Cardiac arrest outcomes in the United Kingdom

by

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Abbreviations

AED	Automated external defibrillator
AHA	American Heart Association
ALS	Advanced life support
ANZICS-CORE	Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation Database
ANZROD	Australia and New Zealand Risk of Death model
aOR	Adjusted odds ratio
APACHE	Acute Physiology and Chronic Health Evaluation
BP	Blood pressure
CMPD	Case mix programme dataset
CIRCA	Critical Illness Related Cardiac Arrest (CIRCA): an investigation of the incidence and outcome of cardiac arrest within Intensive Care Units in the United Kingdom.
COSCA	Core Outcome Set for Cardiac Arrest
CoSTR	Consensus on CPR Science with Treatment Recommendations
CPC	Cerebral performance category
CPR	Cardiopulmonary resuscitation
CQC	Care Quality Commission
CT	Computed tomography
DANARREST	Danish In-Hospital Cardiac Arrest Registry
ECG	Electrocardiograph
ECMO	Extracorporeal membrane oxygenation
ECPR	Extracorporeal cardiopulmonary resuscitation
EMS	Emergency medical services
ERC	European Resuscitation Council
ESICM	European Society of Intensive Care Medicine
GWTG-R	Get-With-Guidelines–Resuscitation registry
HDU	High dependency unit
HR	Heart rate
IABP	Intra-aortic balloon pump
ICNARC	Intensive Care National Audit and Research Centre
ICU	Intensive care unit
IHCA	In-hospital cardiac arrest
ILCOR	International Liaison Committee on Resuscitation
IO	Intraosseous

ISRCTN	International Standard Randomised Controlled Trial Number
IV	Intravenous
LVAD	Left ventricular assist device
mRS	Modified Rankin scale
NCAA	National Cardiac Arrest Audit
NCT	National Clinical Trial number
NIV	Noninvasive ventilation
OHCA	Out-of-hospital cardiac arrest
OHCAO	Out-of-hospital cardiac arrest outcomes registry
OR	Odds ratio
PARAMEDIC2	Prehospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug Administration in Cardiac Arrest 2
PCPC	Paediatric Cerebral Performance Category
RCT	Randomised controlled trial
ROSC	Return of spontaneous circulation
RR	Respiratory rate
RCUK	Resuscitation Council UK
SBP	Systolic blood pressure
SpO_2,	Peripheral oxygen saturation
TTM	Targeted temperature management
VAD	Ventricular assist device
VF	Ventricular fibrillation
VT	Ventricular tachycardia
WLST	Withdrawal of life-sustaining treatment

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I thank Professor Gavin Perkins and Dr Chen Ji for supervising this thesis.

Declaration

This thesis is submitted to the University of Warwick in support of an application
for the degree of Doctor of Philosophy. It has been written by Professor Jerry Nolan under the supervision of Professor Gavin Perkins and Dr Chen Ji and has not been submitted in any previous application for any degree.

The work presented was carried out by Professor Jerry Nolan.

Jerry Nolan

Date 21 August 2022

Abstract

This thesis includes six papers that are related to the incidence and outcome from cardiac arrest in the United Kingdom. The Utstein-style template for reporting in-hospital cardiac arrest defines the data elements of the epidemiology and outcome of cardiac arrest that should be collected so that valid comparisons can be made between emergency medical services (EMS) systems, countries, and regions. Much of this reporting template concerns the documentation of data relating to the post-resuscitation care phase of patient management and links well the papers in this thesis that describe the characteristics and outcome of patients admitted to intensive care units (ICUs) after cardiac arrest.

The first report from the UK National Cardiac Arrest Audit (NCAA) documented the incidence and outcome from in-hospital cardiac arrest in 144 acute hospitals in 2011–2013. Although the incidence overall was 1.6 cardiac arrests per 1000 hospital admissions, there was considerable seasonal variation. The rate of survival to hospital discharge was 18.4 %.

Analysis of the Intensive Care National Audit and Research Centre (ICNARC) case mix programme database (CMPD) provides valuable insights into the increasing numbers of patients admitted to ICUs comatose after resuscitation from cardiac arrest. During the period 1995–2005, mechanically ventilated post-cardiac arrest patients accounted for 5.8% of all ICU admissions; 42.9% survived to leave ICU and 28.6% survived to hospital discharge. A later analysis of the ICNARC CMPD showed that cardiac arrest survivors represented a steadily increasing proportion of mechanically ventilated admissions during 2004 to 2014. Their hospital mortality decreased during the study period. A third analysis of the ICNARC CMPD showed a significant change in temperature management strategy (indicated by a change in the lowest body temperature in the first 24 h of admission) following publication of the Targeted Temperature Management Trial (TTM) trial in December 2013; this change was not associated with a change in the mortality rate.

The final paper in this thesis, a secondary analysis of the PARAMEDIC-2 study showed that the treatment effect of adrenaline on return of spontaneous circulation (ROSC) at hospital admission was the same when given by the intravenous (IV) and intraosseous (IO) routes.

Introduction

Cardiac arrest occurs when cardiac mechanical activity ceases, but this definition is challenging to operationalise because it can be difficult to detect low flow states when the heart is contracting so weakly that a pulse cannot be felt. Cardiac arrest registries will generally include individuals who have received chest compressions and/or defibrillation. There are significant differences in the causes and outcome of in-hospital and out-of-hospital cardiac arrest and differences in the systems of care involved. For these reasons, epidemiological data relating to in-hospital cardiac arrest (IHCA) and out-of-hospital cardiac arrest (OHCA) are collected and reported separately. Data from national registries indicate that the incidence of emergency medical services (EMS)–treated OHCA ranges from 42 per 100,000 population (Singapore) to 97 per 100 000 (Japan); the incidence in the United Kingdom (UK) is 53 per 100,000.[1] There are far fewer national registries for IHCA and for reasons that will be outlined in this thesis, it is more challenging to compare incidence and outcomes for this group.

1.1 Standardising cardiac arrest definitions and reporting templates – the Utstein style

Standardising the definitions applied to the characteristics, interventions, and outcomes after cardiac arrest facilitates reliable comparison of the incidence and outcome from cardiac arrest among different institutions, countries and regions. The first standardised cardiac arrest reporting template was published in 1991 and focused on OHCAs.[2] This was preceded in 1990 by a meeting of international experts at Utstein Abbey near Stavanger, Norway; many subsequent meetings at this location and have resulted in 'Utstein-style' reporting templates on cardiac arrest and related topics. The first Utstein-style reporting template for IHCA was published in 1997 and split the data elements into four domains: hospital, patient, arrest and outcome.[3] In 2004, an update of the Utstein reporting template included both OHCA and IHCA [4] but it was later decided to once again split up these locations and a 2015 update was confined to OHCA.[5] The Utstein reporting template for IHCA was substantially updated following a series of consensus meetings and was published in 2019.[6] This forms the first paper in this thesis and it defines many of the data elements that are included in the analyses undertaken in the other five papers.

1.2 Epidemiology of cardiac arrest in the UK

Ten of the eleven English ambulance services send data relating to OHCA to the out-of-hospital cardiac arrest outcomes (OHCAO) registry at the University of Warwick.[7] In the most recent report (2020), of the 31,698 EMS-treated cardiac arrests (representing 53.4 per 100,000 population), 23% were in an initial shockable rhythm (ventricular fibrillation or ventricular tachycardia (VF/VT)), 25.9% of the total were admitted to hospital with return of spontaneous circulation (ROSC) and 8.3% of the total survived to hospital discharge.[8] The OHCAO registry does not capture data on the treatment of the OHCA survivors after hospital admission.

Data on the epidemiology of in-hospital cardiac arrest in the UK is provided mainly by the National Cardiac Arrest Audit (NCAA) (see 1.3 below). NCAA publishes an annual summary of key statistics (https://www.icnarc.org/Our-Audit/Audits/Ncaa/Reports/Key-Statistics), the most recent being for financial year 2020–21. In this year there were 10,770 cardiac arrests and a cardiac arrest incidence of 1 per 1000 hospital admissions. The rate of ROSC was 48.2% and 21.8% of patients survived to hospital discharge.

1.3 The UK National Cardiac Arrest Audit (NCAA)

In 2007, after completion of a feasibility project, the Resuscitation Council (UK) and ICNARC collaborated to establish the UK National Cardiac Arrest Audit (NCAA). This was termed an audit instead of a registry because it was to include only those cardiac arrests for which there was a 2222 call (the national standard number for calling the cardiac arrest team). This would enable the performance of the hospital response, and in particular the cardiac arrest team, to be audited but excludes those cardiac arrests for which a 2222 call is not made (e.g., many cardiac arrests on ICU and in the emergency department). The initial dataset was limited to just 20 fields covering patient data and short-term outcomes (ROSC and survival to hospital discharge). Reliable comparison between hospitals can be made only by having a high proportion of completed data fields. The number of hospital admissions is also documented which enables a cardiac arrest rate to be calculated. Three hospitals piloted the NCAA dataset in 2009 and other hospitals started to participate from 2010; by 2018 there were 198 participating hospitals in the UK (187 from England). Participating hospitals pay an annual fee and in return receive quarterly reports which enable them to benchmark against the national dataset.

1.4 Post-resuscitation care

Most patients who are resuscitated from cardiac arrest initially remain comatose and develop the post cardiac arrest syndrome.[9] This syndrome comprises 4 components: post-cardiac arrest brain injury,[10] post-cardiac arrest myocardial dysfunction,[11,12] the systemic ischaemia/reperfusion response, and persistent precipitating pathology. Restoration of blood flow and oxygen delivery to tissues that have been rendered ischaemic during a period of cardiac arrest ('no flow') and cardiopulmonary resuscitation ('low flow') can result in the generation of oxygen free radicals, which are highly reactive – they cause cellular injury and provoke an inflammatory response akin to the sepsis syndrome.[13] Guidelines for the treatment of the post cardiac-arrest patient have been published recently by the

European Resuscitation Council (ERC) and European Society of Intensive Care Medicine (ESICM).[14,15] I chaired the writing group for these guidelines. Although several interventions are started immediately after ROSC (and generally outside of the ICU), the majority start after admission to hospital and ICU. The number of patients surviving to reach intensive care after cardiac arrest is increasing and there is some evidence that outcomes are improving. Two of the papers in this thesis provide considerable detail on these aspects of post-cardiac arrest care.[16,17]

1.5 Temperature management after cardiac arrest

Until recently, hypothermic temperature control using a constant temperature between 32°C and 36°C for 24 hours after cardiac arrest was considered a standard of care in the management of patients who were comatose after resuscitation from cardiac arrest. This treatment was implemented widely after the International Liaison Committee on Resuscitation (ILCOR) Advanced Life Support (ALS) Task Force published in 2003 a scientific statement recommending that comatose OHCA survivors should be cooled for 32–34°C for 12–24 h when the initial rhythm was ventricular fibrillation (VF).[18] The science informing this ILCOR statement included supporting experimental data[19] and two randomised controlled trials (RCTs) showing that maintenance of temperature at 32–34°C for 12-24 h in patients comatose after resuscitation from witnessed shockable rhythm OHCA was associated with an improved survival to hospital discharge[20] and functional outcome at 6 months[21] compared with standard care. Partly as a result of concern about the high risk of bias in these studies,[22] the targeted temperature management (TTM) investigators set out to determine if there was any difference in outcome between comatose OHCA patients who received temperature control to a target of 33°C versus a target of 36°C.[23] The TTM trial included 939 patients and showed no difference in all-cause mortality or 6-month neurological function. The findings of this trial led many clinicians to aim for a target temperature of 36°C in post-cardiac arrest patients, while others continued to aim for 33°C.[24,25] Whether this change has been associated with a change in mortality rates for post-cardiac arrest patients is unclear. The 5th paper in this thesis addresses this question.[26]

The 2020 ILCOR Consensus on CPR Science with Treatment Recommendations (CoSTR) recommended temperature control at 32–36°C for at least 24 h for adults after either OHCA or IHCA who remain comatose after resuscitation from cardiac arrest, regardless of the initial rhythm.[27] The 2021 ERC-ESICM Guidelines for Post-resuscitation Care aligned with this recommendation,[14,28] but were later updated to accommodate the results of the TTM-2 trial which showed no difference in 6-month mortality between comatose OHCA survivors treated with temperature control at 33°C and those treated with fever control (37.5°C).[15,29,30]

Thesis overview

This thesis focuses on six papers that are related to the incidence and outcome from cardiac arrest in the United Kingdom. The sequence of papers has been selected to develop the cardiac arrest theme logically instead of following the chronological order in which the papers were published. The first two papers focus on in-hospital cardiac arrest, the third and fourth include both in– and out-of-hospital cardiac arrest and the final two involve only patients with out-of-hospital cardiac arrest. The 6 papers cover a broad range of methodologies, including international consensus guidelines, the first report from a national in-hospital cardiac arrest registry, analyses of a national intensive care database, and a secondary analysis of a large prehospital randomised clinical trial.

- Developing an international registry template for in-hospital cardiac arrest (Paper 1): Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Template for In-Hospital Cardiac Arrest: A Consensus Report from a Task Force of the International Liaison Committee on Resuscitation.
- The UK National Cardiac Arrest Audit (Paper 2): Incidence and outcome of in-hospital cardiac arrest in the United Kingdom National Cardiac Arrest Audit.
- Outcome of cardiac arrest survivors admitted to UK intensive care units (Paper 3): Outcome following admission to UK intensive care units after cardiac arrest: a secondary analysis of the ICNARC Case Mix Programme Database.
- Trends in incidence and outcome for post-cardiac arrest patients receiving intensive care (Paper 4): Increasing survival after admission to UK critical care units following cardiopulmonary resuscitation.
- Temperature management strategies after cardiac arrest (Paper 5): Changes in temperature management and outcome after out-of-hospital cardiac arrest in United Kingdom intensive care units following publication of the Targeted Temperature Management trial.
- Intravascular access after cardiac arrest (Paper 6): Intraosseous versus intravenous administration of adrenaline in patients with out-of-hospital cardiac arrest: a secondary analysis of the PARAMEDIC2 placebo-controlled trial.

Paper 1 describes the modified Delphi process that was used to create an international in-hospital cardiac arrest registry template comprising core and supplemental elements. The core elements are considered essential for a registry and supplemental elements are those deemed desirable for research. Collection of the core elements should enable comparisons between international registries.

Paper 2 describes the rationale for, and the creation of the UK National Cardiac Arrest Audit. It reports the initial results on the incidence and outcome from in-hospital cardiac arrest in the United Kingdom. The highly standardised data collection and reporting will enable trends in incidence and outcome of in-hospital cardiac arrest to be tracked reliably.

Papers 3 and 4 describe the characteristics and outcome for patients admitted to UK ICUs after cardiac arrest. Paper 3 represents the first ever analysis of post-cardiac arrest patients included in the ICNARC CMPD and divided these into community, perioperative, and in-hospital non-perioperative categories. Associations of several physiological variables with outcome are described. This was the first paper to show that mechanically ventilated post-cardiac arrest patients account for 5.8% of all ICU admissions. Paper 4 documents the trends in the number of post-cardiac arrest ICU admissions and their outcome over an 11-year period from 2004 to 2014. It documents a decrease in risk-adjusted hospital mortality during this period. Several other trends were identified which reflect changes in clinical practice during this time.

Paper 5 uses the ICNARC CMPD to determine the impact of the TTM trial on the treatment of patients admitted to UK ICUs after OHCA. This paper highlights the complexities in trying to adjust for case-mix when studying an intervention (temperature control) that artificially manipulates a person's physiology (e.g., temperature). Temperature impacts on several other physiological variables that are used for sickness severity scoring and case mix adjustment – the implications are discussed.

Paper 6 is a secondary analysis of the PARAMEDIC-2 trial – a placebo controlled randomised trial of adrenaline in OHCA. The intraosseous route is being used increasingly for the delivery of drugs in OHCA despite the lack of evidence for benefit or harm from adequately powered randomised clinical trials. Approximately 30% of the patients in the PARAMEDIC-2 trial received the trial drug (adrenaline or placebo) via the intraosseous route. Although the route was not randomised, these data provided an opportunity to adjust for covariates and report adjusted outcomes.

2.1 Paper 1. The Utstein resuscitation registry template for in-hospital cardiac arrest

Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Template for In-Hospital Cardiac Arrest: A Consensus Report From a Task Force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia). Circulation 2019;140:e746–e757 and Resuscitation 2019;144:166–177.
Nolan JP, Berg RA, Andersen LW, Bhanji F, Chan PS, Donnino MW, Lim SH, Ma MH, Nadkarni VM, Starks MA, Perkins GD, Morley PT, Soar J; on behalf of the Utstein Collaborators.

This paper has been cited 147 times

Contribution to Paper 1.

I was the lead author of this paper (60% contribution), which was the result of extensive international collaboration and sets the standard for reporting outcomes from in-hospital cardiac arrest. I chaired four face-to-face international meetings during the period 2013–2017 and five teleconferences during 2016–2018. I designed the web-based survey for the 2-stage Delphi process, wrote the first draft of the paper and co-ordinated the responses to reviewer comments. I submitted the final version of the paper.

Objectives

Reliable comparison of cardiac arrest outcomes in different centres, regions and countries is dependent on consistent definitions of data items and uniform datasets. Failure to standardise will invalidate comparisons and risks incorrect conclusions as 'apples are compared with oranges'. The first Utstein cardiac arrest reporting template was published in 1991 and focussed on OHCA.[2] The first template for IHCA was published in 1997;[3] an update in 2004 incorporated both IHCAs and OHCAs [31] but this combined template was less easy to use and in 2015 an updated Utstein template was restricted to OHCA. The need to produce an updated IHCA template was clear and work on this started in 2013, before the IHCA version had been completed.

Methods

The methodology for producing Utstein cardiac arrest templates has been well-established over 3 decades, although technology has evolved to enable low-cost telephone and videoconferencing and inexpensive web-based survey tools, thus reducing reliance on travel and face-to-face meetings. The initial meetings enabled us to draft a list of potential data items and definitions. With this update of the IHCA reporting template, we retained the concept of core and supplementary data, optimised for registries and research respectively. We allocated the data items into 6 domains: hospital, patient, pre-event, cardiac arrest process, post-resuscitation process, and outome. A 2-stage Delphi process was conducted using a web-based survey (Survey Monkey, Momentive Inc. San Mateo, California, USA) to achieve consensus for the recommendations for core and supplemental elements. During stage 1, the proposals were presented to all members of the ILCOR Advanced Life Support, Basic Life Support, and Paediatric Task Forces. Agreement for core and supplemental elements was sought using a 5-point Likert scale, ranging from 'do not agree' (1) to 'strongly agree' (5); a score of 4 or 5 was considered to be agreement. A video conference was held between Stages 1 and 2. If there was <85% agreement on designation as core or supplemental, items were submitted to a second round of voting.

Results

The elements grouped by core and supplementary and allocated to the six domains are shown in Figure 1. Data definitions are listed in the Table in the paper. Where possible these definitions were based on 2004 and 2015 Utstein definitions and some were adapted from the American Heart Association Get-With-The-Guidelines Resuscitation (GWTG-R) registry.

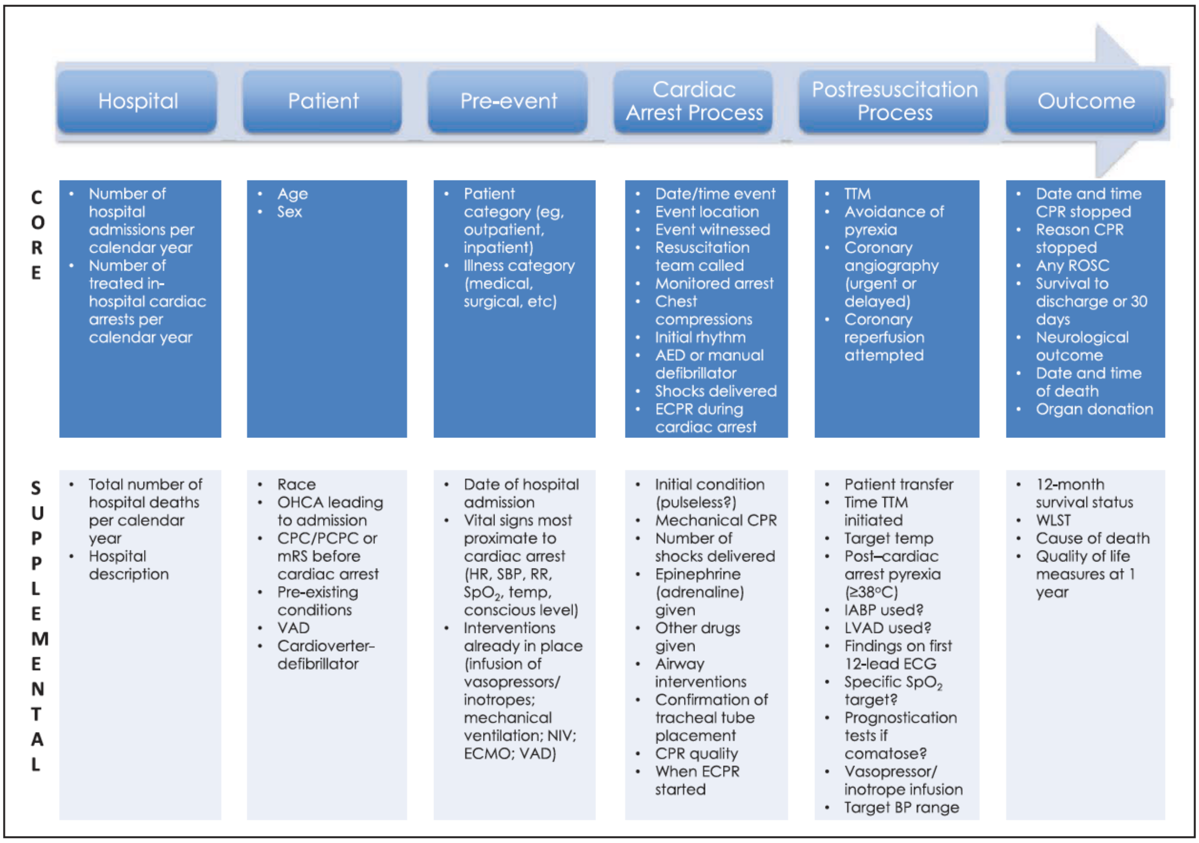

Figure 1. The Utstein updated data element domains for in-hospital cardiac arrest (reproduced from reference 6).

Discussion

The concept of defining core and supplementary data was established in the original Utstein paper[2] and remains the most effective way ensuring that the opinions and suggestions of all participants are incorporated. We used the report forms from the American Heart Association Get-With-Guidelines–Resuscitation (GWTG–R) program to inform our discussions.[32] Many of the data items included in the GWTG–R database were either excluded from the Utstein-style IHCA template or were assigned as supplementary data. There was general agreement within the Utstein collaborator group that core data items should be both important (for comparisons between registries) and easy to collect. Recommending a very large dataset would inevitably increase the amount of missing data and would be expensive to collect, which would restrict its implementation to the wealthiest nations.

A limitation of this IHCA Utstein template is that it has not been tested and currently there are no plans to evaluate its implementation internationally. Core outcome data were restricted to relatively short-term outcomes (ROSC, survival and neurological outcome at hospital discharge/ 30 days). This is consistent with the recommendations of the Core Outcome Set for Cardiac Arrest (COSCA) collaborators,[33] although it is recognised that neurological (better described as 'functional') status can improve over the first 6 months.[34] Long-term functional and cognitive outcomes are prioritised by patients but these outcomes are much more challenging to collect; thus, the IHCA Utstein collaborators defined these outcomes as supplemental. Although we had wide international representation among the contributors to this Utstein template, including two contributors from Asia, we did not include any representatives from low and middle-income countries or patient and public representatives – this relative lack of diversity is a limitation and may be reflected by the comprehensive core dataset.

The extent to which any of the Utstein templates have been implemented is a knowledge gap, which should be addressed by future research.

Impact

The IHCA Utstein template is widely recognised as the benchmark for IHCA registries worldwide. By promoting standardised definitions, it will enable comparison with and learning from different systems. That it has been cited 147 times in the two years since publication reflects its significance. The OHCA Utstein template is being updated and is likely to incorporate some elements from the IHCA version.

2.2 Paper 2. The UK National Cardiac Arrest Audit (NCAA)

Incidence and outcome of in-hospital cardiac arrest in the United Kingdom National Cardiac Arrest Audit. Resuscitation 2014;85:987-992.

Nolan JP, Soar J, Smith GB, Gwinnutt C, Parrott F, Power S, Harrison DA, Nixon E, Rowan K, on behalf of the National Cardiac Arrest Audit.

This paper has been cited 433 times

Contribution to Paper 2.

I was the Lead author (50% contribution) and investigator of this first national description of the incidence and outcome from in-hospital cardiac arrest in the UK. I drafted responses to the peer reviewers, which included the input of all authors, and submitted the final version of the paper. The UK National Cardiac Arrest Audit was conceived by me and implemented in collaboration with colleagues at the Resuscitation Council UK (RCUK) and Intensive Care National Audit and Research Centre (ICNARC). I was the inaugural Chairman of the NCAA Steering Committee and remain in that role.

Objectives

Before 2009 there were very few data on outcome after IHCA in the UK and no national data on the incidence of IHCA. A 6-month audit of IHCAs in 49 UK hospitals in 1997 documented a survival rate to hospital discharge of 17.6% but there were no data on the number of hospital admissions in this period, so the incidence of IHCA was unknown.[35] The UK National Cardiac Arrest Audit (NCAA) was established in 2009 with the aim of promoting improvements in resuscitation care and outcomes by providing hospitals with validated comparative data. The aim of this paper was to report the incidence, characteristics and outcome of adult in-hospital cardiac arrest in the UK NCAA database

Methods

The UK NCAA was established in 2009 as a collaboration between the RCUK and ICNARC. At that time, the ICNARC team had considerable experience in collecting and analysing data from most UK intensive care units (ICUs) using a subscription-based model, but had no experience with the collection of data from patients who were not in ICU. The RCUK already had a well-established network of resuscitation practitioners and the clinical knowledge of resuscitation practice in UK hospitals. Using the combined experience and knowledge of individuals at ICNARC and the RCUK, we established NCAA as a subscription-based national clinical audit of patients who received CPR (chest compressions and/or defibrillation) in response to a 2222 call (Figure 2). Approval to hold patient identifiable data under section 251 of the NHS Act 2006 was obtained from the National Information Governance Board.

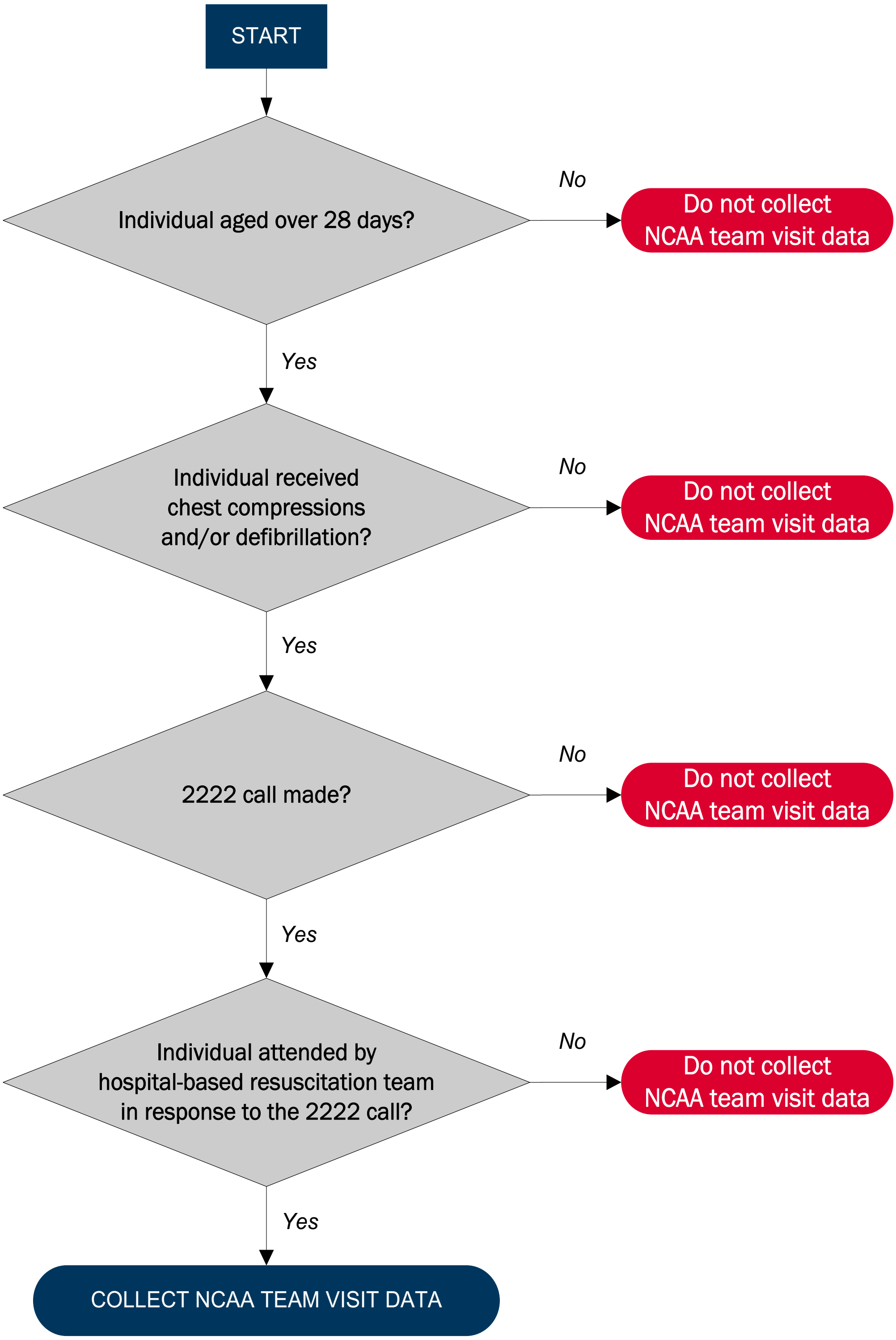

Figure 2. Scope of data collection for the National Cardiac Arrest Audit

We created a precisely defined dataset with aim of collecting only essential data that could be reliably collected and would enable us to determine the incidence and outcome from IHCA (Table 1).

Table 1. National Cardiac Arrest Audit (NCAA) Dataset

Denominator data:

1. Total number of admissions to the hospital
2. Total number of 2222 calls / Total number of 2222 calls solely for cardiac arrest

Team visit data:

3. Team visit number (automated)
4. National Health Service number
5. Date of birth / Estimated age
6. Sex
7. Ethnicity
8. Date of admission to/attendance at/visit to the hospital
9. Reason for admission to/attendance at/visit to the hospital
10. Date/Time of 2222 call
11. Status at team arrival
12. Location of arrest
13. Presenting/first documented rhythm
14. Reason resuscitation stopped at end of team visit
15. Transient post-arrest location
16. Post-arrest location
17. Status at discharge from the hospital
18. Sedated at discharge from the hospital
19. Date of discharge from the hospital
20. Cerebral Performance Category at discharge from the hospital
21. Date/Time of death
22. Additional Information (free text)

The initial scope included only those patients who were actually resuscitated by the resuscitation team, but this was changed to any patient in cardiac arrest who was attended by the team in response to a 2222 call. Thus, the analysis for this paper covered the period 1st April 2011 to 31st March 2013.

Results

During the period of analysis, 144 acute hospitals contributed data on 23,554 IHCAs among 22,268 patients. Only 16.9% of cardiac arrests had an initial shockable rhythm (ventricular fibrillation or ventricular tachycardia (VF/VT)). The total number of hospital admissions (all ages) was 14,784,144, giving an incidence of 1.6 cardiac arrests per 1000 hospital admissions. Incidence varied seasonally, peaking in winter (Figure 3).

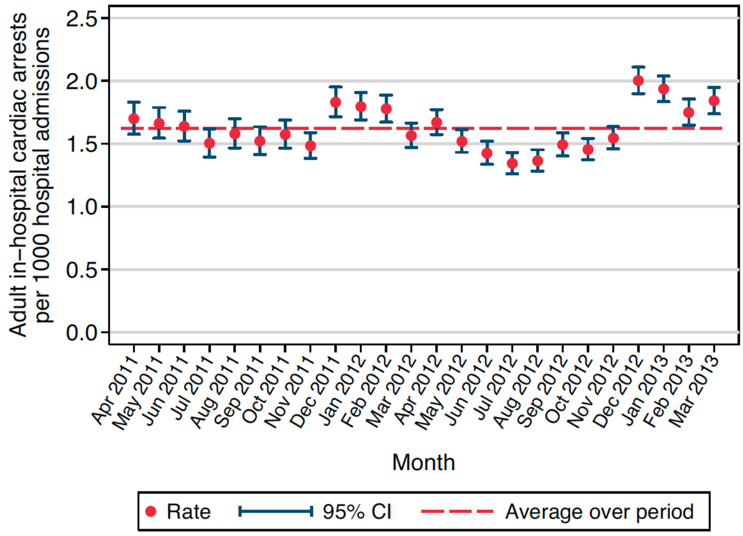

Figure 3. Incidence of adult in-hospital cardiac arrest (per 1000 hospital admissions).

The rate of survival to hospital discharge was 18.4 % overall and 49.0% and 10.5% among those with an initial VF/VT rhythm and a non-shockable rhythm respectively. Hospital survival rates varied substantially by hospital (Figure 4). Of those surviving to hospital discharge, 97.5% were documented as having a Cerebral Performance Category (CPC) of 1 or 2 (normally defined as a favourable functional outcome).

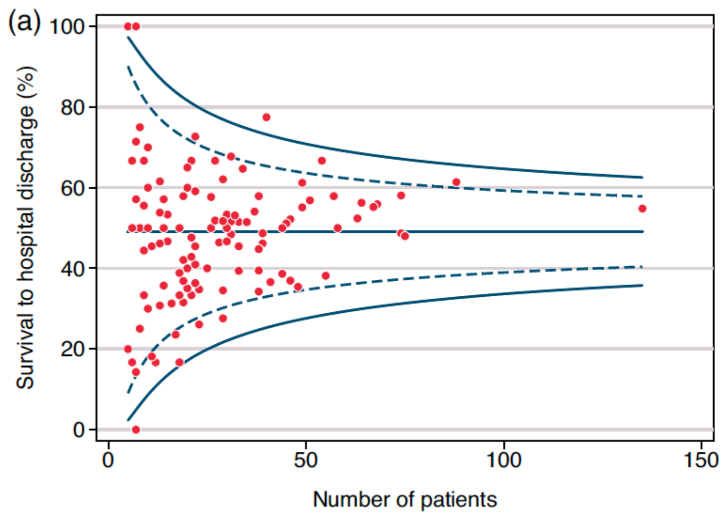

Figure 4. Funnel plot of survival to hospital discharge following adult in-hospital cardiac arrest for shockable rhythms. Each red dot represents an individual hospital. The dashed funnel line represents 2 standard deviations, and the solid funnel line represents 3 standard deviations.

Discussion

This paper described the first results from NCAA, the newly-established UK national audit of IHCA. Although we described variation in survival rates among participating hospitals, these data are unadjusted for case mix. We have subsequently developed risk models to predict return of spontaneous circulation > 20 minutes (ROSC > 20 min) and hospital survival.[36] The final risk model for hospital survival included: age (non-linear), prior length of stay in hospital, reason for attendance, location of arrest, presenting rhythm, and interactions between presenting rhythm and location of arrest. Use of data adjusted for case mix enables valid comparisons between hospitals participating in NCAA. It has also enabled us to show that adjusted outcomes from cardiac arrest are worse at night and at weekends compared with weekday daytime,[37] that the incidence of IHCA is decreasing,[38] and that survival rates were reduced during the first wave of the COVID-19 pandemic.[39]

That NCAA does not capture many of the core data elements defined in the IHCA Utstein template may be considered a weakness, but the difficulties in capturing cardiac arrests that don't result in a 2222 call were thought to be considerable. There has been some concern about the accuracy of the scoring of functional outcomes using CPC scores, but an analysis of these scores based on the source of information documented the highest proportion of CPC 1–2 scores among those assessed using direct patient assessment,[40] which is likely to be more reliable than inference from the notes or communication with the patient's clinical team. However, the survivor's condition may partly determine the information source used, such that survivors with a CPC 1 or 2 are more likely to be assessed directly. A limitation of CPC scores in general is that they do not account for the patient's functional status before their cardiac arrest. Co-morbidities and pre-arrest functional status are not captured by NCAA but these may influence outcome.

Impact

Almost 200 acute hospitals in the UK (mostly in England) have adopted NCAA. This enables benchmarking of performance between hospitals and the quarterly reports that individual hospitals receive enable them to review cases as part of their quality improvement programmes. NCAA has been adopted as a National Clinical Audit and the data are reviewed by the Care Quality Commission (CQC) when the performance of acute hospitals is assessed. While participation in NCAA is not mandated, the CQC's interest in the data provides a strong incentive for acute hospital to contribute their cardiac arrest data.

2.3 Paper 3. Outcome of cardiac arrest survivors admitted to UK intensive care units

Outcome following admission to UK intensive care units after cardiac arrest: a secondary analysis of the ICNARC Case Mix Programme Database. Anaesthesia 2007;62:1207–1216.

Nolan JP, Laver SR, Welch CA, Harrison DA, Gupta V, and Rowan K.

This paper has been cited 352 times

Contribution to Paper 3

I approached the Intensive Care National Audit and Research Centre (ICNARC) with the proposal to study cardiac arrest patients admitted to UK ICUs. I contributed to the analysis plan and was the lead author (60% contribution) of the paper. I drafted responses to the peer reviewers, which included the input of all authors, drafted the first revised version, and submitted the final version of the paper.

Objectives

We undertook an analysis of the ICNARC Case Mix Programme Database (CMPD) to determine the outcomes for patients admitted to UK ICUs after cardiac arrest. By using length of stay data, we also sought to determine the workload generated by post cardiac arrest patients in UK ICUs.

Methods

Data were extracted for patients admitted to ICUs who had received CPR in the 24 hours before ICU admission. At the time, the ICNARC CMPD included data on those admissions who had received CPR in the 24 hours before ICU admission but did not separately identify patients who had an OHCA and those who had an IHCA. We therefore defined OHCA as those whose location immediately before the source of admission to ICU as 'clinic or home' and source of admission as 'A&E, same hospital'. We divided IHCAs into perioperative (defined by source of admission to ICU is 'theatre and/or recovery, same hospital') and not perioperative (defined by excluding all the other categories). We chose to limit our analysis to those who had received ventilation on admission so that we excluded those likely having only a very brief period of CPR. We measured severity of illness by the Acute Physiology and Chronic Health Evaluation (APACHE) II score and the ICNARC Model. We also explored the relationship with mortality of several physiological values that are collected routinely for these severity of illness models.

Results

For the period December 1995 to November 2005 there were 24,132 admissions from 174 ICUs who had received CPR within 24 hours before admission to the ICU and who had received ventilation on admission; these represented 5.8% of all admissions to the ICUs during this period. The ICU mortality was 57.1% and hospital mortality was 71.4%. The APACHE II predicted hospital mortality for all admissions after cardiac arrest was 41.9% compared with 79.7% for the ICNARC model. The median duration of ICU stay was 3.4 days (IQR 1.6–8.1 days) for ICU survivors and 1.0 day (IQR 0.3–2.8 days) for ICU nonsurvivors. Of the 6329 hospital survivors for whom destination data were available, 79.9% were discharged to their normal residence. Treatment was withdrawn in 28.2% of all patients at a median of 2.4 days (IQR 1.5–4.1 days). We showed U-shaped distributions for mortality in association with the lowest values in the first 24 hours of plasma glucose, temperature, and pH.

Discussion

At the time of publication, this was globally the largest study to report outcomes for patients admitted to ICU after cardiac arrest. That mechanically ventilated post-cardiac arrest patients represented 5.8 % of all ICU admissions was an indication of the significant work load presented by these patients. The finding that 80% of the post-cardiac arrest patients who survived to hospital discharge were discharged to their normal residence is important because it implies a favourable functional outcome for the majority of such patients, which was not the perception of some intensivists at the time.[41] In the APACHE II risk model, CPR is treated as a diagnostic category and is given the weighting for outcome prediction, overriding any other diagnostic category. In the ICNARC model, CPR receives a weighting, but this is in addition to a separate diagnostic category weighting based on the primary reason for admission. Thus, the ICNARC model gave much closer overall prediction than the APACHE II model in this cohort – in comparison with the 71.4% hospital mortality of the whole group, the APACHE II model and ICNARC model predicted hospital mortality of 41.9% and 79.7%, respectively. Given that guidelines suggest waiting at least 3 days before making withdrawal of life sustaining treatment (WLST) decisions based on neuroprognostication, our finding that treatment was withdrawn at a median time of 2.4 days implies that in many cases this decision is being made prematurely.

There were several weaknesses of this paper. The most important is that the ICNARC CMP is not a cardiac arrest registry, which means that many data items specified as core in the Utstein template for IHCA are not collected by ICNARC. Most notable among these are the presumed cause of the cardiac arrest, initial monitored rhythm, bystander CPR and functional outcome. We also had to infer the location of the cardiac arrest (OHCA or IHCA) from the location of the patient before admission to the ICU because this this information is also not included in the ICNARC CMPD. Thus, in our analysis, cardiac arrests occurring in the emergency department would be categorised as 'community' (OHCA) even if they had not a cardiac arrest out of hospital. We tried to address the lack of data on functional outcome by using discharge to usual residence as a surrogate for favourable functional outcome. The most commonly used functional outcome scales are the Cerebral Performance Category (CPC) and modified Rankin Scale (mRS). A CPC score of 1 or 2 and an mRS score of 0–3 are generally considered to represent good functional outcome and approximate to an individual who is capable of independent existence. However, a study published in 2011 of 211 post-cardiac arrest patients discharged from hospital in Pittsburgh suggests that the criteria of 'discharge to home' significantly over-estimates the number of patients with a 'good outcome'.[42] In this study, which included both in– and out-of-hospital cardiac arrests, just 20% and 22% had a good outcome using the CPC definition (CPC 1 or 2) and mRS definition respectively; in contrast, 45% of these patients were discharged to home.

Impact

This is the first UK study to report good survival outcomes for those admitted to ICU after cardiac arrest, with many of the survivors returning to home. These findings help to reduce pessimistic outlooks by ICU clinicians. We have also highlighted likely premature withdrawal of life-sustaining treatment (WLST) decisions being made in many cases. These findings have been highlighted in European Resuscitation Council Guidelines from 2010 onwards and we have subsequently shown a lengthening in the time to WLST decisions.

2.4 Paper 4. Trends in epidemiology and outcome of patients admitted to UK ICUs after cardiac arrest

Increasing survival after admission to UK critical care units following cardiopulmonary resuscitation.

Critical Care 2016;20:219.

<u>Nolan JP</u>, Ferrando P, Soar J, Benger J, Thomas M, Harrison DA, Perkins GD.

This paper has been cited 74 times

Contribution to Paper 4

I approached the Intensive Care National Audit and Research Centre (ICNARC) with the proposal to study trends in the epidemiology and outcome of cardiac arrest patients admitted to UK ICUs. I helped to draft the analysis plan and was the lead author (50% contribution) of the paper. I produced the first draft of the paper, drafted responses to the peer reviewers, which included the input of all authors, and I revised and submitted the final version of the paper.

Objectives

We undertook an analysis of the ICNARC Case Mix Programme Database (CMPD) for the period 2004–2011 to determine whether risk-adjusted mortality had decreased for patients admitted to UK ICUs after cardiac arrest. We also aimed to report the lowest temperature of ≤ 34 °C in the first 24 h (as a surrogate for the use of mild induced hypothermia); the proportion of post-cardiac arrest patients having treatment withdrawn and the timing of withdrawal; the length of ICU stay among post-cardiac arrest patients; and the proportion of post-cardiac arrest patients becoming organ donors.

Methods

Data were extracted from the ICNARC CMPD and severity of illness was measured by the ICNARC model. A statistical analysis plan was agreed a priori. Case mix, temperatures, withdrawal, outcome and activity were described annually, and a multivariate logistic regression was performed to analyse the impact on outcome of year of admission.

Results

During the period 1 January 2004 to 31 December 2014, there were 63,417 (4.7% of the total) admissions to 286 ICUs in England, Wales and Northern Ireland who had received CPR within 24 hours before admission to the ICU and received ventilation on admission. One hundred and sixteen ICUs contributed data throughout the study period. Cardiac arrest survivors represented an increasing proportion of mechanically ventilated admissions (from 9.0 % in 2004 to 12.2 % in 2014, $p < 0.001$). The proportion of cardiac arrest patients with a lowest temperature in the first 24 h of ≤ 34°C increased steadily until 2014, when it decreased precipitously (Figure 5).

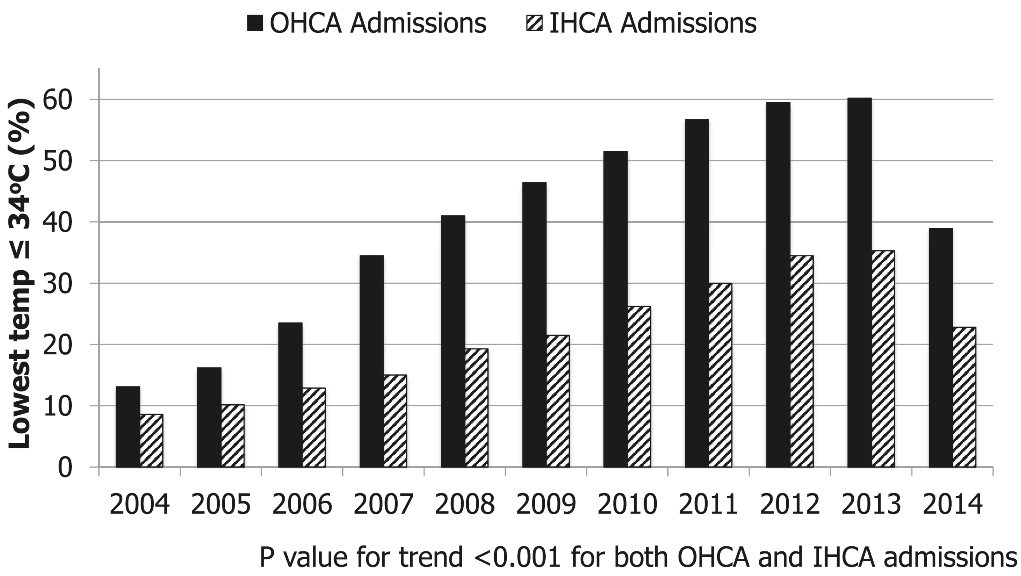

Figure 5. Proportion of post-cardiac arrest patients with lowest temperature ≤ 34^{o}C in the first 24 h (2004–2014) (reproduced from reference 17).

The proportion of post-cardiac arrest patients in whom treatment was withdrawn increased over the analysis period: OHCA 31.5 % in 2004 versus 34.8 % in 2014 (p <0.001); IHCA 27.5 % in 2004 versus 29.6 % in 2014 (p <0.001). The median time to treatment withdrawal has increased over the period of analysis (OHCA: 2.5 days (IQR 1.7 – 3.9 days) in 2004 versus 3.3 days (IQR 2.0 – 5.4 days) in 2014; p <0.001; IHCA = 2.4 days (IQR 1.5 – 4.3 days) in 2004 versus 3.4 days (IQR 2.0 – 6.3 days) in 2014; p <0.001) (Figure 6).

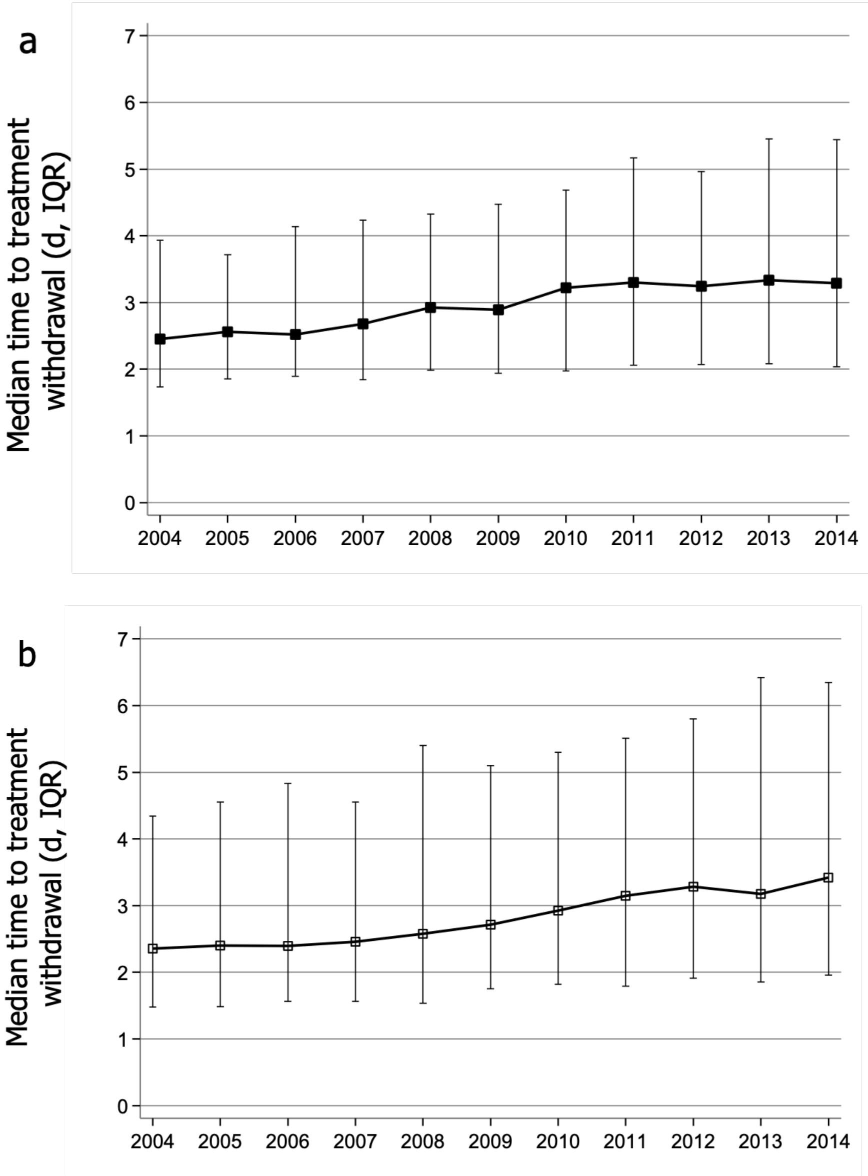

Figure 6. (a) Time to treatment withdrawal following out-of-hospital cardiac arrest 2004–2014 (median, IQR) ($p < 0.001$). (b) Time to treatment withdrawal following in-hospital cardiac arrest 2004–2014 (median, IQR) ($p < 0.001$). IQR interquartile range (reproduced from reference 17)

There was also an increase in the number of solid organ donors and an increase in the proportion of those dying who became solid organ donors, particularly after out-of-hospital cardiac arrest (Figure 7.)

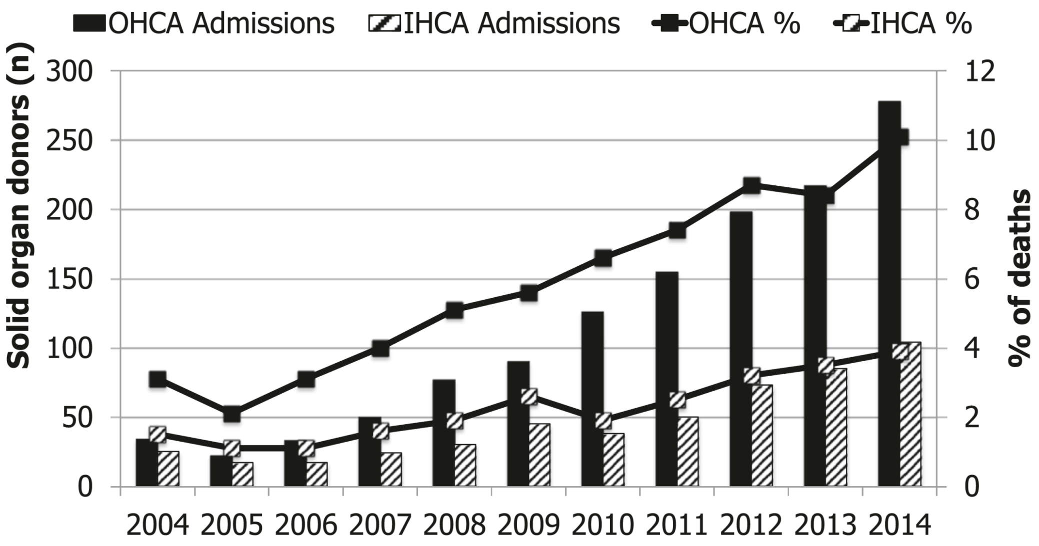

Figure 7. Solid organ donors among those dying after admission to an intensive care unit following cardiopulmonary resuscitation (2004–2014). IHCA in-hospital cardiac arrest, OHCA out-of-hospital cardiac arrest (reproduced from reference 17).

The ultimate acute hospital mortality for OHCA decreased from 70.1 % to 66.4 % (p value for trend 0.024) and for IHCA it decreased from 70.4 % to 60.3 % (p value for trend <0.001) cohorts (Figure 8). These reductions in mortality remained significant after adjustment for case mix [OHCA (adjusted OR per year 0.96 (0.95 to 0.97); p value for trend <0.001); IHCA (adjusted OR 0.96 (0.95 to 0.97); p value for trend <0.001)]. Reanalysis using only the 116 ICUs that contributed data throughout the study period produced results consistent with the primary analysis.

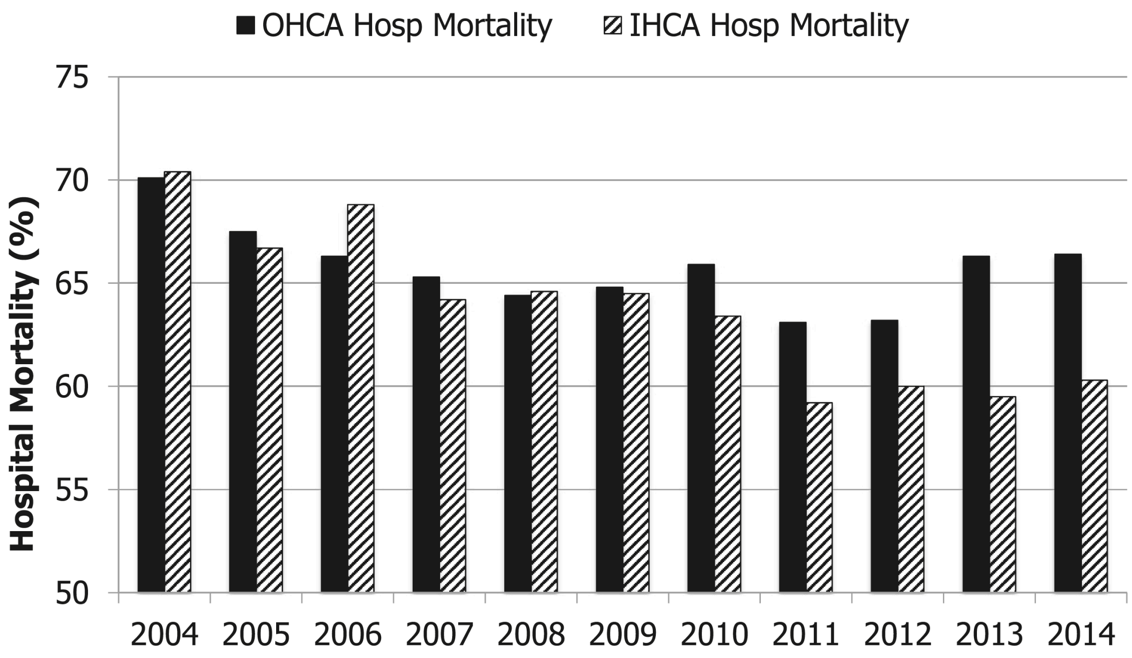

Figure 8. Hospital mortality (2004–2014) (reproduced from reference 17).

Discussion

This study has shown the increasing and substantial ICU workload associated with the treatment of comatose survivors of cardiac arrest: by 2014 they accounted for 1 in 8 of mechanically ventilated patients admitted to the ICU. We also showed that the risk-adjusted mortality had decreased for both IHCAs and OHCAs. Although this had also been shown for similar patients in Finland and the Netherlands,[43,44] it was the first time this had been shown for the UK.

The substantial decrease in the proportion of patients with a lowest temperature in the first 24 h of ≤ 34°C probably reflects the impact of the TTM Study, which showed no difference in outcomes between a target temperature of 33°C and 36°C.[23] We have analysed these changes in detail in paper 5.

The gradual increase in the time to treatment withdrawal over the period of study probably reflects the gradual adoption of international guidelines on multimodal prognostication in comatose post-cardiac arrest patients and increasing recognition of 'late awakeners' (i.e., some of those who eventually achieve a good functional outcome can take many days to awaken).[45,46]

This paper shares several of the weaknesses discussed in Paper 3 above; in particular, the ICNARC CMP is missing many data items specified as core in the Utstein templates for IHCA and OHCA. Although we showed that the proportion of survivors discharged to home remained unchanged throughout the study period (approximately 70%), this is a relatively crude approximation of favourable functional outcome and does not provide a reliable indication of cognitive outcomes. We do not know whether the reduction in the proportion of patients with a lowest temperature in the first 24 h of ≤ 34°C that occurred in 2014 represented a change in target temperature (from 33°C to 36°C) or the abandoning of temperature control altogether by some clinicians.

Impact

This paper was the first to show that outcomes for comatose post-cardiac arrest patients admitted to UK ICUs are improving. This should reduce pessimism among clinicians treating these patients. The sudden change in the lowest temperature in the first 24 hours in the final year of our period of study provided evidence of a significant change in temperature management in post-cardiac arrest patients. This change in practice happened in a remarkably short time following publication of the TTM study.[23] Our findings led many investigators, including ourselves, to look closely for any associated change in outcomes. We have studied this in more detail in Paper 5.

2.5 Paper 5. Temperature management strategies after cardiac arrest

Changes in temperature management and outcome after out-of-hospital cardiac arrest in United Kingdom intensive care units following publication of the Targeted Temperature Management trial. Resuscitation 2021;162:304–311

Nolan JP, Orzechowska I, Harrison DA, Soar J, Perkins GD, Shankar-Hari M.

This paper has been cited 14 times.

Contribution to Paper 5

I was the lead author (60% contribution) and investigator for this analysis of the impact of the TTM trial on temperature management practice and outcomes for post-cardiac arrest patients admitted to UK ICUs. It was my idea to undertake this analysis following the publication of a similar analysis of an equivalent database in Australia and New Zealand.[47] I drafted responses to the peer reviewers, which included the input of all authors, and submitted the final version of the paper.

Objectives

The TTM trial showed no difference in mortality or functional outcome among comatose post-cardiac arrest patients treated with temperature control at 33°C versus 36°C. We aimed to analyse the ICNARC CMP Database and investigate trends in the mean lowest temperature in the first 24 h after admission to ICU following OHCA before and after December 2013 and to determine if this was associated with a change in hospital mortality before and after this date. We also aimed to study trends in the frequency of fever (>38°C), the proportion of post-cardiac arrest patients having treatment withdrawn, the timing of withdrawal, and the proportion of post cardiac arrest non-survivors becoming organ donors.

Methods

We undertook a retrospective analysis of the ICNARC CMP Database for the period 1 January 2010 to 31 December 2017 and identified mechanically ventilated adults admitted to ICU after CPR for OHCA. We excluded cases for which temperature and/or data were missing and those admitted with limitations of treatment in place. The TTM study was published on 5th December 2013. We divided the study population into two cohorts: the pre-TTM study cohort (1 January 2010 to 31 December 2013) and the post-TTM study cohort (1 January 2014 to 31 December 2017). We used the ICNARC model to adjust for case mix. The primary outcome variables were lowest central temperature in the first 24 hours after ICU admission and survival to hospital discharge. A statistical analysis plan was agreed a priori.

Results

The pre-TTM trial cohort included 12,162 patients and the post-TTM cohort included 18,106 patients. Baseline characteristics were similar in the two cohorts, although the incidence of comorbidities listed under past medical history appears higher in the post-TTM cohort and this cohort had a higher ICNARC model predicted risk of mortality. The mean lowest temperature in the first 24 h in ICU was 33.6°C (SD 1.8°C) in pre-TTM patients and 34.7°C (SD 1.6°C) in post-TTM patients (absolute difference 1.12°C; 95% CI 1.08–16°C; $p < 0.001$). The proportion of patients with a fever (>38°C) in the first 24 h was 14.7% in pre-TTM patients versus 24.8% in post-TTM patients (OR 1.91, 95% CI 1.8–2.03 $p < 0.001$). The step change in lowest temperature was statistically significant (OR 0.92, 95% CI 0.85–0.99; $p < 0.001$) as was the change in slope (from a decrease of 0.10°C per year to an increase of 0.19°C per year; $p < 0.001$) (Figure 9).

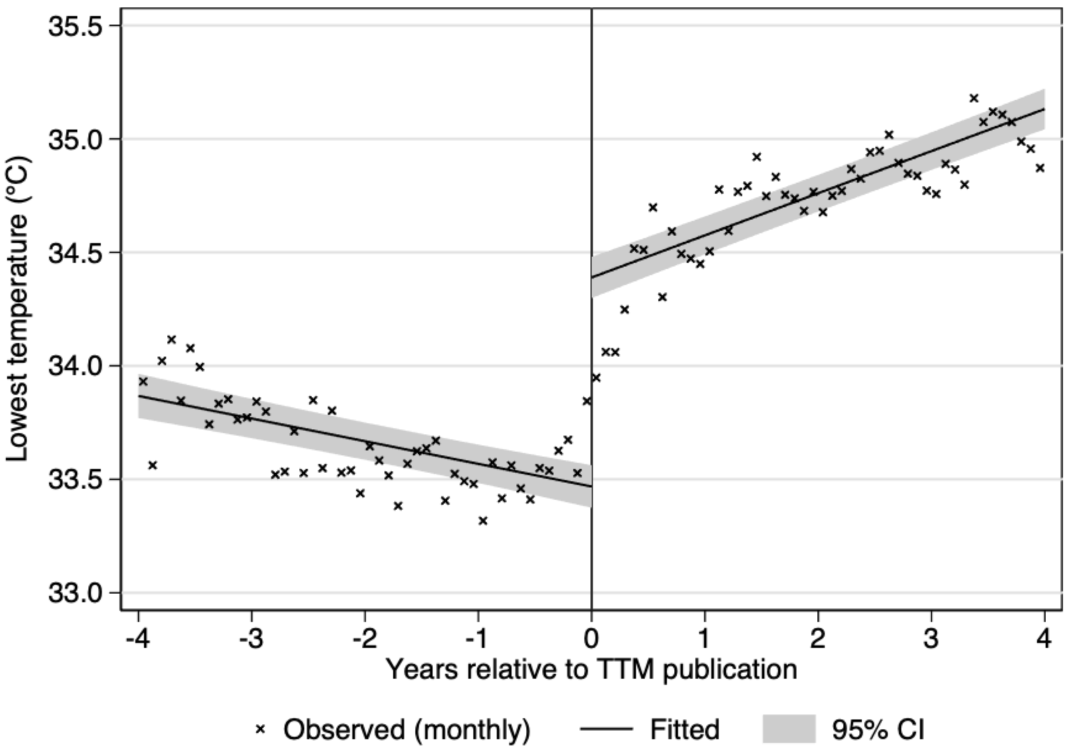

Figure 9. Step change in lowest body temperature in the first 24 hours before and after publication of the targeted temperature management trial on 5th December 2013.

The hospital mortality rate was 61.6% in the pre-TTM cohort and 63.7% in the post-TTM cohort. In a multilevel model, accounting for time trend, neither the step change in hospital mortality following publication of the TTM trial, nor the change in slope, was statistically significant. When adjusted for the ICNARC model probability of death, the step change in mortality in the post-TTM period was statistically significant (OR 1.17, 95% CI 1.04–1.32; $p = 0.008$) (Figure 10). The slope increased from

0.97 per year to 1.02 per year but this was not significant (p = 0.057). When the temperature component and all temperature components (temperature, respiratory rate, heart rate, urine output, pH, and PaO_2) were removed from the ICNARC model the step change in mortality was no longer significant.

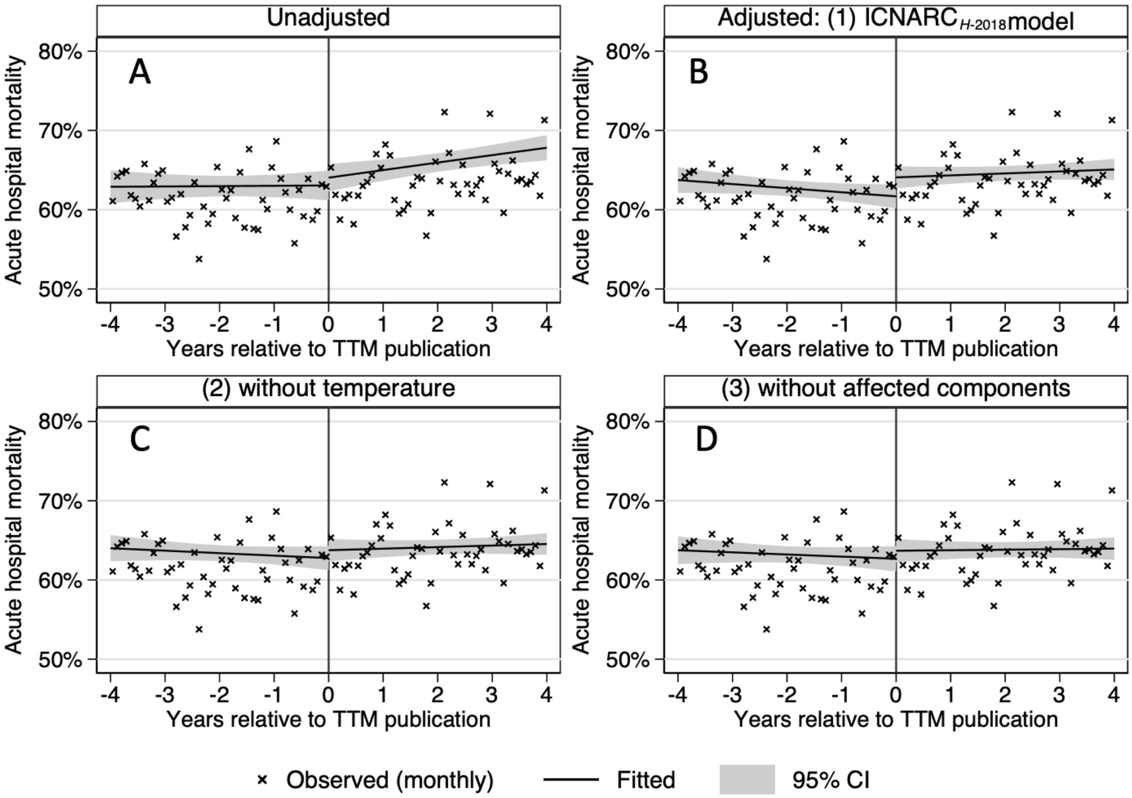

Figure 10. In hospital mortality by month. A — unadjusted data; B — adjusted for ICNARC model risk of death; C — adjusted for ICNARC model risk of death with the temperature component removed; D — adjusted for ICNARC model risk of death with all the temperature affected components removed.

The proportion of patients in whom treatment was withheld or withdrawn was slightly but significantly higher in the post-TTM trial period (40.3% versus 39.1%; p =0.035), as was the time from admission to a withdrawal decision (62.5 h versus 56.5 h; p < 0.001). The proportion of those patients dying in hospital in whom brainstem death was recorded was higher in the post-TTM trial period (11.7% versus 9.4%; p < 0.001). Throughout the period of study, 9.2% of those dying in hospital became organ donors and these were divided roughly equally between donation after circulatory death (DCD – 4.4%) and death by neurological criteria (DBD – 4.7%).

Discussion

This study has shown that publication of the TTM trial results has been associated with a significant change in the lowest temperature in first 24 hours after admission of patients following out-of-hospital cardiac arrest. This was accompanied by an increase in the proportion of patients with fever (> 38.0°C) in the first 24 hours (14.7% versus 24.8%). Analyses of temperature over time showed both a change in slope and step change related to the date of TTM publication. When risk adjusting using all components of the ICNARC model the step change in mortality in the post-TTM period was statistically significant, but this became insignificant when the analysis was repeated with temperature and then all temperature-related components were removed. Our study has highlighted an important potential weakness of risk-adjustment methods – if any of the components of the risk adjustment model are affected by a specific intervention it can seriously affect the reliability and performance of the model.

As discussed previously, an important weakness of this study is that the ICNARC CMP is not a cardiac arrest registry and is missing many of the data that would be of specific interest in relation to cardiac arrest patients, e.g. comorbidities, functional status before cardiac arrest, first monitored rhythm, bystander CPR and functional outcome. Our analyses assume a change in temperature management on a single day; in reality, implementation of such a change would be much more gradual.

Impact

This study was published only last year but its future impact will be a greater caution in the way risk-adjustment models are applied to observational data when a treatment involves direct manipulation of one of the physiological parameters used by the model. We have shown that although the incidence of fever was higher in post-TTM trial cohort, it was associated with an increase in mortality. This finding may mean that there is clinical equipoise for inclusion of a no temperature control arm in a future randomised trial of temperature control after cardiac arrest. This will be included in forthcoming TTM-3 study.

2.6 Paper 6. Intravascular access after cardiac arrest

Intraosseous versus intravenous administration of adrenaline in patients with out-of-hospital cardiac arrest: a secondary analysis of the PARAMEDIC2 placebo-controlled trial.

Intensive Care Medicine 2020;46:954–962

Nolan JP, Deakin CD, Ji C, Gates S, Rosser A, Lall R, Perkins GD.

This paper has been cited 27 times.

Contribution to Paper 6

I was the lead author (40%) of this secondary analysis of the PARAMEDIC2 trial. I wrote the first draft of the introduction and discussion and was particularly involved in interpretation of the results. I drafted responses to the peer reviewers, which included the input of all authors, and submitted the final version of the paper.

Objectives

The primary objective of this paper was to undertake a secondary analysis of the Pre-Hospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug Administration in Cardiac Arrest (PARAMEDIC2) trial to explore the effect of intravenous (IV) and intraosseous (IO) routes for drug delivery on the primary (survival at 30 days) and secondary outcomes (ROSC at handover to hospital, survival at hospital discharge, and favourable neurological outcome at hospital discharge).

Methods

PARAMEDIC2 was a double-blinded placebo-controlled trial in which OHCA patients were randomly allocated to receive either adrenaline or saline placebo.[48] UK paramedics attempt IO access if they fail to obtain IV access (up to two attempts) or if IV access is unlikely to be possible (e.g. restricted access or patient characteristics making it difficult). Treatment effect by the routes was assessed using unadjusted and adjusted logistic regression models. Adjustment was made for categorical variables including gender, whether a bystander commenced CPR, witness to the arrest, aetiology, initial rhythm and continuous variables including age, interval between emergency call and ambulance arrival at scene, and interval between ambulance arrival and drug administration. The primary outcome was also assessed by stratification of treatment and trial drug delivery route using Kaplan–Meier plot and Cox regression.

Results

The baseline characteristics of the patients in the adrenaline and placebo groups in the primary trial were similar. Of the 7317 participants with complete data and included in the analysis, 30.7% and 30.4% in the adrenaline and placebo arms, respectively, received the study drug via the IO route. The baseline characteristics of the patients in the IV and IO groups in this secondary analysis were substantially different. In the IO group there were more females (39.4% versus 33.8%; p < 0.001), a lesser proportion of shockable rhythms (14.2% versus 20.3%; p < 0.001), more unwitnessed cardiac arrests (40.1% versus 36.7%; p = 0.004), a lesser proportion received bystander CPR (54.8% versus 61%; p < 0.001) and a longer time from arrival at scene until administration of drug 18.4 min versus 14 min; p < 0.001).

The odds ratios (adrenaline versus placebo) for ROSC at hospital handover were similar in the IV (aOR 4.07 (95% CI 3.42–4.85)) and IO groups (aOR 3.98 (95% CI 2.86–5.53)); P value for interaction 0.90 (Figure 11). The confidence intervals for survival (discharge and 30 days) and favourable neurological outcomes for IV and IO also overlapped, with no statistical evidence of an interaction.

Outcome	Placebo	Adrenaline	OR (95% CI)	Interaction OR (95% CI)	p value
Survival at 30 days				0.54 (0.22, 1.32)	0.18*
Intravenous (IV)	65/2403 (2.7%)	98/2357 (4.2%)	1.67 (1.18, 2.35)		
Intraosseous (IO)	13/1065 (1.2%)	12/1064 (1.1%)	0.90 (0.40, 2.05)		
ROSC at hospital handover				0.98 (0.67, 1.42)	0.90*
Intravenous (IV)	207/2400 (8.6%)	616/2336 (26%)	4.07 (3.42, 4.85)		
Intraosseous (IO)	52/1061 (4.9%)	174/1059 (16%)	3.98 (2.86, 5.53)		
Survival at hospital discharge				0.48 (0.19, 1.18)	0.11*
Intravenous (IV)	63/2404 (2.6%)	96/2354 (4.1%)	1.72 (1.21, 2.43)		
Intraosseous (IO)	13/1064 (1.2%)	11/1063 (1.0%)	0.82 (0.35, 1.89)		
Favourable neurological outcome at hospital discharge				0.45 (0.15, 1.30)	0.14*
Intravenous (IV)	51/2403 (2.1%)	67/2353 (2.8%)	1.39 (0.93, 2.06)		
Intraosseous (IO)	11/1064 (1.0%)	7/1063 (0.7%)	0.62 (0.23, 1.67)		

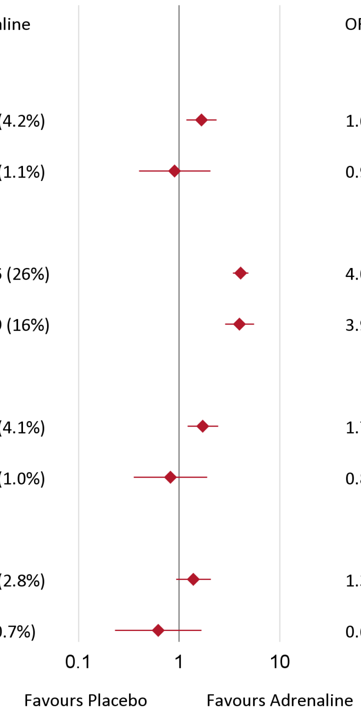

Figure 11. Adjusted treatment effect and interaction with intravenous and intraosseous routes on trial outcomes. *P-value for treatment and route interaction.

Discussion

We have shown that the treatment effect of adrenaline on ROSC at hospital admission was the same when given by the IV and IO routes. We could not detect any difference in the treatment effect between the IV and IO routes on 30-day survival or favourable neurological outcome at discharge. Although the IO route is being used increasingly during resuscitation, the evidence for its efficacy is limited. There is just one small RCT in humans and this showed a significantly higher vascular access success rate and shorter time to initial success with tibial IO compared with peripheral IV or humeral IO.[49] Nearly all observational studies show that the IO route is associated with a worse outcome compared with the IV route but they are all confounded by resuscitation time bias[50] and characteristics that generally favour the IV route.[51] The odds of surviving decrease the longer a resuscitation attempt continues and resuscitation time bias describes the association between any interventions that occur later in the resuscitation and worse outcome. For example, the beneficial effect of adrenaline on outcome diminishes the later it is given. Although the choice of vascular route was not randomised in the PARAMEDIC-2 trials, that it was double-blinded and placebo controlled enabled us to take account of and adjust for known confounders.

Given that the vascular access route was not randomised, and the analysis is under powered, our findings can only be hypothesis-generating. In most cases, it is likely that the IO route was attempted only after failure to achieve IV access, but such failed attempts were not documented. There may hidden confounders that we did not account for.

Impact

These data were shared with ILCOR and the clinical equipoise that resulted from these data prompted ILCOR to recognise the knowledge gap in the optimal method for securing vascular access in cardiac arrest. These data also underpinned the successful grant application to undertake a large RCT of IO versus IV drugs in out-of-hospital cardiac arrest in the UK. This RCT started recruiting patients in November 2021 (ISRCTN14223494). A second RCT of IO versus IV drugs in OHCA has been funded and will recruit patients in Denmark (NCT05205031).

Discussion

This thesis has linked together the international consensus process for updating the Utstein reporting template for IHCA with the first data describing the epidemiology and outcome from IHCA in the UK. Three analyses of the ICNARC CMPD document trends in the epidemiology and outcomes for patients admitted to UK ICUs after cardiac arrest and the impact on these trends of a change in post-cardiac temperature management strategy. The sixth paper focuses on the impact of the route of drug delivery on the outcome after OHCA.

There are always challenges in establishing international consensus because of the wide range of opinions, differing clinical backgrounds and experience, and differing healthcare systems represented by the participants. I have been involved in the development of many of the Utstein updates since 1999 and there is always tension between those wishing to collect a large, comprehensive dataset and those who prefer to restrict the number of data items in the hope that they are more likely to be recorded by most registries worldwide.

There remain relatively few national IHCA registries; to the best of my knowledge, there are currently five – the United States,[52] United Kingdom,[53] Denmark,[54] Sweden,[55] and the most recently established – China.[56] The American Heart Association Get-With-Guidelines–Resuscitation (GWTG–R) registry is the longest established and by far the most comprehensive registry in terms of the number of data items recorded; however, hospitals participating in the registry represent less than 5% of the all acute care hospitals in the US.[57] A registry that is not representative of the whole national healthcare system is of limited value because the data are not widely generalisable. This was a major consideration when we drafted the dataset for the UK NCAA. To enable participation by most UK hospitals we focused on a minimal dataset that would be easy to record and would provide sufficient information to determine the incidence of and outcome from cardiac arrest and to enable risk adjustment so that inter-hospital comparisons could be made. We did not include any intervention data (such as airway management, drugs, defibrillation) but plan to include this in the future.

In comparison with the Get-With-The-Guidelines Resuscitation (GWTG-R) registry in the United States, the proportion of cases with a shockable first documented rhythm (VF/pVT) in NCAA was very similar (16.9% for NCAA and 18.5% for the GWTG-R registry) but the unadjusted survival to hospital discharge from this rhythm was higher in the UK (49.0% versus 37.2%).[58] However, the considerable differences between NCAA and the GWTG-R, make comparisons problematic. As a national clinical audit, NCAA is an audit of the performance of hospital resuscitation processes and the resuscitation team. Unlike GWTG-R, NCAA is not a cardiac arrest registry and does not aim to document every

IHCA. Importantly, cardiac arrests that are managed without calling 2222 will not be captured by NCAA; for example, many cardiac arrests occurring on intensive care units (ICUs), in cardiac catheterisation laboratories and in emergency departments will not be included in NCAA. This may at least partly account for the difference in cardiac arrest incidence, which has been reported as 4.0 per 1000 hospital admissions in the GWTG-R registry compared with 1.6 per 1000 hospital admissions for NCAA. Two-thirds of cardiac arrests in the GWTG-R registry occur in ICUs or in monitored beds,[59] which contrasts with the 6.9% that occurred in ICUs or high dependency units (HDUs) in NCAA, and emphasises the considerable difference in US and UK health systems. An analysis of the Danish In-Hospital Cardiac Arrest Registry (DANARREST) documented an IHCA incidence of 1.8 (n = 4069) per 1000 hospital admissions over a two-year period, which is very similar to the NCAA value.[54] An analysis of the Swedish IHCA Registry reported an incidence of 1.7 per 1000 hospital admissions in 2015.[55] Like NCAA, the Danish and Swedish registries may not capture cardiac arrests for which there is no resuscitation team response, which makes them more reliably comparable with NCAA. The proportion of cardiac arrests occurring on general wards in these three countries are: UK NCAA (56.6%), Denmark (62.0%), and Sweden (50%). The Critical Illness Related Cardiac Arrest (CIRCA) study (NCT04219384), which has been completed but its findings have yet to be reported, will provide valuable data on the incidence and outcome from cardiac arrest in UK ICUs.

Our analysis of the ICNARC CMPD documented the proportion of patients admitted to UK ICUs who had undergone CPR in the previous 24 hours and showed that 28.6% survived to hospital discharge. Given the substantial number of these patients, small increases in the survival rate will translate into many more survivors. An important finding from this paper is that the ICNARC model[60] gave much closer overall prediction than the APACHE II model[61] in this cohort. The actual hospital mortality of the whole group was 71.4%; the APACHE II model predicted a hospital mortality of 41.9% and the ICNARC model 79.7%. The APACHE II model treats CPR as a diagnostic category and is given the weighting for outcome prediction, thus ignoring any other diagnostic category. In the ICNARC model, CPR receives a weighting, but this is in addition to a separate diagnostic category weighting based on the primary reason for admission. Use of the APACHE II model to risk adjust post-cardiac arrest patients may invalidate study results.

In the future, data linkage between the Hospital Episode Statistics for England (HES), the ICNARC CMPD, and NCAA should provide a clearer picture on how cardiac arrest patients are treated and more detail about their co-morbidities and outcomes. However, in practice, data linkage such as this is challenging, not least because of the considerable delay between requests for data and its delivery to investigators. The planned establishment of Trusted Research Environments (TREs) by NHS Digital (https://digital.nhs.uk/coronavirus/coronavirus-data-services-updates/trusted-research-environment-service-for-england) may make data linkage much more efficient.[62]

We also analysed ICNARC CMPD to determine the trends in the epidemiology and outcome of patients admitted to UK ICUs after cardiac arrest during 2004–2014.[17] As well as showing a considerable increase in the number of these patients admitted to ICUs and a reduction in their risk adjusted mortality, we fortuitously documented indirectly a sudden change in the strategy for their temperature management. The ICNARC CMPD does not capture data on whether hypothermic temperature control has been used, but the lowest temperature in the first 24 hours is recorded because this is required for the APACHE physiology score and for the ICNARC model. Guidelines published in 2003, and reinforced in 2005 and 2010, recommended use of hypothermic temperature control at 32–34°C for 24 hours in comatose survivors of OHCA with an initial shockable rhythm, but also suggested possible benefit after cardiac arrest from non-shockable rhythms and after IHCA.[18,63,64] By using a lowest temperature of ≤ 34°C, we were able to track the gradual implementation of hypothermic temperature control from 2004 to 2013 (Figure 5). In December 2013, the results of the Targeted Temperature Management (TTM) study were published – this randomised clinical trial showed no difference in mortality or favourable functional outcome among comatose OHCA survivors who were treated with temperature control at 36°C compared with 33°C.[23] Even though updated guidelines on temperature control after cardiac arrest were not published until 2015,[65] we documented a substantial decrease in 2014 in the proportion of both IHCA and OHCA patients with a lowest temperature ≤ 34°C (Figure 5). It is rare to see the implementation of change so rapidly after new science is published. However, our use of a surrogate marker for hypothermic temperature control (lowest temperature ≤ 34°C) did not enable us to distinguish between clinicians who had adopted temperature control at 36°C and those who had abandoned temperature control altogether. Other investigators have shown similar temperature trends among post-cardiac arrest patients following publication of the TTM study.[66,67]

We followed up this finding with an analysis of the ICNARC CMPD to determine if the change in temperature management was associated with a change in mortality. This study highlighted a major limitation in the use of a risk-adjustment model if any of the components of the model are affected by a treatment intervention – in this case temperature. When temperature was left in the ICNARC model, the step change in mortality after publication of the TTM study was statistically significant, but it became insignificant if temperature and then temperature-related components were removed from the analysis. In our study, the changes in risk-adjusted mortality mirrored the changes in temperature. It is possible that the decreasing temperatures before publication of the TTM trial were interpreted by the risk model as increasing risk of death and the increasing temperature after publication of the TTM trial interpreted as a decrease in risk of death. Thus, the step change and the change in the slope of adjusted mortality either side of the date of the publication of the TTM trial may reflect an artefact of changing temperature management over time. This is best illustrated in Figure 10 which shows no change in the unadjusted hospital mortality over the course of the 4 years before publication of the TTM study but a reducing mortality (albeit not quite statistically significant; $p = 0.057$) when adjusted using the full ICNARC model. The slope is progressively flattened as first the temperature and then all temperature-dependent parameters are removed from the ICNARC model.

Our findings are remarkably similar to those of an analysis of OHCA patients in the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation (ANZICS-CORE) database.[47] These investigators reported changes in lowest temperature in the first 24 hours that were similar to ours and when adjusted using the ANZ Risk of Death (ANZROD) model, mortality was significantly higher in a post-TTM trial cohort compared with a pre-TTM trial cohort (aOR 1.27 (99% CI 1.13–1.43) $p < 0.001$). Fever (> 38°C) in the first 24 hours was also more common in the post-TTM cohort compared with the pre-TTM cohort (16.5% versus 12.8%; OR 1.35 (99% CI 1.16–1.57); $p < 0.001$).

The finding from these two studies that mortality was not increased after a change in temperature management strategy is consistent with the results of the TTM-2 RCT which showed no difference in mortality or functional outcome among OHCA patients treated with temperature control at 33°C versus fever control (active temperature control only if temperature > 37.7°C).[29] In contrast, a single centre observational study that included 782 OHCAs documented that treatment with 36°C compared with 33°C was associated with a reduced odds of a favourable functional outcome (29.7% versus 39.9%; $p < 0.05$); however survival to hospital discharge was not significantly different.[68]

The intraosseous route is increasingly being used to deliver drugs during cardiac arrest and other emergencies, particularly out-of-hospital. The only randomised clinical trial comparing the IO with the IV route in cardiac arrest included only 182 patients and showed a significantly higher vascular access success rate and shorter time to initial success with tibial IO compared with peripheral IV or humeral IO routes.[49] Although virtually all observational studies show the IO route to be associated with a worse outcome compared with the IV route, they are confounded by resuscitation time bias (interventions delivered later during the resuscitation attempt are inevitably associated with a worse outcome)[50] and patient characteristics that bias against the IO route (e.g. fewer shockable rhythms).[51,69-73] Approximately 30% of the patients enrolled in the blinded PARAMEDIC-2 RCT were given the study drug (adrenaline or saline placebo) by the IO route and this provided the opportunity to determine the outcome of these patients in comparison with those receiving the study drug by the IV route. Although the vascular access route was not randomised, that this was a blinded, prospective study enabled us to undertake a robust analysis including adjustment for many of the likely confounders. The almost identical odds ratios for ROSC at hospital handover (approximately 4 for both IV and IO) implies that the IO route is equivalent to the IV route for short-term outcomes. For the longer-term outcomes of survival at hospital discharge and favourable neurological outcome at hospital discharge the odds ratios are lower for the IO route than for the IV route but the interaction statistics are not significant. The challenge in writing this paper was to interpret the findings from the relatively complex statistical analyses and to translate these into clear messages for clinicians. The findings were extremely important in supporting the successful grant application for a randomised trial of IV versus IO routes for drug delivery in OHCA. This PARAMEDIC-3 trial is now recruiting patients (https://warwick.ac.uk/fac/sci/med/research/ctu/trials/paramedic3/). If the IO route enables adrenaline to be delivered earlier than via the IV route it may improve survival – this is the hypothesis underpinning the PARAMEDIC-3 trial.

Conclusion

The six papers forming this thesis include documentation of the incidence and outcome from cardiac arrest, particularly among the cohort of patients who are initially resuscitated and are admitted to an ICU. The last of these papers addressed a prehospital intervention which, if successful, will increase the number of comatose post-cardiac arrest patients admitted to ICUs. Improvements in the ICU management of these patients may increase the chance of converting short-term survival into long-term favourable functional outcome.

Figures

Figure 1. The Utstein updated data element domains for in-hospital cardiac arrest.
Core and supplemental elements are shown for each of the 6 domains. AED indicates automated external defibrillator; BP, blood pressure; CPC, Cerebral Performance Category; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; HR, heart rate; IABP, intra-aortic balloon pump; ICU, intensive care unit; LVAD, left

ventricular assist device; mRS, modified Rankin Scale; NIV, noninvasive ventilation; OHCA, out-of-hospital cardiac arrest; PCPC, Paediatric Cerebral Performance Category; ROSC, return of spontaneous circulation; RR, respiratory rate; SBP, systolic blood pressure; temp, temperature; SpO2, peripheral oxygen saturation; TTM, targeted temperature management; VAD, ventricular assist device; and WLST, withdrawal of life-sustaining treatment.

Figure 2. Scope of data collection for the National Cardiac Arrest Audit

Figure 3. Incidence of adult in-hospital cardiac arrest (per 1000 hospital admissions).

Figure 4. Funnel plot of survival to hospital discharge following adult in-hospital cardiac arrest for shockable rhythms.

Figure 5. Proportion of post-cardiac arrest patients with lowest temperature ≤ 34oC in the first 24 h (2004–2014). IHCA – in-hospital cardiac arrest; OHCA – out-of-hospital cardiac arrest.

Figure 6. (a) Time to treatment withdrawal following out-of-hospital cardiac arrest 2004–2014 (median, IQR) ($p < 0.001$). (b) Time to treatment withdrawal following in-hospital cardiac arrest 2004–2014 (median, IQR) ($p < 0.001$). IQR interquartile range

Figure 7. Solid organ donors among those dying after admission to an intensive care unit following cardiopulmonary resuscitation (2004–2014). IHCA in-hospital cardiac arrest; OHCA out of hospital cardiac arrest.

Figure 8. Hospital mortality (2004–2014). IHCA in-hospital cardiac arrest; OHCA out of hospital cardiac arrest.

Figure 9. Step change in lowest body temperature in the first 24 hours before and after publication of the targeted temperature management trial on 5th December 2013.

Figure 10. In hospital mortality by month. A — unadjusted data; B — adjusted for ICNARC model risk of death; C — adjusted for ICNARC model risk of death with the temperature component removed; D — adjusted for ICNARC model risk of death with all the temperature affected components removed.

Figure 11. Adjusted treatment effect and interaction with intravenous and intraosseous routes on trial outcomes. *P-value for treatment and route interaction.

Tables

Table 1. National Cardiac Arrest Audit (NCAA) Dataset

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Declaration of contributors

Paper 1. The Utstein resuscitation registry template for in-hospital cardiac arrest

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This paper has been cited 90 times

Contribution to Paper 1.

Jerry Nolan was the lead author of this paper (**60% contribution**), which was the result of extensive international collaboration and sets the standard for reporting outcomes from in-hospital cardiac arrest. He chaired four face-to-face international meetings during the period 2013–2017 and five teleconferences during 2016–2018. He designed the web-based survey for the 2-stage Delphi process, wrote the first draft of the paper and co-ordinated the responses to reviewer comments. He submitted the final version of the paper.

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Paper 2. Incidence and outcome of in-hospital cardiac arrest in the United Kingdom National Cardiac Arrest Audit. Resuscitation 2014;85:987-992.

Nolan JP, Soar J, Smith GB, Gwinnutt C, Parrott F, Power S, Harrison DA, Nixon E, Rowan K, on behalf of the National Cardiac Arrest Audit.

This paper has been cited 403 times

Contribution to Paper 2.

Jerry Nolan was the Lead author (50% contribution) of this first national description of the incidence and outcome from in-hospital cardiac arrest in the UK. He drafted responses to the peer reviewers, which included the input of all authors, and submitted the final version of the paper.

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Paper 3. Outcome of cardiac arrest survivors admitted to UK intensive care units

Outcome following admission to UK intensive care units after cardiac arrest: a secondary analysis of the ICNARC Case Mix Programme Database. Anaesthesia 2007;62:1207–1216.

Nolan JP, Laver SR, Welch CA, Harrison DA, Gupta V, and Rowan K.

This paper has been cited 352 times

Contribution to Paper 3.

Jerry Nolan contributed to the analysis plan and was the Lead author (60% contribution) of the paper. He drafted responses to the peer reviewers, which included the input of all authors, and submitted the final version of the paper.

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Contribution to Paper 4

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Paper 5. Temperature management strategies after cardiac arrest
Changes in temperature management and outcome after out-of-hospital cardiac arrest in United Kingdom intensive care units following publication of the Targeted Temperature Management trial. Resuscitation 2021;162:304–311

Nolan JP, Orzechowska I, Harrison DA, Soar J, Perkins GD, Shankar-Hari M.
This paper has been cited 11 times.

Contribution to Paper 5
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Paper 6. Intravascular access after cardiac arrest.

Intraosseous versus intravenous administration of adrenaline in patients with out-of-hospital cardiac arrest: a secondary analysis of the PARAMEDIC2 placebo-controlled trial.

Intensive Care Medicine 2020;46:954–962

<u>Nolan JP</u>, Deakin CD, Ji C, Gates S, Rosser A, Lall R, Perkins GD.

This paper has been cited 27 times.

Contribution to Paper 6

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Appendices of published work

1. Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Template for In-Hospital Cardiac Arrest: A Consensus Report from a Task Force of the International Liaison Committee on Resuscitation.
2. Incidence and outcome of in-hospital cardiac arrest in the United Kingdom National Cardiac Arrest Audit.
3. Outcome following admission to UK intensive care units after cardiac arrest: a secondary analysis of the ICNARC Case Mix Programme Database.
4. Increasing survival after admission to UK critical care units following cardiopulmonary resuscitation.
5. Changes in temperature management and outcome after out-of-hospital cardiac arrest in United Kingdom intensive care units following publication of the Targeted Temperature Management trial.
6. Intraosseous versus intravenous administration of adrenaline in patients with out-of-hospital cardiac arrest: a secondary analysis of the PARAMEDIC2 placebo-controlled trial.

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Critical Care

RESEARCH Open Access

Increasing survival after admission to UK critical care units following cardiopulmonary resuscitation

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Abstract

Background: In recent years there have been many developments in post-resuscitation care. We have investigated trends in patient characteristics and outcome following admission to UK critical care units following cardiopulmonary resuscitation (CPR) for the period 2004–2014. Our hypothesis is that there has been a reduction in risk-adjusted mortality during this period.

Methods: We undertook a prospectively defined, retrospective analysis of the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme Database (CMPD) for the period 1 January 2004 to 31 December 2014. Admissions, mechanically ventilated in the first 24 hours in the critical care unit and admitted following CPR, defined as the delivery of chest compressions in the 24 hours before admission, were identified. Case mix, withdrawal, outcome and activity were described annually for all admissions identified as post-cardiac arrest admissions, and separately for out-of-hospital cardiac arrest and in-hospital cardiac arrest. To assess whether in-hospital mortality had improved over time, hierarchical multivariate logistic regression models were constructed, with in-hospital mortality as the dependent variable, year of admission as the main exposure variable and intensive care unit (ICU) as a random effect. All analyses were repeated using only the data from those ICUs contributing data throughout the study period.

Results: During the period 2004–2014 survivors of cardiac arrest accounted for an increasing proportion of mechanically ventilated admissions to ICUs in the ICNARC CMPD (9.0 % in 2004 increasing to 12.2 % in 2014). Risk-adjusted hospital mortality following admission to ICU after cardiac arrest has decreased significantly during this period (OR 0.96 per year). Over this time, the ICU length of stay and time to treatment withdrawal has increased significantly. Re-analysis including only those 116 ICUs contributing data throughout the study period confirmed all the results of the primary analysis.

Conclusions: Risk-adjusted hospital mortality following admission to ICU after cardiac arrest has decreased significantly during the period 2004–2014. Over the same period the ICU length of stay and time to treatment withdrawal has increased significantly.

Background

In a secondary analysis of the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme Database (CMPD) undertaken 10 years ago, we determined the characteristics and outcomes for patients admitted to United Kingdom (UK) intensive care units (ICUs) [1]. Since then there have been many developments in post-resuscitation care, which are summarised in guidelines published in 2015 by the European Resuscitation Council and the European Society of Intensive Care Medicine [2, 3]. After very little improvement in cardiac arrest survival rates for three decades [4], several investigators have reported increasing survival following both in-hospital [5] and out-of-hospital cardiac arrest [6]. One study from the United States has documented declining mortality rates among those

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hospitalised after cardiac arrest in the period 2001–2009 [7]. Two studies, one from Finland (2000–2008) and one from the Netherlands (1999–2009), have documented an improving trend in outcomes after admission to ICU following cardiac arrest [8, 9].

Other studies have shown considerable variation in outcome for post-cardiac arrest patients admitted to ICUs in the United States [10] and Canada [11].

The ICNARC CMPD includes data on admissions to all adult general ICUs in the UK. This facilitates reliable, representative analyses of most patients in the UK admitted to ICU after cardiac arrest. The objective of this study is to investigate trends in patient characteristics and outcome following admission to UK critical care units following cardiopulmonary resuscitation (CPR) for the period 2004–2014 (11 years). Our hypothesis is that there has been a reduction in risk-adjusted (ICNARC model) mortality during 2004–2014. Secondary objectives of our study are to investigate trends in: the proportion of post-cardiac arrest patients having treatment withdrawn and the timing of withdrawal; the lowest temperature of ≤ 34 °C in the first 24 h (as a surrogate for the use of mild induced hypothermia); length of ICU stay among post-cardiac arrest patients; the proportion of post-cardiac arrest patients becoming organ donors.

Methods

Case Mix Programme Database

The Case Mix Programme (CMP) is a national comparative audit of adult, general ICUs (including intensive care units and combined intensive care and high dependency units, but not coronary care units) in England, Wales and Northern Ireland co-ordinated by ICNARC. The CMP has received approval from the Patient Information Advisory Group to hold patient identifiable information without consent (approval number PIAG 2-10(f)/2005). Approval by a research ethics committee was not required. Details of the data collection and validation have been reported previously [12].

We undertook a prospectively defined, retrospective analysis of the ICNARC CMPD for the period 1 January 2004 to 31 December 2014. Admissions, mechanically ventilated in the first 24 hours in the critical care unit and admitted following CPR, defined as the delivery of chest compressions in the 24 hours before admission, were identified. Patients sustaining a cardiac arrest in ICU (but not before admission) were excluded from the analysis.

The admissions that were identified were then grouped in the following way:

- Out-of-hospital cardiac arrest: location immediately prior to source of admission to the unit as 'clinic or home' and source of admission to the unit is 'A&E, same hospital'.
- In-hospital cardiac arrest: location immediately prior to source of admission to the unit is not 'clinic or home' and source of admission to the unit is not 'A&E, same hospital'.

Case mix

Age, gender, year of admission and past medical history were extracted. Severity of illness was measured by the ICNARC model [13]. The ICNARC model encompasses a weighting for acute physiology (the ICNARC physiology score, defined by derangement from the normal range for twelve physiological variables in the first 24 hours following admission to ICU) and additionally a weighting for age, diagnostic category coefficients and interactions with the physiology score, cardiopulmonary resuscitation within 24 hours prior to admission, and source of admission.

Treatment

Data were extracted on the proportion of people that had the following:

- lowest temperature of ≤ 34 °C in the first 24 h (as a surrogate marker for treatment with therapeutic hypothermia);
- treatment withdrawn;
- timing of treatment withdrawn.

Outcome

Survival data were extracted at discharge from the CMP unit and at ultimate discharge from an acute hospital. The proportion of survivors discharged to home was documented. In those who died, the proportion who became solid organ donors was collected.

Activity

Length of stay in the CMP unit was calculated in fractions of days from the dates and times of admission and discharge. Length of stay in hospital was calculated in days from the dates of original admission and ultimate discharge. Readmissions to the unit within the same hospital stay were identified from the postcode, date of birth and sex, and confirmed by the participating units.

Statistical analyses

A statistical analysis plan was agreed a priori. The analyses performed were as follows.

Descriptive statistics

Case mix, withdrawal, outcome and activity were described annually for all admissions identified as post-cardiac arrest admissions, and separately for out-of-hospital cardiac arrest and in-hospital cardiac arrest. Readmissions were included in the descriptive statistics but were removed from the outcomes. To evaluate changes in study variables by calendar year we used logistic regression for categorical variables and linear regression for continuous, using the year of admission as the predictor variable. For non-normally distributed data, we used the Jonckheere-Terpstra trend test.

Multivariable analyses

A multivariable logistic regression was performed to analyse the impact on outcome of year of admission. To assess whether in-hospital mortality had improved over time, hierarchical multivariate logistic regression models were then constructed, with in-hospital mortality as the dependent variable, year of admission as the main exposure variable (modelled as continuous variable ranging from year 2004 to 2014), and ICU as a random effect. Models were adjusted for illness severity and potential confounding variables, including age, reason for admission and source for admission. This model estimated the adjusted probability of in-hospital mortality per incremental year over the study period. Separated models were developed for out-of-hospital CPR admissions and in-hospital CPR admissions.

All analyses were repeated using only the data from those ICUs contributing data throughout the study period.

All analyses were performed using Stata 13.0 (Stata Corporation, College Station, TX, USA).

Results

During the period 1 January 2004 to 31 December 2014, 1,338,031 admissions to 286 ICUs in England, Wales and Northern Ireland were included in the CMPD. Of these, 63,417 (4.7 %) received CPR within the 24 hours before admission to the ICU and received ventilation on admission.

The number of contributing ICUs, total number of admissions, and number of cardiac arrests (out-of-hospital and in-hospital) by year is shown in Table 1. The number of ICUs contributing data to the CMPD increased steadily during the period of study; 116 ICUs contributed data throughout the study period and separate analyses confined to these ICUs are presented in Additional file 1: Table S1, Additional file 2: Table S2, Additional file 3: Table S3. While mechanically ventilated survivors of cardiac arrest decreased as a percentage of all critical care unit admissions (from 5.1 % in 2004 to 4.7 % in 2014, $p < 0.001$), they represented an increasing proportion of mechanically ventilated admissions (from 9.0 % in 2004 to 12.2 % in 2014, $p < 0.001$).

The proportion of patients with a lowest temperature in the first 24 h of ≤ 34 °C for both out-of-hospital and in-hospital cardiac arrests has increased steadily, peaking in 2013 (p <0.001); the proportion in both cohorts decreases substantially in 2014 (Fig. 1, Tables 2 and 3).

During 2004–2014 the mean ICNARC physiology scores have increased slightly for out-of-hospital cardiac arrest but are unchanged for the in-hospital cohort. The proportion of post-cardiac arrest patients in whom treatment was withdrawn has increased over the analysis period: out-of-hospital cardiac arrest 31.5 % in 2004 versus 34.8 % in 2014 (p <0.001); in-hospital cardiac arrest 27.5 % in 2004 versus 29.6 % in 2014 (p <0.001). The time to treatment withdrawal has increased over the period of analysis (out-of-hospital cardiac arrest median [IQR] = 2.5 [1.7, 3.9] days in 2004 versus 3.3 [2.0, 5.4] days in 2014 (p <0.001); in-hospital cardiac arrest = 2.4 [1.5, 4.3] days in 2004 versus 3.4 [2.0, 6.3] in 2014 (p <0.001) (Fig. 2a and b).

Table 1 A total of 1,338,031 admissions to 286 adult general critical care units in England, Wales and Northern Ireland from 1 January 2004 to 31 December 2014

Year	Number of units	All admissions	Cardiac arrest admissions			
			Out-of-hospital n (%)	In-hospital n (%)	All n (%)	% of ventilated admissions
2004	170	79,681	1582 (2.0)	2446 (3.1)	4028 (5.1)	9.0
2005	170	80,729	1592 (2.0)	2424 (3.0)	4016 (5.0)	9.0
2006	173	82,371	1643 (2.0)	2364 (2.9)	4007 (4.9)	9.2
2007	184	90,053	1938 (2.2)	2418 (2.7)	4356 (4.8)	9.8
2008	194	99,962	2384 (2.4)	2453 (2.5)	4837 (4.8)	10.2
2009	211	109,788	2519 (2.3)	2704 (2.5)	5223 (4.8)	10.6
2010	225	131,785	2926 (2.2)	3178 (2.4)	6104 (4.6)	10.7
2011	235	149,737	3334 (2.2)	3366 (2.2)	6700 (4.5)	11.0
2012	235	161,953	3632 (2.2)	3843 (2.4)	7475 (4.6)	11.5
2013	235	165,770	3924 (2.4)	4083 (2.5)	8007 (4.8)	11.8
2014	254	186,202	4147 (2.2)	4517 (2.4)	8664 (4.7)	12.2
Total	286	1,338,031	29,621 (2.2)	33,796 (2.5)	63,417 (4.7)	10.6

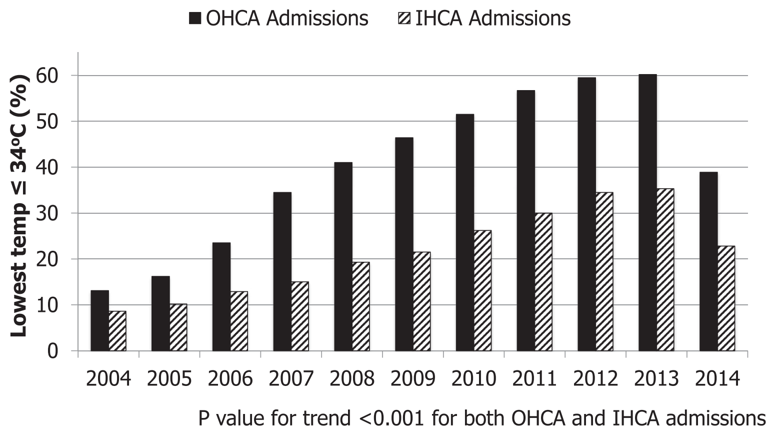

Fig. 1 Proportion of post-cardiac arrest patients with lowest documented temperature ≤ 34 °C in the first 24 hours (2004–2014). *IHCA* in-hospital cardiac arrest, *OHCA* out of hospital cardiac arrest

During the analysis period there has been an increase in both the absolute number of solid organ donors and the proportion of those dying who become solid organ donors (Fig. 3). The increase is particular marked among those dying after out-of-hospital cardiac arrests.

The critical care length of stay (median [IQR]) has increased from 1.9 [0.8, 4.2] to 2.7 [1.0, 5.9] days (p value for a trend <0.001) following out-of-hospital cardiac arrest and from 2.0 [0.6, 5.8] to 3.2 [1.1, 7.4] (p value for a trend <0.001) following in-hospital cardiac arrest. Length of ICU and hospital stay for survivors and non-survivors is given in the Additional file 4: Table S4 and Additional file 5: Table S5. Length of ICU stay for both survivors and non-survivors has increased significantly; hospital length of stay is unchanged following out-of-hospital cardiac arrest but is significantly shorter after in-hospital cardiac arrest.

Over the period of analysis, the ultimate acute hospital mortality for out-of-hospital cardiac arrest has decreased from 70.1 % to 66.4 % (p value for trend 0.024) and for in-hospital cardiac arrest it has decreased from 70.4 % to 60.3 % (p value for trend <0.001) cohorts (Fig. 4). After adjustment for case mix, the reduction in hospital mortality remained significant following both out-of-hospital CPR (adjusted odds ratio (OR) per year 0.96 (0.95 to 0.97); p value for trend <0.001) and in-hospital CPR (adjusted OR per year 0.96 (0.95 to 0.97); p value for trend <0.001). The critical care unit mortality for out-of-hospital cardiac arrests has decreased from 58.1 % to 56.9 % (p value for trend <0.001) and for in-hospital cardiac arrest it has decreased from 57.5 % to 49.5 % (p value for trend <0.001). The proportion of out-of-hospital cardiac arrest survivors discharged home has decreased from 73.1 % to 62.6 % (p value for a trend <0.001). In contrast, the proportion of in-hospital cardiac arrest survivors discharged home has remained unchanged at about 70 % throughout 2004–2014 (p value for a trend 0.559). During 2004–2014 the discharge destinations of survivors following out-of-hospital cardiac arrest were home (66.3 %); other hospital (22.4 %) and rehabilitation (7.3 %). The discharge destinations of survivors of in-hospital cardiac arrest were home (73.6 %); other hospital (16.5 %) and rehabilitation (7.4 %).

Re-analysis using only the 116 ICUs contributing data throughout the study period produced results consistent with the primary analysis of all ICUs (Additional file 1: Table S1, Additional file 2: Table S2, Additional file 3: Table S3). The adjusted OR per year for the reduction in hospital mortality following both out-of-hospital and in-hospital cardiac arrest are 0.96 (0.95 to 0.97; p value for trend <0.001).

Discussion

We have documented a substantial increase in the proportion of mechanically ventilated patients admitted to ICU who have undergone cardiopulmonary resuscitation before admission (9.0 % in 2004 and 12.2 % 2014); the largest increase is in the proportion of out-of-hospital cardiac arrests (3.5 % in 2004 and 5.8 % in 2014).

There has been a reduction in the risk-adjusted hospital mortality following admission to ICU after both out-of-hospital and in-hospital cardiac arrest (OR 0.96 per year) and re-analysis of only the 116 ICUs contributing data throughout the study period shows the same results. This finding is consistent with reports of increasing survival after admission to ICUs in Finland and the Netherlands [8, 9]. We have documented a significant reduction in the proportion of survivors who are discharged home after admission to ICU after out-of-hospital cardiac arrest. Neurological status on discharge is not included in the CMP database but the reduction in the proportion of survivors being discharged home after out-of-hospital cardiac arrest might indicate that the neurological outcome for these individuals is slightly

Table 2 Trends in characteristics and mortality for ICU admissions following out-of-hospital cardiac arrest

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	*p* value for trend
Number of admissions after cardiac arrest, n (%)	1582 (2.0)	1592 (2.0)	1643 (2.0)	1938 (2.2)	2384 (2.4)	2519 (2.3)	2926 (2.2)	3334 (2.2)	3632 (2.2)	3924 (2.4)	4147 (2.2)	<0.001
Age, mean (SD)	60 (17.7)	61 (17.4)	61 (16.6)	60 (18.4)	60 (17.3)	60 (17.2)	61 (16.9)	61 (17.2)	61 (17.8)	61 (17.9)	61 (17.8)	0.478
Gender, males n (%)	954 (60.3)	1000 (62.8)	1022 (62.2)	1224 (63.2)	1529 (64.1)	1614 (64.1)	1878 (64.2)	2139 (64.2)	2382 (65.6)	2537 (64.7)	2626 (63.3)	0.006
ICNARC Physiology Score, mean (SD)	28 (10.0)	28 (10.1)	28 (10.3)	28 (10.0)	28 (10.0)	28 (9.9)	29 (9.9)	29 (9.6)	29 (9.9)	30 (10.0)	29 (10.5)	<0.001
Critical care unit length of stay, mean (SD)	4 (6.8)	4 (5.9)	4 (5.9)	5 (7.3)	4 (6.5)	5 (6.8)	5 (7.4)	5 (7.7)	5 (7.4)	5 (8.1)	5 (8.7)	<0.001[*]
Critical care unit length of stay, median (IQR)	1.9 (0.8 4.2)	2.0 (0.8 4.1)	2.1 (0.9 4.5)	2.3 (1.0 5.0)	2.3 (1.0 4.8)	2.6 (1.1 5.1)	2.6 (1.0 5.3)	2.8 (1.1 5.7)	2.8 (1.2 5.7)	2.9 (1.1 5.8)	2.7 (1.0 5.9)	<0.001[*]
Hospital length of stay, mean (SD)	13 (28.5)	14 (26.6)	14 (24.1)	14 (25.5)	14 (27.2)	15 (30.3)	14 (30.3)	14 (27.8)	13 (25.7)	13 (24.9)	14 (25.3)	0.0020[*]
Hospital length of stay, median (IQR)	3.0 (1.0 12.0)	3.5 (1.0 14.0)	4.0 (1.0 16.0)	4.0 (1.0 15.0)	4.0 (1.0 16.0)	5.0 (1.0 15.0)	4.0 (1.0 15.0)	5.0 (2.0 15.0)	5.0 (1.0 16.0)	4.0 (1.0 15.0)	5.0 (1.0 14.0)	0.0020[*]
lowest temperature of ≤ 34 °C 24 h n (%)	202 (13.1)	250 (16.2)	377 (23.5)	654 (34.5)	964 (41.0)	1160 (46.4)	1495 (51.5)	1870 (56.7)	2143 (59.5)	2344 (60.2)	1603 (38.9)	<0.001
Treatment withdrawn n (%)	498 (31.5)	483 (30.3)	512 (31.2)	573 (29.6)	753 (31.6)	807 (32.0)	972 (33.2)	1171 (35.1)	1240 (34.1)	1394 (35.6)	1444 (34.8)	<0.001
Time to treatment withdrawn (days) mean (SD)	3 (3.8)	3 (3.1)	4 (3.2)	4 (4.1)	4 (2.8)	4 (3.4)	4 (3.3)	4 (4.4)	4 (3.8)	5 (4.6)	4 (4.0)	<0.001[*]
Time to treatment withdrawn (days) median (IQR)	2.5 (1.7 3.9)	2.6 (1.9 3.7)	2.5 (1.9 4.1)	2.7 (1.8 4.2)	2.9 (2.0 4.3)	2.9 (1.9 4.5)	3.2 (2.0 4.7)	3.3 (2.1 5.2)	3.2 (2.1 5.0)	3.3 (2.1 5.5)	3.3 (2.0 5.4)	<0.001[*]
Solid organ donor n (%)[**]	34 (3.1)	22 (2.1)	33 (3.1)	50 (4.0)	77 (5.1)]	90 (5.6)	126 (6.6)	155 (7.4)	198 (8.7)	217 (8.4)	278 (10.1)	<0.001
ICU mortality, n (%)	919 (58.1)	856 (53.8)	859 (52.3)	1009 (52.1)	1248 (52.3)	1348 (53.5)	1620 (55.4)	1800 (54.0)	1957 (53.9)	2255 (57.5)	2361 (56.9)	<0.001
Hospital mortality, n (%)	1098 (70.1)	1059 (67.5)	1076 (66.3)	1251 (65.3)	1514 (64.4)	1617 (64.8)	1917 (65.9)	2089 (63.1)	2287 (63.2)	2590 (66.3)	2739 (66.4)	0.024
Survivors discharged home, n (%)[***]	354 (73.1)	375 (70.4)	383 (67.6)	440 (64.0)	550 (63.2)	575 (63.7)	654 (64.8)	817 (65.6)	850 (63.2)	842 (63.1)	881 (62.6)	<0.001

ICU intensive care unit, *ICNARC* Intensive Care National Audit & Research Centre, *IQR* interquartile range, *SD* standard deviation
[*]Jonckheere-Terpstra test; [**] percentage of hospital deaths, [***]percentage of hospital survivors

Table 3 Trends in characteristics and mortality for ICU admissions following in-hospital cardiac arrest

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	*p* value for trend
Number of admissions after cardiac arrest, n (%)	2446 (3.1)	2424 (3.0)	2364 (2.9)	2418 (2.7)	2453 (2.5)	2704 (2.5)	3178 (2.4)	3366 (2.2)	3,843 (2.4)	4083 (2.5)	4517 (2.4)	<0.001
Age, mean (SD)	64 (16.3)	63 (16.7)	65 (15.6)	64 (16.3)	64 (16.5)	64 (16.2)	64 (15.8)	64 (15.6)	65 (15.3)	65 (15.2)	65 (15.3)	<0.001
Gender, males n (%)	1404 (57.4)	1400 (57.8)	1413 (59.8)	1439 (59.5)	1496 (61.0)	1623 (60.0)	1893 (59.6)	2059 (61.2)	2399 (62.4)	2554 (62.6)	2916 (64.6)	<0.001
ICNARC Physiology Score, mean (SD)	29 (11.2)	29 (10.9)	29 (11.1)	29 (10.9)	29 (10.6)	29 (10.5)	29 (10.4)	29 (10.2)	29 (10.1)	29 (10.4)	28 (10.5)	0.121
Critical care unit length of stay, mean (SD)	5 (9.0)	6 (10.1)	5 (8.5)	5 (9.5)	6 (10.1)	6 (9.9)	6 (10.4)	7 (12.2)	6 (9.4)	6 (9.4)	6 (10.5)	<0.001*
Critical care unit length of stay, median (IQR)	2.0 (0.6 5.8)	2.2 (0.7 6.3)	2.0 (0.6 5.9)	2.2 (0.8 6.0)	2.5 (0.8 7.1)	2.5 (0.9 6.9)	2.7 (0.9 6.7)	2.9 (1.0 7.1)	3.2 (1.1 7.4)	3.1 (1.0 7.3)	3.2 (1.1 7.4)	<0.001*
Hospital length of stay, mean (SD)	22 (35.8)	24 (39.7)	21 (32.3)	23 (34.2)	22 (33.0)	22 (37.5)	23 (43.9)	23 (37.4)	22 (33.1)	22 (35.9)	21 (33.4)	0.1128 *
Hospital length of stay, median (IQR)	10.0 (3.0 27.0)	11.0 (3.0 28.0)	10.0 (3.0 26.0)	11.0 (3.0 26.0)	11.0 (4.0 28.0)	11.0 (3.0 26.0)	10.0 (3.0 26.0)	11.0 (4.0 27.0)	11.0 (4.0 27.0)	10.0 (4.0 26.0)	11.0 (4.0 25.0)	0.1128 *
lowest temperature of ≤ 34 °C 24 h n (%)	200 (8.6)	237 (10.2)	293 (12.9)	352 (15.0)	464 (19.3)	575 (21.5)	817 (26.2)	997 (30.0)	1305 (34.5)	1,420 (35.3)	1014 (22.8)	<0.001
Treatment withdrawn n (%)	672 (27.5)	638 (26.3)	602 (25.5)	628 (26.0)	682 (27.8)	786 (29.1)	927 (29.2)	923 (27.4)	1149 (29.9)	1,198 (29.4)	1336 (29.6)	<0.001
Time to treatment withdrawn (days) mean (sd)	4 (6.6)	4 (5.2)	4 (5.6)	4 (5.4)	5 (6.5)	5 (7.2)	5 (8.8)	5 (7.3)	5 (6.5)	5 (6.9)	5 (6.1)	<0.001*
Time to treatment withdrawn (days) median (IQR)	2.4 (1.5 4.3)	2.4 (1.5 4.6)	2.4 (1.6 4.8)	2.5 (1.6 4.6)	2.6 (1.5 5.4)	2.7 (1.8 5.1)	2.9 (1.8 5.3)	3.2 (1.8 5.5)	3.3 (1.9 5.8)	3.2 (1.9 6.4)	3.4 (2.0 6.3)	<0.001*
Solid organ donor n (%)**	25 (1.5)	17 (1.1)	17 (1.1)	24 (1.6)	30 (1.9)	45 (2.6)	38 (1.9)	50 (2.5)	73 (3.2)	85 (3.5)]	104 (3.9)	<0.001
ICU mortality, n (%)	1406 (57.5)	1308 (54.0)	1302 (55.1)	1234 (51.0)	1281 (52.2)	1434 (53.1)	1662 (52.3)	1631 (48.5)	1909 (49.7)	2023 (49.6)	2235 (49.5)	<0.001
Hospital mortality, n (%)	1683 (70.4)	1592 (66.7)	1593 (68.8)	1526 (64.2)	1555 (64.6)	1719 (64.5)	1988 (63.4)	1965 (59.2)	2280 (60.0)	2400 (59.5)	2687 (60.3)	<0.001
Survivors discharged home, n (%)***	521 (68.3)	583 (70.1)	530 (68.7)	622 (69.7)	624 (69.5)	681 (69.1)	839 (70.5)	1012 (72.2)	1136 (72.7)	1209 (71.8)	1292 (70.6)	0.559

ICU intensive care unit, *ICNARC* Intensive Care National Audit & Research Centre, *IQR* interquartile range, *SD* standard deviation
*Jonckheere-Terpstra test; ** percentage of hospital deaths; ***percentage of hospital survivors

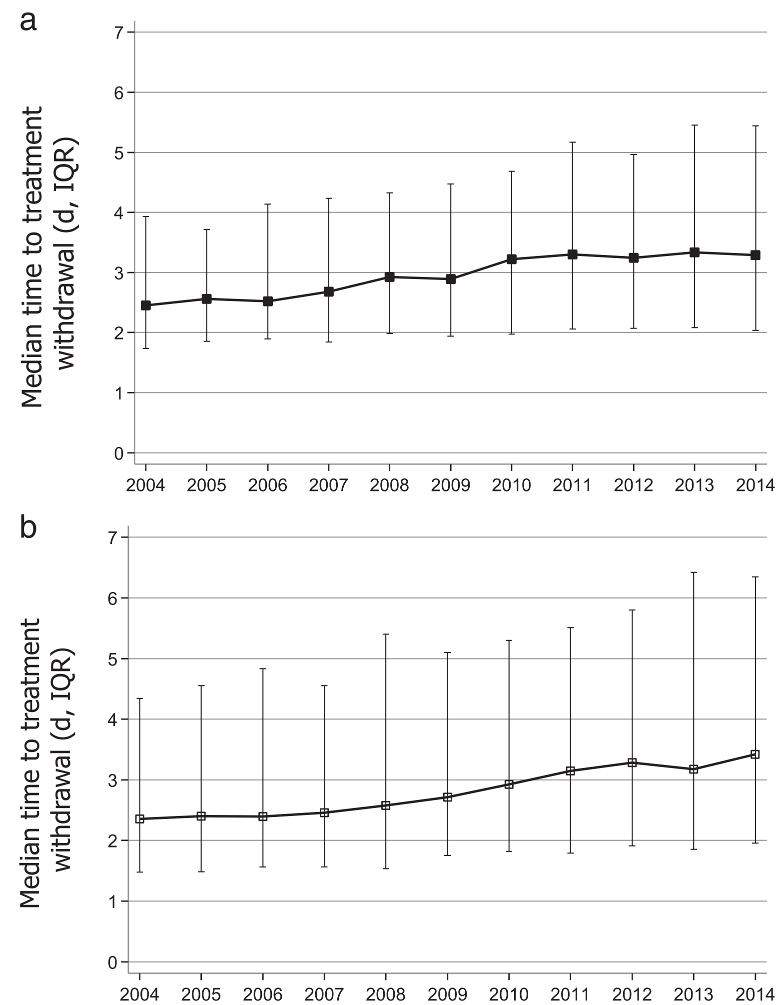

Fig. 2 a Time to treatment withdrawal following out-of-hospital cardiac arrest 2004–2014 (median, IQR) ($p < 0.001$). **b** Time to treatment withdrawal following in-hospital cardiac arrest 2004–2014 (median, IQR) ($p < 0.001$). *IQR* interquartile range

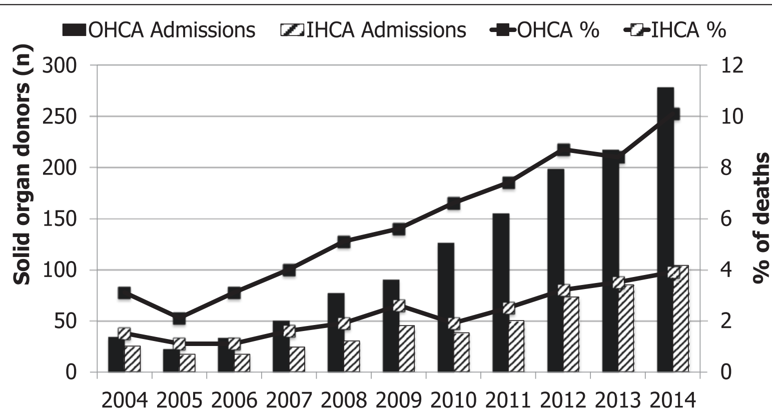

Fig. 3 Solid organ donors among those dying after admission to an intensive care unit following cardiopulmonary resuscitation (2004–2014). *IHCA* in-hospital cardiac arrest, *OHCA* out of hospital cardiac arrest

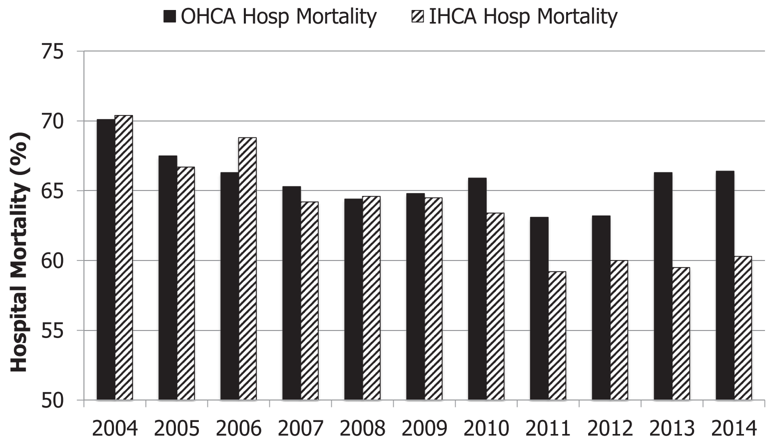

Fig. 4 Ultimate acute hospital mortality (2004–2014). *IHCA* in-hospital cardiac arrest, *OHCA* out of hospital cardiac arrest

worse over the period of study. This trend is not a feature among the survivors of in-hospital cardiac arrest. We do not know if discharge to home is a reliable surrogate for neurological outcome and this requires further study.

Trends of reducing ICU mortality have also been shown for other pathologies and relative to some of these (e.g. severe sepsis) the reduction in mortality that we have shown for cardiac arrest patients is comparatively modest [14].

Like the previous studies from Finland and the Netherlands, we have also shown a substantial increase in the implementation of mild induced hypothermia (increasing from 13.1 % in 2004 and peaking at 38.9 % in 2013 in the out-of-hospital cohort). In 2014 there was a substantial decrease in the proportion of patients (in both groups) with a documented lowest temperature in the first 24 hours. The results of a randomised trial of targeted temperature management (TTM) at 33 °C versus 36 °C after cardiac arrest were published in 2013 [15]. The TTM trial showed no difference in all-cause mortality between the two groups. Our findings may reflect a change in practice as a result of this study, with clinicians electing to use a target temperature of 36 °C instead of 33 °C or possibly abandoning the use of TTM altogether. There have been several other developments (e.g. changes in prognostication strategy, and use of percutaneous coronary intervention) in post-resuscitation care during the study period and one or more of these could contribute to improved survival.

We used the ICNARC model instead of Acute Physiology and Chronic Health Evaluation (APACHE) II for risk adjustment because we have shown previously that the ICNARC model gives much better discrimination than APACHE II in post-cardiac arrest patients [1]. In APACHE II, CPR is treated as a diagnostic category and is given the weighting for outcome prediction, overriding any other diagnostic category. In the ICNARC model, CPR receives a weighting but this is in addition to a separate diagnostic category weighting based on the primary reason for admission.

Our data document a significant change in the ICU management of post-cardiac arrest patients. The proportion of patients in whom treatment was withdrawn has increased slightly after both out-of-hospital and in-hospital cardiac arrest but the median time to treatment withdrawal has increased considerably from 2.5 to 3.3 days for out-of-hospital cardiac arrests and from 2.4 to 3.4 days after in-hospital cardiac arrest. For the last few years many investigators have advocated a much more cautious approach to prognostication, including delaying decisions to withdraw life-sustaining treatment until at least 3 days after cardiac arrest [16–19]. Our data suggest that in this respect practice is already changing [20].

Post-cardiac arrest patients who die after ICU admission are increasingly being recognised as potential solid organ donors [21, 22]. Organ survival rates after donation from post-cardiac arrest patients are comparable to those from other donors [21, 23]. Over the 11-year period of our study there has been a substantial increase in the proportion of non-survivors who have become solid organ donors: for out-of-hospital cardiac arrests this proportion has increased from 3.1 % (34) of non-survivors in 2004 to 10.1 % (278) in 2014. The latest National Health Service Blood and Transplant activity report (http://www.odt.nhs.uk/uk-transplant-registry/annual-activity-report/) indicates that, excluding Scotland (Scottish ICUs do not contribute data to the ICNARC CMP), there were 1185 deceased donors in the UK for the 2014–2015 year. Given that our data does not include every ICU in England, Wales and Northern Ireland, it seems likely that those admitted to an ICU after out-of-hospital cardiac arrest account for at least 25 % of the deceased solid organ donors in the UK.

Our study has several weaknesses. The CMP was not designed to collect data on cardiac arrest patients specifically and many of the essential data included in the Utstein template for reporting cardiac arrest data are missing [24]. Most notable among these are the presumed aetiology of the cardiac arrest, first monitored rhythm, bystander CPR and neurological outcome. The CMP dataset was modified to include location of cardiac arrest in 2009 but as this was not recorded throughout our study period, we have inferred this from the location of the patient before admission to the ICU and applied this to all patients in the study. We made inferences about the location of cardiac arrest: patients having a cardiac arrest in the emergency department will have been included in the out-of-hospital group. We have used lowest temperature within the first 24 h of ≤ 34 °C as a surrogate for the use of mild induced hypothermia but it is possible that some of these patients spontaneously had a temperature of less than 34 °C. By including only those patients undergoing mechanical ventilation at the time of admission to the ICU, we have attempted to exclude those patients who had only a brief period of CPR within 24 hours of admission, but required admission to the ICU for other reasons. We have documented the proportion of hospital survivors who were discharged home but this has not been validated as a surrogate for good neurological outcome.

Conclusions

In conclusion, during the period 2004–2014 survivors of cardiac arrest accounted for an increasing proportion of mechanically ventilated admissions to ICUs in the ICNARC CMP (9.0 % in 2004 increasing to 12.2 % in 2014). Risk-adjusted hospital mortality following admission to ICU after cardiac arrest has decreased significantly during this period (OR 0.96 per year). Over this time, the ICU length of stay and time to treatment withdrawal has increased significantly. It seems likely that non-survivors of out-of-hospital cardiac arrest account for at least a quarter of the solid organ donors in the UK.

Additional files

Additional file 1: Table S1. A total of 753,290 admissions to the 116 adult general critical care units in England, Wales and Northern Ireland that contributed data throughout the period 1 January 2004 to 31 December 2014. (DOCX 74 kb)

Additional file 2: Table S2. Trends in characteristics and mortality for ICU admissions following out-of-hospital cardiac arrest. Data from the 116 ICUs contributing data throughout the study period. (DOCX 16 kb)

Additional file 3: Table S3. Trends in characteristics and mortality for ICU admissions following in-hospital cardiac arrest. Data from the 116 ICUs contributing data throughout the study period. (DOCX 16 kb)

Additional file 4: Table S4. Length of stay for survivors and non-survivors. Data from all 286 ICUs contributing data to the case mix programme database. (DOCX 14 kb)

Additional file 5: Table S5. Length of stay for survivors and non-survivors. Data from the 116 ICUs contributing data throughout the study period. (DOCX 90 kb)

Abbreviations

APACHE, Acute Physiology and Chronic Health Evaluation; CMPD, Case Mix Programme Database; CPR, cardiopulmonary resuscitation; ICNARC, Intensive Care National Audit & Research Centre; ICU, intensive care unit; IHCA, in-hospital cardiac arrest; IQR, interquartile range; OHCA, out-of-hospital cardiac arrest; TTM, targeted temperature management

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Authors' contributions

JPN, JS, JB, MT and GDP were responsible for conception and design, data interpretation, manuscript writing and final approval of the manuscript. PF and DH were responsible for conception and design, data analysis and interpretation, manuscript writing and final approval of the manuscript.

Competing interests

JPN is Editor-in-Chief of *Resuscitation*. GDP and JS are Editors of *Resuscitation*. GDP is Director of Research for the Intensive Care Foundation and a NIHR Senior Investigator. PF, JB, MT and DH declare no conflicts of interest.

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