complex than MIRACLE2. It uses 10 main factors with 37 subcategories: age, initial blood pH, arrest setting, use of epinephrine, zero-flow time, initial rhythm, low-flow time, corneal or pupillary reflex at ROSC, initial arterial carbon dioxide partial pressure and motor GCS score.

STUDY OUTCOMES

Our study outcomes were defined a priori. The primary outcome was poor neurological recovery/mortality at hospital discharge,[7] defined as CPC 3–5. Secondary outcomes included poor neurological recovery/mortality at 6 months.[3]

Statistical analysis

Continuous variables were expressed as median and IQR. Categorical variables were expressed as numbers and percentages (%). Fisher's exact test was used to compare two groups when the outcome was a categorical variable. After using the Shapiro-Wilk test to confirm normal distribution, the Student's t-test or Mann-Whitney U test was used to compare continuous variable means between the two groups. The variables studied included age, length of hospital stay, lab results and vital signs. Univariable

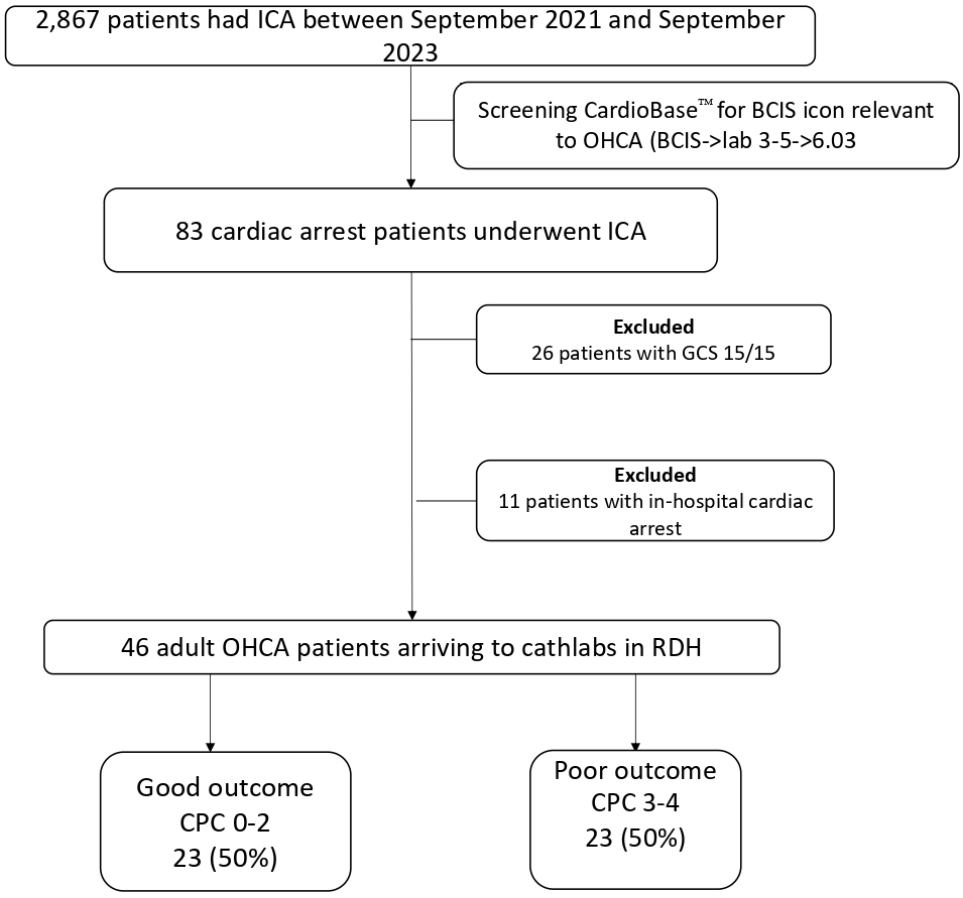

Figure 1 Flow chart of the study's selection criteria and neurological outcomes. CPC, Cerebral Performance Category; GCS, Glasgow Coma Scale; ICA, invasive coronary angiogram; OHCA, out-of-hospital cardiac arrest; RDH, Royal Derby Hospital.

and multivariable logistic regression models were used to investigate the relationship between poor neurological outcomes and predictive variables. Risk estimates were calculated as adjusted ORs with a 95% CI. The DeLong test compared the AUC between the MIRACLE2 and other predictive scores. All p values were two-sided and were presented without adjustment for multiple testing, with a value of <0.05 considered statistically significant. Statistical analysis was performed using GraphPad Prism V.9.5 for Mac (San Diego, California, USA; www.graphpad.com). The DeLong test was conducted using R: A language and environment for statistical computing. R Foundation for Statistical Computing (Vienna, Austria, www.R-project.org).

RESULTS

Cohort details

A total of 2867 patients underwent ICA during the study period. Among them, 46 satisfied the study's inclusion and exclusion criteria (figure 1). Half the patients had good neurological outcomes at discharge, defined by a CPC of 0–2. Demographics, ECG post-ROSC and ICA details stratified by the neurological outcome are demonstrated in table 1. The median age was 64; most patients were male (93%). Almost half of the patients (48%) had left ventricular ejection fraction of <40%, and percutaneous coronary intervention was performed in all patients, with 42 patients (91%) having early ICA. Patients with previous ischaemic heart disease had worse neurological outcomes compared with patients with first presentation (8 (36%) vs 2 (8%); p=0.037). OHCA circumstances are demonstrated in table 2. Missed arrest occurred in 11 patients (24%). An initial shockable rhythm was encountered in 35 patients (76%), and a changing rhythm was observed in 22 patients (48%). On ROSC, 25 patients (54%) had reactive pupils, and 20 of them (43%) had an initial pH<7.20. None of the patients was treated by extracorporeal membrane oxygenation during the study period due to its local unavailability.

MIRACLE2 scoring and outcome prediction

The split across the MIRACLE2 score risk categories was balanced: low (CPC 0–2), 14 patients (30%); intermediate (CPC 3–4), 16 patients (35%); high (CPC≥5), 16 patients (35%). A stepwise increase in the risk of poor neurological outcomes was observed with increasing MIRACLE2 score (figure 2A). Poor neurological outcome rates at discharge with high and low admission MIRACLE2 scores were 88% and 0%, respectively. Intermediate MIRACLE2 scores balanced good and poor neurological outcomes (50% for each arm). Univariable and multivariable logistic regression regarding predictors

Table 1 Baseline characteristics and investigation details

Variable	Total (n=46)	CPC 0–2 (n=23, 50%)	CPC 3–5 (n=23, 50%)	P value
Demographics, n (%) or median (IQR)				
Age (years)	64 (57–70)	53 (51–69)	65 (59–73)	0.44
Male	43 (93%)	20 (87%)	23 (100%)	0.23
Diabetes mellitus	11 (24%)	6 (26%)	5 (22%)	0.99
Dyslipidaemia	24 (52%)	14 (61%)	10 (43%)	0.55
Smoking	14 (30%)	6 (26%)	8 (35%)	0.99
Ischaemic heart disease	10 (22%)	2 (9%)	8 (35%)	0.032
12-leads ECG after ROSC, n (%)				
Anterior/anterolateral ST elevation	21 (35%)	12 (55%)	9 (39%)	0.072
Lateral ST elevation	4 (9%)	2 (9%)	2 (9%)	0.99
Inferior ST elevation	12 (26%)	6 (26%)	6 (26%)	0.99
Posterior ST elevation	1 (2%)	0 (0%)	1 (4%)	0.89
LBBB	2 (4%)	1 (4%)	1 (4%)	0.96
No ST elevation or LBBB	6 (13%)	2 (9%)	4 (17%)	0.67
Left ventricular ejection fraction assessed by transthoracic echocardiogram, n (%)				
50% or more	9 (20%)	5 (22%)	4 (17%)	0.84
40–49%	15 (32%)	8 (35%)	7 (30%)	0.22
<40%	22 (48%)	10 (43%)	12 (52%)	0.76
Primary coronary intervention details, n (%)				
Early intervention strategy	42 (91%)	19 (83%)	23 (100%)	0.11
Multivessel disease	26 (57%)	12 (52%)	14 (61%)	0.23
PCI to left anterior descending artery	32 (70%)	18 (78%)	14 (61%)	0.33
PCI to left main stem	5 (11%)	0 (0%)	5 (22%)	0.049
PCI to left circumflex artery	8 (17%)	5 (22%)	3 (13%)	0.35
PCI to the right coronary artery	13 (28%)	7 (30%)	6 (26%)	0.64

CPC, Cerebral Performance Category; LBBB, left bundle branch block; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation.

Table 2 Out-of-hospital arrest details and initial in-hospital assessment

Variable	Total (n=46)	CPC 0–2 (n=23, 50%)	CPC 3–5 (n=23, 50%)	P value
Resuscitation details, n (%) or median (IQR)				
Missed arrest	11 (24%)	6 (26%)	6 (26)	0.97
Low-flow time (min)	25 (15–37)	17 (9.3–28)	31 (22–46)	<0.001
Initial shockable rhythm	35 (76%)	22 (96%)	13 (57%)	0.02
Changing rhythm	22 (48%)	7 (30%)	15 (65%)	0.02
Epinephrine given	29 (63%)	9 (39%)	20 (87%)	0.001
Initial pH<7.20	20 (43%)	8 (35%)	13 (57%)	0.14
Reactivity of pupils	15 (33%)	3 (13%)	12 (52%)	0.004
MIRACLE2 risk category, n (%)				
Low score (≤2)	14 (30%)	14 (61%)	0 (0%)	<0.001
Intermediate score 3–4	16 (35%)	8 (35%)	8 (35%)	0.94
High score (≥5)	16 (35%)	2 (9%)	14 (61%)	<0.001

CPC, Cerebral Performance Category; GCS, Glasgow Coma Score.

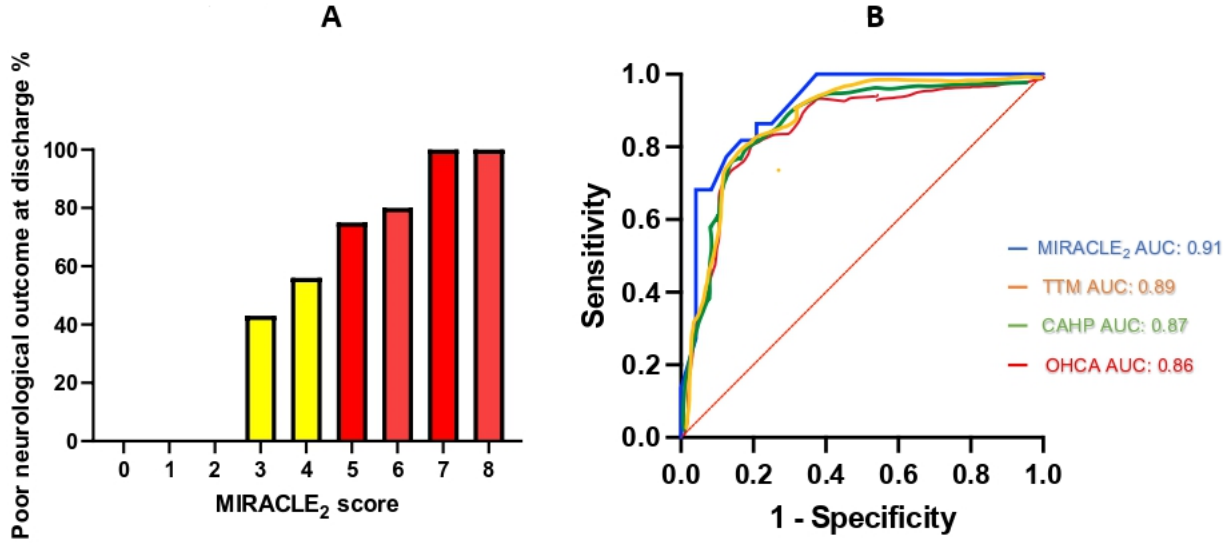

Figure 2 (A) Correlation between MIRACLE2 score and percentage of patients having poor neurological outcome defined by Cerebral Performance Category of 3–5 on discharge. (B) Comparison of the discrimination performance of the MIRACLE2, OHCA, CAHP and TTM scores. AUC, area under the curve; CAHP, cardiac arrest hospital prognosis; OHCA, out-of-hospital cardiac arrest; TTM: target temperature management.

of poor neurological outcomes is demonstrated in table 3. The multivariable analysis was conducted using the MIRACLE2 score components.

MIRACLE2 performance against other predicting scores

ROC curves emanated from the MIRACLE2 score and three other prognostication scoring systems. The AUC for the MIRACLE2 score was 0.91 when predicting poor neurological outcomes at discharge. The G squared was 28.9, and Tjur's R was 0.53. The AUC for the OHCA, CAHP and TTM scores was 0.86, 0.87 and 0.89, respectively (figure 2B). The DeLong test showed no statistically significant difference in performance between the MIRACLE2 and the three predictive scores (p>0.05 for all). A MIRACLE2 score ≥5 had a positive predictive value of 91%, while a MIRACLE2 score ≤2 had a negative predictive value of 92% for poor neurological outcomes at discharge.

DISCUSSION

Although a recent study validated the MIRACLE2 score in a tertiary care centre,[9] this is the first study to validate the score in a DGH with an HAC. The study's main finding is that a high-risk MIRACLE2 score had a positive predictive value of 91% for poor neurological outcomes. A MIRACLE2 score ≤2 had a negative predictive value of 92% for poor neurological outcomes. Intermediate MIRACLE2 was less predictive of neurological outcome, with nearly equal distribution between the study arms. DGHs often operate with limited resources. Early and practical prognostic tools are crucial for guiding clinical

Table 3 Univariable and multivariable logistic regression analysis regarding prediction of poor neurological outcomes

Predictor	Univariable analysis, OR (95% CI)	P value	Multivariable analysis, aOR (95% CI)	P value
Unwitnessed arrest	1.1 (0.57 to 2.2)	0.860	1.2 (0.7 to 1.9)	0.752
Initial non-shockable rhythm	5.1 (2.1 to 15.4)	<0.001	7.9 (2.5 to 28)	0.028
Changing rhythm	2.4 (1 to 6.3)	0.007	7.64 (1.01 to 93)	0.042
Age: 60–80 years*	1.4 (0.91 to 2.9)	0.120	3.2 (1.4 to 7.2)	0.047
Age: >80 years*	4.2 (2.1 to 5.7)	<0.001	9.5 (2.4 to 74)	0.032
pH<7.20	1.8 (0.8 to 4.2)	0.080	2 (0.96 to 5.2)	0.062
Unreactive pupils	2.1 (1 to 4.7)	0.002	10.8 (1.3 to 100)	0.049
Any epinephrine dose given	7.5 (2.1 to 48)	0.001	23 (2.8 to 366)	0.008
LVEF: 40%–49%†	1.2 (0.9 to 1.2)	0.870		
LVEF: <40%†	1.3 (0.8 to 1.6)	0.120		

*Reference: age <60.
†Reference left ventricular systolic function ≥50%.
aOR, adjusted OR; LVEF, left ventricular ejection fraction.

decisions in this setting. Our study demonstrates that the MIRACLE2 score performs well in a real-world DGH, maintaining high predictive accuracy comparable to tertiary centres. Its simplicity makes it a valuable adjunct to clinical judgement, aiding early discussions with families, guiding ICU resource allocation and informing referral decisions. By validating the score in a DGH, our findings support its broader implementation, potentially improving standardised neuroprognostication in non-tertiary settings. The MIRACLE2 score was developed from various demographic and clinical factors.[3] Pareek *et al* identified a simplified model of seven independent predictors of poor outcomes with the highest statistical association, practical applicability and clinical relevancy. Excellent agreement was shown with the original study.[3] Although the MIRACLE2 shows excellent negative and positive predictive values for poor neurological outcomes in patients with low and high scores, outcomes seem more uncertain for intermediate-risk patients (MIRACLE2: 3–4). These patients represented 35% of our cohort. Half had good neurological recovery at discharge, regardless of the presenting ECG. This advocates the need for case-by-case consideration of overall individual risk, potentially involving the multidisciplinary team and using other variables not included in the MIRACLE2, such as functional baseline and zero/low-flow time, in the decision-making process. In our cohort, the variables associated with the most significant increase in the probability of poor neurological outcome were age category, initial non-shockable rhythm, non-reactivity of pupils and any use of epinephrine in keeping with previous evidence.[3] An earlier study demonstrated that age is an independent poor prognostic factor in OHCA patients, supporting this study's findings and the original MIRACLE2 trial data.[3 13] This can be explained by a higher comorbid status in the elderly population.

Several factors have been shown to independently predict poor neurological outcomes in OHCA patients, including initial rhythm type, pupillary reflex, and the use of epinephrine. Our findings confirm that these variables significantly contribute to the likelihood of poor outcomes, which aligns with previous studies. It is well known that OHCA patients with shockable rhythms have preferable outcomes to patients with non-shockable rhythms due to the generally more effective management strategies.[14] Therefore, it is no surprise that in keeping with the original data, an initial non-shockable rhythm was associated with an eightfold increase in the probability of poor neurological outcomes compared with the sevenfold increase in the original trial. The change in rhythm had a threefold increase in the likelihood of poor neurological outcomes, similar to the original research. Although a shift from a non-shockable rhythm to a shockable one was associated with preferable outcomes,[15] most of the changes in rhythm in this study were from shockable to non-shockable, which is presumed to carry a poorer prognosis. Epinephrine remains in the European Resuscitation Council recommendations,[16] although randomised clinical trials did not prove any neurological benefit in an arrest situation.[17] Our study showed a 23-fold increase in the probability of poor neurological outcomes when epinephrine was used. Its use can indicate a prolonged zero-flow time (time from arrest to initiation of CPR) and a complicated course with multiple arrest cycles. Pupillary reflex involves a subjective assessment with a possible improvement in recovery response. This poses a challenge in using it as a prognostic factor, with a specificity of around 50% for neurological outcomes,[18 19] possibly due to confounding factors like drugs and ambient light. However, the OR for poor neurological outcomes was 10.8 (compared with 2.49 in the original study).

Compared with the OHCA, TTM and CAHP scores, the MIRACLE2 score had equivalent discrimination performance with the added significant benefit of being practical for clinical application on admission. It is vital to note that the intention of the MIRACLE2 score is not to replace clinical judgement but to provide a practical method for objectively evaluating risk for poor neurological outcomes before delivering potentially invasive and expensive treatment. Unlike tertiary care centres with access to advanced neuroprognostication tools,

Limitations

The single-centre design of our study offers advantages. The consistent detailed data collection and clinical protocols allow for a comprehensive evaluation of the MIRACLE2 score in this DGH. Furthermore, patient populations in a single centre are likely more homogeneous, making it easier to control for local confounding factors and better assess specific intervention effects in that setting. However, this limits the generalisability of our findings to other centres, where patient populations and care protocols may differ. Moreover, the smaller sample size reduces the statistical power, potentially limiting our ability to detect significant differences in secondary outcomes.

The study included only routinely collected data from medical records and the number of patients who presented to the hospital. The data on the MIRACLE2 score are based on an immediate assessment of critically ill patients, and the response represents an initial assessment of the presentation (within the first hour). The pupillary response is a factor that might evolve as patients progress through their post-ROSC care. Ongoing evaluation of pupillary response is needed as part of the patient's neuroprognostication. The utility of patients with an intermediate score seems to be low. This cohort requires careful consideration of the best approach on a case-by-case basis in a multidisciplinary approach. In addition, the retrospective nature of this analysis introduces limitations such as potential selection bias, incomplete records and the inability to control for all confounders. These challenges highlight the need for future prospective, multicentre studies to confirm our findings and provide more generalisable data on the utility of the MIRACLE2 score in neuroprognostication.

CONCLUSIONS

The MIRACLE2 score provides an accurate and practical neuroprognostication tool in patients with OHCA of cardiac origin presenting to DGHs with HACs. It can facilitate rapid decision-making at the front door, guide the delivery of invasive and costly therapies to the appropriate patients and avoid futility.

Contributors SD and FS collected the data. IA and SD accessed and verified the data. IA and SD are the guarantors. IA analysed the data. IA, FS and SD wrote the first draft of the manuscript. MB supervised the project and edited the manuscript.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants but the research reported in this article adhered to the Declaration of Helsinki. The project was conducted as part of an audit approved by the hospital board and involved prospective analysis of retrospectively collected anonymised data (reference: UHDBM239). Therefore, the hospital board waived the need for consent. The research reported in this article adhered to the Declaration of Helsinki. The project was conducted as part of an audit approved by the hospital board and involved prospective analysis of retrospectively collected anonymised data (reference: UHDBM239). Therefore, the hospital board waived the need for consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Data are available on reasonable request. Data may be obtained from a third party and are not publicly available. All data relevant to the study are included in the article or uploaded as supplementary information. Data relating to this study are available on reasonable request from the corresponding author.

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