Clinical paper

Therapeutic hypothermia in Italian Intensive Care Units after 2010 resuscitation guidelines: Still a lot to do

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A B S T R A C T

Background: Therapeutic hypothermia (TH) is one of three interventions that have demonstrated to improve patients’ neurological outcome after cardiac arrest. The aim of this study was to investigate the effect of the 2010 resuscitation guidelines on TH implementation in various Italian Intensive Care Units (ICU).

Methods: A structured questionnaire was submitted to Italian ICU. The questionnaire was addressed to determine the procedures of TH in each ICU or, on the contrary, the reason for not employing the therapy.

Results: We obtained complete information from 770 of 847 Italian ICU (91%). Out of 405 Units included in the analysis only 223 (55.1%) reported to use TH in comatose patients after return of spontaneous circulation. The trend of TH implementation shows a stable increase, particularly after 2006 but there is no evident acceleration after the strong indication of the 2010 guidelines. There was a rise of about 3.4 times in the number of Italian ICU using TH as compared to the 2007 survey (an increase of 68% per year). One hundred and eighty-two (44.9%) units did not use TH mainly because of lack of equipment, economic issues or the conviction of the difficulty of execution.

Conclusions: TH is still under-used in Italy (55.1%) even though the therapy is strongly recommended in the 2010 guidelines. However, the increase in the adoption of hypothermia has been significant in the past 5 years (68%/years) and the awareness of the efficacy is almost consolidated among intensivists, being logistic problems the leading cause for non-adoption.

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1. Introduction

The incidence of out-of-hospital cardiac arrest (CA) in Italy ranges between 95 and 87/100,000/year1–2 and coronary artery disease is the leading cause. For the patients who survive to hospital discharge, about 30% develops post-anoxia neurological damage with different degrees of disability.3 Therapeutic hypothermia (TH) developed after 2 trials published in 2002, which showed that the reduction of body temperature to 32–34°C for 12–24 h after out-of-hospital ventricular fibrillation significantly improve neurological outcome and, in one of these, long-term survival as well.4,5 The experience and research in the last decades have elucidated that hypothermia holds significant promise for improving outcome in patients suffering from any type of post-ischemic reperfusion injury such ischemic stroke, perinatal asphyxia encephalopathy and myocardial infarction.6,7

Despite a heterogeneous but satisfactory level of implementation in most part of Europe8–11 an Italian survey performed in 2007 showed poor adoption of TH: only 16% of Intensive Care Units (ICU) had used TH after CA.12

The 2010 resuscitation guidelines stress the primary role of TH in the setting of post CA care, placing it in the first class of recommendation for out-of-hospital CA secondary to initial ventricular fibrillation.13,14 On the basis of current evidence, TH should be considered as the standard of care in post CA patients regardless of the initial rhythm or location.15

To evaluate the endorsement of TH in clinical practice after the new resuscitation guidelines, we conducted a survey in Italian
ICU. This survey was addressed to determine how many units use hypothermia for post CA care and for other indications, the procedures of TH induction, maintenance and rewarming, and the reasons for non-supporting it. We wanted also elucidate the impact of resuscitation guidelines in the adoption of TH in the years.

2. Methods

All ICU with entries in the 2012 list of the GiViTI (“Italian Group for the evaluation of Intensive Care Units”) (n = 424) and all Italian Intensive Cardiac Care Units (ICU) with entries in the website list of the ANMCO (“National Association of Hospital Cardiologists”) (n = 423), were contacted between February and July 2012. A presentation letter with a questionnaire was sent by e-mail to the GiViTI network participants. The ICU that had not responded and all ICU were contacted by telephone up to 4 times to increase the rate of responses. In this case, the consultant on-call for the unit that day was asked to participate voluntarily in the survey.

We considered ineligible the ICU located in hospital without Emergency Department, all the ICU unable to manage intubated patients or without patients potentially treated with TH.

Questionnaire gathered information on the hospital characteristics (university hospital or not), the number of ICU beds and the type of ICU (Cardiac or Cardiosurgery Units, Neurosurgery Units, Pediatric Units, Postoperative Units or general ICU). Those which used TH after CA were asked to define the application fields of hypothermia, the mean number of patients treated per year, the underlying rhythm of CA, the place where TH started. Data regarding induction, maintenance and the rewarming phase characteristics (target temperature, timing, and equipment) were also obtained. The ICU contacted by phone, which did not use TH, were asked to justify the reason for not implementing TH by filling in a multiple-choice section.

Quantitative and qualitative data are expressed in mean value with standard deviation (SD) and in frequency with percentage (%) respectively. Data were analyzed using a spreadsheet application (Excel, Microsoft, Redmond, Washington, USA). Data on the year in which cooling was started in each ICU were used for determine the yearly increase in TH adoption.

Ethical approval was not deemed necessary given the lack of any patient identifiers or clinical intervention in this study.

3. Results

Out of the 847 ICU contacted, complete data were obtained from 770 Units (91%). Of these Units, 365 ICU were deemed ineligible according to the methods of the study design (Fig. 1). Among the 405 eligible Units: 298 (73.6%) were general ICU, 39 (9.6%) ICU, 20 (4.9%) Cardiosurgery Units, 18 (4.4%) Neurosurgery Units, 13 (3.2%) Pediatric Units, and 17 (4.2%) Postoperative Units.

The total number of beds of the 405 eligible ICU was 3280 and the mean number was 8 ± 3.6 beds/ICU. Eighty-three ICU (20.5%) belonged to University or affiliated hospitals.

Two hundred and twenty-three (55.1%) eligible ICU have implemented TH following CA, 35 used TH in intracranial hypertension (22.9% Neurosurgery Units) and 4 in perinatal asphyxia (75% Pediatric Units). Other fields of TH application were traumatic brain injuries (5 Units), status epilepticus (2 Units), cardiogenic shock (2 Units), ischemic stroke (2 Units) and aortic aneurysm rupture (1 Unit). Only one ICU (Pediatric ICU) adopted TH for perinatal asphyxia and not for CA and it was excluded from the analysis.

We estimated that more than 7800 post CA patients had already been treated with TH in Italy (Fig. 2). Fig. 3 shows different adoption of TH among Italian regions. The ICU of the northern regions have implemented TH more than those of the southern regions.
The type of ICU that use TH, and the execution modality of this procedure are summarized in Table 1. Most of these units are general ICU (179, 80.3%), while the remaining are ICU (12, 5.4%) or other types of specialist ICU (32, 14.3%).

For out-of-hospital CA, 39 (17.5%) institutions induce hypothermia in the pre-hospital phase by Emergency Medical Service, 57 (25.6%) induce hypothermia in the Emergency Department and 127 (56.9%) induce hypothermia only after the arrival of the patient on ICU.

Out of the 223 ICU currently performing TH for CA, most of them (185, 83%) use it both for non-shockable and shockable rhythms, regardless an in-hospital or out-of-hospital CA. Among remaining ICU, 36 (16.1%) use TH only for shockable rhythms (in two case for only out-of-hospital ventricular fibrillation/ventricular tachycardia CA) and 2 (0.9%) consider it only for non-shockable rhythms (one of this cooled only patients with in-hospital CA due to non-shockable rhythms).

Most responders use a target temperature between 32 and 34 °C (203/223 Units; 91%), while a maintenance temperature between 34 and 35 °C is chosen by a small proportion (20/223 Units; 9%). The ICU that choose 24 h as maintenance phase are 188 (84.3%), 18 (8.1%) ICU choose less than 24 h and 17 (7.6%) more than 24 h. At the end of maintenance phase, 67 (30%) units rewarmed passively while 156 (70%) rewarmed at a controlled rate in 13 ± 9.6 h (rate of 0.41 ± 0.28 °C/h).

The methods use to induce, maintain and rewarmed are very different as well as the methods use to check the body temperature (Table 1).

Table 1

| Details of 223 Units that use therapeutic hypothermia after cardiac arrest and characteristics of hypothermic procedure. Values are number (proportion) or mean ± SD. |
| Type of ICU | General | 179 (80.3%) | Cardiac ICU | 12 (5.4%) | Other specialist ICU (Neurosurgery ICU, Cardiosurgery ICU, Pediatric ICU, Postoperative ICU) | 32 (14.3%) |
| Years from TH adoption | 3.6 ± 2.5 | Number of patients/year treated with TH | 9.2 ± 7.4 |
| Place of induction | Out-of-hospital | 39 (17.5%) | Emergency Department | 57 (25.6%) | ICU | 127 (56.9%) |
| Cardiac arrest rhythms | Shockable rhythms only | 36 (16.1%) | Non-shockable rhythms only | 2 (0.9%) | Both shockable and non-shockable rhythms | 185 (83%) |
| Target temperature | 32–34 °C | 203 (91%) | 34–35 °C | 20 (9%) |
| Duration of maintenance phase | 12–23 h | 18 (8.1%) | 24 h | 188 (84.3%) | 25–36 h | 9 (4%) | >37 h | 8 (3.6%) |
| Rewarming | Passive (uncontrolled) | 67 (30%) | Controlled rate | 156 (70%) | Rate (°C/h) | 0.41 ± 0.28 |
| Methods of cooling | Induction with cold fluids | 165 (74%) | Dedicated surface cooling | 137 (61.4%) | Intravascular cooling device | 31 (13.9%) |
| | Non-specific cooling methods | 55 (24.7%) |
| Temperature measurement (more answers possible) | Rectum | 32 (14.3%) | Bladder | 125 (56.1%) | Axillary | 12 (5.4%) |
| | Tympanum | 15 (6.7%) | Esophagus | 94 (42.1%) | Intravascular | 25 (11.2%) |

TH, therapeutic hypothermia; ICU, Intensive Care Unit; SD, standard deviation.

4. Discussion

This survey shows that TH in Italian ICU, after the strong indication of the 2010 resuscitation guidelines, is however under-used. With this study we obtained information from a significant number of Italian ICU (91%) and we may consider the results as representative for the clinical practice in the field of post CA care in Italy. Moreover, this is the second complete survey concerning TH in Italy and the first after the new resuscitation guidelines.

The main conclusion is that up to 45% of ICU do not use this therapy routinely after resuscitation for CA despite the class I recommendation.

The Italian result (55.1% of TH adoption) is far from Scandinavian, Dutch18 and UK2 practice where the rate of the adoption of TH in ICU is over 80%. Our results are more consistent with studies from other parts of Europe, including Poland where at the end of 2010 only 21.7% of ICU were using TH after CA.15

The trend of TH implementation over the past 10 years in Italy is shown in Fig. 2. There has been a rise of about 3.4 times in the number of ICU using TH as compared to the 2007 survey (68% more per year) with a rate similar to other European countries (e.g. UK 75%, Poland 56%). Although there is a significant delay, there has been a continuous progression in TH use particularly after 2006 (1 year after the 2005 guidelines for CPR), but there is no significant variation after the strong indication of the 2010 resuscitation guidelines.

One hundred and twenty-tree ICU that have never performed TH after CA have provided reasons for this. Fortunately, it does not appear that critical care clinicians are failing to keep up with clinical developments because the main reasons for non-adoption are logistic problems and economic burden. This situation is in contrast with the evidence of the last Italian survey (2007),12 in which the main reason for not cooling was the perceived lack of evidence or consensus. We can say that critical care physicians have understood the effectiveness of TH. On the other hand, they are not aware of the simplicity and the possibility to perform this therapy with low-cost.1,14 In fact, more than 36% of ICU rarely treat patients after CA and they said that cost-effectiveness does not justify the introduction in their clinical practice. This perception may be modifiable and the experience of the other ICU must be a guide to change this conviction, since it is well known that TH is low-cost and easy to do.

TH is used for both shockable and non-shockable rhythms in the majority of Italian ICU (83%), even though the guidelines give a higher level of indication for the first one. However, this is in agreement with the evidences reported by literature, that the outcome of the patient does not differ from these two groups of patients.19

This characteristic was already present in the previous Italian survey and reflects the fact that physicians, who use TH, are up-to-date and they do not simply follow the strong indications of the guidelines. This is also confirmed by the use of TH both for in-hospital and out-of-hospital CA. In our opinion, the main concept is that TH is beneficial for the brain regardless of the first rhythm to the monitor and the location of CA, considering the low cost and the low risk of this therapy.
Regarding time to cooling several animal studies suggest that the effectiveness of mild TH could be improved if initiated as soon as possible\(^2\) also during CPR.\(^3\) This benefit seems similar for humans,\(^4\) even if an Australian trial by Bernard et al.\(^5\) was not able to demonstrate an improvement of neurological outcome at discharge compared with cooling commenced in the hospital. This trial shows a modest reduction of patients’ body temperature and the loss of the initial result in the first phase of the admission in the Emergency Department. However some studies show that prehospital cooling seems to be safe and feasible.\(^4\)-\(^6\) In our survey most hospitals (56.9\%) initiated TH in the ICU while a minority started TH in the Emergency Department or in the pre-hospital setting (25.6\% and 17.5\%, respectively).

Italian ICU generally respects the target temperature (32–34 °C) and duration of cooling (12–24 h), as recommended by ILCOR. These ranges simply derive from the set level in the first two trials in 2002 and they are accepted all over the world in the field of post CA care. However, a recent Spanish trial has compared 2 levels of target temperature (32 vs 34 °C) demonstrating how a lower cooling level may be associated with a better outcome in patients after ventricular fibrillation CA.\(^6\) Some ICU claimed to cool patients between 34 and 35 °C (9\%) and others for a period of less than 12 h or more than 24 h (7.6\% cumulative percentage).

The rapid infusion of cold fluids is a well-known method to induce TH in Italian ICU (74\%). This is a recognized method to achieve a significant and rapid reduction in patient’s body temperature without the risk of pulmonary oedema\(^7\) but with a favorable impact on circulatory stability.

Although the maintenance phase of TH can be performed without specific machines, most of ICU are provided with cooling methods in particular with non-invasive ones, being used by 137 (61.4\%) units. This is an evolution from the analysis by Bianchin et al.\(^8\) in 2007 when the “home made” methods (e.g. ice packs, wet towels, gastric lavage) were the most used. However, the most important thing is to perform TH, not the method applied, as demonstrated by the literature.\(^9\) Ice or wet towels are the cheapest methods but the control of temperature during maintenance phase and rewarming is difficult to manage because of the absence of an automatic control of temperature. Surface cooling techniques are easy to use as well low cost but the presence of thermal inertia decreases the rate of cooling and temperature variations, while endovascular techniques are invasive but provide better temperature management as well as a more favorable complication profile.\(^9\)

After maintenance phase the patient should be rewarmed slowly (0.2–0.5 °C per hour) using a passive or active method. Most of ICU (70.3\%) use rewarming at controlled rate with the use of the same device that was used for cooling with an average rate of 0.4 °C per hour, while the others use passive uncontrolled rewarming. It is important to avoid the negative consequences of rapid rewar- ming and hyperthermia following a period of hypothermia for any type of neurological damage. If the patient’s temperature exceeded 37 °C within 48 h from CA it is associated with a worse outcome.\(^10\)

We are convinced that, as for time to intervention for myocardial infarction, TH will need many years to become a standard practice and it is important to extend the experience at all ICU in particular for southern regions of Italy, making it clear that TH is a successful therapy, easy to do, also without any specific machines or knowledge needed. The challenge is to increase the rate of TH adoption among ICU, and inform them that the failure to adopt TH is an important medical liability as well as not performing CPR of defibrillation for a CA due to ventricular fibrillation. We underline the need for educational program targeted to several specialists and nurses involved in the treatment of post CA patients, to create “a chain of cold” from Emergency Service to ICU through the Emergency Department.

5. Conclusion

TH after CA is used only slightly more than a half of Italian ICU despite a strong recommendation from the last resuscitation guidelines. In the past 5 years the increase of TH adoption by Italian ICU has been about 68% per years, a value quite similar to previous survey from other centers. The awareness of the importance of TH treatment for patients after CA is well established among physicians but logistic and economical problems are now the main reasons for non-adoption.

We are convinced that an educational program on a large scale could be the way to overcome the “fear” to start this simple but highly effective therapy.

Conflicts of interest statement

None.

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References