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Citation for published version:
McGuigan, PJ, Edwards, J, Blackwood, B, Dark, P, Doidge, JC, Harrison, DA, Kitchen, G, Lawson, I, Nichol, AD, Rowan, KM, Shankar-Hari, M & McAuley, DF 2023, 'The association between time of in hospital cardiac arrest and mortality: a retrospective analysis of two UK databases', *Resuscitation*. https://doi.org/10.1016/j.resuscitation.2023.109750

Digital Object Identifier (DOI):
10.1016/j.resuscitation.2023.109750

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Resuscitation

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Download date: 17. Apr. 2023

RESUSCITATION xxx (2023) xxx–xxx

Available online at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

The association between time of in hospital cardiac arrest and mortality; a retrospective analysis of two UK databases

Peter J McGuigan[a,b,*], *Julia Edwards*[c], *Bronagh Blackwood*[b], *Paul Dark*[d], *James C. Doidge*[c], *David A. Harrison*[c], *Gareth Kitchen*[e,f], *Izabella Lawson*[c], *Alistair D. Nichol*[g,h,i], *Kathryn M. Rowan*[c], *Manu Shankar-Hari*[j,k], *Danny F McAuley*[a,b]

Abstract

Aims: The incidence of in hospital cardiac arrest (IHCA) varies throughout the day. This study aimed to report the variation in incidence of IHCA, presenting rhythm and outcome based on the hour in which IHCA occurred.

Methods: We conducted a retrospective analysis of the National Cardiac Arrest Audit (NCAA) including patients who suffered an IHCA from 1st April 2011 to 31st December 2019. We then linked the NCAA and intensive care Case Mix Programme databases to explore the effect of time of IHCA on hospital survival in the subgroup of patients admitted to intensive care following IHCA.

Results: We identified 115,690 eligible patients in the NCAA database. Pulseless electrical activity was the commonest presenting rhythm (54.8%). 66,885 patients died in the immediate post resuscitation period. Overall, hospital survival in the NCAA cohort was 21.3%.

We identified 13,858 patients with linked ICU admissions in the Case Mix Programme database; 37.0% survived to hospital discharge. The incidence of IHCA peaked at 06.00. Rates of return of spontaneous circulation, survival to hospital discharge and good neurological outcome were lowest between 05.00 and 07.00. Among those admitted to ICU, no clear diurnal variation in hospital survival was seen in the unadjusted or adjusted analysis. This pattern was consistent across all presenting rhythms.

Conclusions: We observed higher rates of IHCA, and poorer outcomes at night. However, in those admitted to ICU, this variation was absent. This suggests patient factors and processes of care issues contribute to the variation in IHCA seen throughout the day.

Keywords: Cardiac arrest, Circadian rhythm, Critical care, Mortality

Introduction

One in 625 patients admitted to UK hospitals suffer in-hospital cardiac arrest (IHCA).[1] Mortality is high, with less than one in five patients surviving to hospital discharge.[1] Rates of IHCA and outcomes vary throughout the day.[2,3] Patients who suffer an IHCA at night are less likely to achieve return of spontaneous circulation (ROSC) and survive.[2–7]

It is unclear whether circadian rhythm, patient characteristics or processes of care drive diurnal IHCA differences.[6,7] Circadian rhythm is defined as cyclical changes in physiology throughout the day.[8] Variations in physiology which predispose to ischaemic and thromboembolic events may result in a night time nadir and morning peak in rates of IHCA.[5,9–11]

The National Cardiac Arrest Audit (NCAA) is the UK national clinical audit of IHCA. Previous NCAA database analysis found no differences in patient characteristics who suffered IHCA at night, leading authors to conclude that poorer outcomes were due to processes of care.[7] However, the limited patient dataset collected by NCAA in turn limits the scope for research based on analysis of NCAA data alone.[7,12] Patients who suffer IHCA often have severe comorbidities and are dependent on others for care.[13] The case mix programme (CMP) is the national clinical audit of patient outcomes from adult, general intensive care units (ICUs) in England, Wales and Northern Ireland. The CMP contains additional information which includes pre-

* Corresponding author.
E-mail address: peter.mcguigan@belfasttrust.hscni.net (P.J McGuigan).

https://doi.org/10.1016/j.resuscitation.2023.109750
Received 22 December 2022; Received in Revised form 2 February 2023; Accepted 18 February 2023

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Please cite this article as: Peter J McGuigan, J. Edwards, B. Blackwood et al., The association between time of in hospital cardiac arrest and mortality; a retrospective analysis of two UK databases, RESUSCITATION, https://doi.org/10.1016/j.resuscitation.2023.109750

admission level of dependency and diagnostic categories. Thus, linkage of the NCAA and CMP databases represents an opportunity to correct for patient characteristics in those with IHCA admitted to ICU. Furthermore, consultant-level input at the point of referral to ICU may address process of care issues previously identified in IHCA which contribute to poorer outcomes at night.[13,14]

We hypothesized that the incidence of IHCA, presenting rhythm and mortality following IHCA varies based on hour in which the IHCA occurred but that patient factors and processes of care, and not circadian rhythm, may explain variation in IHCA outcomes.

Methods

Data source

In the UK, the Intensive Care National Audit and Research Centre (ICNARC) administer both NCAA and CMP. Support for the collection and use of data from these national clinical audits was obtained under Section 251 of the National Health Service Act 2006. Approval was granted by the Health Research Authority (NCAA approval number ECC 2–06(n)/2009, CMP approval number: PIAG 2–10(f)/2005).

Acute hospitals in England, Wales, Scotland and Northern Ireland participate in NCAA. All resuscitation events, which commence in-hospital, where defibrillation or chest compressions are delivered by the hospital-based resuscitation team are eligible for inclusion in NCAA. NCAA contains data on the patient, hospital admission, cardiac arrest, survival and neurological outcomes.

The CMP is the national clinical audit of patient outcomes in intensive care. All adult, general ICUs in England, Wales and Northern Ireland contribute to the CMP. ICUs in Scotland do not participate. In addition, not all specialist ICUs or stand-alone high dependency units (HDUs) participate.[15] For consecutive admissions, trained data collectors record data on physiological and non-physiological predictors of mortality. Diagnostic categories are recorded using ICNARC Coding Method with diagnoses available for 99.8% of patients.[16] Data collected for NCAA and CMP undergoes extensive validation to assess completeness, logical consistency and biological plausibility prior to their use in audit and research.

Study design and population

We included all adult patients ($\geq$16 years) in the NCAA database where the cardiac arrest team provided CPR or defibrillation ('NCAA cohort'). We included patients with IHCA recorded between 1st April 2011 (when the current NCAA dataset commenced) and 31st December 2019 (to exclude the COVID-19 pandemic which may have affected provision of in-patient hospital services, rates of do not resuscitate orders, resuscitation guidelines and the provision of ICU services[17–19]).

We also investigated a subset of patients admitted to ICU following IHCA, with a linked CMP record ('ICU linked cohort'). In keeping with national guidelines on emergency admissions to ICU, we only included those admitted to ICU within 4 hours of their cardiac arrest as delays beyond 4 hours are associated with poorer outcomes.[14,20]

We excluded cardiac arrests that began pre-hospital. IHCA occurring in ICU were excluded as they show little diurnal variation[3]; this may represent disrupted circadian rhythm or staffing models in ICU where night time staffing closely resembles day time staffing.[3,21] We excluded those with a Do Not Attempt Cardio-Pulmonary Resuscitation (DNACPR) decision in place before the arrest, and those with missing date and time of IHCA.[7,12] Where patients were attended to by the cardiac arrest team on more than one occasion or had more than one ICU admission within the same hospital stay, the first was selected for analysis.

Statistical analysis

Patient characteristics, IHCA details and patient outcomes are summarised descriptively using frequencies and percentages (categorical variables) or mean (SD) or median (IQR) (continuous variables) for the NCAA and ICU linked cohorts. Frequencies of IHCA are presented graphically by hour and presenting rhythm.

We considered time of IHCA as the primary exposure. We treated time of IHCA as a categorical variable with 24 hourly categories. Binary logistic regression was used to model unadjusted ROSC > 20 minutes, hospital survival and good neurological outcome (defined as cerebral performance category (CPC) 1–2 at hospital discharge, as recorded in NCAA) for the NCAA cohort, and survival to ICU discharge for the ICU linked cohort.

Hospital survival was the primary outcome measure in keeping with the Core Outcome Set for Cardiac Arrest and the majority of studies in cardiac arrest.[22,23] To ensure comparability between the NCAA and ICU linked cohorts, the primary outcome was derived from the NCAA database. In the ICU linked cohort, there was 99% agreement in hospital survival between the NCAA and CMP records. For the ICU linked cohort, we adjusted for age, sex, pre-admission dependency, presence of severe comorbidity as defined by APACHE II, diagnosis resulting in ICU admission, NCAA documented reason for admission to/attendance at/visit to hospital, length of hospital stay prior to IHCA, year, clinical status at arrival of cardiac arrest team and location of IHCA (Supplementary Table 1).[6,7,12] Four location categories were used to reflect IHCA at the point of admission to hospital, in-patient locations, in specialist treatment areas and, finally, in HDU/coronary care. The level of missing data was low. Therefore, full case analysis was undertaken with no imputation of missing data. Results are presented as odds ratios for hospital survival and corresponding 95% confidence intervals.

Analysis was conducted for each rhythm; shockable (ventricular fibrillation, pulseless ventricular tachycardia, and unknown shockable rhythm), pulseless electrical activity (PEA), asystole and rhythm never determined. The hour with the lowest proportion of patients achieving each outcome was used as the reference category.

We conducted two sensitivity analyses. The first was restricted to IHCA occurring between Monday 08.00 and Saturday 07.59 which aimed to further reduce the effects of processes of care on survival. The second included all patients admitted to ICU up to 24 hours following IHCA.

All analyses were performed in Stata 16.1 (StataCorp LP, College Station, TX).

Results

Of the 150,636 IHCAs recorded in 228 acute hospitals during the ten-year study period, 115,690 were included in the NCAA cohort, of which 13,858 were subsequently admitted to ICU and included in the ICU linked cohort (Fig. 1). The commonest reason for exclusion from the ICU linked cohort was death, which occurred in 66,885 patients. A total of 137 patients were excluded from the complete case analysis due to missing data. Baseline demographics and cardiac arrest characteristics are presented in Table 1.

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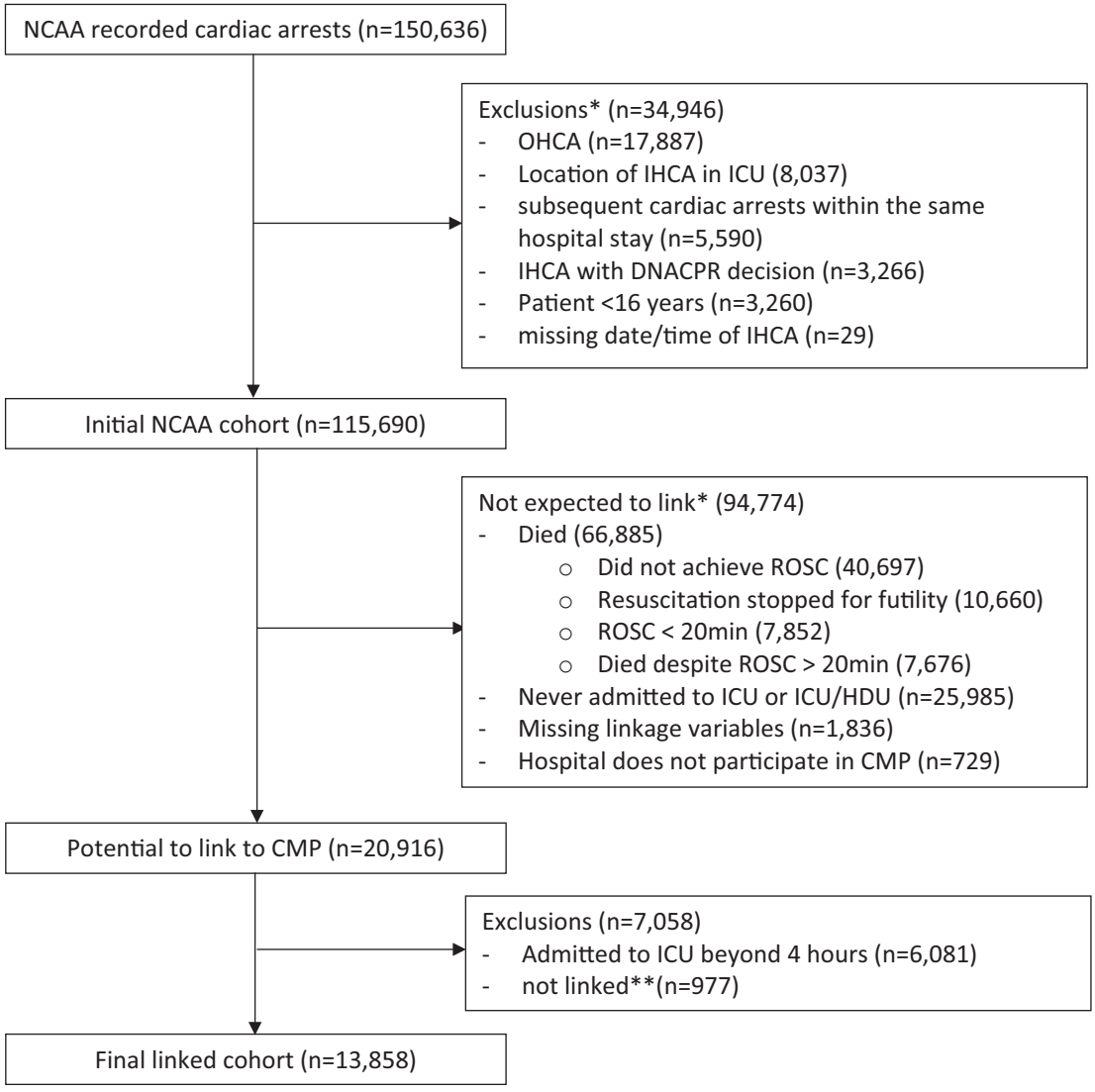

*May be excluded for >1 reason

**For records not linked this may be due to a hospital participating in the CMP but the individual intensive care unit does not.

Fig. 1 – Consort diagram.

NCAA cohort

PEA was the commonest presenting rhythm in the NCAA cohort (54.8%). Patient outcomes are presented in Tables 2 and 3. The ward location, where patients who achieved sustained ROSC were cared for, is presented in Supplementary Table 2. Hospital survival was 21.3%. Rates of IHCA (Fig. 2 and Supplementary Fig. 1), ROSC > 20 minutes (Supplementary Fig. 2), unadjusted hospital survival (Fig. 3) and survival with good neurological outcome (Supplementary Fig. 3) varied throughout the 24 hour period. Outcomes were typically worst between 05.00 and 07.00.

Shockable rhythm

Shockable rhythm incidence was highest at 09.00, and lowest at 01.00 with clear diurnal variation. Rates of ROSC > 20 minutes, unadjusted hospital survival and good neurological outcome were all lowest at 05.00 or 06.00 and highest at 15.00 or 16.00.

PEA

PEA incidence was highest at 09.00, with smaller peaks at 06.00 and 22.00, again diurnal variation was seen. Rates of ROSC > 20 minutes, unadjusted hospital survival and good neurological outcome were all lowest at 05.00 and highest at between 11.00 and 13.00.

Asystole

Rates of asystole peaked at 06.00; asystole was three times more frequent at 06.00 than 15.00 (Fig. 2). There was a sharp decline in the number of patients presenting with asystole between 06.00 and 07.00. Rates of ROSC > 20 minutes, unadjusted hospital survival

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Table 1 – Patient demographics.

Patient characteristics	NCAA cohort (n = 115,690)	ICU linked cohort (n = 13,858)
Age (years), Median (IQR)	76 (66–84)	69 (58–78)
Male sex, n (%)	67,984 (58.8)	8,248 (59.5)
Ethnic group, n (%)		
White	95,197 (82.3)	11,134 (80.3)
Not stated	11,030 (9.5)	1191 (8.6)
Asian/Asian British	5,373 (4.6)	880 (6.4)
Black/African/Caribbean/Black British	1,955 (1.7)	325 (2.3)
All other	1,492 (1.3)	221 (1.6)
Mixed/multiple ethnic group	642 (0.6)	107 (0.8)
Pre-admission dependency, n (%)		
Able to live without assistance in daily activities	NA	8,854 (64.3)
Minor assistance with some daily activities	NA	3,684 (26.8)
Major assistance with majority of/all daily activities	NA	1,082 (7.9)
Total assistance with all daily activities	NA	150 (1.1)
Presence of severe comorbidity*, n (%)	NA	2,661 (19.2)
Diagnosis resulting in ICU admission, n (%)		
Acute coronary syndrome	NA	5,370 (38.8)
Cardiac arrhythmia	NA	3,683 (26.6)
Other	NA	2,798 (20.2)
Sepsis	NA	2,007 (14.5)
APACHE-II physiology score, median (IQR)	NA	15 (11–21)
Length of hospital stay prior to arrest (days), median (IQR)	2 (0–6)	1 (0–5)
Reason for admission to/attendance at/visit to your hospital, n (%)‡		
In-patient - medical	99,809 (86.3)	11,245 (81.2)
In-patient - surgical	13,945 (12.1)	2,334 (16.8)
Outpatient	1,490 (1.3)	217 (1.6)
Staff or visitor	371 (0.3)	60 (0.4)
Location of cardiac arrest, n (%)		
In-patient location	69,607 (60.2)	7,697 (55.5)
At the point of presentation to hospital	22,727 (19.7)	3,180 (23.0)
High dependency/coronary care unit	13,160 (11.4)	1,064 (7.7)
Treatment area	10,159 (8.8)	1,915 (13.8)
Status at team arrival, n (%)		
Resuscitation ongoing	97,853 (84.6)	11,814 (85.3)
ROSC achieved before team arrival	10,201 (8.8)	961 (6.9)
Deteriorating (not yet arrested)	6,706 (5.8)	1,080 (7.8)
Dead - resuscitation stopped	809 (0.7)	0 (0.0)
Presenting rhythm, n (%)		
Shockable	18,885 (16.3)	2,524 (18.2)
VF	12,883 (11.1)	1,839 (13.3)
VT	5,412 (4.7)	608 (4.4)
Unknown (shockable)	590 (0.5)	77 (0.6)
PEA	63,387 (54.8)	8,642 (62.4)
Asystole	25,110 (21.7)	1,868 (13.5)
Rhythm never determined	8,308 (7.2)	824 (5.9)

*Using APACHE II definition of severe co-morbidity.

‡ **Reason for admission to/attendance at/visit to your hospital, n (%)**.

In-patient include all patients from the point of triage in the emergency department to discharge from hospital.

Outpatients include all those who attended the hospital for clinic or appointment.

In-patient location: In-patient ward, obstetric clinical areas or other inpatient intermediate care area.

At the point of presentation to hospital: Emergency department, emergency admissions unit (or equivalent), outpatient clinic, non-clinical area.

Treatment area: Theatre and recovery, imaging department, cardiac catheter laboratory or other specialist treatment area.

High dependency/coronary care unit: HDU, CCU.

and good neurological outcome were all lowest between 05.00 and 07.00 and highest between 13.00 and 16.00.

Rhythm never determined

Rates of IHCA where the rhythm was never determined peaked at 09.00. Rates of ROSC > 20 minutes, unadjusted hospital survival and good neurological outcome were lowest between 03.00 and 05.00 and highest at 11.00.

ICU linked cohort

In patients admitted to ICU following their IHCA, again PEA was the commonest presenting rhythm (62.4%). Hospital survival was

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Table 2 – Patient outcomes in the NCAA cohort.

Outcome	Entire NCAA cohort n = 115,690 (%)	Shockable n = 18,885 (%)	PEA n = 63,387 (%)	Asystole n = 25,110 (%)	Rhythm never determined n = 8,308 (%)
ROSC > 20 minutes	56,420 (48.8)	14,434 (76.4)	28,732 (45.3)	7,105 (28.3)	6,149 (74.5)
Survival to hospital discharge	24,592 (21.3)	9,775 (51.9)	8,828 (13.9)	2,284 (9.1)	3,705 (45.0)
CPC* 1 or 2 (% of all IHCA)	21,089 (18.7)	8,609 (48.3)	7,334 (11.8)	1,975 (8.0)	3,171 (40.5)
CPC 1 or 2 (% of all survivors to hospital discharge)	21,089 (88.7)	8,609 (88.1)	7,334 (83.1)	1,975 (86.5)	3,171 (85.6)

* Cerebral performance category (CPC) at hospital discharge. CPC is a five-point scale used to classify neurological outcomes. CPC 1 (good performance) and 2 (moderate disability) are considered good outcomes. CPC 3 (severe disability), 4 (coma or vegetative state) or 5 (death) are considered poor outcomes.

Table 3 – Patient outcomes in the ICU linked cohort.

Outcome	Entire ICU (CMP) cohort n = 13,858 (%)	Shockable n = 2,524 (%)	PEA n = 8,642 (%)	Asystole n = 1,868 (%)	Rhythm never determined n = 824 (%)
ICU survival	6,055 (43.8)	1,615 (64.2)	3,396 (39.4)	574 (30.8)	470 (57.3)
Survived to hospital discharge	5,106 (37.0)	1,417 (56.3)	2,822 (32.7)	440 (23.7)	427 (52.0)
CPC 1 or 2 (% of all IHCA)	4,326 (32.7)	1,205 (51.2)	2,395 (28.8)	378 (20.8)	348 (46.3)
CPC 1 or 2 (% of all survivors to hospital discharge)	4,326 (84.7)	1,205 (85.0)	2,395 (84.8)	378 (85.9)	348 (81.5)
ICU length of stay (days), median (IQR)					
Survivors	NA	3.3 (1.8–6.5)	5.2 (2.5–10.7)	5.0 (2.4–11.8)	3.6 (1.8–7.5)
Non-survivors	NA	1.6 (0.5–4.1)	1.2 (0.4–3.9)	1.3 (0.4–3.6)	1.3 (0.4–4.2)
Hospital length of stay (days), median (IQR)					
Survivors	NA	15 (8–29)	20 (10–37)	19 (9–41)	16 (8–34)
Non-survivors	NA	2 (1–4)	1 (0–4)	1 (0–4)	1 (0–4)

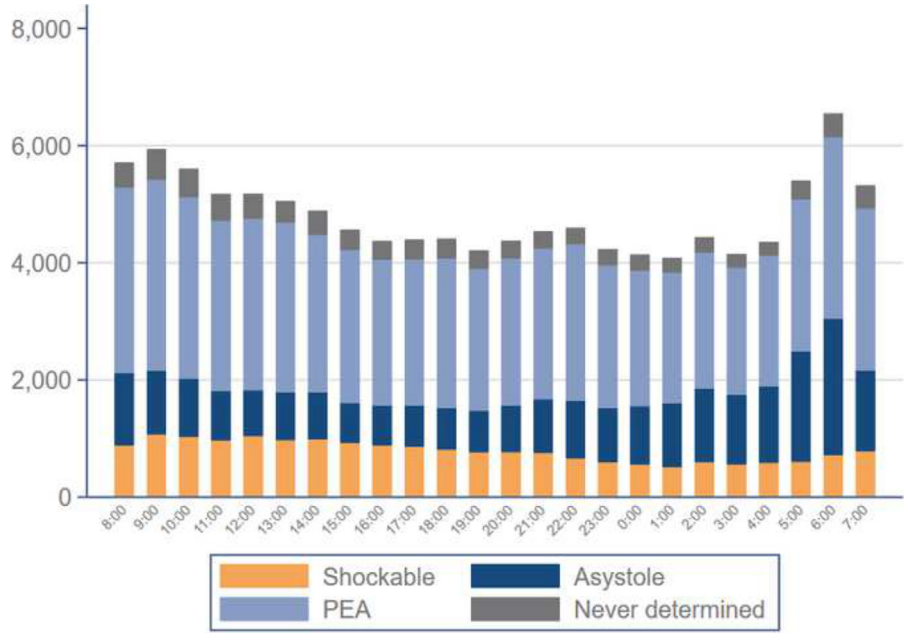

Fig. 2 – Incidence of IHCA throughout 24-hour period for the NCAA cohort (n = 115,690).

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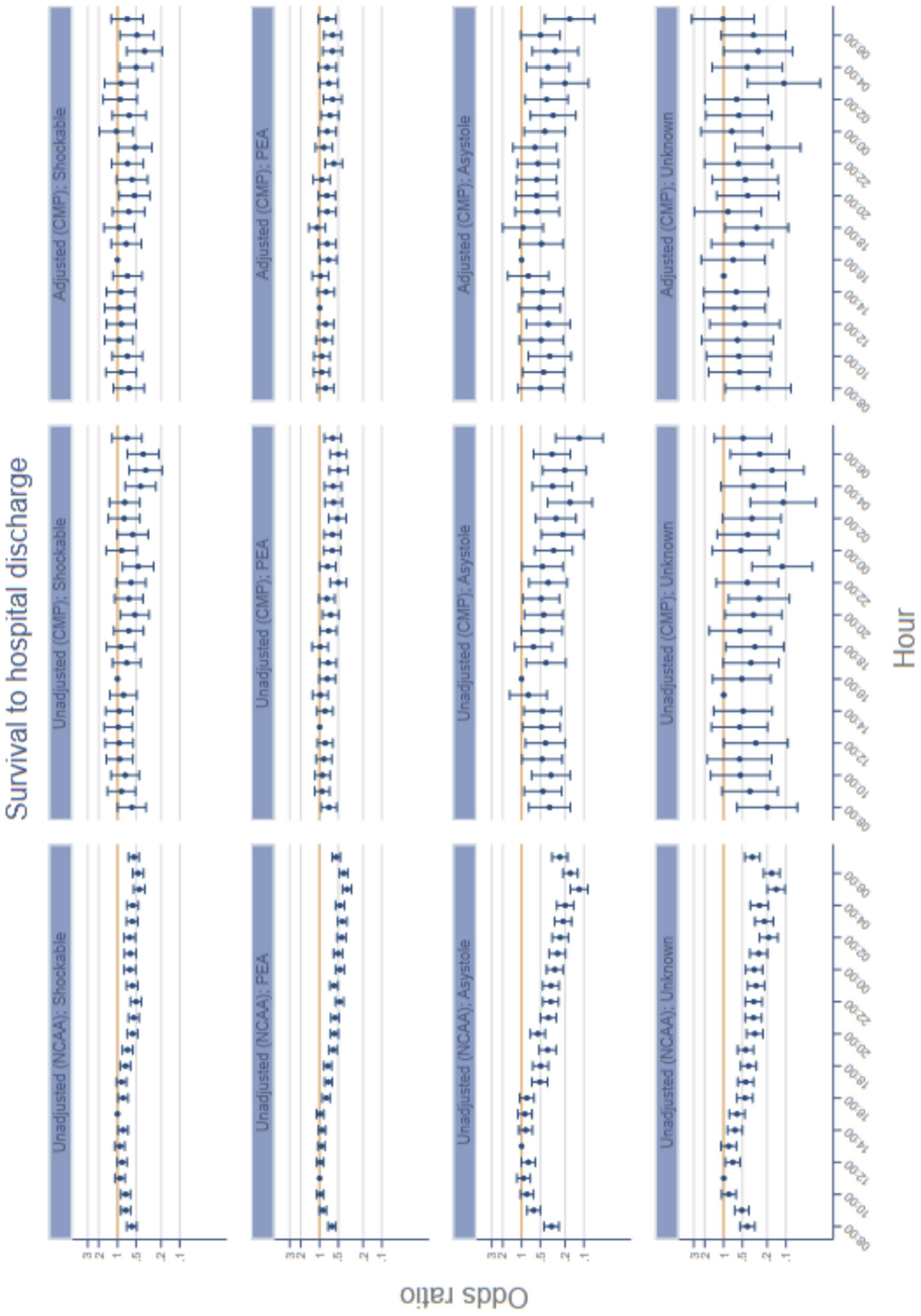

Fig. 3 – Rates of hospital survival Unadjusted rates of hospital survival in the NCAA cohort, unadjusted rates of hospital survival in the ICU (CMP) linked cohort and adjusted rates of hospital survival in the ICU (CMP) linked cohort divided by hour and presenting rhythm.

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37.0%; rates of unadjusted and adjusted hospital survival in the ICU linked cohort are presented in Fig. 3.

Shockable rhythm

The primary outcome measure of adjusted odds ratio for hospital survival was lowest at 05.00 and highest at 00.00 in those with shockable IHCA admitted to ICU. However, there was no clear diurnal variation in either unadjusted or adjusted hospital survival in ICU linked cohort (Fig. 3).

PEA

Once again, little diurnal variation was seen in unadjusted or adjusted hospital survival (Fig. 3); the primary outcome measure of adjusted hospital survival was lowest at 22.00 and highest at 18.00 in those with PEA.

Asystole

Adjusted hospital survival was lowest at 07.00 and highest at 16.00 in those with asystole admitted to ICU, with no clear diurnal variation seen in adjusted hospital survival.

Rhythm never determined

The number of patients where rhythm was never determined who were admitted to ICU was small (n = 824). Therefore, confidence intervals for adjusted hospital survival were wide; survival was lowest at 03.00 but highest at 07.00.

Sensitivity analysis

Sensitivity analyses produced similar results to the primary analysis demonstrating no clear diurnal variation in adjusted hospital survival in those admitted to ICU having suffered IHCA on a weekday (Supplementary Fig. 4) or when all patients admitted to ICU up to 24 hours after their IHCA were included (Supplementary Fig. 5).

Discussion

We conducted a retrospective observational study of IHCA including 115,690 patients from a UK population. We also studied a cohort of patients admitted to ICU following their IHCA; the commonest reason for exclusion from this ICU cohort was death. Only one in five patients survived to hospital discharge in our study, similar to survival rates seen in other registries.[2,3,6,7,24] Between 20.00 and 08.00, we observed higher rates of IHCA, lower rates of ROSC > 20 minutes, lower hospital survival and poorer neurological outcomes. However, patients subsequently admitted to ICU demonstrated no diurnal variation in hospital survival either before or after adjustment.

Previous studies have demonstrated diurnal variation in the incidence of shockable rhythms.[2,3,5,6] However, these have included both patients receiving care at ward level and those in ICU.[2,3,6] In our study of a homogenous cohort of patients at ward level, we observed a night time nadir and morning peak in shockable rhythms in keeping with other studies.[3,5] A morning rise in blood pressure, increased vascular tone, catecholamine secretion, changes in cortisol levels and platelet activation may predispose to cardiac arrhythmias, ischaemic and thromboembolic events and account for a morning peak in IHCA.[5,9–11] It is notable that two thirds of patients in the ICU linked cohort had an underlying diagnosis of acute coronary syndrome or cardiac arrhythmia.

A night time nadir and morning peak in out of hospital cardiac arrest (OHCA) has been reported.[9–11,25] However, concern exists that the reduced incidence of shockable rhythms overnight may be due to prolonged ambulance response times and lower rates of bystander intervention in an OHCA population.[9,11] Presentation with non-fatal acute myocardial infarction,[26,27] malignant ventricular arrhythmias detected by internal cardiac defibrillators[28,29] and stroke[30] all demonstrate a night time nadir and morning peak.[8] These conditions share similar pathophysiology to IHCA, but are unaffected by processes of care seen in hospitals.

In the NCAA cohort, we identified variation in rates of IHCA throughout the 24-hour period with a peak at 06.00. This is in keeping with other studies.[3,5] Rates of ROSC > 20 minutes, hospital survival, and survival with a good neurological outcome were consistently lowest between 05.00 and 07.00. Whilst this may suggest a circadian effect on IHCA, no diurnal variation was seen in those subsequently admitted to ICU. Therefore, unmeasured patient factors and processes of care must also be considered.

The 06.00 peak in IHCA was primarily driven by an increase in asystole, being three times more frequent at 06.00 than at 15.00. Normal circadian rhythm results in elevated vagal but reduced sympathetic tone at night. This leads to nocturnal bradycardia, delayed conduction via the atrioventricular node and lengthening of QRS duration.[8] This may explain an increase in asystole seen overnight.[5,6] However, the abrupt decline in rates of asystole between 06.00 and 07.00 lacks biological plausibility and suggests processes of care may play a role. The 06.00 peak in asystole and reduced rates of shockable rhythm overnight may represent multiple patients across many hours with undetected IHCA who subsequently deteriorated into asystole.[7]

Cardiac arrests at night time are less likely to be monitored or witnessed.[6] Being cared for on a ward without telemetry monitoring is an independent risk factor for presenting with a non-shockable rhythm.[3] In our study, 11.4% of IHCA occurred in a high dependency or coronary care unit and 8.8% occurred in a specialist treatment area. Therefore, rates of cardiac monitoring in the NCAA cohort were likely to have been low. Despite this, we observed rates of asystole (21.7%) lower than that reported in studies with high levels of witnessed or monitored IHCA.[2,6]

The absence of co-morbidity data in the NCAA database has previously been recognized as a limitation.[12] In 2012, a National Confidential Enquiry into Patient Outcome and Death (NCEPOD) examined cases of ward based IHCA in the UK. Here, over a quarter of patients were physically dependant on others and 81% had a severe co-morbidity.[13] In our study, linkage of the NCAA and CMP databases allowed us to adjust for level of dependency and presence of severe comorbidity.

The NCEPOD enquiry found that no decision had been made regarding resuscitation status in 78% of cases and attempts at resuscitation were “inappropriate” in a quarter of cases.[13] In a study examining timing of DNACPR orders, the mean time to institution was 3.2 days, longer than the median length of stay prior to IHCA in our study.[31] Therefore, absence of a DNACPR order, may have meant patients who were unlikely to benefit from CPR were resuscitated. In contrast, national standards in the UK dictate that all decisions to admit to ICU are made by a consultant in Intensive Care Medicine.[14] Consultant level decision making in those referred to ICU is likely to have excluded patients with severe co-morbidities or high levels of dependency that would not benefit from ICU support.

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Consequently, the ICU linked cohort likely represents a selected group of patients much more likely to survive. This consultant-level input, may have eliminated important process of care issues, resulting in loss of diurnal variation in hospital survival even prior to adjustment.

Our study has several strengths. Our NCAA cohort excluded patients in ICU at the time of IHCA and thus represents a homogeneous cohort. In contrast, in previous studies of comparable size, half of all patients were in ICU with a quarter mechanically ventilated at the time of IHCA.[3,6] Diurnal variation in the incidence of IHCA in the UK has previously been reported.[1] However, previous studies examined 12-hour blocks that coincide with staffing patterns but lack biological plausibility.[7] Due to the cohort size we were able to generate 24 one-hour blocks and stratify on rhythm. Hourly blocks have been shown to model diurnal variations in IHCA best.[5] This enabled identification of changes in rates of asystole on an hourly basis that were biologically implausible.

Previous studies using the NCAA database have been unable to correct for patient characteristics.[7] Our study uniquely linked the NCAA and CMP databases. Crucially, this allowed adjustment for important prognostic variables present in a UK IHCA population admitted to ICU.[13] We demonstrated the incidence of IHCA, presenting rhythm and survival following IHCA varied throughout the day in the NCAA cohort. However, the absence of diurnal variation in survival seen in the ICU cohort prior to adjustment, suggest this variation is likely explained by patient factors and processes of care, not circadian rhythm.

Our study has some weaknesses. As fewer hospitals submit data to NCAA than CMP, we will have failed to capture some patients who suffered an IHCA and been admitted to ICU. Furthermore, our exclusion criteria may mean the ICU cohort is not fully representative of an IHCA population in the UK. However, whilst our ICU cohort only contained 12.0% of all eligible IHCA, the majority were excluded as they did not achieve ROSC or died in the immediate post resuscitative period. The exclusion of patients admitted to ICU > 4 hours after IHCA may have excluded patients who were receiving treatment for the cause of their IHCA prior to ICU admission. Analysis of patients who suffered an IHCA and ST-elevation myocardial infarction included in the UK Myocardial Ischaemia National Audit Project database revealed the median time to revascularization was 0.76 hours (IQR 0.51–1.2).[32] The rapid access to coronary angiography would suggest receiving appropriate treatment is unlikely to result in a delay of > 4 hours in admission to ICU. A sensitivity analysis including those admitted to ICU up to 24 hours following IHCA produced results similar to the primary analysis.

The aetiology of IHCA is not recorded in NCAA. Whilst we present diagnosis resulting in ICU admission as recorded in CMP, these diagnoses lack detail and likely contain heterogenous groups of patients with variable circadian biology who are subject to different processes of care. The inclusion of patients who suffered an IHCA following surgery or trauma may have included patients who arrested due to bleeding, the timing of which is unlikely to be influenced by circadian rhythm. However, exsanguination (4–6%), cardiac tamponade (3%) and pneumothorax (0.1%) are all uncommon causes of IHCA.[33–35]

We are unable to comment on patient wake time which may govern circadian rhythm. Admission to hospital may disrupt circadian rhythm.[10] However, in our study the median time to IHCA was 2 days in the NCAA cohort and 1 day in the ICU linked cohort. Therefore, circadian rhythm is unlikely to have been significantly disrupted.

We were unable to correct for witnessed status, as this is not recorded in the NCAA or CMP databases. In a UK healthcare setting, the level of cardiac monitoring is likely to have been low. The peak in asystole at 06.00 may represent unwitnessed IHCA which has gone unrecognised. Hence, outcomes may have been influenced by processes of care which we were unable to adjust for. We were unable to adjust for duration of IHCA (a predictor of mortality) as this was only reliably recorded in the NCAA database from 2016. However, we corrected for variables recorded in the NCAA dataset which has good discrimination (c index 0.811) for predicting hospital survival.[12] The NCAA model has better ability to predict hospital survival than other models which adjust for intra-arrest variables.[12] We were unable to correct for institutional factors including staffing, therefore residual confounding relating to processes of care may remain. Finally, we presented CPC as a measure of neurological outcome. Inter-rater variability may affect the quality of CPC data.[12,22,36] CPC is assessed by note review in 72.6% of cases in NCAA, and has previously been shown to overestimate disability.[36] Reassuringly, our rates of good neurological outcome was similar to other studies.[2]

Conclusion

We conducted a large retrospective observational study examining the effect of circadian rhythm on outcomes following IHCA and linked two UK national audits to adjust for important confounders. We observed higher rates of IHCA, and poorer outcomes between 20.00 and 08.00. However, in those admitted to ICU, no diurnal variation was seen. This suggests patient factors and processes of care issues contribute to the variation in outcomes following IHCA seen throughout the day. Strategies directed towards improving processes of care may improve outcomes.

Conflicts of interest

None.

Data statement

The data that support the findings of this study are available from ICNARC but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of ICNARC's independent Data Access Advisory Group.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2023.109750.

Author details

[a]Regional Intensive Care Unit, Royal Victoria Hospital, Belfast, UK[b]Wellcome-Wolfson Institute for Experimental Medicine, Queen's University Belfast, UK [c]Intensive Care National Audit & Research Centre, Napier House, 24 High Holborn, London, UK [d]Division of

Please cite this article as: Peter J McGuigan, J. Edwards, B. Blackwood et al., The association between time of in hospital cardiac arrest and mortality; a retrospective analysis of two UK databases, RESUSCITATION, https://doi.org/10.1016/j.resuscitation.2023.109750

Infection, Immunity and Respiratory Medicine, University of Manchester, Manchester, UK [e]Faculty of Biology, Medicine, and Health, Manchester Academic Health Sciences Centre, University of Manchester, Manchester, UK [f]Manchester Foundation Trust, Manchester, UK [g]University College Dublin Clinical Research Centre, St Vincent's University Hospital, Dublin, Ireland [h]The Australian and New Zealand Intensive Care Research Centre, Monash University, Melbourne, Australia [i]The Alfred Hospital, Melbourne, Australia [j]Centre for Inflammation Research, Institute of Regeneration and Repair, University of Edinburgh, UK [k]Royal Infirmary of Edinburgh, NHS Lothian, UK

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