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Research paper

Magnetic resonance imaging in comatose adults resuscitated after out-of-hospital cardiac arrest: A posthoc study of the Targeted Therapeutic Mild Hypercapnia after Resuscitated Cardiac Arrest trial

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ABSTRACT

Background: Neuroimaging with magnetic resonance imaging (MRI) may assist clinicians in evaluating brain injury and optimising care in comatose adults resuscitated after out-of-hospital cardiac arrest (OHCA). However, contemporary international data on its use are lacking.
Aim: The primary aim was to compare the patient characteristics, early postresuscitation care, and neurological outcomes of patients according to MRI use.
Methods: We performed a posthoc analysis of the Targeted Therapeutic Mild Hypercapnia after Resuscitated Cardiac Arrest (TAME) trial, a multinational randomised trial comparing targeted mild hypercapnia or normocapnia in comatose adults after OHCA.
Results: After exclusions, 1639 patients enrolled in the TAME trial were analysed. Of these, 149 (9%) had an MRI. Compared to non-MRI patients, MRI patients were younger (58.9 versus 61.7 years, p: 0.02), had a longer median time from OHCA to return of spontaneous circulation (30 versus 25 min, $p < 0.0001$), and had a higher average arterial lactate level (8.78 versus 6.74 mmol/L, $p < 0.0001$) on admission to hospital. MRI patients were more likely to receive additional advanced diagnostic assessments during intensive care unit admission ($p < 0.0001$). At 6 months, 23 of 140 patients (16.4%) in the MRI group had a favourable neurological outcome, compared with 659 of 1399 patients (47.1%) in the no-MRI group ($p < 0.001$). On multivariable modelling, country of enrolment was the dominating predictor in the likelihood of an MRI being performed.

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Conclusions: In the TAME trial, 9% of patients had an MRI during their intensive care unit admission. Among these patients, only 16% had a favourable neurological outcome at 6 months.

1. Background

Out-of-hospital cardiac arrest (OHCA) is a life-threatening event associated with high mortality.[1] Among survivors, hypoxic ischaemic brain injury is the leading cause of disability and has considerable immediate and long-term consequences on individual patients, their families, and the broader community.[2,3] For comatose adults resuscitated after OHCA, accurate prognostication is crucial to avoid false pessimistic prediction of unfavourable outcome and subsequent withdrawal of life-sustaining therapies (WLST).[3–5]

International guidelines recommend a multimodal approach to the prognostication of patients who are comatose after resuscitation from OHCA.[3–5] Prognostic assessment typically involves clinical examination, electrophysiology, brain injury biomarkers, and neuroimaging.[5,6] These assessments are often performed between 72 and 96 h after OHCA and after major confounders have been excluded (e.g., residual sedation and/or hypothermia).[5,6]

Neuroimaging, particularly magnetic resonance imaging (MRI) of the brain, may contribute to understanding the extent of structural injury and may guide decisions related to ongoing care.[6] To date, however, research on postresuscitation MRI has been based on single-centre studies or systematic reviews of such single-centre studies focussed on the timing[6] or diagnostic accuracy of MRI[7–9] for poor outcomes or mortality after cardiac arrest (CA). Thus, there are no contemporary data drawn from multicentre randomised trials to describe the use of MRI along with the characteristics, early post-resuscitation care, and neurological outcomes of patients after CA.

Accordingly, using data from the Targeted Therapeutic Mild Hypercapnia after Resuscitated Cardiac Arrest (TAME) trial,[10] we sought to describe the CA characteristics, early post-CA care, and neurological outcomes of patients who received a brain MRI after resuscitation from an OHCA.

2. Methods

2.1. Trial design

We performed a posthoc analysis of the TAME trial, a multicentre, parallel-group, open-label, randomised trial conducted in 63 intensive care units (ICUs) in 17 countries between 2018 and 2021 (ClinicalTrials.gov number: NCT03114033).[10] The rationale for, ethical approval of (reference: HREC/17/Austin/209) consent model applied, and results of the trial have been previously reported.[11]

2.2. Patient population

Hospitalised comatose adults (18 years or older) resuscitated from OHCA of a presumed cardiac or unknown cause with sustained return of spontaneous circulation (ROSC) of greater than 20 min were eligible for inclusion. Patients were excluded if the time from ROSC to screening exceeded 180 min, the CA was unwitnessed with an initial rhythm of asystole, and/or there were limitations of care. Full details of eligibility are shown in the Supplementary Appendix.

2.3. Randomisation and intervention

Randomisation was stratified according to trial site and, whenever able, coenrolment in the Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial.[12] Patients were randomised in a 1:1 ratio and were assigned to targeted mild hypercapnia (arterial carbon dioxide tension of 50–55 mm Hg) or to targeted normocapnia (arterial carbon dioxide tension of 35–45 mm Hg) for a 24-h period beginning at randomisation.

2.4. Assessment of neurological prognosis and withdrawal of life-sustaining therapy

To assess for poor neurologic prognosis, at 96 h after randomisation or later, a clinician who was blinded to allocation performed a protocol-guided assessment of patients who remained in the ICU.[12] An MRI was encouraged but not mandated. Full details of the neurological assessment are provided in the Supplementary Appendix. Supported by international guidelines, decisions regarding WLST were made at the discretion of the treating medical team.

2.5. General data collection

Managed in a web-based case report form, trained site research coordinators collected demographics and prehospital and hospital data. They also recorded the performance of neurological prognosis assessments (e.g., serum neuron-specific enclose, computerised topography [CT], electroencephalograms [EEGs], somatosensory evoked potentials, and neuroimaging) as well as WLST events. Outcome assessors blinded to allocation assessed 6-month outcomes from the participant (as the primary candidate) or their proxy.

2.6. Classification of TAME patients based on MRI

Using MRI brain scans that were performed during admission to the ICU, patients enrolled in the TAME trial were classified into the MRI group and those who did not were classified into the No-MRI group.

2.7. Primary aim and objectives

The primary aim was to compare the patient characteristics, early postresuscitation care, and neurological outcomes of patients according to MRI use.

Aligned with the TAME trial,[10] the key secondary objective was to report the proportion of patients in each MRI group who had a favourable neurological outcome defined by a Glasgow Outcome Scale-Extended (GOSE) score of 5–8 at 6 months. A GOSE score of 1 indicates death, 2 indicates vegetative state, 3 to 4 indicates severe disability, 5 to 6 indicates moderate disability, and 7 to 8 indicates good recovery. Additional secondary objectives were to compare patient survival and cause of death obtained at 6 months between the two groups.

2.8. Statistical analysis

Baseline comparisons between those that did versus those that did not receive an MRI were performed using Chi-square tests for equal proportion, student t-tests for normally distributed data, and Wilcoxon rank-sum tests otherwise, with results reported as frequency (%), mean (standard deviation), and median (interquartile range), respectively. To determine baseline features that were independently predictive of whether a patient would receive an MRI or not, multivariable logistic regression was used, with results reported as odds ratios (95% confidence interval). Candidate variables for the multivariable model were chosen according to clinical relevance and baseline imbalance. This list included country, age, coronary angiogram, Full Outline of UnResponsiveness (FOUR)[13] motor score, lactate, initial rhythm, cardiopulmonary resuscitation (CPR), arrest location, time from CA arrest to ROSC, coenrolment in TTM2 trial, and treatment allocation in the TAME trial. To facilitate inclusion of key variables with missingness, FOUR motor score (scores 0–4) and lactate (quartiles) were modelled as categorical variables, with missingness treated as an additional category. To further facilitate convergence and enable greater understanding of heterogeneity, four countries with low recruiting numbers (<5) were collapsed together, and the country was included as a fixed variable.

As MRI status was established post randomisation, to enable an unbiased estimate with patient survival, proportional hazards regression was used with MRI treated as a time-dependent variable adjusting for the previously described covariates, with country treated as a random effect and results reported as hazard ratios (95% confidence interval) and presented as a Kaplan–Meier curve. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), and a two-sided p value of 0.05 was used to indicate statistical significance.

3. Results

3.1. Patients

There were 1700 patients enrolled into the TAME trial. After the exclusion of 61 patients, 1639 patients were included in the analysis (Fig. 1). Patients were excluded for the following reasons: consent was withdrawn entirely or partially for 24 patients, there was refusal of consent for follow-up data in 21 patients, 180-day mortality status was unavailable for 15 patients, and one patient had missing information pertaining to MRI (Fig. 1).

Overall, 149 of 1639 patients (9%) underwent MRI of the brain. MRI patients came from trial sites located in 14 of the 17 (82%) countries. Countries with the highest number of MRI group patients were Australia, Switzerland, and Norway (Appendix Table S1).

As shown in Table 1, of the 1639 patients, 1291 (78.8%) were male, and the median age was 61.5 years (standard deviation: 13.8 years). Most patients experienced their OHCA at home (920/1639 patients, 56.1%), the majority had an initial shockable rhythm (1167/1639 patients, 71.2%), and the median time from OHCA to ROSC was 25 min (interquartile range: 17–40 min).

In addition, as shown in Table 1, compared to no-MRI patients, MRI patients were younger (58.9 versus 61.7 years, p 0.02) and had a longer median time from OHCA to ROSC (30 versus 25 min, $p < 0.0001$) and a higher average arterial lactate level (8.78 versus 6.74 mmol/L, $p < 0.0001$) on admission to hospital. At the time of the MRI assessment, most patients (56%) had a documented FOUR score motor response of 2 or less (range: 0–4, with higher scores indicating better motor function). The median time from randomisation into the TAME trial to the MRI being performed was 4.9 days (3.01–7.83 days). Finally, countries in which patients had an MRI performed before the median of 4.9 days from randomisation were France, Ireland, and Switzerland (Appendix Table S2).

Overall, on univariate analysis, the relationship between MRI and mortality by country identified variability in the likelihood of death by country (Appendix Table S3). The country with the strongest relationship between MRI and mortality was Finland, followed by Denmark and Switzerland (Appendix Table S3).

3.2. Comparison of characteristics and early post-CA care

3.2.1. Prehospital and early post-OHCA care

As shown in Table 2, compared to no-MRI patients, MRI patients were statistically more likely to have active mechanical CPR

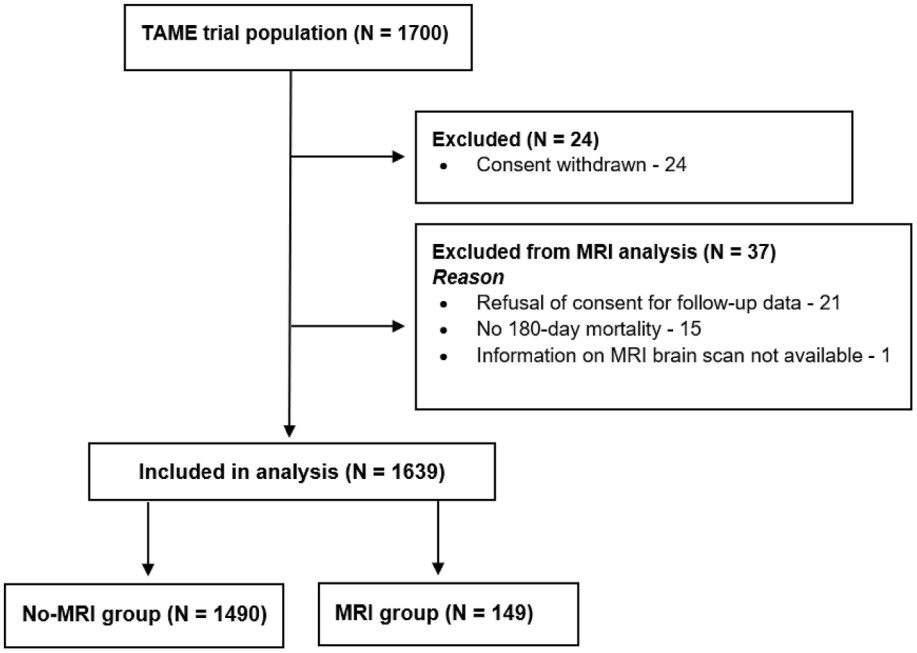

Fig. 1. Flow diagram of study participants.

Table 1
Baseline characteristics.

	All patients (n = 1639)	No MRI (n = 1490)	MRI (n = 149)
Demographic characteristic			
Age—yr, mean (SD)	61.5 (13.8)	61.7 (13.8)	58.9 (14.2)
Male sex—no. (%)	1291 (78.8)	1176 (78.9)	115 (77.2)
Medical history			
Hypertension, no./total. (%)	558/1567 (35.6)	515/1429 (36)	43/138 (31.2)
Diabetes, no. (%)	298 (18.2)	266 (17.9)	32 (21.5)
PCI, no./total. (%)	226/1567 (14.4)	206/1429 (14.4)	20/138 (14.5)
Myocardial infarction, no. (%)	222 (13.5)	209 (14)	13 (8.7)
COPD, no. (%)	166 (10.1)	154 (10.3)	12 (8.1)
Heart failure, no. (%)	132 (8.1)	123 (8.3)	9 (6)
Coronary artery bypass grafting, no./total. (%)	104/1567 (6.6)	98/1429 (6.9)	6/138 (4.3)
NYHA III or IV heart failure, no./total. (%)	28/1587 (1.8)	27/1444 (1.9)	1/143 (0.7)
Characteristic of the cardiac arrest			
Location of the cardiac arrest, no. (%)			
Place of residence	920 (56.1)	837 (56.2)	83 (55.7)
Public place	531 (32.4)	488 (32.8)	43 (28.9)
Work place	123 (7.5%)	106 (7.1)	17 (11.4)
Other	65 (4)	59 (4)	6 (4)
Bystander witnessed cardiac arrest	1447 (88.3)	1316 (88.3)	131 (87.9)
Bystander performed CPR	1326 (80.9)	1213 (81.4)	113 (75.8)
First monitored rhythm, no. (%)			
Shockable rhythm	1167 (71.2)	1058 (71)	109 (73.2)
Unknown rhythm, shock administered	42 (2.6)	38 (2.6)	4 (2.7)
Nonshockable rhythm	352 (21.5)	319 (21.4)	33 (22.1)
Unknown, no shock administered	24 (1.5)	22 (1.5)	2 (1.3)
Minutes from cardiac arrest to sustained ROSC, median (IQR)	25 (17–40)	25 (16–39)	30 (20–50)
Clinical characteristic on hospital admission			
Tympanic temperature—°C, mean (SD)	35.4 (1.07)	35.4 (1.04)	35.3 (1.27)
FOUR[a] motor score, mean (SD)	0.31 (0.82)	0.33 (0.84)	0.11 (0.47)
Bilateral corneal reflexes present, no./total. (%)	229/547 (41.9)	205/496 (41.3)	24/51 (47.1)
Bilateral pupillary reflexes present, no./total. (%)	1026/1307 (78.5)	922/1179 (78.2)	104/128 (81.3)
Arterial pH, median (IQR)	7.21 [7.10–7.29]	7.21 [7.10–7.29]	7.18 [7.09–7.27]
Arterial lactate level—mmol/litre, mean (SD)	6.88 (3.78)	6.74 (3.68)	8.78 (4.53)
First measured arterial carbon dioxide tension, mean (SD)	52.7 (18.9)	52.6 (18.2)	53.6 (25.4)
Shock—no. (%)	452 (27.6)	404 (27.1)	48 (32.2)
ST-segment elevation myocardial infarction, no. (%)	661 (41.1)	600 (41)	61 (41.8)

Abbreviations: °C, degrees Celsius; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; IQR, interquartile range; MRI, magnetic resonance imaging, mmol/litre, millimole per litre; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; SD, standard deviation.

[a] FOUR motor score, The scale for the Full Outline of Unresponsiveness (FOUR) motor score ranges from 0 to 4, with higher scores indicating better motor function. Data on the FOUR motor score were available for 775 patients in the mild hypercapnia group and for 781 in the normocapnia group.

commenced prehospital ($p < 0.0001$) and have a coronary angiography procedure prior to ICU admission.

While in the ICU, MRI patients were more likely to receive EEG, neuron-specific enclose, and somatosensory evoked potential diagnostic assessments during ICU admission. Of these diagnostic assessments, for MRI patients, EEG was the most common and was performed in 125 of 149 patients (83.9%) compared to 446 of 1489 patients (30%) in no-MRI patients (Table 2). For no-MRI patients, the most common diagnostic assessment was computerised tomography (CT) of the brain, which was performed in 1068 of 1490 patients (71.7%).

Overall, 720 of 1638 patients (44%) had prognostication performed at 96 h or later. In addition, 125 of 149 (82%) MRI patients had such 96-h prognostication compared to 595 of 1489 (40%) no-MRI patients. Of note, a poor prognosis based on this assessment occurred in 58 of 125 (46%) MRI patients compared to 135 of 595 (22%) no-MRI patients. In developing a 96-h prognosis, the results of the MRI were used in 75 of 149 (49%) of MRI patients. On sensitivity analysis, in patients in whom prognostication was performed, the substantive characteristics and outcomes for patients with MRI and those with no MRI were similar (Appendix Table S4). While in the ICU, compared to no-MRI patients, MRI patients had a longer median duration of invasive mechanical ventilation (189 versus 66 h). A comparison of multiple investigations and treatments received and performed on patients in both groups is shown in Table 2. Finally, compared to no-MRI patients, MRI patients had a significantly longer stay in the ICU and in hospital (Table 2).

3.3. Neurological outcomes at six months

For the 149 MRI patients, mortality data were available for all patients, and full categorical GOSE outcome data were available for 140 (92%). At 6 months, 23 of 140 (16.4%) MRI patients had a favourable neurological outcome (GOSE score: 5–8), compared to 659 of 1399 (47.1%) no-MRI patients ($p < 0.001$) (Table 3). Across the individual categories of the GOSE, more MRI patients were classified as having “lower severe disability” and fewer as “upper good recovery” than no-MRI patients (both, $p < 0.0001$) (Table 3).

3.3.1. Mortality and cause of death at six months

By 6 months, 101 of 149 MRI patients (67.8%) and 665 of 1490 no-MRI patients (44.6%) had died ($p < 0.0001$). Death due to a presumed “cerebral cause” was the most common reported cause of death for patients in both groups but was statistically higher in MRI patients (64 of 96 patients, 66.7%) than in no-MRI patients (302 of 617 patients, 48.9%) ($p < 0.0001$) (Table 3). The proportion and comparison of causes of death are also shown in Table 3. Kaplan–Meier curves displaying patient survival censored at 250 days from randomisation for patients who did or did not have an MRI performed while admitted to the ICU are shown in Fig. 2.

Table 2
Investigations and treatments.

	All patients (n = 1639)	No MRI (n = 1490)	MRI (n = 149)	*p* values
Additional cardiac arrest characteristics				
Active mechanical CPR device, no./total (%)	640/1638 (39.1)	555 (37.8)	85 (57)	<0.0001
Number of defibrillations, median (IQR)	2 (1–4)	2 (1–4)	2 (1–4)	0.45
Artificial airway inserted, no. (%)	1470 (89.7)	1342 (90.1)	128 (85.9)	0.11
Adrenaline dose - total, mg, median (IQR)	1 (0–3)	1 (0–3)	2 (1–4)	<0.001
Investigations prior to ICU admission, no./total (%)				
Coronary angiography	878/1235 (71.1)	782/1119 (69.9)	96/116 (82.8)	0.004
CT brain	722/1188 (60.8)	657/1068 (61.5)	65/120 (54.2)	0.12
Time to intervention				
Hours from CA to coronary angiography, median (IQR)	2.55 (1.92–3.62)	2.55 (1.92–3.68)	2.53 (1.88–3.17)	0.15
PCI, no./total (%)	580 (35.4)	527 (35.4)	53 (35.6)	0.96
Hours from CA to PCI, median (IQR)	2.42 (1.87–3.17)	2.45 (1.87–3.17)	2.33 (1.62–3.17)	0.42
Diagnostic procedures during ICU admission				
CT brain, no. (%)	1188 (72.5)	1068 (71.7)	120 (80.5)	0.02
EEG, no./total. (%)	571/1638 (34.9)	446 (30)	125 (83.9)	<0.0001
NSE, no./total. (%)	548/1638 (33.5)	478 (32.1)	70 (47)	<0.0001
SSEP, no./total. (%)	192/1638 (11.7)	151 (10.1)	41 (27.5)	<0.0001
Interventions during ICU admission, no./total (%)				
CABG	11/1638 (0.6)	10/1489 (0.6)	1/149 (0.6)	1.0
Coronary angiography	243/1638 (14.8)	225/1448 (15.1)	18/149 (12.1)	0.32
PCI	110/1638 (6.7)	98/1489 (6.6)	12/149 (8.1)	0.49
Device used for targeted temperature management	1100/1638 (67.2)	997/1489 (67)	103/149 (69.1)	0.59
Assessment of neurological prognostication[a]				
Prognostication at ≥96 h no./total. (%)	720/1638 (44)	595/1489 (40)	125/149 (83.9)	<0.0001
Poor prognosis likely, no./total. (%)	193/720 (26.8)	135/595 (22.7)	58/125 (46.4)	<0.0001
MRI available at the time of prognostication, no. (%)	75 (4.6)	0 (0)	75 (49)	<0.0001
Duration of invasive mechanical ventilation				
Hours receiving mechanical ventilation in the ICU, median (IQR)	72 (41.9–136)	66 (40.8–119)	189 (113–303)	<0.0001
Renal replacement therapy during ICU stay, no. (%)				
CRRT	156 (9.5)	139 (9.3)	17 (11.4)	0.41
Length of time from randomisation to ICU and hospital discharge, median (IQR)				
Hours from randomisation to the ICU discharge	103 (61.5–172)	96.9 (57.3–162)	210 (130–336)	<0.0001
Days from randomisation to hospital discharge	8.31 (4.05–16.1)	8.01 (3.82–15.7)	11.6 (5.93–22)	<0.0001

Abbreviations: CA, cardiac arrest; CABG, coronary artery bypass graft surgery; CPR, cardiopulmonary resuscitation; CRRT, continuous renal replacement therapy; CT, computerised tomography, EEG, electroencephalogram; IABP, intra-aortic balloon pump; ICD, Implantable cardiac defibrillator; ICU, intensive care unit; IQR, interquartile range; MRI, magnetic resonance imaging; NSE, neuron-specific enclose; PCI, percutaneous coronary intervention; SSEP, somatosensory evoked potential; TAME, Targeted Therapeutic Mild Hypercapnia after Resuscitated Cardiac Arrest.

[a] Assessment of neurological prognostication was performed according to the TAME trial protocol for the assessment and is described in the supplementary appendix.

Table 3
Neurological outcomes at 180 days.

	No MRI	MRI	*p* value
Primary outcome, no./total (%)			
Favourable outcome (GOSE score: 5–8)	659/1399 (47.1%)	23/140 (16.4%)	<0.0001
GOSE category, no./total (%)			<0.0001
Dead (1)	665 (44.6%)	101 (67.8%)	
Vegetative state (2)	3 (0.2%)	0 (0%)	
Lower severe disability (3)	30 (2.1%)	10 (7.1%)	
Upper severe disability (4)	42 (3.0%)	6 (4.3%)	
Lower moderate disability (5)	80 (5.7%)	7 (5%)	
Upper moderate disability (6)	138 (9.9%)	5 (3.6%)	
Lower good recovery (7)	208 (14.9%)	7 (5%)	
Upper good recovery (8)	233 (16.7%)	4 (2.9%)	
Day 180 mortality, no. (%)	665 (44.6%)	101 (67.8%)	<0.0001
Cause of death[a], no. (%)			<0.0001
Cerebral	302 (48.9)	64 (66.7)	
Cardiovascular	178 (28.8)	16 (16.7)	
Multiorgan failure	98 (15.9)	8 (8.3)	
Other	39 (6.3)	8 (8.3)	

Abbreviations: GOSE, Glasgow Outcome Scale Extended; MRI, magnetic resonance imaging. Scores for the GOSE range from 1 to 8, with 1: dead, 2: vegetative state, 3: lower severe disability, 4: upper severe disability, 5: lower moderate disability, 6: upper moderate disability, 7: lower good recovery, 8: upper good recovery. A favourable neurological outcome was defined as a GOSE score of 5 to 8.

[a] Presumed cause of death (COD) data were collected at hospital discharge only resulting in differing cumulative totals to that of Day 180 mortality.

3.4. Likelihood of MRI use and outcomes

On univariate analysis, several predictors of use of MRI were identified. These included workplace as location of CA, time from CA to ROSC, active mechanical CPR, age at randomisation, coronary angiography before ICU admission, and country of enrolment (Table 4). However, following multivariable analysis, only country of enrolment along with age at randomisation were significant predictors of the use of MRI for prognostication (Table 4). In their aggregate, the dominant predictor of the use of MRI for prognostication was the country of enrolment (Table 4).

Overall, on univariate analysis, the relationship between MRI and mortality by country identified variability in the likelihood of death by country (Appendix Table S3). The country with the strongest relationship between MRI and mortality was Finland, followed by Denmark and Switzerland (Appendix Table S3).

On multivariable analysis, compared to no-MRI patients, patients who had an MRI performed were greater than three times more likely to die (Appendix Table S5). Additionally, apart from MRI being performed, several patient characteristics were identified as predictors of worse outcomes. These characteristics included having a CA of a nonshockable rhythm, longer time from CA to ROSC, higher lactate levels on admission to hospital, greater level of unconsciousness on admission to hospital (FOUR score motor

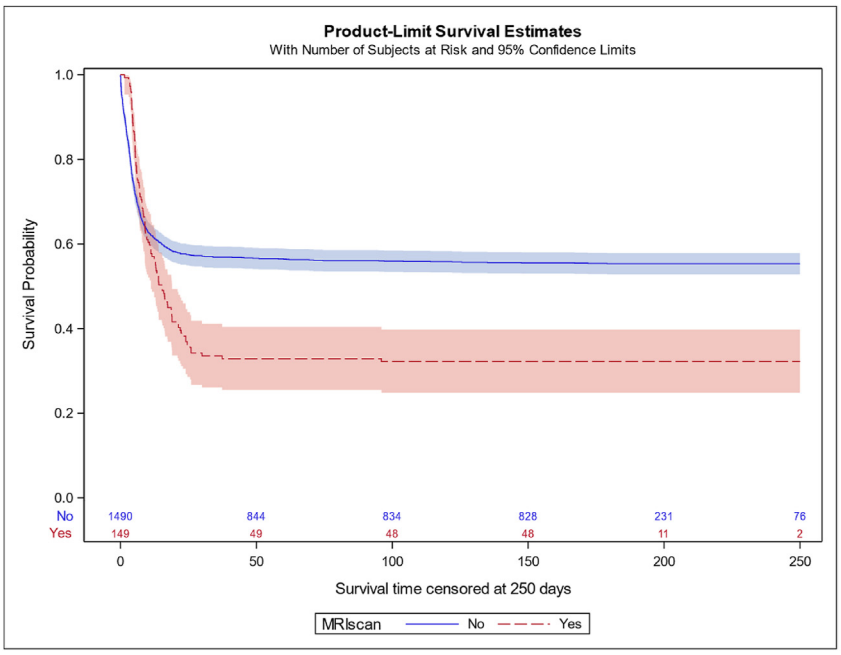

Fig. 2. Kaplan–Meier curves displaying patient survival censored at 250 days from randomisation of patients who did or did not have an MRI performed while admitted to the intensive care unit. MRI, magnetic resonance imaging.

response), and increasing age, with each additional year increasing the risk of death by 3% (Appendix Table S5).

4. Discussion

4.1. Key findings

In this posthoc analysis of the TAME trial, we evaluated the patient characteristics, early care, and outcomes of patients who received an MRI brain scan. There were five key findings. First, approximately one in 10 patients had an MRI performed during their ICU admission. Second, compared to no-MRI patients, MRI patients were younger, had a longer duration from OHCA to ROSC, were more likely to have received active mechanical CPR, and remained mechanically ventilated for longer. Moreover, they had more additional neurology-oriented diagnostic assessments performed while in the ICU, and their stay in the ICU and hospital was longer than that of no-MRI patients. Third, patients who underwent an MRI were >3 times more likely to die than no-MRI patients. Fourth, only one in six MRI group patients had a favourable neurological outcome at 6 months, approximately a third of the rate in no-MRI patients. Finally, country of enrolment was the strongest predictor of the likelihood of MRI use for prognostication.

4.2. Comparison with other studies

Our findings build mostly on the observational, retrospective, and single-centre studies that have explored the incidence of MRI and the outcomes of patients following OHCA. A systematic review and meta-analysis of such studies, published in 2020,[6] provided a description of 21 MRI studies that included a total of 1105 patients (range of 9–185 patients per study) in an attempt to evaluate the prognostication value of MRI. Timing of MRI assessment was either unspecified or varied from 24 to 96 h, within the first 5–7 days or out to 10 or 28 days post OHCA.[6] In our study, the median time from randomisation to the MRI being performed was 4.9 days.

Data from our study show that OHCA event characteristics and early post–CA care treatments, interventions, and hospital outcomes in the MRI group patients were similar to those in previous studies.[6,12] Moreover, as expected, patients who received an MRI were also likely to receive other neurologic diagnostic assessments while in the ICU. Additionally, MRI findings were commonly incorporated into the overall assessment of likely neurological outcome during ICU admission. This is concordant with international postCA guidelines concerning the application and use of a multimodal approach to prognostication in such patients.[4]

International postCA guidelines recommend neuroimaging as part of the multimodal approach to prognostication particularly when deciding to continue or withdraw life-supporting therapies.[4] For TAME trial patients, a range of neuroimaging tests was performed, with MRI being used in 9% of cases. The rate of MRIs performed in TAME (published in June 2023) was similar to that of the TTM2 trial[12] (published in June 2019) at approximately 8% of patients, though greater than the approximately 4% of TTM1 trial patients (published in December 2013).[14] Though the rate of MRI performance is low, it is likely to reflect current practice as it differs from the high-rate of MRI performance in a single-centre study within a prospectively dedicated investigational program.[ref] For the first time, however, we show the dominant nature of the "country of enrolment" as a predictor of MRI. This finding appears to reflect a level of regional variation that is not easily explained by patient characteristics but may be subject to tradition and resource availability.

Within previous studies of MRI after CA, neurological assessment was typically performed at ICU or hospital discharge using the Cerebral Performance Category scale or the Modified Rankin Score, whereas long-term follow-up was absent.[6] We are unable to report the method or findings of the MRI assessment for TAME trial patients as these data were not captured in the trial database. We are, however, the first to report 6-month neurological outcomes,

Table 4
Univariable and multivariable prediction of MRI status.

Effect	Raw odds ratio (95% CI)	P value	Adjusted odds ratio (95% CI)	P value
Countries (ref = United Kingdom)		<0.0001		<0.0001
Australia	4.71 (2.08–10.69)		4.74 (1.97–11.41)	
Belgium	1.72 (0.43–6.83)		1.99 (0.49–8.11)	
Denmark	2.42 (0.92–6.37)		2.36 (0.86–6.49)	
Finland	1.01 (0.21–4.98)		0.91 (0.17–4.75)	
France	1.56 (0.18–13.19)		1.17 (0.13–10.44)	
Ireland	12.00 (4.46–32.32)		16.41 (5.53–48.65)	
Norway	4.09 (1.59–10.5)		3.52 (1.28–9.68)	
New Zealand	0.80 (0.23–2.76)		1.06 (0.29–3.84)	
Saudi Arabia	13.50 (4.65–39.22)		14.41 (4.41–47.04)	
Slovenia	0.89 (0.11–7.38)		1.20 (0.14–10.34)	
Sweden	6.50 (2.25–18.76)		8.58 (2.73–26.93)	
Switzerland	26.24 (11.12–61.89)		21.32 (8.32–54.64)	
Canada, Italy, Netherlands, and Singapore[a]	5.57 (0.60–51.58)		5.34 (0.55–51.48)	
Coronary angiography before ICU admission	1.64 (1.16–2.33)	0.006	1.30 (0.85–2.00)	0.23
FOUR[b] motor score (ref = missing [n = 109 (6.6%])		<0.0001		0.33
0 (n = 1319)	1.23 (0.61–2.48)		0.85 (0.37–1.94)	
1 (n = 38)	0.95 (0.24–3.72)		0.59 (0.13–2.62)	
2 (n = 95)	0.62 (0.20–1.91)		0.49 (0.14–1.67)	
3 (n = 72)	0.16 (0.02–1.26)		0.11 (0.01–0.91)	
4 (n = 6)	0 (0-.)		0 (0-.)	
Lactate quartiles (ref = missing (n = 976 [59.6%])		<0.0001		0.16
Lactate 1st quartile	0.31 (0.13–0.72)	0.03	0.41 (0.17–1.01)	
Lactate 2nd quartile	0.69 (0.37–1.28)	0.92	0.79 (0.39–1.63)	
Lactate 3rd quartile	0.56 (0.28–1.09)	0.53	0.48 (0.23–1)	
Lactate 4th quartile	1.12 (0.66–1.88)	0.03	0.85 (0.47–1.56)	
Initial rhythm of PEA	1.04 (0.7–1.57)	0.83	0.84 (0.52–1.35)	0.47
Active mechanical CPR	2.24 (1.59–3.15)	<0.0001	1.3 (0.86–1.96)	0.21
Workplace as place of CA	1.68 (0.98–2.89)	0.06	1.63 (0.88–3.02)	0.12
Age at randomisation	0.99 (0.97–1)	0.02	0.98 (0.97–1)	0.02
Enrolled in TTM2 and TAME trials	0.49 (0.3–0.8)	0.005	0.97 (0.55–1.73)	0.93
Time from CA to ROSC, in hours	1.63 (1.15–2.31)	0.006	1.3 (0.86–1.99)	0.22
Allocated to mild hypercapnia	0.82 (0.58–1.15)	0.24	0.8 (0.55–1.15)	0.23

Abbreviations: CA, cardiac arrest; CI, confidence interval; CPR, cardiopulmonary resuscitation; ICU, intensive care unit; MRI, magnetic resonance imaging; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; TAME trial, Targeted Therapeutic Mild Hypercapnia after Resuscitated Cardiac Arrest trial; TTM2, Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest trial; UK, United Kingdom.
Predicative model: to determine baseline features that were independently predictive of whether a patient would receive an MRI or not, multivariable logistic regression was used with results reported as odds ratios (95% CI). Candidate variables for the multivariable model were chosen according to clinical relevance and baseline imbalance.
[a] Grouping of low recruitment counties: Canada (one patient), Italy (two patients), Netherlands (one patient), and Singapore (four patients).
[b] FOUR motor score: the scale for the Full Outline of Unresponsiveness (FOUR) motor score ranges from 0 to 4, with higher scores indicating better motor function. Data on the FOUR motor score were available for 775 patients in the mild hypercapnia group and for 781 in the normocapnia group.

including full categorical GOSE, for 140 TAME patients who had an MRI.

4.3. Study implications

Our study findings imply a selection bias in the performance of MRI in OHCA patients. Specifically, patients who received an MRI tended to be younger, have greater illness severity, and received more additional investigations. These characteristics may reflect the fact that neuroprognostication was difficult in such patients and that MRI scanning was used in an effort to reduce uncertainty.[15] Moreover, we identified that MRI use varied greatly by country. Between-country variation may in itself be related to health service provision, resource availability, or local culture pertaining to neurological assessment following resuscitation from OHCA. Nonetheless, our findings support the view that despite lack of robust data regarding its prognostic contribution, MRI continues to be used in the evaluation of brain injury and outcome prognostication of comatose CA patients.

4.4. Strengths and limitations

Our study has three key strengths. First, data on the prevalence of MRI were drawn from a contemporary multicentre trial that incorporated a systematic approach to the assessment and reporting of neurological prognostication in comatose adults after CA. Second, this study is the first to describe key OHCA characteristics, early post-OHCA care, and longer-term outcomes of such patients. Third, as the TAME trial enrolled patients in 17 countries, we were able to report regional variation in the performance of MRI in comatose adults after CA.

We acknowledge several limitations. First, as we used data derived from the TAME trial, we do not have data on the findings of the MRI scans in individual patients or how the MRI scan was performed (e.g., use of contrast agent, diffusion-weighted imaging, or arterial spin labelling). As such, we cannot describe the relationship between specific MRI findings and potential disabilities experienced by survivors. Second, this is a posthoc analysis based on a randomised controlled trial designed primarily to address the original hypothesis of the TAME trial. Accordingly, we recommend caution when interpreting our findings and view our findings as hypothesis-generating. Third, the use of dichotomised outcomes for the neurological outcomes of CA patients at 6 months is a crude assessment that fails to acknowledge the nuances of societal participation and cognitive function. Fourth, as an MRI was not performed in patients who died or were discharged from the ICU prior to 96 h, our study is prone to survival bias. However, to negate this, when considering patient survival, we treated MRI status as a

time-dependent variable. Finally, while TAME was conducted in many sites and counties, there was significant regional variation in the rate of MRI scans being performed.

5. Conclusion

In conclusion, from our posthoc analysis of the TAME trial, we found that almost one in 10 patients had an MRI scan during their ICU admission and that country of enrolment was the strongest predictor of the likelihood of MRI use. MRI group patients were younger, had a longer duration from OHCA to ROSC, were more likely to have received active mechanical CPR, and had more additional neurology-oriented diagnostic assessments performed while in the ICU. In these patients, at 180 days, only one in 6 had a favourable neurological outcome. This information provides the necessary epidemiologic background to the conduct of more in-depth studies of the role of MRI in neuroprognostication.

CRediT authorship contribution statement

GE: conceptualisation, methodology, formal analysis, writing—original draft, writing—review and editing validation, visualisation, supervision, project administration, Funding acquisition.
MB: formal analysis, writing—review and editing, visualisation.
AN: writing—review and editing, Funding acquisition.
JD: writing—review and editing.
NN: writing—review and editing.
RP: writing—review and editing, Funding acquisition.
TC: writing—review and editing.
TO: writing—review and editing.
AMG: writing—review and editing.
MI: writing—review and editing.
MH: writing—review and editing.
PM: writing—review and editing.
FW: writing—review and editing.
MMK: writing—review and editing.
ML: writing—review and editing.
RB: Conceptualisation, methodology, writing—review and editing.

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Data available statement

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data are not available.

Conflict of interest

Associate Professor Rachael Parke is an Editor with Australian Critical Care. This manuscript has been managed by Senior Editor, Associate Professor Tom Buckley, and Associate Professor Parke has had no input into the decision-making process.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aucc.2024.09.015.

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