Resuscitation 116 (2017) 84–90

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

A survey on general and temperature management of post cardiac arrest patients in large teaching and university hospitals in 14 European countries—The SPAME trial results

Christian Storm[a,*,1], J. Nee[a,1], Kjetil Sunde[b], Michael Holzer[c], Pia Hubner[c], Fabio Silvio Taccone[d], Hans Friberg[e], Esteban Lopez-de-Sa[f], Alain Cariou[g], Joerg C. Schefold[h], Giuseppe Ristagno[i], Marko Noc[j], Dirk W. Donker[k], Janusz Andres[l], Pawel Krawczyk[l], Markus B. Skrifvars[m,n], James Penketh[o], Alexander Krannich[a], Michael Fries[p]

[a] *Charité-Universitätsmedizin Berlin, Germany*
[b] *Dept. of Anaesthesiology, Division of Emergencies and Critical Care, Oslo University Hospital, and Institute of Clinical Medicine, University of Oslo, Norway*
[c] *Department of Emergency Medicine, Medical University of Vienna, Vienna, Austria*
[d] *Dept. of Intensive Care, Erasme Hospital—Université Libre de Bruxelles (ULB) Brussels, Belgium*
[e] *Dept. of Anesthesiology and Intensive Care Medicine, Skåne University Hospital, Lund University, Lund, Sweden*
[f] *Dept. of Cardiology, La Paz-Idipaz University Hospital Madrid, Spain*
[g] *Medical Intensive Care Unit, Cochin Hospital (Assistance Publique Hôpitaux de Paris)—INSERM U970 (Team 4) and Paris Descartes University, France*
[h] *Dept. of Intensive Care Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland*
[i] *Dept. of Cardiovascular Research, IRCCS-Istituto di Ricerche Farmacologiche "Mario Negri", Milan Italy and Italian Resuscitation Council, Bologna, Italy*
[j] *Centre of Intensive Internal Medicine, University Medical Centre, Ljubljana, Slovenia*
[k] *Dept. of Intensive Care Medicine, University Medical Center Utrecht, Utrecht, The Netherlands*
[l] *Dept. of Anaesthesiology and Intensive Care, Jagiellonian University Medical College Cracow, Poland*
[m] *Australian and New Zealand Intensive Care Research Centre, School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia*
[n] *Division of Intensive Care, Department of Anaesthesiology, Intensive Care and Pain Medicine, Helsinki University and Helsinki University Hospital, Finland*
[o] *Dept. of Anaesthesia and Intensive Care Medicine, Royal United Hospital Bath, UK*
[p] *Dept. of Anaesthesiology and Intensive Care Medicine, St. Vincenz-Hospital, Limburg, Germany, Germany*

ARTICLE INFO

Article history:
Received 13 February 2017
Received in revised form 22 March 2017
Accepted 30 March 2017

Keywords:
European survey
Post-resuscitation care
Target temperature management
Standard operating procedure

ABSTRACT

Introduction: International guidelines recommend a bundle of care, including targeted temperature management (TTM), in post cardiac arrest survivors. Aside from a few small surveys in different European countries, adherence to the European Resuscitation Council (ERC) and European Society of Intensive Care Medicine (ESICM) recommendations are unknown.
Methods: This international European telephone survey was conducted to provide an overview of current clinical practice of post cardiac arrest management with a main focus on TTM. We targeted large teaching and university hospitals within Europe as leading facilities and key opinion leaders in the field of post cardiac arrest care. Selected national principal investigators conducted the survey, which was based on a predefined questionnaire, between December 2014 and March 2015, before the publication of the ERC Guidelines 2015.
Results: The return rate was 94% from 268 participating intensive care units (ICU). The majority had a predefined standard operating procedure (SOP) protocol for post cardiac arrest patients. Altogether, 68%

* Corresponding author at: Charité-Universitätsmedizin Berlin CC 13, Dept. of Nephrology and Intensive Care Medicine Cardiac Arrest Center of Excellence Augustenburger Platz 1 13353 Berlin, Germany.
E-mail addresses: christian.storm@charite.de (C. Storm), jens.nee@charite.de (J. Nee), kjetil.sunde@medisin.uio.no (K. Sunde), michael.holzer@meduniwien.ac.at (M. Holzer), pia.hubner@meduniwien.ac.at (P. Hubner), ftaccone@ulb.ac.be (F.S. Taccone), hans.a.friberg@gmail.com (H. Friberg), e.lopezdesa@terra.com (E. Lopez-de-Sa), alain.cariou.perso@gmail.com (A. Cariou), joerg.schefold@insel.ch (J.C. Schefold), gristag@gmail.com (G. Ristagno), marko.noc@mf.uni-lj.si (M. Noc), dirkdonker@ymail.com (D.W. Donker), janusz.andres@uj.edu.pl (J. Andres), p.krawczyk@uj.edu.pl (P. Krawczyk), Markus.Skrifvars@hus.fi (M.B. Skrifvars), jpenketh@nhs.net (J. Penketh), alexander.krannich@biostats.de (A. Krannich), m.fries@st-vincenz.de (M. Fries).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.resuscitation.2017.03.038
0300-9572/

of the ICUs provided TTM at a target temperature of 32–34 °C for 24 h, and 33% had changed the target temperature to 36 °C. The minority provided a written SOP for neurological prognostication, which was generally initiated 72 h after return of spontaneous circulation (ROSC). Electroencephalography and somatosensory evoked potentials were used by most ICUs for early prognostication. Treating more than fifty patients a year was significantly associated with providing written SOPs for TTM and prognostication ($p < 0.01$), as well as the use of a computer feedback device ($p = 0.03$) for TTM.

Conclusion: This international European telephone survey revealed a high rate of implementation of TTM in post cardiac arrest patients in university and teaching hospitals. Most participants also provided a SOP, but only a minority had a SOP for neurological prognostication.

Introduction

Post cardiac arrest management has changed considerably over the last decade, especially following several milestone trials on the use of targeted temperature management (TTM) in comatose survivors after cardiac arrest [1–4]. In 2010, the European Resuscitation Council (ERC) guidelines recommended to cool comatose patients to a constant temperature between 32 and 34 °C for 24 h [4]. In 2013, however, the pragmatic "TTM trial" showed that there was no difference in outcome among cooled patients if the target temperature was 33 °C or 36 °C [5]. Accordingly, the ERC guidelines from 2015, co-established with the European Society of Intensive Care Medicine (ESICM), recommended a wider range of target temperatures between 32 °C and 36 °C in this setting [4].

In addition to TTM for the treatment of ischemic-hypoxic brain injury, structured post-arrest treatment bundles including hemodynamic – optimization, early percutaneous coronary interventions (whenever indicated), controlled oxygen and carbon dioxide levels during mechanical ventilation and tight glucose control provide a substantial reduction of secondary brain insults [6,7] and were also included into recent recommendations to manage cardiac arrest (CA) survivors (4). However, the rate of implementation of these therapies widely varies between different European countries and TTM may still be an underused part of a standardized post-arrest clinical management [8–10]. Additionally, some centers stopped to use TTM after CA and moved to normothermia or fever control because of misinterpretation of the TTM study [11]. Thus, it would be of great importance to understand current clinical practice for CA survivors to better understand how current guidelines have been implemented.

This international European survey was therefore conducted to give an overview of current practice of post cardiac arrest management in Europe focusing on large teaching and University hospitals as leading facilities with key opinion leaders in the field of post cardiac arrest care. Importantly, the survey was performed at a time when the ERC guidelines still recommended TTM in the 32°–34 °C range, but after the publication of the TTM trial.

Methods

National investigators in 14 European countries were recruited to be responsible for a structured telephone survey between December 2014 and March 2015 using a predefined questionnaire (Fig. 1). Large teaching hospitals and University hospitals as leading facilities and key opinion leaders in the field of post cardiac arrest care were targeted. Core data about type and size of the intensive care unit (ICU) as well as data about implementation of post arrest management, whether, standard protocols for TTM and prognostication were used and target population were surveyed. The leading physician of the ICU was contacted, at least twice if the first contact was without success. As the structure of hospitals varies in Europe the number of ICUs within a hospital admitting post cardiac arrest patients varies; there is also variation between hospitals and countries. All completed questionnaires were computer-analyzed and final data double-checked before entering statistical analysis. The department for medical computer science at the medical faculty of the University Aachen, Germany, was responsible for data analysis, calculations and presentation of data. To analyze if the number of patients being treated in the ICU had any association with the care provided as part of the post cardiac arrest bundle, a differentiation between less/more than 50 treated cardiac arrest patients per years was made. Statistical analysis was performed using the R environment for statistical computing and graphics, version 3.2.2 (Fire Safety). For group comparisons chi-square test was used and a p-value <0.05 was considered to indicate statistical significance. Diagrams were generated using the R-packages ggplot2, rworldmap 1.3-1, and Map Projections (Packaged for R by Ray Brownrigg and Thomas P Minka, transition to Plan 9 codebase by Roger Bivand), version 1.2-4.

Table 1
Detailed data from different European countries participating in the survey are given. Number of ICUs per country, total number of beds per country and participating ICUs and number of post cardiac arrest patient per year (<10, 10–50 or >50) are given (* no data from 2 ICUs; ** no data from 13 ICUs).

Country	no. of ICUs	no. of beds	<10	10–50	>50
Austria	15	145*	4 (27%)	8 (53%)	3 (20%)
Belgium	7	198		4 (57%)	3 (43%)
Finland	5	119		2 (40%)	3 (60%)
France	45	906	3 (6%)	26 (58%)	16 (36%)
Germany	81	1495**	10 (12%)	27(33%)	27 (33%)
Italy	21	247	6 (28%)	14 (67%)	1 (5%)
Netherlands	8	244		2 (25%)	6 (75%)
Norway	7	88		2 (29%)	5 (71%)
Poland	15	183	3 (20%)	10 (67%)	2 (13%)
Slovenia	2	26		1 (50%)	1 (50%)
Spain	10	109		9 (90%)	1 (10%)
Sweden	8	116		3 (38%)	5 (62%)
Switzerland	7	197	1 (14%)	5 (72%)	1 (14%)
UK	36	1003	3 (8%)	14 (39%)	19 (53%)

Results

Core data

In total, 268 ICUs in 14 European countries (Table 1) were contacted. Among those, 94% provided a full data set as defined in the questionnaire and 16 ICUs declined to participate (Fig. 1).

Post cardiac arrest management

General characteristics

In 68% of the ICUs in leading hospitals a written SOP was implemented to treat post cardiac arrest patients whereas 26% and 6%, of the ICUs, respectively, either did not have a written protocol or did not answer (Fig. 2). 73% of ICUs used early coronary angiography

PI: M. Fries, University RWTH Aachen; C. Storm, University Charité Berlin; Germany

core data

1. country:
2. university name:
3. specialty of ICU: Anaesthesiology/ Internal Medicine/ Surgical/ Interdisciplinary
4. number of beds:

post-arrest managment data

1. target temperature		☐ 36°	☐ 32-34°	
2. changed after TTM-trial		☐ yes	☐ no	
3. duration of TTM		☐ 24 hrs	☐ longer	☐ shorter
4. target population		☐ OHCA	☐ IHCA	☐ both
4. feedback device in use		☐ yes	☐ no	
5. Controlled rewarming (<0.5°/h)		☐ yes	☐ no	
6. TTM for all rhythms		☐ yes	☐ no	
7. PCI for VF/VT CA survivors		☐ yes	☐ no	
8. PCI for non-VF/VT survivors		☐ yes	☐ no	
9. number of CA patients/year		☐ <10	☐ 10-50	☐ >50
10. written SOP		☐ yes	☐ no	
11. pre-defined targets for	MAP	☐ yes	☐ no	
	pCO_2	☐ yes	☐ no	
	pO_2	☐ yes	☐ no	
	glucose	☐ yes	☐ no	
12. routine use of cardiac output measurement		☐ yes	☐ no	
13. standard for prognostication		☐ yes	☐ no	
14. type of prognostication	EEG	☐ yes	☐ no	
	SEP	☐ yes	☐ no	
	NSE	☐ yes	☐ no	
	cCT	☐ yes	☐ no	
15. timing of prognostication		☐ <24 hrs	☐ >24-72 hrs	☐ >72 hrs

Fig. 1. Questionnaire used for telephone survey in all participating countries. ICU intensive care unit; TTM target temperature management; OHCA out-of-hospital cardiac arrest; IHCA in-hospital cardiac arrest; PCI percutaneous catheter intervention; VF ventricular fibrilation; VT ventricula tachycardia; CA cardiac arrest; SOP standard operating procedure; MAP mean arterial pressure; EEG electroencephalography; SEP somatosensory evoked potentials; NSE neuron specific enolase; cCT cerebral computer tomographie; hrs hours.

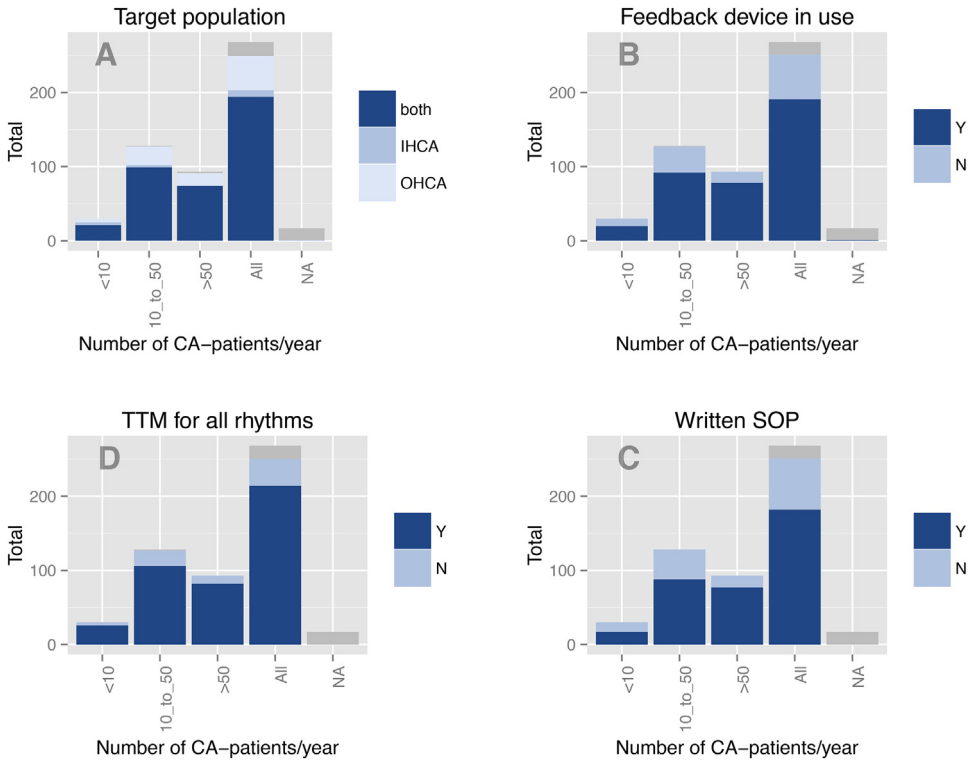

Fig. 2. (A) Target population concerning location of cardiac arrest (IHCA, in-hospital arrest; OHCA, out-of-hospital arrest) in all ICUs and separated by number of patients per year (B) Whether a computer feedback device was used or not (Y, yes, N, no) in all ICUs and separated by number of patients per year (C) Figure shows the answer to whether or not ICUs have a written SOP (standard operating procedure) for TTM (Y, yes; N, no) in all ICUs and separated by number of patients per year (D) Target temperature management towards all rhythms (shockable or not-shockable; Y, yes; N, no) in all ICUs and stratified by number of patients per year.

(ECA) with subsequent percutaneous coronary intervention (PCI) for initial shockable cardiac rhythm if the cause of arrest was most likely cardiac (missing data in 21 sites). In 40% of ICUs, patients with initial non-shockable rhythms also received ECA if the cause was likely cardiac. A target for mean arterial pressure (MAP), blood glucose levels, partial pressure of carbon dioxide (pCO_2) and oxygen (pO_2) was predefined in 59%, 66%, 56% and 51% of the ICUs, respectively (missing data in 18 sites). Invasive cardiac output monitoring was routinely used in 26% of the ICUs (Fig. 2).

Target temperature management

In 63% of the ICUs the target temperature was in the 32°–34 °C range, whereas 30% of the ICUs used 36 °C as their target temperature (missing data in 18 sites; see Fig. 3). 79% of the ICUs applied TTM for 24 h, 12% of ICUs cooled even longer and 2% shorter (missing data in 18 sites). In 72% of the ICUs, TTM was used for both in-and-out-of-hospital cardiac arrest and in 80% regardless of initial rhythm (in 7% no answer was given) (Fig. 2). A computer feedback cooling device was used by 76% (missing data in17 sites) and 77% performed a feedback controlled rewarming procedure (missing data in 18 sites).

Neurological prognostication

A written SOP for neurological prognostication was available in 50% of the ICUs (missing data in 18 sites). The timing varied with 2% of ICUs initiating prognostication after 24 h, 30% between 24 and 72 h and 60% at 72 h or later (missing data in 21 sites). Electroencephalography (EEG), cerebral computer tomography (CT), somatosensory evoked potentials (SSEPs) and neuron-specific enolase (NSE) were used in 71%, 60%, 53% and 46% of the ICUs, respectively (Fig. 4).

Treatment and number of annually treated patients

ICUs treating a large number of patients (over 50 patients per year) had significantly more often a written SOP implemented for post-cardiac-arrest management as well as a written standard protocol for neurological prognostication ($N = 93$, $p < 0.01$). In addition, the use of a computer feedback device for TTM was also significantly more often used in those ICUs treating a large number of patients ($p = 0.03$).

Discussion

Our results currently represent the largest survey describing the core of the post cardiac arrest treatment protocols in large European teaching and university hospitals. It was performed prior to the latest recommendations from ERC/ESICM in 2015, but 13–16 months after the publication of the TTM trial. The survey showed significant variations within the European countries, but the majority of the ICUs used a SOP for the general management and a target temperature of 32–34 °C. Noteworthy, only 50% had a SOP for prognostication [5].

Core data and baseline characteristics

Of the 268 ICUs asked to participate, a total of 94% completed the survey. We think the participation of dedicated and interested key opinion leaders in each country, contributed to this high rate.

A SOP can improve patient safety and quality of treatment in a variety of settings, and makes the treatment less physician and/or nurse-dependent [6,7,12]. A general pathway for clinical management and treatment and known pitfalls or side effects of the treatment should be highlighted in a SOP, with the possibility to apply individual treatment strategies when considered necessary. According to our results most, but not all, of the participating ICUs

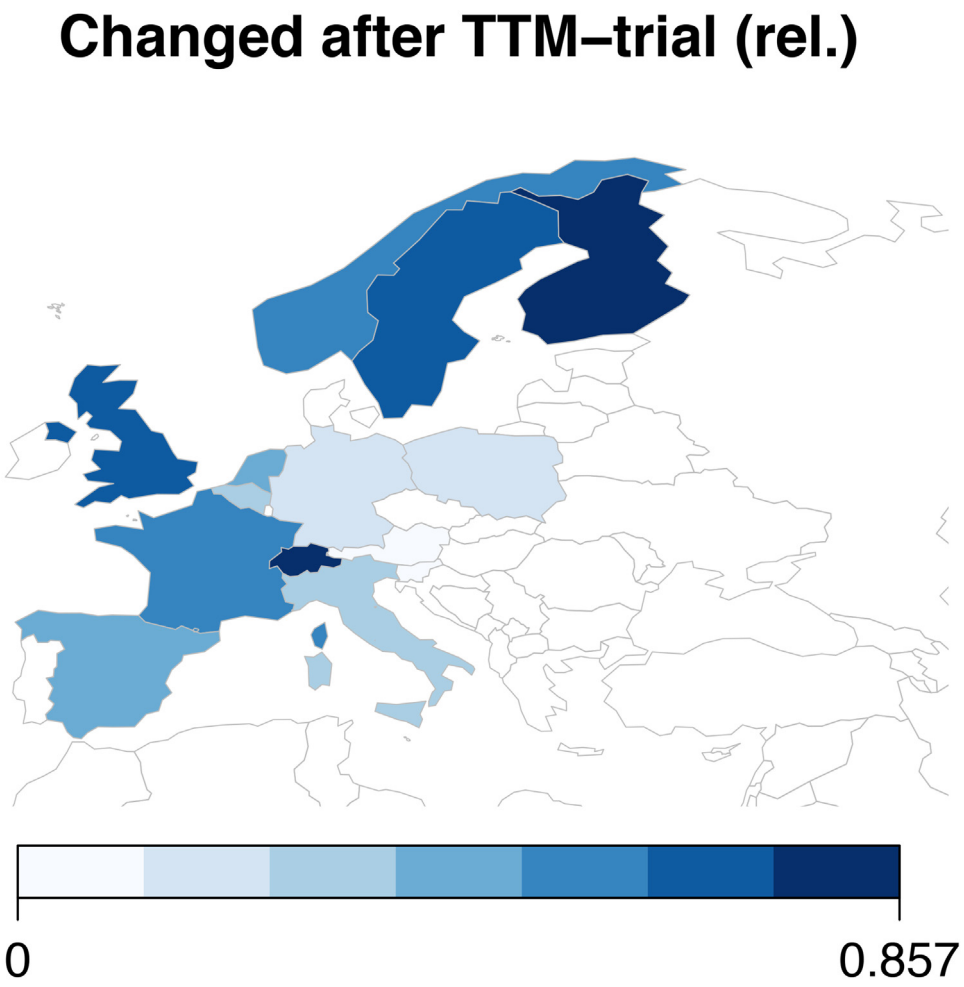

Fig. 3. Geographical plot for Europe with colored effect indicating the number of ICUs that have changed the local target temperature after the TTM-trial by Nielsen et al. to 36 °C in relative numbers compared to total answers. Darker colors reflect a higher rate of change from 0% to 100%. For example in Switzerland 6/7 ICUs have changed (86%) to 36°.

used a SOP, indicating further need for improvement. Importantly, the likelihood of having a SOP was significantly associated with the number of treated cardiac arrest patients per year.

In cardiac arrest patients with ST-elevation myocardial infarction, ECA with subsequent PCI was performed in the majority of sites. Whether immediate ECA is necessary in survivors after CA without ECG changes or in patients with non-shockable rhythms is still under debate [13,14]. Our data suggest that a minority of ICUs provide ECA with subsequent PCI in patients with non-shockable rhythms, and only when a cardiac arrest of cardiac cause is suspected. Several studies have indicated that many patients without ECG changes have significant culprit lesions as an underlying cause for their cardiac arrest requiring PCI [15]. Most recently, Staer-Jensen and colleagues demonstrated that the ECG is actually of limited value in predicting which patients had culprit lesions or not, and even in patients with initial asystole and PEA, half of the patients had coronary stenosis of more than 50% [16].

The question whether ECA vs. later coronary angiography among NSTEMI patients saves more lives, is currently being investigated in several large RCTs (TOMAHAWK trial Germany, NCT02750462 (ClinicalTrials.gov Identifier); DISCO trial Sweden, NCT02309151; COACT trial Netherlands, NTR 4973 (trialregister.nl); EMERGE trial France, NCT02876458; PEARL trial USA, NCT02387398).

Although ERC guidelines in 2010 also recommended normoxia (80–120 mmHg) and normocapnia (35–45 mmHg) during mechanical ventilation, a MAP within normal targets (65–80 mmHg) for ICU patients as well as avoiding hyper-and hypoglycemia, our data indicated that only a minority of ICUs had predefined targets for MAP, oxygenation and ventilation, however, the majority of ICUs had a predefined target of blood glucose [17]. Those predefined targets need to be interpreted with caution as the evidence is low due to lack of data in post-cardiac arrest care. Especially an intensive glucose management was shown to increase mortality in intensive care patients [18].

This might be improved by dissemination of best practice SOPs from ICUs using such targets and protocols.

Target temperature management

According to our survey results, collected 13–16 months after the TTM trial, but still at a time with the 2010 ERC guidelines recommendations of TTM to 32°–34 °C, the majority of European ICUs applied TTM to 32°–34 °C for 24 h. This was in general offered all comatose survivors irrespective of initial rhythm and location of arrest if active treatment was decided. Moreover, the rate of using a feedback device for TTM was high. Our results show a difference between countries concerning the current target temperature after cardiac arrest (Fig. 4). Especially the change to 36 °C as new target temperature showed a decline from north to south in Europe. A webmail based survey among 518 emergency physicians in France by Deye at al. revealed that 44% had changed to a target temperature of 36 °C one year after the publication of the TTM results [19]. Although results from both studies were collected before publica-

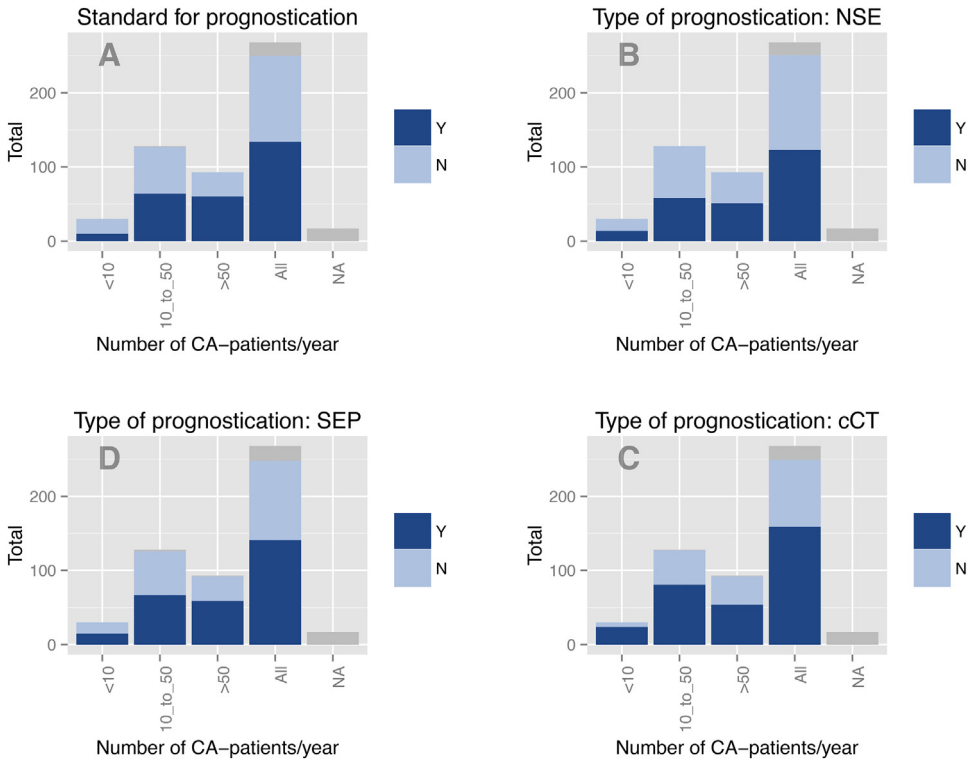

Fig. 4. (A) Written standard for neurological outcome prognostication (Y, yes; N, no) in all ICUs and separated by number of patients per year (B) Whether participants use NSE (neuron specific enolase) or not as biomarker in prognostication (Y, yes; N, no) in all ICUs and separated by number of patients per year (C) Whether participants use cCT (cerebral computer tomography) or not in prognostication (Y, yes; N, no) in all ICUs and separated by number of patients per year (D) Whether participants use SEP (somatosensory evoked potentials) or not in prognostication (Y, yes; N, no) in all ICUs and separated by number of patients per year.

tion of the new guidelines it is known that implementation of new therapies or guidelines in general takes time [20]. Another publication revealed an adoption rate of 25% of the target temperature of 36 °C after CA in the Netherlands 8 months after the TTM trial results were published [21].

The current guidelines recommend the use of a feedback controlled TTM device to maintain a constant target temperature, although there are no data to show that the use of such devices improves neurological outcome. But there is some evidence that if the temperature inadvertently rises over 37 °C, which could occur by cooling with simple ice packs, neurologic outcome of the patients might be affected [22].

Neurological prognostication

Prognostication after cardiac arrest has changed remarkably over the last years. Neurological prognostication should allow optimizing identification of those individuals that benefit from post cardiac arrest care and avoid premature withdrawal of life-sustaining treatment (WLST) which is a frequent cause of death in the ICU [23]. A multimodal approach including the use of biomarkers, SSEP, EEG and clinical examination should therefore be combined to enhance the reliability of prognostication. The current advisory ERC/ESICM statement on prognostication in comatose survivors after cardiac arrest strongly recommends a multimodal approach which should not be performed before 72 h after ROSC and after ensuring the clearance of sedation and elimination of other possible confounders [4,24]. A prolonged time of clinical monitoring and reassessment, at least 3–5 days, is recommended to determine any change in neurology. Despite these recommendations, only 50% of the ICUs have a formalized SOP for prognostication, giving EEG and brain CT the highest priority. Most ICUs (60%) perform testing after 72 h, but 30% evaluate the patient already between 24 and 72 h. As the optimal type of sedation is unknown so far in post cardiac arrest survivors very short acting drugs might add a benefit and will increase the reliability at the time of prognostication [25]. If a decision of WLST is made too early, we might loose survivors with the potential to recover as a relevant number will regain consciousness later than 72 h, especially if lower target temperatures were used [26].

Differentiation according to the number of patients treated in the ICU

Our data show that experienced ICUs with a large number of patients treated per year will more often provide a written SOP for TTM and prognostication. They are also more likely to have a computer feedback device compared with ICUs treating less than 50 patients per year. As we can provide no outcome data, this information needs to be interpreted with caution, but there is evidence that patients with Simplified Acute Physiologic Score II (SAPS II) between 20 and 60 selectively did benefit from being treated in high volume centers [27]. The impact on outcome of specialized cardiac arrest centers with high patient volumes requires further evaluation.

The general management of post cardiac arrest patients, however, consists of a bundle of several different steps. To enhance patient safety and generate a high degree of implementation and acceptance a formalized standard operating procedure (SOP) is indispensable. However, university and teaching hospitals should feel responsible to share best clinical practice and current knowledge by education and sharing of protocols. The ESICM recently started an online library calling for TTM protocols (http://www.esicm.org/research/TTMlibrary).

The current guidelines for post-resuscitation care also discuss the need for high-volume cardiac arrest centers, which may

improve the quality of treatment [28,29]. Such a strategy is similar to that of established stroke or trauma centers and needs to be further discussed in the years to come [27].

Conclusions

This international European telephone survey revealed a high rate of implementation of TTM in post cardiac arrest patients in university and teaching hospitals. Most ICUs also had a SOP for the treatment of post-cardiac arrest patients but only a minority used a SOP for neurological prognostication.

Limitations

The selection of participants by the national investigators is a possible confounder. A large number of ICUs were included, however, and very few declined participation.

Our survey was conducted after the publication of the TTM trial but before the latest guideline update by ERC and ESICM in October 2015 emphasizing a target temperature range between 32°–36°. At the time of our survey the guidelines thus recommended a target temperature of 32–34°, and it is possible that more centers have changed to a target temperature of 36° following the latest changes in ERC/ESICM guidelines.

Ethics approval and consent to participate

No experimental, patient or personal data were recorded or analyzed. This was a survey among intensive care physicians without need for ethical approval by the local ethics committees.

Funding

No funding.

Authors' contributions

All listed authors were national investigators. CS, JN, AK and MF drafted the protocol, analyzed the data and were major contributors in writing of the manuscript. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Acknowledgments

We would like to thank Dr. rer. nat. Cord Spreckelsen, Department of Biostatistics University Aachen, RWTH Aachen, Germany for statistical consultancy, calculation and preparation of figures. We also would like to thank all local national sub-investigators being of assistance to the national principle investigator and thank you very much to all participants of this survey.

References

[1]. The Hypothermia After Cardiac Arrest Study G. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med 2002;346:549–56.
[2]. Hachimi-Idrissi S, Corne L, Ebinger G, Michotte Y, Huyghens L. Mild hypothermia induced by a helmet device: a clinical feasibility study. Resuscitation 2001;51:275–81.
[3]. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557–63.
[4]. Nolan JP, Soar J, Cariou A, Cronberg T, Moulaert VR, Deakin C, et al. European Resuscitation Council Guidelines for Resuscitation: Section 5. Post resuscitation care. Resuscitation 2015;95:202–22.
[5]. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, et al. Targeted temperature management at 33 °C versus 36 °C after cardiac arrest. N Engl J Med 2013;369:2197–206.
[6]. Sunde K, Pytte M, Jacobsen D, Mangschau A, Jensen LP, Smedsrud C, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. Resuscitation 2007;73:29–39.
[7]. Walters EL, Morawski K, Dorotta I, Ramsingh D, Lumen K, Bland D, et al. Implementation of a post-cardiac arrest care bundle including therapeutic hypothermia and hemodynamic optimization in comatose patients with return of spontaneous circulation after out-of-hospital cardiac arrest: a feasibility study. Shock 2011;35:360–6.
[8]. Gasparetto N, Scarpa D, Rossi S, Persona P, Martano L, Bianchin A, et al. Therapeutic hypothermia in Italian Intensive Care Units after 2010 resuscitation guidelines: still a lot to do. Resuscitation 2014;85:376–80.
[9]. Storm C, Meyer T, Schroeder T, Wutzler A, Jorres A, Leithner C. Use of target temperature management after cardiac arrest in Germany – a nationwide survey including 951 intensive care units. Resuscitation 2014;85:1012–7.
[10]. Orban JC, Cattet F, Lefrant JY, Leone M, Jaber S, Constantin JM, et al. The practice of therapeutic hypothermia after cardiac arrest in France: a national survey. PloS one 2012;7:e45284.
[11]. Nielsen N, Wetterslev J, Friberg H, Group TTMTS. Targeted temperature management after cardiac arrest. N Engl J Med 2014;370:1360.
[12]. Puskarich MA, Marchick MR, Kline JA, Steuerwald MT, Jones AE. One year mortality of patients treated with an emergency department based early goal directed therapy protocol for severe sepsis and septic shock: a before and after study. Crit Care 2009;13:R167.
[13]. Dankiewicz J, Nielsen N, Annborn M, Cronberg T, Erlinge D, Gasche Y, et al. Survival in patients without acute ST elevation after cardiac arrest and association with early coronary angiography: a post hoc analysis from the TTM trial. Intens Care Med 2015;41:856–64.
[14]. Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. Circ Cardiovasc Intervent 2010;3:200–7.
[15]. Camuglia AC, Randhawa VK, Lavi S, Walters DL. Cardiac catheterization is associated with superior outcomes for survivors of out of hospital cardiac arrest: review and meta-analysis. Resuscitation 2014;85:1533–40.
[16]. Staer-Jensen H, Nakstad ER, Fossum E, Mangschau A, Eritsland J, Draegni T, et al. Post-resuscitation ECG for selection of patients for immediate coronary angiography in out-of-hospital cardiac arrest. Circ Cardiovasc Intervent 2015;8.
[17]. Nolan JP, Soar J, Zideman DA, Biarent D, Bossaert LL, Deakin C, et al. European resuscitation council guidelines for resuscitation 2010 section 1. Executive summary. Resuscitation 2010;81:1219–76.
[18]. Investigators N-SS, Finfer S, Chittock DR, Su SY, Blair D, Foster D, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med 2009;360:1283–97.
[19]. Deye N, Vincent F, Michel P, Ehrmann S, da Silva D, Piagnerelli M, et al. Changes in cardiac arrest patients' temperature management after the 2013 TTM trial: results from an international survey. Ann Intens Care 2016;6:4.
[20]. Berdowski J, Schmohl A, Tijssen JG, Koster RW. ime needed for a regional emergency medical system to implement resuscitation Guidelines 2005–The Netherlands experience. Resuscitation 2009;80:1336–41.
[21]. Wils EJ, van den Berg T, van Bommel J. Current practice of target temperature management post-cardiac arrest in The Netherlands, a post-TTM trial survey. Resuscitation 2015;97:e1–2.
[22]. Bray JBJ, Stub D, Segan L, Mitra B, Smith K, Finn J, et al. Impact of change to target temperature management on post-arrest care for out-of hospital cardiac arrest patients. Resuscitation 2015;96(1):37.
[23]. Dragancea I, Rundgren M, Englund E, Friberg H, Cronberg T. The influence of induced hypothermia and delayed prognostication on the mode of death after cardiac arrest. Resuscitation 2013;84:337–42.
[24]. Sandroni C, Cariou A, Cavallaro F, Cronberg T, Friberg H, Hoedemaekers C, et al. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. Resuscitation 2014;177:9–89.
[25]. Krannich A, Leithner C, Engels M, Nee J, Petzinka V, Schroder T, et al. Isoflurane sedation on the ICU in cardiac arrest patients treated with targeted temperature management: an observational propensity-matched study. Crit Care Med 2017;45(Apr (4)):e384–90.
[26]. Ponz I, Lopez-de-Sa E, Armada E, Caro J, Blazquez Z, Rosillo S, et al. Influence of the temperature on the moment of awakening in patients treated with therapeutic hypothermia after cardiac arrest. Resuscitation 2016;103:32–6.
[27]. Schober A, Holzer M, Hochrieser H, Posch M, Schmutz R, Metnitz P. Effect of intensive care after cardiac arrest on patient outcome: a database analysis. Crit Care 2014;18:R84.
[28]. Callaway CW, Schmicker R, Kampmeyer M, Powell J, Rea TD, Daya MR, et al. Receiving hospital characteristics associated with survival after out-of-hospital cardiac arrest. Resuscitation 2010;81:524–9.
[29]. Soholm H, Wachtell K, Nielsen SL, Bro-Jeppesen J, Pedersen F, Wanscher M, et al. Tertiary centres have improved survival compared to other hospitals in the Copenhagen area after out-of-hospital cardiac arrest. Resuscitation 2013;84:162–7.