Australian Critical Care 38 (2025) 101264

Contents lists available at ScienceDirect

Australian Critical Care

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

Review paper

Targeted temperature management to minimise secondary brain injury after cardiac arrest: A systematic review

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ARTICLE INFORMATION

Article history:
Received 9 December 2024
Received in revised form
12 May 2025
Accepted 13 May 2025

Keywords:
Neuroprotection
Nursing care
Post–cardiac arrest syndrome
[Secondary] brain injury
Targeted temperature management

ABSTRACT

Background: A patient recovering from an in-hospital or out-of-hospital cardiac arrest (CA) requires interventions for recovery, particularly for minimising secondary brain injury. Targeted temperature management (TTM) is the intervention with the greatest impact on neurological recovery.
Aim: The aim of this systematic review was to describe current TTM in adult CA patients and its impact on functional outcomes.
Methods: This systematic review was developed between March and May 2024 according to the Joanna Briggs Institute guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for reporting. Eligibility criteria were established. We systematically reviewed studies enrolling adult CA patients who received TTM and reported functional outcomes. The search strategy was applied in the following databases: Medline and CINAHL Ultimate, the Cochrane Central Register of Controlled Trials, through EBSCO, and Scopus. The Rayyan software was used for the final extraction and selection.
Results: The studies retrieved highlight the following interventions for neuroprotection: the use of a continuous temperature feedback system (continuous temperature monitoring with vesical, oesophageal, or parenthetic probes) for temperature induction; conducting a preinduction time between 390 min (6.5 h) and 12 h and an induction time greater than 440 min (7.3 h); setting the target temperature between 32 °C and 37.5 °C according to the patient's characteristics for a maintenance period between 24 and 48 h; the administration of sedatives, antipyretics, and neuromuscular blockers; and the assessment of neurological prognosis only after the rewarming phase, using scales such as the Cerebral Performance Category and the Modified Rankin Score.
Conclusions: Continuous research and investment in this area of knowledge are highly encouraged, particularly in terms of refining accurate neurological prognostic tools and assessment scales.
Registration: PROSPERO Registration ID: CRD42024588646.

1. Introduction

Cardiac arrest (CA) is the abrupt and unexpected cessation of cardiac, respiratory, and consciousness functions. It usually results from an electrical problem in the heart in adults, which interrupts its ability to pump blood effectively. This condition is a medical emergency that, if not treated immediately with cardiopulmonary resuscitation (CPR) and eventually defibrillation measures, can lead to death within minutes.[1] Resuscitation can occur in both intra-hospital and extrahospital settings, requiring advanced teams equipped with skills to address these emergent CA situations[2] and to act in the post-CA period to prevent secondary brain injury.[1–3]

Data from the United States, Europe, Asia, and Australasia show that the annual incidence of CAs treated by emergency medical services ranges from 30 to 100 per 100 000 people.[4]

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https://doi.org/10.1016/j.aucc.2025.101264

According to the CARES 2023 Annual Report,[5] the survival rate up to hospital admission was 26.1%, and the rate of survival until hospital discharge was 10.2%.[5] As the heart is more tolerant of ischaemia than the brain, even where the initial 76% resuscitation efforts are successful, up to 70% of patients die from the effects of post-CA brain injury, and of those who survive to hospital discharge, 19% have moderate to severe neurological impairments, preventing return to work and activities of daily living.[6,7] Another study refers that one in three patients admitted to intensive care will survive, many of whom will need intensive, tailored rehabilitation after discharge to have the best outcomes.[7] Thus, it is crucial to prevent secondary brain injury by optimising neurological recovery to restore brain function to pre-CA levels.[8,9]

Secondary brain injury refers to brain damage that occurs after the primary injury, such as trauma, ischaemia, or haemorrhage. This additional injury is often caused by a series of biochemical and physiological processes triggered by the initial event. Factors contributing to secondary brain injury include cerebral oedema, increased intracranial pressure, hypoxia, ischaemia, metabolic changes, inflammation, and excitotoxicity. It can significantly worsen the patient's prognosis and increase the extent of neurological damage.[10] After the return of spontaneous circulation (ROSC), secondary brain injury can be minimised by optimising the neurological recovery of the individuals; aiming to restore brain function to the level before CA is crucial.[7] To support this crucial goal, targeted temperature management (TTM) should be initiated as soon as possible[1] to prevent coma, anoxic-ischaemic encephalopathy, or multiple organ failure.[11] This process requires close monitoring and surveillance by the by the multidisciplinary team, which includes nurses to identify signs and symptoms that demand intervention.[12] To achieve this, nurses must rely on the latest scientific evidence, enabling them to accurately interpret their assessments.[12]

Current guidelines strongly recommend the use of TTM for patients who experience in-hospital CA. However, there is a need for greater clarity on the benefits and specificities of the treatment associated with TTM[13,14] (e.g., how assessments should be performed), which justifies the need to find more evidence in this field, with a systematic review (SR).[13] The issue was then contextualised according to the needs identified in clinical practice too.[15] Thus, considering the most recently available evidence published from 2019, this SR aimed to describe current TTM practice and the reported functional outcomes of patients (e.g., neuroprotection). This date was defined with the purpose of getting the most recent evidence that may not have been considered in the latest existing guidelines in 2020 from the American Heart Association (AHA)[16] and which could be the basis for the new 2025 guidelines. We intend to obtain results that could support the subsequent guidelines in this area, which will be published in 2025.

2. Methods

This SR was conducted between March and May 2024, in accordance with the Joanna Briggs Institute (JBI)[15] and, for reporting this type of study, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines.[17]

Firstly, the topic of the SR was defined based on an identified gap in the existing literature that required further study.[15] We systematically reviewed studies enrolling adult CA patients who received TTM and reported functional outcomes. To address this, an initial search was conducted in Medline and CINAHL Ultimate, Cochrane Database of Systematic Reviews, and PROSPERO databases, to know if similar SRs were available from 2019 and no existing SR on the subject was found with this complete vision of how to do this intervention and how effective it is, to improve neuroprotection.

Subsequently, the research question was formulated using the PI[C]O mnemonic:[15] What temperature management interventions are effective (I) in minimising secondary brain injury (O) in patients after CA (P)?

To answer the research question, the following eligibility criteria were defined. Following were the inclusion criteria: (i) studies considering adults after CA[2,18] and involving individuals who had both out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA); (ii) studies related to TTM as an intervention,[1] which include continuous monitoring measures only available in hospital settings;[13] (iii) studies with secondary brain injury reduction (Cerebral Performance Category 1 or 2) as an outcome[7]; (iv) studies published from 2019 onwards were included due the most recent guidelines on TTM date back to 2020[16] to ensure our review includes recent articles, including those that may not have been considered in the 2020 guidelines;[13] (v) primary studies[19] with quantitative designs (e.g., experimental studies and cohort studies);[19] and (vi) all articles written in different languages understood by the authors (e.g., English, Spanish, Portuguese, French, and Italian) were included. Following were the exclusion criteria: (i) paediatric population (aged under 18 yrs) which has usually another specificity (e.g., cause of CA [hypoxia][20]); (ii) studies not focussed in TTM as an intervention; (iii) studies focussed in other outcomes (e.g., mortality); (iv) studies before 2019; (v) studies with qualitative design, secondary research, conference papers, and discussion papers, according to JBI methodology;[19] and (vi) articles in other languages. We excluded grey literature, clinical trial registries, and conference abstracts to maintain a focus on peer-reviewed studies with rigorous methodological standards. Grey literature and unpublished trials often lack standardised peer review, which can impact the reliability of findings. Likewise, conference abstracts were omitted due to their limited methodological details, making it challenging to assess study quality and replicability.[21]

Subsequently, searches in databases were conducted between March 2024 and May 2024, for studies published between 2019 and 2024, in the Medline and CINAHL Ultimate databases, the Cochrane Central Register of Controlled Trials, trough EBSCO, and Scopus, using search terms related to the population, intervention, and outcome, which were adapted for each database. This review integrates search terms from previous reviews, thus broadening the results. Additionally, we have expanded our search to include trial registries and two were found[22] (ID: jRCT1062220035 and ACTRN12623001057673). However, we did not have access to the data.

The search strategy was developed through an iterative process to ensure the comprehensive identification of relevant studies. Initially, key concepts related to the research question were identified using natural language. Keywords and synonyms were then refined by analysing terms used in relevant SRs, primary studies, and indexed database thesaurus. The indexed terms or keywords were combined using the Boolean operators “AND” and “OR”, adapting each term for the specific databases mentioned (see complete search strategy in Supplementary File 1). The search strategy was reviewed by HRH to ensure its comprehensiveness and methodological rigour. The review followed established guidelines, including the Peer Review of Electronic Search Strategies checklist,[23] which assesses key aspects such as the appropriateness of search terms, Boolean operators, truncation, and database selection. Based on this review, necessary refinements were made before finalising the search to enhance the accuracy and reliability of the retrieved studies.

For extraction and selection, Rayyan software was used[24] in blind-on mode to allow the selection of the final results, independently, by each researcher. Titles and abstracts retrieved from the

database searches were screened independently by two reviewers (JS and MO) based on predefined inclusion and exclusion criteria.

Any discrepancies during this process were resolved through discussion among the three researchers (MM), with input from a fourth author to reach consensus (JFT).

Full-text articles were assessed for eligibility by two independent reviewers following the same process as the title and abstract screening. Data from the included studies were extracted by three reviewers (JS, MO, and MM) using a standardised data extraction form. The form was piloted on a subset of studies to ensure consistency. Any discrepancies were resolved by discussion or consultation with a fourth reviewer (JFT).

All authors contributed to the final decision. The whole process is described in the PRISMA flow diagram. First, duplicates were excluded, followed by the exclusion of the articles due to the wrong study design and date. The subsequent phases included applying the population, intervention, and outcome eligibility criteria. The first exclusion was done by reading the title and abstract, and the final phase was done by reading the full text. This SR was registered in the PROSPERO (CRD42024588646).

The data extracted from each article were fully presented in a tabular format that includes title, author/year, country, study type, aim, population/sample, interventions, indicators, results, conclusions, and implications for future research. Another table was presented with quantitative data (intervention, sample size, temperature, and mean outcome for control group and intervention group). To evaluate the methodological quality of each final study, the critical appraisal tools from the JBI were used.[15] According to each type of study, the corresponding tool for quality assessment was applied. The level of evidence was determined also according to the JBI.[25]

In this SR, a meta-analysis was initially planned, according to Grove and Gray,[26] to conclude the overall effects across the included studies,[27] specifically to determine whether TTM significantly improves neurological outcomes or has minimal or no effect. Since most of the necessary criteria for conducting a meta-analysis were not met, it was decided not to proceed with it.

3. Results

A total of 4795 initial articles were identified from the databases. Following the previously defined eligibility criteria, the selection process was carried out independently by three researchers, supported by Rayyan software.[24] After removing duplicates and abstract screening, 27 studies were reviewed in full text. Of these, nine studies met the inclusion criteria and were included in the SR. The PRISMA flow diagram in Fig. 1 illustrates this process and shows the results of the search and the reason why studies were excluded.

This process yielded eight to nine articles for analysis (Tables 1 and 2). Each article underwent an assessment of methodological quality (Table 3) and level of evidence (Table 2)[15,25] which are presented in a tabular format. Then, the most relevant information from each study was extracted and organised in a spreadsheet (Tables 1 and 2) to systematically present the data, facilitating the interpretation and analysis of the results and guiding the discussion.

3.1. Characteristics of the included studies

We identified variability in TTM in the included studies. The data obtained from the final articles are organised chronologically in Table 2. The number of participants ranged from 22 to 597. In terms of study designs, there were two (n = 2) randomised studies[31,29] and seven (n = 7) cohort studies.[28,32,33,36,30,35,34] 27–32. Following the JBI Levels of Evidence,[25] the articles fall into the following levels: 3.e (n = 7) and 1.c (n = 2) (Table 2).

3.2. Risk of bias assessment

Based on the JBI critical appraisal of the included qualitative studies, the overall methodological quality was high, with an average score of 90.4%[15] (Table 3). Most studies demonstrated strong congruity between their stated philosophical perspectives, chosen methodologies, and data collection and analysis methods. The majority also clearly articulated how researchers' positions influenced the research process and interpretation of findings. Ethical considerations were generally well addressed, with formal approval reported in nearly all cases. Furthermore, conclusions were closely tied to the data. These findings suggest a robust level of methodological rigour across the studies assessed.

3.3. CPC Scale

All articles used the CPC Scale to monitor the neurological status of post-CA patients (Tables 1 and 4). Some authors describe this scale as follows: Scores of one and two indicate a positive neurological outcome, while scores above two indicate a negative neurological outcome.[36,30] Other authors use the full designation of the scale: one as good cerebral performance, two as moderate disability (disabled but independent), three as severe disability (conscious but disabled and dependant), four as vegetative state or coma, and five as brain death.[25–27,31,29,33]

3.4. Preinduction temperature

A retrospective cohort study by Li et al.[36] concluded that an initial spontaneous temperature below 35 °C is associated with higher mortality and worse neurological outcomes.[36]

3.5. Methods of temperature induction

Effective TTM requires appropriate methods for temperature induction and maintenance categorised as invasive, superficial, and noninvasive. Most studies administered sedatives, anaesthetics, and muscle relaxants, though these drugs can obscure neurological assessments, as noted by Kobata et al.,[28] who used an extracorporeal membrane oxygenation circuit with a heat exchanger. Invasive methods such as intravascular cooling catheters were used by Lascarrou et al.,[29] Blanc et al.,[31] and Chiu et al.,[32] with the latter also employing the ZOLL® intravascular system, which was associated with better neurological outcomes. Noninvasive approaches included closed-circuit surface cooling systems, gel pads,[30] and cooling blankets,[36] while Jiang et al.[35] combined endovascular cooling with external methods like ice packs and ibuprofen. Wang et al.[33] induced TTM with cold Ringer's lactate followed by surface cooling, whereas Li et al.[36] also used intravenous cooled saline when needed. Leadbeater et al.[34] use the Arctic Sun® 5000 as a noninvasive temperature management system that regulates patient temperature through hydrogel cooling pads placed on the body, with continuous core temperature monitoring via oesophageal, rectal, or bladder probes to ensure precise thermal control.

3.6. Preinduction and induction time[g]

The analysis of the data provided by Wang et al.[33] reveals that the duration of TTM (24 h vs. 48 h) did not demonstrate a significant difference in 28-d survival.[33] Survivors, however, had a

[g] Preinduction time is the period from the return of spontaneous circulation to the start of cooling. Induction time is the period from the start of cooling to the achievement of the target temperature.[33]

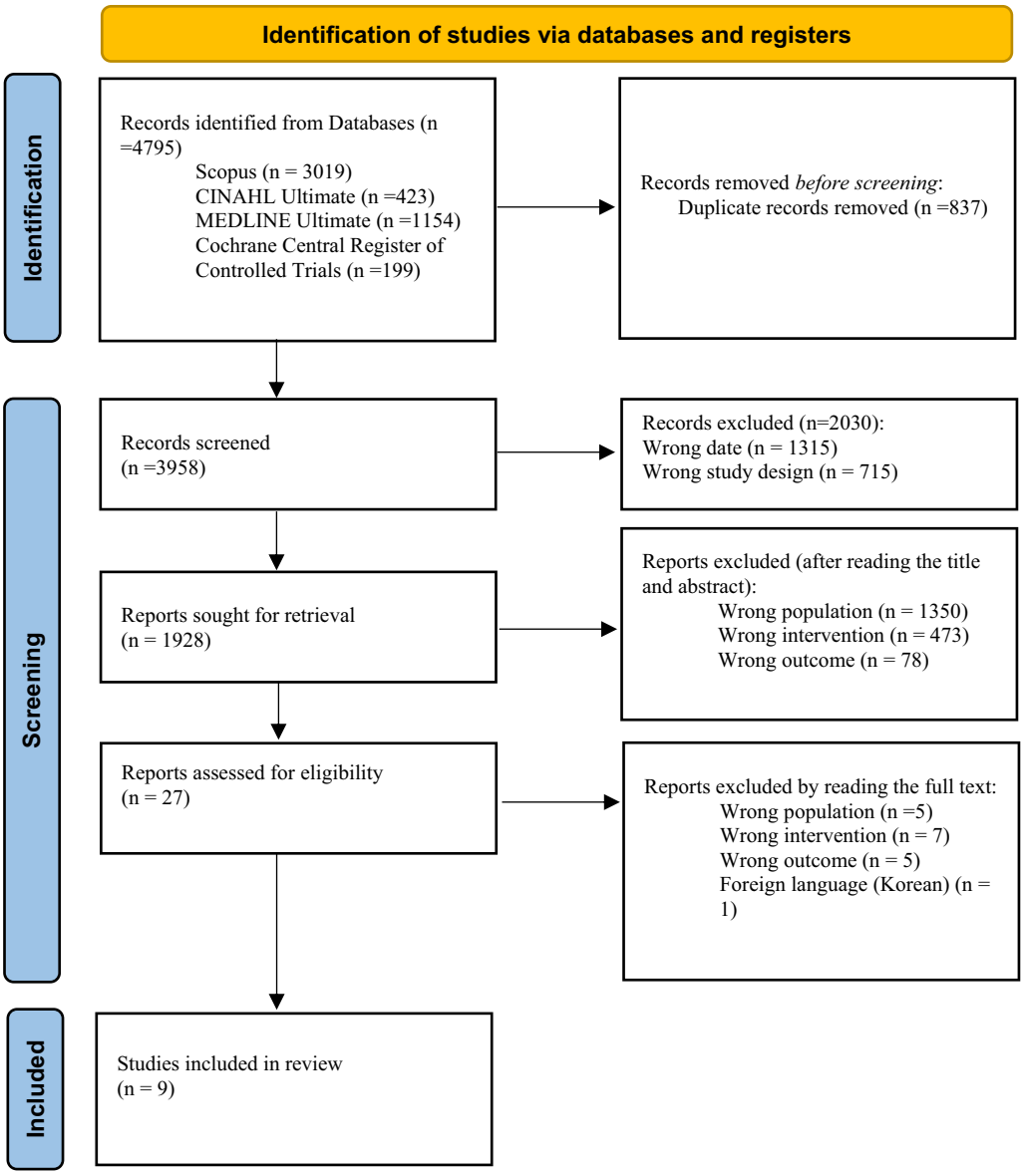

Fig. 1. PRISMA flow diagram. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

significantly lower Acute Physiology and Chronic Health Evaluation II[h] score, indicating a better initial health state.[33] On the other hand, the preinduction and induction times were critical. Preinduction times longer than 390 min (>6.5 h) and induction times greater than 440 min (>7.3 h) were associated with improved survival rates and neurological outcomes, highlighting the importance of TTM.[33]

3.7. Temperature monitoring methods

To ensure that post-CA patients reach and maintain the target temperature during TTM, continuous monitoring of body temperature is essential. Several different methods were reported for continuous temperature monitoring (Table 5), including oesophageal, bladder, rectal, and pulmonary artery catheter temperature. The choice of monitoring method may have been influenced by equipment availability, researchers' preferences, clinical context, or the clinical characteristics of the patients.

3.8. Target temperature values

The included studies primarily compared hypothermia (T = 32–34 °C) with normothermia (T = 36–37 °C) in post-CA patients. Kobata et al.[28] targeted 34 °C for most patients, with adjustments for comorbidities, while Lascarrou et al.[29] and Blanc et al.[31] focussed on hypothermia at 33 °C for 24 h, showing improved neurological outcomes compared to normothermia in patients with nonshockable rhythms. Other studies, such as those by Cordoza et al.,[30] Chiu et al.,[32] and Wang et al.,[33] varied in temperature settings, duration, and rewarming rates, with Wang et al.[29] noting no significant survival differences between 24 h and

[h] This prognostic index, known as the Acute Physiology and Chronic Health Evaluation system, is used in intensive care units to predict hospital mortality. Additionally, this score allows for the determination of patient severity by assessing organ dysfunction based on clinical and laboratory changes.[37]

Table 1
Characteristics of the included studies.

Study	Participants	Arrest type	Cooling method	Cooling duration	Cooling initiation	Target temperature	Outcome measure	Outcome assessment time
Kobata et al., 2020	22	Predominantly OHCA	ECMO with heat exchanger	24 h + rewarming + maintain <37 °C for 72 h	Start after ECPR	34 °C or 36 °C	CPC	Discharge and 6 months
Lascarrou et al., 2019	581	27.4% IHCA, 72.6% OHCA	Intravascular, surface, basic external	24 h (33 °C), 48 h (normothermia)	Median 16 min after randomisation	33 °C vs 37 °C	CPC	90 d
Cordoza et al., 2021	237	IHCA and OHCA	Surface gel pads	24 h + rewarming + 48 h normothermia	After reaching target temperature	36 °C	CPC	Hospital discharge
Blanc et al., 2022	159	IHCA	Internal and external	24 h + rewarming + 24 h normothermia	Immediately after randomisation	33 °C vs 37 °C	CPC	90 d
Chiu et al., 2022	580	IHCA and OHCA	ECMO, intravascular (ZOLL), noninvasive	≥24 h	Up to 12 h after ROSC	33–35 °C	CPC	Hospital discharge
Wang et al., 2023	177	76.8% OHCA, 23.2% IHCA	Cold Ringer's + surface blanket	24 h or 48 h	Post-ROSC (mean ~6 h)	33 °C	CPC	28, 90, 180 d
Leadbeater et al., 2023	183	OHCA	Surface (TTM phase) vs fever prevention	Not specified	TTM phase vs fever prevention phase	36 °C vs <37.5 °C	CPC	Hospital discharge
Jiang et al., 2024	423 (before matching)	IHCA	Endovascular (Thermogard XP)	≥72 h	After ROSC >20 min	33–35 °C	CPC	Hospital discharge
Li et al., 2024	597	61% OHCA	Cooling blanket, refrigerated saline	24 h + rewarming + fever prevention up to 96 h	Post hospital admission	32–34 °C	CPC	Hospital discharge

CPC: Cerebral Performance Category; ECMO: extracorporeal membrane oxygenation; ECPR: extracorporeal cardiopulmonary resuscitation; IHCA: in-hospital cardiac arrest; OHCA: out-of-hospital cardiac arrest; ROSC: return of spontaneous circulation; TTM: targeted temperature management

48 h hypothermia. Jiang et al.[35] used endovascular cooling (33–35 °C for 72 h), finding better survival at discharge but no neurological advantage over normothermia. Li et al.[36] applied TTM at 32–34 °C for 24 h with strict fever control post rewarming. Leadbeater et al.[34] compare a period of protocolised targeted TTM (36 °C) and a period of fever prevention (<37.5 °C).

Overall, hypothermia showed potential benefits, particularly in neurological outcomes; one study[34] concludes that there was no difference in the proportion of patients discharged with a CPC one or two between the groups and that variations in protocols and study populations influenced the findings.

3.9. Postinduction temperature variation[i]

Cordoza et al.[30] conducted a retrospective cohort study to investigate the association between temperature variation, defined as 0.5 °C ± 36 °C during the maintenance phase, and neurological outcome. The authors concluded that there is no association between temperature variation during the maintenance phase and the likelihood of a negative outcome. However, the study revealed that positive neurological outcomes were associated with factors such as having a shockable rhythm post CA and the use of neuromuscular blockers during hospital stay.[30]

3.10. Quantitative analyses

Only nine studies were included, and they did not consistently measure the same outcomes, apply the intervention in the same way, or include both a control and a treatment group. Therefore, as suggested by Polit and Beck,[38] it was opted to conduct an in-depth integrated analysis, as described in the previous sections.

To identify the temperature that promotes the best neurological outcomes, the temperatures used in both control and treatment groups were analysed, when available, and their correlation with positive neurological outcomes was evaluated, as reported in the studies.

The analysis of the temperatures used in both control and treatment groups or before and after intervention across multiple studies indicates that lower temperatures, typically in the range of 33 °C–35 °C, are associated with more favourable neurological outcomes than normothermic conditions or higher temperatures. Specifically, studies like those by Lascarrou et al.[31] and Blanc et al.[29] showed improved neurological outcomes (CPC score: one to 2) at 33 °C, while others like those by Cordoza et al.[30] and Leadbeater et al.[34] used a temperature of 36 °C or higher without significant variability in neurological outcomes. Wang et al.[33] noted that survivors with good neurological function had a mean temperature of 36.7 °C, suggesting a potential variation depending on patient context (Table 4). However, the variability across studies and the lack of statistical significance indicate that the benefit of TTM at lower temperatures may depend on individual patient factors and specific treatment protocols. Overall, no statistically significant difference in neurological outcomes between control and treatment groups was found in most studies.

4. Discussion

All the analysed articles used the CPC Scale to assess the neurological prognosis of patients post CPR. However, there are other neurological assessment scales that can complement this one once this scale does not differentiate between mild and moderate

[i] Postinduction temperature variation refers to the ability to maintain body temperature at the target level after this desired value has been reached.[30]

Table 2
Results table with level of evidence.

Author/year	Country	Study type	Aim	Population/sample	Intervention	Indicators/outcomes	Results	Level of evidence
(Kobata et al., 2020)[28]	Japan	Prospective observational study	Assess the feasibility and potential usefulness of amplitude-integrated EEG in cardiac arrest (CA) patients undergoing extracorporeal cardiopulmonary resuscitation and targeted temperature management (TTM).	Twenty-two CA patients (IHCA and OHCA).	An ECMO circuit with a heat exchanger. The target temperature was set at 34 °C or 36 °C. The core temperature was monitored via a Foley catheter. Patients at 34 °C remained there for 24 h, then were rewarmed to 36 °C over 8 h. All patients were kept below 37 °C for 3 d post rewarming.	Patients' wakefulness was assessed after TTM, and neurological outcomes (CPC) were evaluated at discharge and 6 months later.	All patients underwent TTM: 18 at 34 °C and four at 36 °C. The target temperature was reached in 94 min, and TTM lasted 37.5 h. Nine patients (41%) regained consciousness, with six (67%) showing good neurological outcomes at discharge and 6 months later.	3.e
(Lascarrou et al., 2019)[29]	France	Randomised controlled trial	Evaluate whether moderate therapeutic hypothermia at 33 °C, compared to targeted normothermia at 37 °C, would enhance neurological outcomes in successfully resuscitated CA patients with a nonshockable rhythm and coma.	581 patients, with 284 patients in the hypothermia group and 297 in the normothermia group. CA transpired within the hospital for 27.4% of the patients and outside the hospital for 72.6%.	Patients in the hypothermia group were cooled to 33 °C (±0.5 °C) for 24 h using various cooling methods, followed by slow rewarming to 36.5 −37.5 °C, maintained for 24 h. In the normothermia group, the body temperature was maintained at 36.5 −37.5 °C for 48 h.	Surviving participants were monitored until day 90 post randomisation. The primary outcome was survival with a favourable neurological outcome (CPC score: one or 2) at day 90, assessed via a blinded telephone interview. Secondary outcomes included mortality, ventilation duration, ICU and hospital stay length, infections, and haematologic adverse events.	At day 90, 29 of 284 patients in the hypothermia group had a CPC score of one or 2, compared to 17 of 297 in the normothermia group. Deaths within 90 days totalled 231 in the hypothermia group and 247 in the normothermia group.	1.c.
(Cordoza et al., 2021)[30]	United States	Retrospective cohort study	Investigate the relationship between body temperature fluctuations during the maintenance phase of TTM and neurological outcomes in patients undergoing TTM at 36 °C following CA.	237 patients participated.	TTM followed three phases: Phase 1, surface cooling gel pads were used with a temperature management system for 24 h after reaching 36 °C, monitored with an oesophageal temperature probe. Phase 2, rewarming occurred at 0.3 °C per hour until reaching 37 °C. Phase 3, after rewarming, surface cooling gel pads maintained normothermia at 37 °C for an additional 48 h for all patients, regardless of neurological status.	The primary outcome was neurological condition at hospital discharge, assessed using the CPC Scale. CPC scores were determined through a review of medical records, including physician notes, cognitive evaluations, and discharge.	Patients with temperature variability were more likely to have a shockable rhythm, receive less bystander CPR, have a longer CA duration, and experience more shivering. An initial shockable rhythm and the use of neuromuscular blocking agents were significantly associated with better neurological outcomes and higher odds of survival to hospital discharge while temperature variability was not. Temperature variability was defined as having at least one body temperature	3.e

							outside the 36 °C ± 0.5 °C range during the maintenance phase.	
(Blanc et al., 2022)[31]	France	Randomised controlled trial	To investigate if TTM at 33 °C is associated with better neurological outcomes after IHCA in a nonshockable rhythm than normothermia at 37 °C.	Out of 584 patients in the original study, 159 with IHCA were included in this study, with 73 randomised to 33 °C and 86 to 37 °C.	In the hypothermia group, cooling to 33 °C (±0.5 °C) was induced and maintained for 24 h using both external and internal devices. Slow rewarming occurred at 0.25−0.50 °C/h to 36.5 −37.5 °C, maintained for 24 h. Sedation was adjusted to achieve a RASS score of −5 according to each centre's protocol. In the NT group, body temperature was maintained at 36.5 −37.5 °C for 48 h using both external and internal cooling methods, including cooling devices, intravascular cooling catheters, closed-loop surface cooling systems, and basic external cooling devices.	The primary outcome was survival with a good neurological outcome (CPC score: one or 2) on day 90, and the secondary outcome was day 90 mortality.	Of the 159 IHCA patients, 12 (16.4 %) in the hypothermia group and 5 (5.8 %) in the TN group survived with a CPC score of one or 2. The number of deaths was 50 (68.5%) in the hypothermia group and 66 (76.7%) in the TN group (P = 0.24). Hypothermia at 33 °C was significantly associated with better neurological outcomes on day 90 (P = 0.03).	1.c
(Chiu et al., 2022)[32]	Taiwan	Retrospective cohort study	The goal is to identify predictors of outcomes for TTM and use artificial neural networks to develop reliable models that predict survival and favourable neurological outcomes in patients with ROSC treated with TTM.	580 patients were included in this study across 10 medical centres and regional hospitals in Taiwan.	Patients were treated with the following TTM protocol: they received either invasive ECMO, the ZOLL® intravascular temperature management system, or a noninvasive device (e.g., Arctic Sun or cold blanket) to lower core body temperature to 33°C−35 °C. This temperature was maintained for at least 24 h, followed by a gradual rewarming at 0.25 °C per hour until reaching 36.5 °C.	Survival was defined as having a CPC score of 0 −four at discharge, while death was defined as a CPC score of five at discharge. A favourable neurological outcome was classified as a CPC score of 0−2, whereas a poor outcome was classified as a CPC score of 3−5.	After TTM, 346 patients (59.7%) died and 234 patients (40.3%) survived and were discharged. The mean CPC of survivors ranged from 1.3 to 2.5. Among survivors, 119 patients (50.9%) had favourable neurological outcomes, while 115 (49.1%) had poor outcomes. Patients with better survival outcomes were younger, had shorter CPR duration, higher blood pressure, better motor response at ROSC, and lower prevalence of diabetes, heart failure, and end-stage renal disease. Intravascular cooling using the Icy catheter was associated with the highest survival rate and good neurological	3.e

(*continued on next page*)

Table 2 (*continued*)

Author/year	Country	Study type	Aim	Population/sample	Intervention	Indicators/outcomes	Results	Level of evidence
							outcomes (47%), followed by Arctic Sun cold blanket (22%), ECMO (21%), and traditional cold blanket (16%).	
(Wang et al., 2023)[33]	Taiwan	Retrospective analysis.	The purpose of this study was to investigate if the timing and rate of TTM would affect the outcomes in these patient groups.	All nontraumatic adult ROSC patients with OHCA or IHCA who received TTM at Mackay Memorial Hospital (Taipei and Tamsui branches, Taiwan) between July 2015 and July 2021−177.	TTM was initiated with a 4 °C Ringer's lactate solution, followed by a surface cooling blanket (Arctic Sun Model 2000/5000) for 24 or 48 h, targeting 33 °C. After hypothermia, controlled rewarming was performed at 0.15 °C per hour until 36.5 °C. Active temperature management, including fever prevention (>37.2 °C), continued for 24 h. Core temperature was monitored via anal or oesophageal probe.	Neurological outcomes were evaluated using the CPC Scale: 1 (good recovery), 2 (moderate disability), 3 (severe disability), 4 (coma/ vegetative state), and 5 (death/brain death). CPC scores of 3−5 were considered poor neurological outcomes.	A total of 177 patients were enrolled (136 OHCA [76.8%], 41 IHCA [23.2%]). Overall, 68 (38.42%) survived, while 109 (61.58%) died, with no significant differences in 28-d survival or neurological outcomes between OHCA and IHCA. TTM was applied for 24 h in 116 patients (65.53%) and 48 h in 61 patients (34.47%), with no significant survival difference between durations. Survivors had lower APACHE II scores, shorter no/low flow times, slower cooling rates, and longer times to reach the target temperature. Good neurological outcomes (CPC 1−2) were observed in 25 patients (15.52 %), while 136 (84.47 %) had poor outcomes. Patients with good outcomes were younger, had lower APACHE II scores, shorter no-/low-flow times, longer induction times, and higher temperatures at ROSC and cooling initiation. Longer preinduction times (>390 min) were associated with better survival and lower CPC scores. The multivariate analysis showed preinduction times >390 min and induction times >440 min were linked to higher survival.	3.e

							The Kaplan–Meier analysis revealed significantly longer 28-d survival for those with preinduction times >390 min and induction times >440 min, with trends extending to 90 and 180 d, respectively. Cox regression identified an induction time >440 min as the only factor significantly reducing 28-d mortality risk.	
(Leadbeater et al., 2023)[34]	United Kingdom	Retrospective observational cohort study	The aim is to identify any effect of changing from TTM to fever prevention on neurological outcome following OHCA	183 patients	Comparison was made between a period of protocolised TTM to 36 °C and a period of fever prevention.	CPC evaluation	There was no difference in the proportion of patients discharged with a CPC score of 1 or two between the groups (42% vs. 40%, P = 0.88): Survival to hospital discharge with a CPC score of one or two occurred in 42% of patients in the TTM group and 40% in the fever prevention group (P = 0.88).	3e
(Jiang et al., 2024)[35]	China	Propensity-matched cohort study.	This study aimed to assess the prognostic impact and outcomes of extending endovascular cooling therapy to 72 h in patients with IHCA.	We included 440 IHCA patients	TTM is performed using an endovascular cooling device (Thermogard XP) to maintain 33–35 °C for at least 72 h to prevent fever. After cooling, gradual rewarming to 37 °C occurs at 0.25 °C per hour. Alternatively, normothermia (≤37.5 °C) is maintained using ice packs, cooling blankets, or ibuprofen. Temperature is monitored with a bladder thermometer.	The CPC Scale ranges from one to 5: 1 (mild or no neurological disability), 2 (moderate disability), 3 (severe disability), 4 (coma/vegetative state), and 5 (brain death).	Endovascular cooling improved survival-to-discharge rates but did not significantly impact neurological outcomes. A higher proportion of patients in the endovascular cooling group had CPC scores of 1–2. Cox regression indicated that prolonged endovascular cooling independently improved survival in comatose IHCA patients. Adverse events were similar between groups, with no significant differences.	3.e
(Li et al., 2024)[36]	United States	Single-centre retrospective cohort study.	The objective was to examine 24 h temperature trends related to impaired thermoregulation, including transient temperatures above 37.5 °C, during a 48 h	597 patients	The standard temperature control protocol involves maintaining a core temperature between 32 °C and 34 °C for 24 h, with continuous monitoring and hourly	Neurological status was assessed using a simplified CPC score, where a score of ≤2 indicated good neurological status and a score >2 indicated poor neurological status.	Of the 597 patients, 325 (54%) died in the hospital. Logistic regression showed low spontaneous body temperature was linked to higher in-hospital mortality and increased	3.e

(*continued on next page*)

Table 2 (*continued*)

Author/year	Country	Study type	Aim	Population/sample	Intervention	Indicators/outcomes	Results	Level of evidence
			hypothermia therapy period.		documentation. Cooling is achieved using a cooling blanket and nonheated airway humidification or refrigerated normal saline if needed. After 24 h, passive rewarming begins with a target of 37.5 °C within 6 h. If passive rewarming is ineffective, active rewarming with a warming blanket is used. Hyperthermia prevention (temperature >37.5 °C) is maintained from 24 to 96 h post cooling. Core temperature is monitored hourly using oesophageal, bladder, or pulmonary artery catheter measurements, with oesophageal probes predominantly used.		risk of poor neurological outcomes (32% had poor outcomes). ICU stay was shorter for those with low temperatures, but this was due to higher ICU mortality. No significant difference in hospital length of stay was found among survivors.	

APACHE: Acute Physiology and Chronic Health Evaluation; CPC: Cerebral Performance Category; CPR: cardiopulmonary resuscitation; ECMO: extracorporeal membrane oxygenation; EEG - Electroencephalogram; ICU: intensive care unit; IHCA: in-hospital cardiac arrest; OHCA: out-of-hospital cardiac arrest; ROSC: return of spontaneous circulation; NT: normal temperature; RASS - Richmond Agitation-Sedation Scale.

Table 3
Quality assessment of the included studies.

Type of study	Methodological quality of studies													% Quality
Randomised studies	1	2	3	4	5	6	7	8	9	10	11	12	13	
Blanc et al., 2022[31]	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	92%
Lascarrou et al., 2019[29]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%
Cohort studies	1	2	3	4	5	6	7	8	9	10	11			
Kobata et al., 2020[28]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y			82%
Chiu et al., 2022[32]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y			91%
Wang et al., 2023[33]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y			91%
Li et al., 2024[36]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y			91%
Cordoza et al., 2021[30]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y			91%
Jiang et al., 2024[35]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y			100%
Leadbeater et al., 2023[34]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y			91%
													Average quality	90.4%

Y: Yes; N: No.

disability. Therefore, the use of the modified Rankin Scale (mRS) is recommended, especially to complement the CPC three category, which is nonspecific.[39,40]

Previous studies from 2010 highlighted the association between spontaneous hypothermia after ROSC, defined as a temperature below 35 °C, and worse neurological outcomes in patients treated with therapeutic hypothermia than in those with a temperature above 35 °C at intensive care unit admission.[41,42] This association is supported by Li et al.[36] However, the conditions of the CA and the duration of CA are also important predictors of neurological prognosis, so it is not clear whether spontaneous temperature after ROSC can be used as an independent predictor.[41] In a study by Hartog et al.,[42] logistic regression showed that factors such as age, acute-chronic physiological assessment, the Sequential Organ Failure Assessment scale, and a low spontaneous temperature at intensive care unit admission were associated with an increased *odds ratio* of a negative neurological outcome.[42] The study by Li et al.[36] did not include predictors such as the duration of CA, time to CPR, and no-flow or low-flow times. Future studies should explore the association between predictors considered relevant for neurological prognosis and low spontaneous temperature. Additionally, it is necessary to investigate whether low spontaneous temperature can be used as an independent predictor of neurological outcome.

For effective TTM, the use of sedatives, analgesics, and appropriate devices for inducing the TTM is necessary.[43] These medications help reduce shivering, which generates heat, resulting in longer induction times, significant temperature variability during the maintenance phase, and faster rewarming.[43] Antipyretics are commonly used during normothermia to prevent or minimise fever as adjunctive therapy.[43] Finally, the addition of muscle relaxants is also effective in inducing TTM to allow the target temperature to be reached quickly and to prevent temperature fluctuations.[43]

Among the various methods available for inducing TTM, automated devices using a temperature feedback system provide a faster time to reach the target temperature, less temperature variability, and precise and slow rewarming compared to external methods.[44] Although nonautomated methods are cheaper and easier to apply, TTM is more challenging, and their use should be limited to the induction phase in combination with automated devices.[43] This approach aligns with the findings of Wang et al.[33] and Li et al.,[36] where both studies used invasive and noninvasive methods simultaneously. Calabró et al.[44] concluded that the use of central devices is associated with a lower probability of poor neurological outcomes, contrasting with the findings of Chiu et al.,[32] who found better neurological outcomes with noninvasive methods like cooling blankets than central/invasive methods such as ice catheters.

There is still no consensus on the ideal time to initiate TTM.[45] However, evidence suggests no significant difference in outcomes between TTM durations of 24, 48, or 72 h. On the other hand, the interval between 390 min (6.5 h) and 12 h of preinduction time is associated with better neurological outcomes, as well as an induction time greater than 440 min (7.3 h).[33,45] Thus, future studies should explore the relationships between preinduction, induction, and TTM duration times and neurological outcomes, accounting for the various existing variables.[33]

When initiating TTM, body temperature should be assessed using a vesical,[28,32,36,35] oesophageal,[32,33,36,30] or parenteral probe[36] as these methods are the most accurate for measuring core temperature.[43] Leadbeater et al.[34] used a noninvasive temperature management system through hydrogel cooling pads placed on the body, with continuous core temperature monitoring via oesophageal, rectal, or bladder probes to ensure precise thermal control.

Other methods, such as oral probes, infrared ear, or axillary thermometry, should be avoided, and rectal temperature,[33] which lags behind core temperature changes, is not recommended.[43]

According to the 2020 guidelines of the AHA[16] and the 2021 guidelines from the European Resuscitation Council,[3] it is recommended that during temperature management in post-CA patients, both inside and outside the hospital, the temperature should be maintained between 32 °C and 36 °C for at least 24 h.[16] The study by Chiu et al.[32] used a target temperature range of 33 °C–35 °C for 24 h. Meanwhile, Cordoza et al. 3131 used a target temperature of 36 °C for 24 h. Li et al.[36] used target temperatures between 32 °C and 34 °C for 24 h.

Thus, these three studies utilised temperature values that fall within the ranges indicated by both guidelines.[3,16] Kobata et al.[28] used a target temperature of 34 °C, except in patients with comorbidities, such as a risk of haemorrhage, where the target temperature was 36 °C. Taccone et al.[43] suggest that a target temperature of 36 °C may be preferable in patients at an increased risk of adverse events at lower temperatures, such as haemorrhage or severe haemodynamic compromise. On the other hand, a lower temperature of 33 °C might be preferred in patients at a higher risk of neurological damage, such as seizures or evidence of cerebral oedema, which can be exacerbated by higher temperatures.[43]

Wang et al.[33] set a target temperature of 33 °C for both 24 and 48 h and found no significant difference in 28-d survival between the two durations. Therefore, their findings are aligned with the AHA and the European Resuscitation Council guidelines, which recommend maintaining TTM for 24 h with a target temperature consistent with the proposed ranges.[3,16]

The updated 2023 AHA guidelines recommend a broader temperature range of 32 °C–37.5 °C for temperature control in post-CA patients.[46] This is in accordance with the findings of Leadbeater et al.[34] who used a TTM with 36 °C and another period with fever prevention (<37.5 °C) for post-CA patients to compare neurological outcomes and highlight there are no differences between the two

Table 4
Quantitative data.

Study	Intervention	Outcome measured	N_{CG}	N_{TG}	$Temperature_{CG}$	$Temperature_{TG}$	Mean temperature				Patients with CPC 1 to 2	
							CG	SD_{CG}	TG	SD_{TG}	N_{CG}	N_{TG}
Kobata et al., 2020[28]	TTM	Cerebral Performance Category (CPC) score: one to 2	4	18	36 °C	34 °C					1	2
Lascarrou et al., 2019[29]	TTM	Survival with favourable neurologic outcomes (CPC score: 1 to 2)	297	284	37 °C	33 °C	37 °C	0.7	33.5 °C	1.1	17	29
Cordoza et al., 2021[30]	TTM	Neurological outcome at hospital dicharge (CPC score $\leq$ 2)	62	124	36 °C (no variability)	36 °C ± 0.5 °C	–	–	–	–	12	35
Blanc et al., 2022[31]	TTM	Survival with favourable neurologic outcome (CPC score: one to 2) on day 90	86	73	37 °C	33 °C	–	–	–	–	5	12
Chiu et al., 2022[32]	TTM Cooling methods: Artic Sun cold blanket, Icy catheter, traditional cold blanket, and ECMO	Survival and favourable neurological outcome (CPC score: 0 to 2)	–	580	–	33ºC–35 °C	–	–	–	–	–	119
Wang et al., 2023[33]	TTM	Survival with favourable neurologic outcome (CPC score: one to 2) on day 28	–	177	–	–	35.65 °C (survivors with poor neurological function)	1.56	36.68 °C (survivors with good neurological function)	1.15	34	4
Leadbeater et al., 2023[34]	Arctic Sun® 5000 (Franklin, NJ, USA) cooling device	CPC evaluation at discharge	65	118	<37.5 °C	36 °C	37.9 °C		35.6 °C		48	87
Jiang et al., 2024[35]	TTM Extended cooling	Survival within a 30-day period with favourable neurologic outcome (CPC score: one to 2)	48	16	Normothermia	Endovascular cooling	–	–	–	–	–	–
Li et al., 2024[36]	Various cooling methods	In-hospital death and neurologic outcomes at discharge	–	597	Initial spontaneous body temperature ≥35 °C	Initial spontaneous body temperature <35 °C	–	–	–	–	362/387	195/208

CG: control group; ECMO: extracorporeal membrane oxygenation; TG: treatment group; TTM: targeted temperature management; SD: standard deviation.

Table 5
Temperature monitoring methods employed in the selected articles.

Study	Monitoring methods
Kobata et al., 2020[28]	Bladder temperature probe
Lascarrou et al., 2019[29]	–
Cordoza et al., 2021[30]	Oesophageal temperature probe
Blanc et al., 2022[31]	–
Chiu et al., 2022[32]	Bladder or oesophageal temperature probe
Wang et al., 2023[33]	Rectal or oesophageal temperature probe
Leadbeater et al., 2023[34]	Noninvasive method (sensor)—Arctic Sun® 5000 (Franklin, NJ, USA) cooling device
Jiang et al., 2024[35]	Bladder temperature probe
Li et al., 2024[36]	Oesophageal, bladder, or pulmonary artery catheter temperature probe

groups. However, it is also mentioned that there is still no consensus on the ideal temperature, especially for populations who suffered CA from noncardiac causes, who might benefit from a lower temperature.[46] On the other hand, for TTM, a continuous monitoring is necessary,[45] only possible in hospital settings, which means that the goal in the first hour after CA is to avoid fever, aligned with the study by Leadbeater et al.[34]

Lascarrou et al.[29] and Blanc et al.[31] conclude that hypothermia at 33 °C shows a higher percentage of patients surviving with favourable neurological outcomes after 90 d than normothermia at 37 °C. Thus, these findings are not aligned with the updated AHA guidelines.[46]

Chiu et al.[45] recommended continuous temperature monitoring to prevent unexpected temperature variations during TTM. They recommend continuous temperature monitoring during the development of TTM treatment to avoid temperature variations greater than 1 °C from the target temperature.[45] However, according to Cordoza et al.,[30] there is no association between the temperature variation (defined as a variation of 0.5 °C) and negative neurological outcomes at a target temperature of 36 °C. These divergent results may arise from the use of different target temperatures (33 °C vs. 36 °C) and different phases of TTM. Future studies will be necessary to determine whether temperature variation influences neuroprotection in the different phases of TTM, according to different target temperatures.

Some studies suggest that patients with different conditions may benefit from different target temperatures. Additionally, it was shown that the temperature maintenance phase of 24 or 48 h does not impact the neurological outcome.

The methods of temperature induction can be divided into invasive or noninvasive, central or superficial, and with or without continuous temperature monitoring. Automated devices using a temperature feedback system are associated with better neurological outcomes. A preinduction time between 390 min (6.5 h) and 12 h and an induction time longer than 440 min (7.3 h) were associated with better neurological outcomes. Regarding temperature monitoring, bladder, oesophageal, and parenteral probes were found to be the most accurate. Pharmacological measures to prevent shivering include the administration of antipyretics and sedatives, while the administration of muscle relaxants can be administered so that the target temperature is reached more quickly. Neurological prognosis should be assessed only after rewarming, ideally using a multimodal approach with the CPC scale, complemented by the mRS scale to better distinguish between mild and moderate neurological disability.

Finally, it was identified that spontaneous hypothermia below 35 °C after ROSC was associated with worse neurological outcomes, while a temperature variation greater than 0.5 °C during the TTM maintenance phase, with a target temperature of 36 °C, did not influence the neurological outcomes. These findings corroborate the idea that hypothermia does not benefit the patient's neurological outcome but, on the other hand, refute the idea of the benefit of 36 °C TTM, taking into account the target temperature mentioned in the latest AHA guidelines.[1]

This analysis is aligned with Meyer and Lavin's Vigilance Theory (Table 6), highlighting the importance of detecting the relevance of signals presented by the patient and attributing meaning to them, combined with scientific knowledge, to enhance the delivery of individualised and fundamental care.[12]

5. Limitations of the study

This SR identified heterogeneity in TTM in the included trials, despite the availability of guidelines, particularly in study design and the reporting of functional results, which prevented a meta-analysis from being carried out.

Our search strategy was predefined and did not include citation searching. While citation searching can help mitigate the risk of missing relevant studies, it was not part of our initial methodology, so some studies may have been missed. Overall, there is uncertainty in neurological assessment scales and the ideal time to initiate TTM, neurological predictors for IHCA and OHCA patients separately, and TTM for patients with different conditions.[43] Although some

Table 6
Alignment of the results with the theory of Meyer and Lavin.

Elements of vigilance theory	Data obtained	Explanation of the relation with the theory
Attaching meaning to what is	Descriptions of the various TTM methods (e.g., invasive and noninvasive), CPC Scale definitions and temperature monitoring methods.	Establishing a baseline understanding of TTM practices, neurological status classifications, and the role of different interventions in clinical outcomes.
Anticipating "what might be"	Outcomes of TTM practices in different studies, target temperature settings and the significance of preinduction and induction times.	Recognising potential outcomes based on the interventions (e.g., hypothermia vs. normothermia) and foreseeing their impact on survival and neurological status.
Calculating the risk	Findings on preinduction temperatures and their relation to mortality, comparison of target temperatures (e.g., 33 °C vs. 36 °C), and the effects of temperature variation during TTM maintenance.	Weighing the risks and benefits of different target temperatures, understanding how initial conditions (such as low spontaneous temperature) influence mortality and neurological outcomes.
Staying ready to act	Protocols for temperature induction, continuous monitoring strategies, adjusting treatment based on clinical needs (e.g., switching between invasive and noninvasive methods).	Highlighting the importance of adaptability and readiness in applying TTM methods according to patient-specific needs and treatment goals.
Monitoring results/outcomes	Data on survival rates, neurological outcomes at different time points, analysis of temperature control and maintenance phases, and overall methodological quality assessment.	Evaluating the impact of TTM practices on patient outcomes, considering long-term neurological recovery and survival, and assessing the overall effectiveness and quality of applied methodologies.

CPC: Cerebral Performance Category; TTM: targeted temperature management.

articles[31,29,28,32,33,36,30] included samples covering both IHCA and OHCA patients, they did not distinguish the results between these two groups, which affected the analysis and discussion of the results. In addition, the variables and neurological predictors for IHCA patients are distinct from those who experienced OHCA, especially with the presence or absence of assistance at the scene, no-flow and low-flow times,[36] how these are accounted for, and the time of arrival at a hospital for advanced/specialized care.

6. Implications for future research

Continuous research and investment in this area of knowledge are highly encouraged, particularly in terms of refining accurate neurological prognostic tools and assessment scales. Future research should explore whether a target temperature between 32 °C and 37.5 °C is more suitable for patients with different health conditions (namely in hemodynamically unstable patients and patients with increased neurological risk, such as the presence of seizures or cerebral oedema). Future studies should also assess the neurological status of patients over longer periods, given the potential for neurological improvement up to six months after the ROSC. Additionally, research should investigate distinct neurological predictors for IHCA and OHCA patients separately, assessing their response to TTM treatment and considering these findings with previously established predictors. Future guidelines should consider these distinctions when analysing the effectiveness of interventions for each group.

7. Conclusion

This SR described current TTM in adult CA patients and the impact of it on functional outcomes. The findings suggest that tailored approaches to TTM considering factors such as patient stability, risk of neurological damage, and optimal preinduction and induction times can significantly influence neurological outcomes. Surveillance, automated devices with temperature feedback systems, the use of accurate monitoring methods (such as bladder, oesophageal, and parenteral probes), and pharmacological measures to control shivering are key components of successful interventions, implemented in a multicomponent and multidisciplinary way. The review also emphasises the importance of surveillance, as a nursing competence, as well as the early initiation of TTM and maintaining it within a specific range based on individual patient conditions to optimise neuroprotection, as preconised by the Meyer and Lavin Theory.

Future research should focus on refining these interventions, investigating the long-term neurological outcomes across diverse patient populations, and developing precise prognostic tools to enhance post-CA care. This evidence supports the need for nursing protocols, articulated with a multidisciplinary approach, that are adaptable and evidence-based, ensuring optimal patient recovery and advancing clinical practice in intensive care settings.

CRediT Authorship Contribution Statement

Joana Costa Seixas: Conceptualisation, Data curation, Formal analysis, Methodology, Visualisation, Writing – original draft, Writing – review & editing.

Mariana Oliveira: Conceptualisation, Data curation, Formal analysis, Methodology, Writing – original draft.

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Maria do Rosário Pinto: Visualisation, Writing – review & editing.

Cândida Durão: Project administration, Visualisation, Writing – review & editing.

Gisela Teixeira: Methodology, Visualisation, Writing – review & editing.

Helga Rafael Henriques: Funding acquisition, Methodology, Project administration, Visualisation, Writing – review & editing.

Joana Ferreira Teixeira: Conceptualisation, Formal analysis, Methodology, Visualisation, Writing – original draft, Writing – review & editing.

Acknowledgements

There are no acknowledgements relevant to this manuscript.

Statement of Financial Support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Not applicable.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aucc.2025.101264.

References

[1] Sinz E, Navarro K, Cheng A, Hunt E, Johnson S, Brooks S, et al. Suporte Avançado de Vida Cardiovascular. American Heart Association; 2021.
[2] Neto P, Marques N, Vaz F, Olasveengen T, Soar J, Lott C, et al. Manual de Suporte Avançado de Vida, vol. 1. INEM; 2019.
[3] Perkins G, Gräsner J, Semeraro F, Olasveengen T, Soar J, Lott C, et al. European resuscitation council guidelines 2021: executive summary. Resuscitation 2021;161:1–60.
[4] Perkins GD, Neumar R, Hsu CH, Hirsch KG, Aneman A, Becker LB, et al. Improving outcomes after post–cardiac arrest brain injury: a scientific statement from the international liaison committee on resuscitation. Circulation 2024;150:158–80.
[5] Cardiac arrest registry to enhance survival. Cares 2023 annual report - data highlights, successes, and future directions. 2023. p. 1–58.
[6] Sandroni C, Cronberg T, Sekhon M. Brain injury after cardiac arrest: pathophysiology, treatment, and prognosis. Intensive Care Med 2021;47:1393–414.
[7] Perkins G, Callaway C, Haywood K, Neumar R, Lilja G, Rowland M, et al. Brain injury after cardiac arrest. Lancet 2021;398:1269–78.
[8] Benner P, Kyriakidis PH, Stannard D. Clinical wisdom and interventions and acute and critical care: a thinking-in-action approach. 2nd ed. Springer Publishing Company; 2011.
[9] Ordem dos Enfermeiros. Padrões de qualidade dos Cuidados de Enfermagem Enquadramento conceptual enunciados descritivos. 2001. https://www.ordemenfermeiros.pt/media/8903/divulgar-padroes-de-qualidade-dos-cuidados.pdf [Accessed 20 March 2024].
[10] Bullard SE, Griss M, Greene S, Gekker A. Encyclopedia of clinical neuropsychology. Arch Clin Neuropsychol 2013;28:92. 92.
[11] Santos A, Alburquerque A, Assis A, Fernández A, Nunes A, Bejarano A, et al. Enfermagem em terapia intensiva práticas integrativas. 1st ed. 2017.
[12] Meyer G, Lavin M. Vigilance: the essence of nursing. OJIN: Online J Issues Nurs 2005;10:1–8.
[13] Hirsch KG, Abella BS, Amorim E, Bader MK, Barletta JF, Berg K, et al. Critical care management of patients after cardiac arrest: a scientific statement from the American heart association and neurocritical care society. Neurocritical Care 2024;40:1–37.
[14] Rasmussen TP, Bullis TC, Girotra S. Targeted temperature management for treatment of cardiac arrest. Curr Treat Options Cardiovasc Med 2020;22:1–39.
[15] Aromataris E, Lockwood C, Porritt K, et al. JBI manual for evidence synthesis. 2024. https://doi.org/10.46658/JBIMES-24-01. [Accessed 27 May 2024].

[16] Panchal AR, Bartos JA, Cabañas JG, Donnino MW, Drennan IR, Hirsch KG, et al. Part 3: adult basic and advanced life support: 2020 American heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2020;142:366–468.
[17] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021:1–71.
[18] Oliveira F. Suporte Básico de Vida. 2022. Lisbon PH, https://lisbonph.pt/blog/suporte-basico-de-vida/ [Accessed 27 May 2024].
[19] Whiting P, Rutjes AW, Reitsma JB, Reitsma JB, Bossuyt PM, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol 2003;3:1–25.
[20] Martins C, Gala C, Abecassis F, Campos G, Feu J, Lourenço J, et al. Manual de Suporte Básico de Vida Pediátrico. INEM DFEM 2022:1–33.
[21] Hartling L, Featherstone R, Nuspl M, Shave K, Dryden DM, Vandermeer B, et al. Grey literature in systematic reviews: a cross-sectional study of the contribution of non-English reports, unpublished studies and dissertations to the results of meta-analyses in child-relevant reviews. BMC Med Res Methodol 2017;17:64.
[22] World Health Organization. International clinical trials registry platform search portal. https://trialsearch.who.int.
[23] McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol 2016;75:40–6.
[24] Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev 2016;5:1–10.
[25] Munn Z, Porrit K, Aromataris E, Lockwood C, Peter M. JBI levels of evidence. Joanna Briggs Institute; 2020. p. 1–5.
[26] Grove S, Gray J. Understanding nursing research building an evidence-based practice. 8th ed. St. Louis, Missouri: Elsevier; 2022.
[27] Sen S, Yildirim I. A tutorial on how to conduct meta-analysis with IBM SPSS statistics. Psych 2022;4:640–67.
[28] Kobata H, Tucker A, Sarapuddin G, Negoro T, Kawakami M, et al. Continuous amplitude-integrated electroencephalography for prognostication of cardiac arrest patients undergoing extracorporeal cardiopulmonary resuscitation with targeted temperature management. Resuscitation 2020;156:107–13.
[29] Lascarrou J-B, Merdji H, Le Gouge A, Colin G, Grillet G, Girardie P, et al. Targeted temperature management for cardiac arrest with nonshockable rhythm. N Engl J Med 2019;381:2327–37.
[30] Cordoza M, Thompson H, Bridges E, Burr R, Carlbom D. Association between target temperature variability and neurologic outcomes for patients receiving targeted temperature management at 36°C after cardiac arrest: a retrospective cohort study. Ther Hypothermia Temp Manag 2021;11:103–9.
[31] Blanc A, Colin G, Cariou A, Merdji H, Grillet G, Girardie P, et al. Targeted temperature management after in-hospital cardiac arrest. Chest 2022;162:356–66.
[32] Chiu W, Chung C, Huang C, Chien Y, Hsu C, Wu C, et al. Predicting the survivals and favorable neurologic outcomes after targeted temperature management by artificial neural networks. J Formos Med Assoc 2022;121:490–9.
[33] Wang I-T, Wang C-J, Chen C-H, Yang SH, Chen CY, Huang YC, et al. Optimal timing of targeted temperature management for post-cardiac arrest syndrome: is sooner better? J Clin Med 2023;12:2610–28.
[34] Leadbeater P, Warren A, Adekunle E, Fielden H, Barry J, Proudfoot AG. Comparative before-after study of fever prevention versus targeted temperature management following out-of-hospital cardiac arrest. Resusc Plus 2024;17:100538.
[35] Jiang L, Bian Y, Liu W, Zheng W, Zheng J, Li C, et al. Treatment of comatose survivors OF IN-hospital cardiac arrest with extended endovascular cooling method for 72 h: a propensity score-matched analysis. Shock 2024;61:204–8.
[36] Li A, Hegazy AF, Vasquez LEM, Liu L, Durocher AM, Vucetic A, et al. Characterizing the impact of thermoregulation in patients after cardiac arrest: a retrospective cohort study. Canadian J Anesth J Canadien d'Anesth 2024:1–12.
[37] Moreno RP, Nassar Júnior AP. Is Apache II a useful tool for clinical research? Rev Bras Ter Intensiva 2017;29:264–7.
[38] Polit D, Beck C. Nursing research: generating and assessing evidence for nursing practice. 11th ed. Philadelphia: Wolters Kluwer; 2021.
[39] Zeltzer L. Modified Rankin scale (MRS). Stroke Engine 2008:1–4.
[40] Gutiez MT, Beuchat I, Novy J, Ben-Hamouda N, Rossetti AO. Outcome of comatose patients following cardiac arrest: when mRs completes CPC. Resuscitation 2023;192:1–6.
[41] Wörner J, Oddo M. Too cold may not be so cool: spontaneous hypothermia as a marker of poor outcome after cardiac arrest. Crit Care 2010;14:1002.
[42] den Hartog AW, de Pont A-CJ, Robillard LB, Binnekade JM, Schultz MJ, Horn J. Spontaneous hypothermia on intensive care unit admission is a predictor of unfavorable neurological outcome in patients after resuscitation: an observational cohort study. Crit Care 2010;14:121.
[43] Taccone FS, Picetti E, Vincent J-L. High quality targeted temperature management (TTM) after cardiac arrest. Crit Care 2020;24:6.
[44] Calabró L, Bougouin W, Cariou A, De Fazio C, Skrifvars M, Soreide E. Effect of different methods of cooling for targeted temperature management on outcome after cardiac arrest: a systematic review and meta-analysis. Crit Care 2019;23:285.
[45] Chiu W, Lin K, Tsai M, Hsu C, Wang C, Kuo L, et al. Post-cardiac arrest care and targeted temperature management: a consensus of scientific statement from the Taiwan society of emergency & critical care medicine. Taiwan Society of critical care medicine and Taiwan society of emergency medicine. J Formos Med Assoc 2021;120:569–87.
[46] Perman SM, Elmer J, Maciel CB, Uzendu A, May T, Mumma BE, et al. 2023 American heart association focused update on adult advanced cardiovascular life support: an update to the American heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2024;149:254–73.