

Advances in adult cardiopulmonary resuscitation: a narrative review

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Abstract

Cardiac arrest occurs rapidly, requires high timeliness in treatment, and has a poor prognosis. Cardiopulmonary resuscitation (CPR) is a key intervention to save the lives of patients with cardiac arrest. In recent years, CPR has made significant progress with the update of evidence-based research and technological development. The evolution of specific recommendations in international guidelines reflects the changes in the certainty of and understanding about emerging evidence. To unravel the logical progression of cognitive development in the CPR field, this review systematically clarifies the evidence base and evolutionary history of recommendations for core components of adult CPR, including the chain of survival, interruptions in compressions, high-quality CPR, early defibrillation, dispatcher-assisted CPR, extracorporeal CPR, and temperature control. Moreover, it identifies knowledge gaps and proposes potential development directions to provide systemic insights and strategic thinking in CPR for providers, researchers, and healthcare administrators.

Keywords: Chain of survival, Dispatcher-assisted CPR, Early defibrillation, Extracorporeal CPR, High-quality CPR, Interruptions in compressions, Temperature control

Introduction

Cardiac arrest is the sudden cessation of cardiac mechanical activity confirmed by the absence of signs of circulation.^[1] As a major global critical event, cardiac arrest poses a severe public health challenge because of its high burden and mortality.^[2] The annual incidence of out-of-hospital cardiac arrest (OHCA) worldwide is approximately 50–100 per 100,000 population, whereas 750,000 cases of OHCA are assessed by the emergency

medical service (EMS) in China every year.^[3,4] More critically, the survival of patients with shockable rhythms decreases by 7%–10% for every 1-minute delay in defibrillation,^[5] which highlights the extreme timeliness required for rescue. Meanwhile, cardiac arrest management is not a single-link intervention but a whole-chain process covering the community response, prehospital services, emergency department (ED), intensive care unit (ICU), and rehabilitation stages. The disruption or delay of any link will directly lead to resuscitation failure, imposing extremely high requirements on the continuity of rescue.^[6]

Cardiopulmonary resuscitation (CPR) is an essential method for maintaining the patient's perfusion and oxygen supply and restoring spontaneous circulation. The core components of modern CPR techniques, including chest compression, ventilation, and defibrillation, were initially developed during the 1950s and 1960s.^[7–9] Subsequently, evidence-based research gradually emerged, resulting in continuous evolution in both knowledge and techniques. The concept of the “chain of survival” has further improved the systematicness and continuity of CPR. Since its first introduction in 1991, it has become the core framework for global resuscitation efforts, with all links closely interconnected.^[10]

The International Liaison Committee on Resuscitation (ILCOR) was established in 1992 and is the authoritative academic organization in the global resuscitation field.^[11] By systematically reviewing global evidence-based research, it regularly releases Consensus on Science and Treatment Recommendations (CoSTR) every 5 years, guiding the development direction of global CPR knowledge and practice. The first edition of CoSTR in 2000 was a standardized update based on the integration of the core contents of previous national guidelines from the American Heart Association and European Resuscitation Council, laying the foundation for the homogenization of global resuscitation practice.^[12] Since then, with the increasing number of high-quality clinical studies, the development and application of new technologies, and the integration of humanistic medical

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Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Emergency and Critical Care Medicine (2026) 6:1

Received: 30 January 2026; Accepted: 12 February 2026.

Published online: 27 March 2026

<http://dx.doi.org/10.1097/EC9.000000000000179>

concepts, many important advancements have emerged in the field of adult CPR. ILCOR gradually optimized its guideline update model, adjusting from the initial 5-year periodic update to continuous evidence assessment and annual updates after 2016, ensuring that guideline recommendations are always in line with the latest evidence.^[13] Despite this, high-certainty evidence within the domain of CPR remains limited, and numerous knowledge gaps still require filling.

The evolution process of CoSTR and international guidelines reflects the cognitive changes in this field based on the accumulation of evidence and reflection. Behind each recommendation lies a multitude of data, evaluations, discussions, and balance. Only by understanding the historical context of its origin, growth, and transformation can one better affirm and criticize it, and thus better move toward the future. The CPR progress encompasses a wide range of aspects, and we cannot cover all of them in 1 article. The purpose of this review is to clarify the advancing history and challenges of some key components of CPR, enabling providers and researchers to understand the logical progression of this field and draw analogies to gain a comprehensive understanding of the overall situation.

Given the foundational role and central position, this review focuses on elaborating the development history and challenges of the chain of survival, minimizing interruptions of compressions, high-quality CPR, early defibrillation, and dispatcher-assisted CPR (DA-CPR) in basic life support (BLS). Meanwhile, because there are relatively clear evolutionary processes of recommendations for extracorporeal CPR (ECPR) in advanced life support (ALS) and temperature control in postresuscitation care based on randomized controlled trials (RCTs), detailed explanations have been provided. Finally, based on the current status of CPR research, various challenges and prospects are summarized to facilitate further progress.

Methods

A narrative review was conducted drawing on literature from PubMed/MEDLINE, Embase, Scopus, and the Cochrane Library, covering publications from database inception to December 2025. Search terms encompassed key concepts such as “cardiac arrest,” “CPR,” “ILCOR,” “chain of survival,” “interruptions in compressions,” “high-quality CPR,” “early defibrillation,” “dispatcher-assisted CPR,” “extracorporeal CPR,” and “temperature control.” The review focused on adult cardiac arrest and included peer-reviewed English-language studies such as RCTs, observational studies, manikin studies, animal experiments, systematic and scoping reviews, clinical guidelines, and expert consensus statements. Non-adult studies, irrelevant reports, duplicates, and unpublished gray literature were excluded. The selection of literature was based on the review team’s comprehensive judgment of the relevance to the topic and academic quality, and consensus was reached through repeated discussions. Data extraction was centered around key concepts and practical frameworks, with a focus on distilling theoretical and empirical findings.

Results

Chain of survival

The chain of survival is a series of key actions that must be carried out rapidly and continuously to maximize the survival of patients with cardiac arrest.^[14] As evidence and understanding have continued to evolve, the content of the core links has gone through an evolution from 4 links to 5 and then to 6 (Fig. 1).

Four-link chain. This concept was first systematically proposed in 1991, and the original chain included 4 links: early access, early CPR, early defibrillation, and early advanced care.^[14] Early

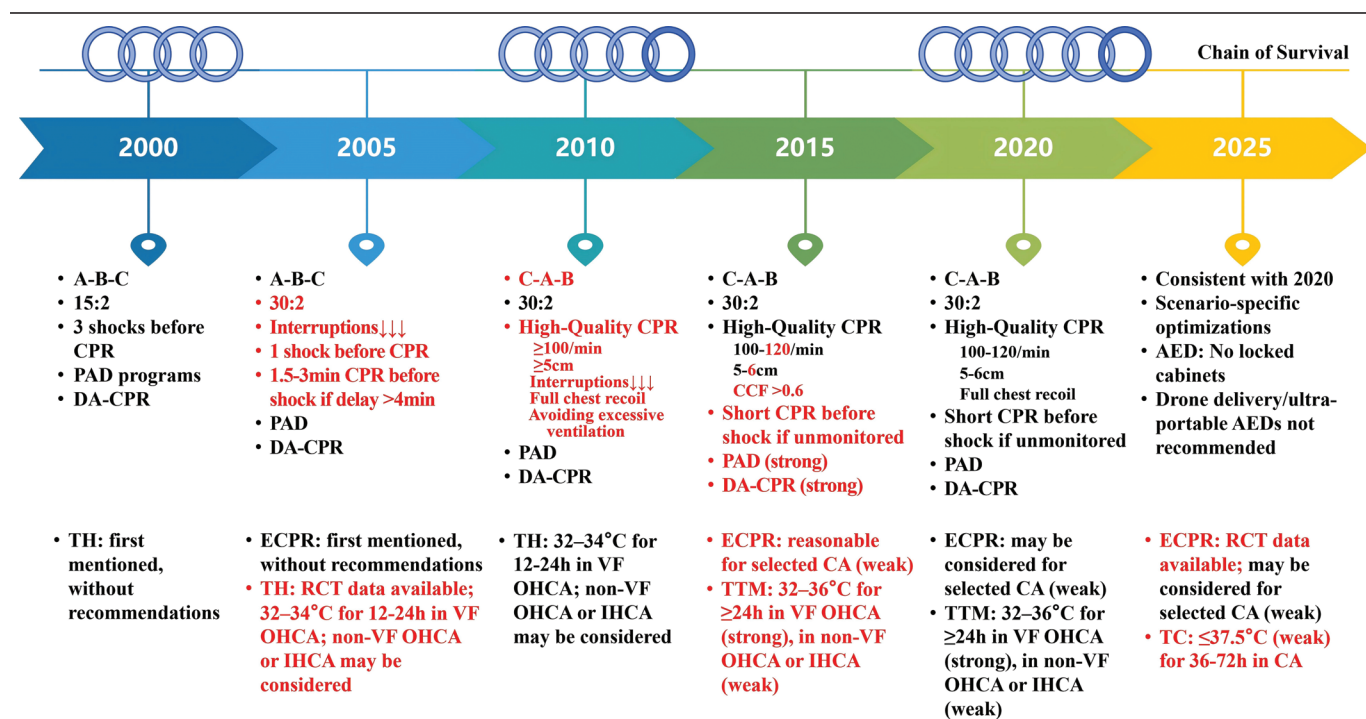


Figure 1. Evolution of recommendations in international guidelines for selected key components of adult CPR (2000–2025). AED, automated external defibrillator; CA, cardiac arrest; CCF, chest compression fraction; CPR, cardiopulmonary resuscitation; DA-CPR, dispatcher-assisted CPR; ECPR, extracorporeal CPR; IHCA, in-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; PAD, public access defibrillation; RCT, randomized controlled trial; TC, temperature control; TH, therapeutic hypothermia; TTM, targeted temperature management; VF, ventricular fibrillation.

access was evidenced by the effectiveness of universal emergency numbers in reducing response delays and public education programs that improved emergency recognition and EMS activation.^[15, 16] Early CPR's value was confirmed by data that bystander-initiated CPR prolonged ventricular fibrillation (VF) duration and improved survival.^[17, 18] Early defibrillation programs raised VF survival from 3% to 19% in rural communities.^[19] Paramedic-led interventions (intubation, medications) enhanced survival when combined with early defibrillation, from 18% to 38%.^[20, 21] The chain of survival was introduced into the first edition of ILCOR's CoSTR in 2000 and remains the cornerstone of international resuscitation guidelines to this day.^[12]

Five-link chain. In 2010, the chain of survival was expanded to 5 links, with the addition of postcardiac arrest care/postresuscitation care.^[22–24] This extension was based on the clinical observation that patients still faced a high mortality rate within 24 hours after return of spontaneous circulation (ROSC), mainly because of hemodynamic instability, multiple organ failure, and brain injury, collectively known as the postcardiac arrest syndrome.^[25–27] Since 2002, high-quality studies have confirmed that targeted interventions after ROSC can significantly increase the rate of neurologically intact survival.^[28–31] Two landmark RCTs showed that implementing 24-hour mild hypothermia treatment at 32–34 °C for comatose OHCA patients with VF after ROSC could increase the favorable neurological survival significantly (Table 1).^[28, 29] Multicenter observational studies demonstrated that a bundled treatment approach combining hemodynamic optimization, neuroprotection, coronary intervention, and metabolic management could improve the survival to hospital discharge of ROSC patients, and the volume of cases treated in the hospital was positively correlated with survival outcomes.^[30, 31, 43, 44]

Six-link chain. In 2020, as the sixth link, recovery was added to the chain of survival, indicating that the focus on survival has extended from ROSC and discharge survival to high-quality long-term survival.^[45] Data showed that among cardiac arrest survivors, 25%–50% had long-term neurocognitive impairment, and 13%–61% suffered from psychological trauma.^[46, 47] Multicenter cohort studies and RCTs have shown that comprehensive rehabilitation (physical, cognitive, and psychological) could improve quality of life scores, increase the return-to-work rate, and reduce long-term mortality.^[48, 49] In addition, the single chain was expanded into 4 independent chains: adult OHCA, adult in-hospital cardiac arrest (IHCA), pediatric OHCA, and pediatric IHCA. The core basis is that there are significant differences in the causes, physiological characteristics, rescue resources, and prognosis requirements of cardiac arrest among different populations and in different scenarios. The out-of-hospital chain highlighted the popularization of bystander CPR and public access defibrillation (PAD), the in-hospital chain emphasized team collaboration and rapid response systems, and the pediatric chain prioritized prevention and respiratory support.^[50–52]

In 2025, these 4 chains were integrated into a unified 6-link chain again, applicable to adult and pediatric populations and both in-hospital and out-of-hospital settings.^[53] The unified framework aims to simplify training processes, reduce implementation inconsistencies caused by multiple chains, and enhance the coordination of resuscitation care across different scenarios.

Knowledge gaps. The exploration of the content and form of the chain of survival is still ongoing, and discussions are also underway

on whether to add a seventh link, prevention, at the beginning of the chain.^[53] In the global application of the chain of survival, the heterogeneity of its constituent elements is gradually increasing.^[10] In response to the particularity of different patient groups and rescue scenarios, customized elements have emerged, with the core being to supplement exclusive interventions in the basic links, even applied to other emergency scenarios, such as stroke, acute myocardial infarction (AMI), sepsis, and so forth.^[10] Except for a few publications mentioning that the chain of survival had a positive effect on patient outcomes (such as improving survival and the rate of bystander CPR), no related reports on its impact on the educational or implementation level have been found.^[54, 55] Further exploration is needed of its value in education, implementation, and clinical outcomes. ILCOR suggested retaining the basic version of the 6 links (recognition and prevention, early call for help, high-quality CPR, early defibrillation and ALS, postcardiac arrest care, and recovery and rehabilitation) and making localized adjustments in combination with the concept of adaptable resources and environment to avoid confusion caused by too many versions.^[55]

Minimizing interruptions in chest compressions

The decisive role of timeliness and continuity of compressions in the prognosis of patients with cardiac arrest has been gradually recognized, with the goal of maximizing myocardial and cerebral perfusion during resuscitation. The guidelines consistently convey a principle that minimizing interruptions in compressions is the core of the high-quality CPR and entire CPR process, and adjustments to key operations such as ventilation and defibrillation must be based on this premise.

Pauses for ventilation. The 2000 CoSTR continued to adopt the traditional airway–breathing–circulation (A-B-C) sequence.^[56, 57] And the compression–ventilation ratio was updated from 5:1 (previously used for 2-rescuer CPR) to 15:2 (applicable to both 1-rescuer and 2-rescuer CPR). A manikin experiment indicated that a 15:2 compression-to-ventilation ratio for a 2-rescuer CPR could provide more chest compressions per unit time than the 5:1 ratio (approximately 64 vs. 50 times/min), whereas the quality of compressions (such as depth and recoil) remained unaffected.^[58]

The 2005 CoSTR first established minimizing interruptions of chest compressions as a core principle.^[59] To reduce ventilation-related interruptions and increase the number of compressions per minute, the guidelines updated the compression–ventilation ratio from 15:2 to 30:2 for 1-rescuer CPR. According to the literature evidence at that time, the 30:2 ratio was the scientifically validated optimal compromise in BLS. Animal experiments showed that in nonasphyxial cardiac arrest (such as VF or AMI models), 30:2 was superior to 15:2 or compression-only CPR in balancing blood flow generation and oxygen supply.^[60, 61] Theoretical modeling studies further demonstrated that 30:2 achieved a dynamic optimal balance in maintaining compression continuity, ventilation effectiveness, and operational feasibility, maximizing effective perfusion to the heart and brain per unit time.^[62] Multiple observational studies also demonstrated that, under previous 15:2 ratio, there was consistently substandard quality of real CPR, including insufficient compression rate, frequent interruptions, and incomplete chest recoil.^[63–65]

The 2010 CoSTR proposed the C-A-B sequence to replace the traditional A-B-C, establishing the absolute priority of chest compressions, marking a milestone breakthrough.^[66]

Table 1**Summary of Selected RCTs on Adult CPR**

Year	Journal	Title	Study Duration	Center Type	Study Population	Intervention and Control	Primary Endpoint	Key Results	Guideline Impact
BLS									
2010 ^[32]	N Engl J Med	CPR with chest compression alone or with rescue breathing	2004–2009 (King County), 2005–2009 (Thurston County), 2005–2008 (London)	Multicenter (King County/Thurston County, USA; London, UK)	1941 Adults with OHCA	Intervention: Chest compression alone (n = 981) Control: Chest compression + rescue breathing (n = 960)	Survival to hospital discharge	No significant difference between the 2 groups in survival to hospital discharge (12.5% in intervention group vs. 11.0% in control group, $P = 0.31$) Similar proportions survived to hospital admission (43.2% vs. 42.7%; $P = 0.87$), survived to hospital discharge (13.3% vs. 10.6%; $P = 0.19$), and achieved ROSC before physician arrival (47.0% vs. 48.6%; $P = 0.65$)	2015 and later ILCOR CoSTR: Recommend that dispatchers provide chest compression-only CPR instructions to callers for adults with suspected OHCA (strong recommendation, low-quality evidence)
2010 ^[33]	Circulation	DEFI 2005: A randomized controlled trial of the effect of automated external defibrillator cardiopulmonary resuscitation protocol on outcome from out-of-hospital cardiac arrest	2005–2008	Multicenter cluster RCT (Paris and its suburbs)	845 Patients with OHCA requiring defibrillation	Intervention: No stacked shocks (n = 421) Control: Sequences of up to 3 stacked countershocks (n = 424)	Survival to hospital admission	No significant difference between the 2 groups in survival to hospital admission (43.2% vs. 42.7%; $P = 0.87$), survived to hospital discharge (13.3% vs. 10.6%; $P = 0.19$), and achieved ROSC before physician arrival (47.0% vs. 48.6%; $P = 0.65$)	2015 and later ILCOR CoSTR: Suggest immediate resumption of chest compressions after shock delivery for adults in cardiac in any setting (weak recommendation, very low-quality evidence)
2011 ^[34]	N Engl J Med	Early versus later rhythm analysis in patients with out-of-hospital cardiac arrest	2007–2009	Multicenter (10 Resuscitation Outcomes Consortium sites in the United States and Canada)	9933 Adults with OHCA	Intervention: Early analysis of cardiac rhythm (n = 5290) Control: Later analysis (n = 4643)	Survival to hospital discharge with satisfactory functional status (a modified Rankin scale score of ≤ 3)	No significant difference between the 2 groups in primary endpoint (5.9% in early group vs. 5.9% in later group, $P = 0.59$)	2020 and later ILCOR CoSTR: Suggest a short period of CPR until the defibrillator is ready for analysis and/or defibrillation in unmonitored cardiac arrest (weak recommendation, low-certainty evidence)
2004 ^[35]	N Engl J Med	Public-access defibrillation and survival after out-of-hospital cardiac arrest	2000–2003	Multicenter cluster RCT (993 community units in 24 North American regions)	More than 19,000 volunteer responders	Intervention: Lay volunteers trained in CPR + AEDs (n = 11015) Control: Lay volunteers trained in CPR alone (n = 8361)	Survival to hospital discharge	CPR plus AED training was associated with a higher rate of survival to hospital discharge compared with CPR-only training (23.4% vs. 14.0%; RR: 2.0, $P = 0.03$)	2015 and later ILCOR CoSTR: Recommend the implementation of PAD programs for patients with OHCA (strong recommendation, low-quality evidence)

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Table 1

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Year	Journal	Title	Study Duration	Center Type	Study Population	Intervention and Control	Primary Endpoint	Key Results	Guideline Impact
ECPR									
2020 ^[36]	Lancet	Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomized controlled trial	2019–2020	Single center (the University of Minnesota Medical Center, USA)	30 Adults with OHCA and refractory VF	Intervention: Early ECMO-facilitated resuscitation (n = 15) Control: Standard ACLS treatment (n = 15)	Survival to hospital discharge	Survival to hospital discharge: 6/14 (43%) (95% CI: 21.3–67.7) in the early ECMO group vs. 1/15 (7%) (95% CI: 1.6–30.2) in the standard ACLS group (RD: 36.2%, 3.7–59.2; posterior probability of ECMO superiority 0.9861)	2023 ILCOR CoSTR: Suggest that ECPR may be considered as a rescue therapy for selected patients with OHCA (weak recommendation, low-certainty evidence) or IHCA (weak recommendation, very low-certainty evidence) when conventional CPR is failing to achieve ROSC in settings in which this can be implemented
2021 ^[37]	Ann Emerg Med	Extracorporeal Cardiopulmonary Resuscitation for Refractory Out-of-Hospital Cardiac Arrest (EROCA): Results of a Randomized Feasibility Trial of expedited out-of-hospital transport	2017–2020	Single center (University of Michigan Health System, USA)	15 Adults with refractory shockable or witnessed OHCA	Intervention: Expedited transport with ongoing mechanical CPR to a hospital capable of initiating ECPR in the ED (n = 12) Control: Continued standard care in the field (n = 3)	The proportion of subjects with a 911 call to ED arrival	In the intervention group, 5/12 patients had an ED arrival time of ≤30 min, 3/5 patients had flow initiated in ≤30 min of ED arrival; no subject in either group survived with a good neurologic outcome	2023 ILCOR CoSTR: Suggest that ECPR may be considered as a rescue therapy for selected patients with OHCA (weak recommendation, low-certainty evidence) or IHCA (weak recommendation, very low-certainty evidence) when conventional CPR is failing to achieve ROSC in settings in which this can be implemented
2022 ^[38]	JAMA	Effect of intra-arrest transport, extracorporeal cardiopulmonary resuscitation, and immediate invasive assessment and treatment on functional neurologic outcome in refractory out-of-hospital cardiac arrest: A randomized clinical trial (Prague)	2013–2020	Single center (Prague, Czech Republic)	256 Adults with a witnessed OHCA of presumed cardiac origin without ROSC	Intervention: Mechanical compression was initiated, followed by intra-arrest transport to a cardiac center for ECPR and immediate invasive assessment and treatment (n = 124) Control: Regular ACLS was continued on-site (n = 132)	Survival with a favorable neurologic status at 180 d	39 Patients (31.5%) in the invasive strategy group and 29 (22.0%) in the standard strategy group survived to 180 d with a good neurologic outcome (OR: 1.63, 95% CI: 0.93–2.85; RD: 9.5%, 95% CI: -1.3% to 20.1%; P = 0.09)	2023 ILCOR CoSTR: Suggest that ECPR may be considered as a rescue therapy for selected patients with OHCA (weak recommendation, low-certainty evidence) or IHCA (weak recommendation, very low-certainty evidence) when conventional CPR is failing to achieve ROSC in settings in which this can be implemented

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Table 1

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Year	Journal	Title	Study Duration	Center Type	Study Population	Intervention and Control	Primary Endpoint	Key Results	Guideline Impact
2023 ^[39]	N Engl J Med	Early extracorporeal CPR for refractory out-of-hospital cardiac arrest (INCEPTION)	2017–2021	Multicenter (The Netherlands)	134 Patients with refractory OHCA	Intervention: EPCR (n = 70) Control: Conventional CPR (n = 64)	Survival with a favorable neurologic outcome at 30 d	Survival with a favorable neurologic outcome: 14/70 (20%) in the EPCR group vs. 10/64 (16%) in the control group (OR: 1.4, 95% CI: 0.5–3.5, P = 0.52)	2024 ILCOR CoSTR: Suggest that EPCR may be considered as a rescue therapy for selected patients with OHCA (weak recommendation, low-certainty evidence) or IHCA (weak recommendation, very low-certainty evidence) when conventional CPR is failing to achieve ROSC in settings in which this can be implemented
Temperature control									
2002 ^[28]	N Engl J Med	Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest	1996–2001	Multicenter (9 centers in 5 European countries)	Comatose survivors of OHCA, 18–75 yr, witnessed OHCA because of VF/pVT (cardiac origin); 5–15 min from collapse to first resuscitation, ROSC within 60 min	Intervention: Mild therapeutic hypothermia (32–34 °C, for 24 h) + standard care (n = 137) Control: Normothermia + standard care (n = 138)	Favorable neurologic outcome (CPC 1/2) at 6 mo	6-mo Favorable neurologic outcome: 55% (intervention) vs. 39% (control), RR = 1.40 (95% CI: 1.08–1.81, P = 0.009); mortality: 41% vs. 55%, RR = 0.74 (95% CI: 0.58–0.95, P = 0.02)	2005 ILCOR CoSTR: Unconscious adult patients with ROSC after OHCA should be cooling to 32–34 °C for 12–24 h when the initial rhythm was VF. Such cooling may be considered for other rhythms or IHCA
2002 ^[29]	N Engl J Med	Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia	1996–1999	Multicenter (4 hospitals in Melbourne, Australia)	Comatose survivors of OHCA with initial VF; ≥18 yr (men), ≥50 yr (women); excluded cardiogenic shock, noncardiac arrest causes	Intervention: Induced hypothermia (33 °C for 12 h) (n = 43) Control: Normothermia (37 °C) (n = 34)	Survival to hospital discharge with good neurologic function (discharged home/rehabilitation facility)	Good neurologic outcome: 49% (hypothermia) vs. 26% (normothermia), P = 0.046; mortality: 51% vs. 68%, P = 0.145	2005 ILCOR CoSTR: Unconscious adult patients with ROSC after OHCA should be cooling to 32–34 °C for 12–24 h when the initial rhythm was VF. Such cooling may be considered for other rhythms or IHCA
2013 ^[40]	N Engl J Med	Targeted temperature management at 33 °C versus 36 °C after cardiac arrest (TTM)	2010–2013	Multicenter (36 ICUs in Europe and Australia)	Unconscious adults (GCS < 8) after OHCA of presumed cardiac cause; ≥18 yr; ROSC > 20 min; excluded unwitnessed arrest with asystole, acute intracranial hemorrhage/stroke, body temperature < 30 °C	Intervention: TTM at 33 °C (n = 473) Control: TTM at 36 °C (n = 466)	All-cause mortality through the end of the trial	Mortality: 50% (33 °C) vs. 48% (36 °C), HR = 1.06 (0.89–1.28), P = 0.51; 180-d poor neurologic outcome (CPC 3–5): 54% vs. 52%, P = 0.78	2015 ILCOR CoSTR: Recommend TTM for unresponsive adults after ROSC from shockable OHCA (strong recommendation, low-quality evidence), from nonshockable OHCA or from IHCA with any rhythms (weak recommendation, very low-quality evidence), 32–36 °C (strong recommendation, moderate-quality evidence) for ≥ 24h (weak recommendation, very low-quality evidence)

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Table 1

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Year	Journal	Title	Study Duration	Center Type	Study Population	Intervention and Control	Primary Endpoint	Key Results	Guideline Impact
2019 ^[41]	N Engl J Med	Targeted temperature management for cardiac arrest with nonshockable rhythm (HYPERION)	2014–2018	Multicenter (25 ICUs in France)	Comatose patients (GCS ≤ 8) resuscitated from IHCA/OHCA with nonshockable rhythm (asystole/PEA); ≥ 18 yr; excluded no-flow time > 10 min, low-flow time > 60 min, major hemodynamic instability	Intervention: Moderate therapeutic hypothermia (33 °C for 24 h) (n = 284) Control: Targeted normothermia (36.5–37.5 °C) (n = 297)	Survival with a favorable neurologic outcome (CPC: 1–2) at 90 d	Favorable neurologic outcome at 90 d: 10.2% (hypothermia) vs. 5.7% (normothermia), difference 4.5% (0.1%–8.9%), P = 0.04; 90-d mortality: 81.3% vs. 83.2%, P = 0.67	2020 ILCOR CoSTR: Recommend TTM for unresponsive adults after ROSC from shockable OHCA (strong evidence), from nonshockable OHCA or from IHCA with any rhythms (weak recommendation, very low-quality evidence), 32–36 °C (strong recommendation, moderate-quality evidence) for ≥ 24h (weak recommendation, very low-quality evidence)
2021 ^[42]	N Engl J Med	Hypothermia versus normothermia after out-of-hospital cardiac arrest (TTM2)	2017–2020	Multicenter (International)	Unconscious adults (FOUR score < 4) after OHCA of presumed cardiac/unknown cause; ≥ 18 yr; ROSC > 20 min; excluded unwitnessed arrest with asystole, limitations in care	Intervention: Targeted hypothermia (33 °C for 28 h, then rewarming) (n = 930) Control: Targeted normothermia (≤ 37.8 °C with fever control) (n = 931)	All-cause mortality at 6 mo	6-mo Mortality: 50% (hypothermia) vs. 48% (normothermia), RR = 1.04, P = 0.37; poor functional outcome (mRS 4–6): 55% vs. 55%, P = 0.87; hemodynamic arrhythmias more common in hypothermia group (24% vs. 17%; P < 0.001)	2022 and later ILCOR CoSTR: Suggest actively preventing fever by targeting a temperature < 37.5 °C for patients who remain comatose after ROSC from cardiac arrest (weak recommendation, low-certainty evidence)

ACLS, advanced cardiac life support; AED, automated external defibrillator; CI, confidence interval; CoSTR, Consensus on Science and Treatment Recommendations; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; EPCR, extracorporeal CPR; ED, emergency department; FOUR, Full Outline of Unresponsiveness; GCS, Glasgow Coma Scale; HR, hazard ratio; ICU, intensive care unit; IHCA, in-hospital cardiac arrest; ILCOR, International Liaison Committee on Resuscitation; LOE, level of evidence; mRS, modified Rankin scale; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; PAD, public access defibrillation; PEA, pulseless electrical activity; pVT, pulseless ventricular tachycardia; RCT, randomized controlled trial; RD, risk difference; ROSC, return of spontaneous circulation; RR, relative risk; TTM, targeted temperature management; VF, ventricular fibrillation.

This recommendation was based on a manikin study evidence, which showed that prioritizing compression could significantly shorten the initial compression delay time.^[67] Although there were no direct human or animal studies that confirm its ability to improve survival outcomes, it emphasized that the timely initiation of high-quality compression is a key component for successful resuscitation. This strategy has been incorporated into the standard BLS process and is applicable to OHCA and IHCA in adults until now. Meanwhile, the definition of chest compression fraction (CCF) was mentioned in this CoSTR, which was the proportion of total resuscitation time during which compressions are delivered. An observational study involving 506 patients with OHCA found that the survival to discharge improved with an increase in CCF, and the best prognosis was achieved when CCF was >0.60.^[68] Based on this, the guidelines emphasized in the treatment recommendation to perform compressions at a rate of $\geq 100/\text{min}$ and minimize interruptions as much as possible to increase the number of effective compressions per minute. CCF's core optimization strategy is to shorten all noncompression interruptions (such as ventilation, rhythm checks, defibrillation charging, etc). This recommendation has become one of the core indicators for measuring the quality of CPR in subsequent international guidelines. For compression-only CPR, it was recommended for untrained rescuers and a reasonable choice for trained rescuers who are unable or unwilling to perform artificial respiration. The basis for this was that multiple high-quality observational studies had shown that compared with no rescue at all, bystanders performing compression-only CPR could significantly improve the survival of adult patients with OHCA.^[69–71] Three RCTs confirmed that compression-only CPR under the instructions of dispatchers was at least as effective as CPR with ventilation in terms of survival to discharge.^[32, 72, 73] It was emphasized that compression-only CPR simplified the operation and enhanced the willingness of bystanders to participate, which was a key strategy for improving the coverage of the “first link” in the chain of survival.

In 2015, the recommendations were based on systematic reviews and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE). However, the overall quality of the evidence was generally low.^[74] First, regarding the sequence of compression and ventilation, although there was no high-quality human research to support it, multiple manikin studies consistently showed that prioritizing compression (C-A-B) over ventilation (A-B-C) could significantly shorten the initial compression initiation time (averaging about 20–26 seconds less).^[67, 75–77] Therefore, it was weakly recommended in adult OHCA that chest compressions should be initiated before opening the airway and providing artificial respiration. Second, regarding the compression–ventilation ratio, 4 before-and-after studies showed that the 30:2 group had slightly better outcomes in terms of survival to discharge and ROSC.^[78–81] Although the evidence was of very low quality, it still weakly recommended the use of a 30:2 ratio, emphasizing its practical consistency and operational advantages as part of a comprehensive intervention package. Third, regarding CCF, it was recommended that CCF should be at least 60% (weak recommendation, low-quality evidence). Based on 3 observational studies, shorter ventilation/rhythm analysis pause and higher CCF were significantly associated with survival benefits.^[68, 82, 83] Finally, regarding compression-only CPR, multiple observational studies and DA-CPR trials showed that compression-only CPR had no statistical difference in survival and a favorable neurological prognosis compared with conventional CPR.^[32, 71, 84]

Therefore, it was strongly recommended that all cardiac arrest patients should receive chest compressions (very-low-quality evidence), and weakly recommended that trained and willing rescuers should provide compression with artificial respiration (very-low-quality evidence), especially in scenarios with EMS response delay or asphyxial arrest.

In 2017, ILCOR conducted a systematic review on the compression–ventilation ratio, including 20 studies on adult patients, among which 17 were cohort studies, 2 were RCTs, and 1 was a cluster-crossover RCT.^[85] The analysis revealed that there were clear differences in the effectiveness of different compression–ventilation ratios in adult CPR, and the effect highly depended on the type of rescuer. For CPR performed by bystanders (including dispatcher-assisted), the analysis did not find any consistent statistical significant differences in the main outcome between compression–ventilation ratios (such as 30:2 vs. 15:2) or whether ventilation was given (ie, compression-only CPR vs. 30:2). However, a large cohort study involving over 350,000 patients showed that compared with 30:2, compression-only CPR performed by bystanders significantly reduced ROSC, survival, and good neurological prognosis.^[86] For CPR performed by EMS personnel, 30:2 significantly improved good neurological prognosis and survival compared with 15:2; whereas 50:2 was also shown to significantly improve survival and ROSC compared with 15:2. In addition, continuous chest compression combined with asynchronous ventilation (such as 10 times/min) was slightly lower in ROSC compared with 30:2, but the difference disappeared after adjusting for confounding factors. In conclusion, in adult CPR, 30:2 is currently the most evidence-supported standard protocol with the best comprehensive benefits, especially suitable for professional rescuers. For bystanders, although compression-only is easier to initiate, 30:2 should still be prioritized when conditions permit.

The 2020 and 2025 CoSTR continued the core recommendations of the 2015 version, with updates focusing on scenario-specific optimizations.

Pauses for defibrillation. In 2000, it was recommended to perform 3 consecutive defibrillations before 1 minute of CPR for patients with VF/pulseless ventricular tachycardia (pVT),^[87, 88] based on several considerations. Data showed that the survival of patients with VF was negatively correlated with defibrillation delay (decreasing by 7%–10% for each minute of delay), consecutive defibrillations could seize the shockable window with a cumulative success rate, and repeated shocks lowered transthoracic impedance and enhanced the effectiveness of the shock.^[15, 89]

In 2005, the CoSTR replaced the traditional 3 consecutive shocks with a single shock followed by immediate CPR.^[90] Given the high first-shock success rate of biphasic waveform defibrillation (85%–98%), multiple shocks were unnecessary.^[91, 92] A porcine model study showed that the rate of ROSC with a single shock was significantly higher than that with 3 shocks, while reducing defibrillation-related interruptions.^[93] Furthermore, for unwitnessed cardiac arrest with an EMS response delay >4 minutes, the guidelines suggested performing short-duration CPR before defibrillation. A before-and-after study and an RCT showed that when the EMS response delay was >4–5 minutes, performing 1.5–3 minutes of CPR before defibrillation was associated with an increased survival for patients with VF.^[94, 95] A randomized controlled study in a porcine model demonstrated that CPR before defibrillation could improve myocardial readiness for defibrillation by enhancing coronary perfusion pressure and

stabilizing myocardial electrical activity (increasing the median frequency of VF), thereby increasing the success rate of defibrillation and the rate of ROSC.^[96]

In 2015, it was clearly stated for the first time that the total interruption time should be as short as possible, with a manual defibrillation preshock pause of ≤ 10 seconds (strong recommendation, low-quality evidence).^[74] This recommendation was based on 1 RCT and 3 large-sample observational studies, all of which consistently showed that shorter interruption times or higher compression fractions ($\geq 60\%$) significantly improve ROSC and survival.^[68, 82, 83, 33] Regarding whether to immediately defibrillate or perform CPR for patients with VF/ pVT, a systematic review of 5 RCTs concluded that for patients without monitoring, 1.5–3 minutes of preshock CPR did not offer any benefit over preparing the defibrillator while compressing, analyzing as soon as possible, and defibrillating.^[97, 95, 34, 98, 99] Especially for the subgroup with EMS response time > 5 minutes, although 1 study suggested that 180 seconds of CPR might be beneficial, the other 3 RCTs failed to confirm this, and 1 exploratory analysis even indicated that prolonged CPR (180 seconds) might reduce survival. Therefore, it was recommended that in unmonitored arrests, brief CPR should be performed until the defibrillator was ready for analysis and defibrillation (weak recommendation, low-quality evidence). In addition, the consensus opposed immediately checking the rhythm after a shock (weak recommendation, very low-quality evidence). Three observational studies showed that this performance significantly reduced survival.^[100–102] It was pointed out that there was no clinical outcome evidence to support the technique of rhythm analysis during compressions, so the routine application of filtering algorithms was not recommended (weak recommendation, very low-quality evidence).

In 2020, CoSTR refined and clarified previous recommendations based on new evidence, but the evidence remained of low- or very-low-certainty.^[103] Regarding immediate defibrillation after compression rather than immediate rhythm analysis, a meta-analysis of 3 RCTs (1 new) and 3 observational studies indicated that immediate rhythm analysis significantly reduced the rate of ROSC and survival, mainly because of a decrease in CCF.^[33, 100–102, 104, 105] The first systematic assessment of real-time rhythm analysis technology during CPR was conducted based on 14 methodological studies from 2007 to 2019. There was no patient outcome data. A weak recommendation against routine application of this technology was added (very-low-certainty evidence), emphasizing that its clinical benefits had not been confirmed and needed to be verified through high-quality RCTs.

Knowledge gaps. Although the management of chest compression interruptions has been strongly emphasized, it is difficult to precisely quantify and optimize in practice, especially during transportation, airway management, and equipment operation. The physiological impact of interruptions and the optimal intervention threshold remain unclear. Regarding the sequence of chest compressions and ventilation (CAB vs. ABC), although the 2025 ILCOR still maintains a weak recommendation (very-low-certainty evidence) for CAB, all supporting evidence comes from manikin studies and lacks clinical outcome data from real cardiac arrest patients. Moreover, for special causes like drowning, there is no direct evidence to guide whether ventilation should be prioritized (ABC). The recommendation for the compression-to-ventilation ratio (30:2) is also based on indirect, low-quality observational studies, and the benefits may stem from the overall update of the guidelines rather than the ratio itself. Currently, there is no high-quality study to separately evaluate the independent

effects of different ratios (such as 50:2 or higher). The problem of chest compression interruptions caused by defibrillation is prominent. Existing evidence has not clarified the optimal sequence of compressions before defibrillation or immediate compressions after rapid defibrillation, and there is a lack of differentiated strategies for different rhythms. The timing of rhythm assessment (every 2 minutes) continues to adhere to the 2015 recommendation. However, there is low-certainty evidence to support this, and the key issue of whether the analysis interval should be dynamically adjusted based on the initial rhythm remains unaddressed.

High-quality cardiopulmonary resuscitation

High-quality CPR refers to the process of resuscitation in which multiple key parameters are optimized to ensure the maximum effect of chest compressions. Its core components consist of 5 parts: adequate compression rate, adequate compression depth, full chest wall recoiling, avoidance of excessive ventilation, and minimizing interruptions of chest compressions as mentioned above.

Chest compression rate, depth, and recoil. The international guidelines first established the core elements framework of high-quality CPR in 2005, although the term was not explicitly defined. It proposed key requirements, such as a compression frequency of $\geq 100/\text{min}$, a depth of $\geq 4\text{--}5\text{ cm}$, complete chest recoil, and minimizing interruptions.^[59] A compression rate of 100/min was recommended in 2000^[56] based on theoretical, animal, and patient data, which showed that a rate $> 80/\text{min}$ could achieve optimal forward blood flow.^[106–114] Some animal studies showed that compared with standard CPR, high-rate compressions (120–150/min) could improve hemodynamics without increasing injuries,^[108, 110, 115] although some studies did not find such an effect.^[116] One human study presented that high-rate compressions (120/min) improved hemodynamics better than the conventional strategy.^[113] But in mechanical CPR in humans, high-rate compressions (140/min) did not improve hemodynamics compared with 60/min.^[117] The guidelines before 2000 recommended a compression depth of $4\text{--}5\text{ cm}$.^[56] But in animal studies, compared with standard depth compressions, deeper compressions were associated with higher rates of ROSC and improved neurological prognosis at 24 hours.^[118–120] As to the wall recoil, 1 animal study provided the association between incomplete chest recoil and significantly increased intrathoracic pressure, decreased venous return, and decreased coronary and cerebral perfusion during CPR.^[121]

In 2010, ILCOR introduced the term “high-quality CPR” as compressions at a rate of $\geq 100/\text{min}$, a depth of $\geq 5\text{ cm}$, full chest recoil, minimizing interruptions in compressions, and avoiding excessive ventilation.^[66] An observational study of 97 IHCA patients showed that a higher rate of chest compressions was significantly associated with the initial ROSC. The average rate for patients achieving ROSC was $90 \pm 17/\text{min}$, whereas for those not achieving ROSC, it was $79 \pm 18/\text{min}$ ($P = 0.0033$).^[65] Multiple observational studies suggested that a compression depth of 5 cm or more was associated with improved defibrillation success and ROSC rate.^[122–125]

In 2015, ILCOR added the upper limits for compression rate and depth.^[74] It recommended a chest compression rate of 100–120/min (strong recommendation, very-low-quality evidence) and a chest compression depth of approximately 5 cm (strong recommendation, low-quality evidence), whereas avoiding greater than 6 cm (weak recommendation, low-quality evidence)

during manual CPR. Rescuers performing manual CPR should avoid leaning on the chest between compressions to allow full chest wall recoil (weak recommendation, very-low-quality evidence). The basis for adding an upper limit to the compression rate mainly came from several observational studies. After adjusting the CCF and depth, the group with 100–119/min had the highest survival to discharge, when compared with high rate (>140/min), medium high rate (120–139/min), medium low rate (80–99/min), and low rate (<80/min).^[126] Moreover, the higher the rate, the shallower the compression depth.^[126] The ROSC peaked at a compression rate of approximately 125/min and then declined.^[127] Physiologically, when the frequency reached 140/min, systolic blood pressure dropped to the baseline level of 74%, and there was no significant difference in end-tidal carbon dioxide (ETCO₂).^[117] The addition of an upper limit of compression depth was mainly based on safety considerations. An observational study showed that when the depth was greater than 6 cm, the incidence of chest wall injuries (rib fractures, sternum fractures) was significantly higher than that of the <6 cm group (63% vs. 31%).^[128] In addition, a multicenter cohort indicated that an increased depth of chest compressions was closely associated with better survival. However, the maximum survival occurred within the range of 40.3–55.3 mm (with a peak at 45.6 mm), suggesting that the recommended depth of more than 5 cm might be too high.^[129]

In 2020, ILCOR conducted a scoping review on research related to compression rate, depth, and chest recoil.^[130] A total of 22 articles were summarized, but no sufficient new evidence was found to support the revision of current guideline recommendations. Only 1 RCT directly studied the components of chest compressions. The RCT on 292 nontraumatic OHCA patients who arrived at the ED found that between the 100/min and the 120/min group, there was no difference in the ROSC and survival to hospital discharge/30-day survival.^[131] This review pointed out significant gaps in the research evidence related to the compression components, including a lack of high-quality evidence, a scarcity of studies on IHCA, and the failure to consider the possible interactions among the components of chest compressions.

Avoiding excessive ventilation. In the adult BLS guidelines, ventilation recommendations have been optimized around the balance between effectiveness (oxygenation/ventilation) and safety (avoiding complications).

In 2000, the tidal volume and inspiratory time were adjusted based on whether oxygen supplementation was provided.^[56] When no oxygen was supplemented, a sufficient tidal volume of 10 mL/kg (700–1000 mL) delivered over 2 seconds was required to maintain oxygenation. With oxygen supplementation, a smaller tidal volume of 6–7 mL/kg (400–600 mL) given over 1–2 seconds was recommended to reduce complications. All ventilation should be marked as effective when there is obvious chest movement, and the inspiratory speed should be controlled to avoid overventilation. An RCT showed that when relying solely on air (with an oxygen concentration of 21%), a small tidal volume (6–7 mL/kg) could not ensure arterial blood oxygen saturation.^[132]

In 2010, based on multiple human and mechanical studies, the guidelines recommended that, regardless of whether oxygen supply was available, the tidal volume for mouth-to-mouth ventilation or bag-mask ventilation should be approximately 600 mL, with the inspiration time for each ventilation controlled within 1 second to achieve chest rise.^[66] Human studies showed that when using room air, a tidal volume of 600 mL was sufficient to

maintain oxygenation and normal blood carbon dioxide levels in asphyxiated patients.^[133,134] Mechanical model studies found that there was no clinically significant difference in tidal volume when the inspiration time was 1 or 2 seconds.^[135–137]

Knowledge gaps. Regarding the recommendations on rate and depth of compression, most existing studies are observational or simulation-based, lacking high-quality RCTs to confirm their direct causal impact on survival and neurological outcomes. Insufficient chest wall recoil (ie, leaning) is consistently advised to be avoided, but there is no reliable clinical data quantifying its degree of harm, nor are there individualized recoil standards for patients of different body types, ages, or underlying conditions. The specific operational thresholds for avoiding excessive ventilation are not clearly defined in the BLS section, and the relevant evidence mainly comes from ALS contexts. Furthermore, the interaction between parameters has not yet been clarified, and there is a lack of dynamic adjustment strategies applicable to different scenarios. Also, the real-time correlation models between physiologically feedback indicators (such as ETCO₂ and coronary perfusion pressure) and the quality of compression should be widely promoted. Therefore, current practice highly relies on standardized training and technical feedback devices, but its real-world effectiveness is still limited by weak evidence and individual heterogeneity.

Early defibrillation with automated external defibrillators

For cardiac arrest caused by shockable rhythm (VF or pVT), the most effective treatment is defibrillation. CPR alone is unlikely to successfully convert VF to an organized rhythm. The time window for shock is extremely narrow, and only a few minutes' delay may lead to conversion to asystole, significantly reducing the success rate of resuscitation. Clinical data showed that every minute of delayed defibrillation results in a 7%–10% decrease in survival.^[5] Therefore, the timeliness of defibrillation and the accessibility of defibrillators are of utmost importance.

In 2000, international guidelines set specific requirements for early defibrillation and clearly defined the core value of PAD.^[87] Real-world data showed that the PAD program in King County and rural Iowa increased the survival of patients with VF significantly.^[19,138] RCTs and observational studies demonstrated that the success rate of terminating VF with biphasic waveforms was 86%–97%, with less myocardial damage.^[139–141] A prospective controlled simulation study demonstrated that untrained sixth-grade students could safely and accurately perform AED operations with only basic term prompts. The average time for the first shock was 90 seconds, which was only 23 seconds slower than that of regularly trained EMTs/paramedics.^[142] These studies collectively supported the core recommendations of the guidelines and laid a scientific foundation for the promotion of early defibrillation.

In 2005, ILCOR's recommendations were refined in aspects such as the detailed classification of PAD scenarios, quality control of AEDs, in-hospital application, and operational norms.^[90] Regarding the PAD programs, it was clearly stipulated that AEDs should be deployed in "high incidence of witnessed cardiac arrest" scenarios such as airports and casinos, along with a complete response plan involving equipment maintenance, personnel training, and coordination with EMS. A cluster RCT confirmed that trained laypersons can use AEDs safely and effectively on the public scene, increasing the number of survivors to

hospital discharge.^[35] Observational studies in scenarios such as casinos and passenger planes showed that survival from timely defibrillation exceeded 40%.^[143, 144] The quality assurance system for AEDs should be updated with clear control requirements, including regular verification of heart rhythm analysis accuracy, battery/electrode status, operator performance, and system response time.^[145] Through simulation exercises, the process was optimized.^[146] The in-hospital application of AEDs was recommended for deployment in noncritical areas (outpatient departments, diagnostic departments), allowing authorized nurses and other first responders to use them, according to the positive results of clinical and simulation studies.^[147, 148] In operational norms for defibrillation, the waveform was preferentially recommended to be a biphasic waveform (energy ≤ 200 J), as its effect in terminating VF had been proved to be equivalent to or better than that of a monophasic incremental energy waveform in several RCTs.^[91, 92, 149, 150] Although there was no definite optimal biphasic waveform, the energy should be selected according to the type of equipment. The initial energy of the biphasic truncated exponential waveform in the biphasic defibrillator should be 150–200 J, the linear biphasic waveform 120 J, and the initial energy of the single-phase defibrillator 360 J. Subsequent biphasic defibrillation can maintain the initial energy or increase it, both of which were safe and effective. On the edge-patient interface, based on RCTs' results,^[151, 152] the self-adhesive electrode patch had a comparable effect to traditional paddles and was recommended as an alternative. The anterior–posterior position and apical–posterior position of the electrode were effective alternative positions for the anterior position. Patients with large breasts should avoid placing electrodes on the breasts.

In 2017, 2 systematic reviews focusing on the application value of AEDs in OHCA were published, providing more evidence from 2 dimensions on bystander use behavior and PAD programs.^[153, 154] In 1 review including 44 observational studies, 3 randomized trials, and 13 cost-effectiveness analysis studies, the meta-analysis indicated that bystander use of AEDs was associated with increased survival to hospital discharge and good neurological prognosis. In environments with a high incidence of cardiac arrest, AEDs were cost-effective.^[153] Another review, including 41 PAD-related studies, showed that the median survival to hospital discharge after PAD treatment for OHCA was 40%.^[154] Although the quality of the evidence was low-to-very low, the 2020 guidelines continued the strong recommendation for the implementation of PAD programs for patients with OHCA made in 2015.

In 2025, new technologies were evaluated with caution.^[155] The drone delivery of AEDs was first mentioned, and a scoping review was completed,^[156] but the existing evidence was insufficient to support routine recommendation, and no new treatment suggestions were made. Regarding the accessibility of AEDs, it was not recommended to store public AEDs in locked cabinets (good practice statement). Locked cabinets would prolong the time to obtain AEDs, and the theft/vandalism rate of AEDs was extremely low (<2%), with no significant difference from unlocked cabinets.^[157] Ultra-portable/pocket AEDs were not suggested because of insufficient clinical effectiveness evidence. No human studies have confirmed that rhythm analysis during compressions can improve survival, so it is only recommended for evaluation in research rather than in clinic practice.

Knowledge gaps. Public access to and use of AEDs are still limited by issues such as device availability, environmental barriers, lack of operational confidence, and insufficient dispatcher

instruction efficiency. The effectiveness of ultra-portable AEDs, the impact of drone delivery on survival outcomes in real-world scenarios, and the direct effect of different electrode sizes/positions (especially within the first 3 shocks) on patient neurological prognosis are all lacking in conclusive human research support. There is a lack of optimized defibrillation strategies for different populations (such as obese individuals, drowning adults, and pregnant women). Evidence-based clinical guidance on the compatibility of AED deployment strategies (eg, heat map-based layout) with local community cultural contexts is currently insufficient. Furthermore, the optimal approach to integrating technical feedback, such as real-time impedance monitoring, for effectively elevating the first-shock defibrillation success rate, remains elusive. This thus underscores the urgent imperative for multicenter, prospective, patient-centered pragmatic research to address these critical knowledge gaps.

Dispatcher-assisted cardiopulmonary resuscitation

Dispatchers are the crucial bridge between bystanders, victims, and EMS personnel. They need to quickly identify cardiac arrest and provide CPR guidance over the phone, which is key to achieving continuous chest compressions and early defibrillation as soon as possible.

In 2000, the international guidelines systematically and clearly defined the role of DA-CPR.^[56] The guidelines recommended that dispatchers should receive specialized training to master standardized medical dispatch protocols, prehospital instruction skills, and the ability to grade the severity of conditions. To simplify the operation and eliminate the action barriers for bystanders, it was recommended that in the DA-CPR instructions, chest compression-only CPR should be used for untrained bystanders. An RCT of DA-CPR demonstrated that the survival to discharge in the chest compression-only group was not different from that in the group combining mouth-to-mouth ventilation. Only performing chest compressions might be the preferred method for bystanders without CPR experience.^[72]

The 2010 guidelines strengthened the recommendations regarding dispatcher recognition of cardiac arrest.^[66] When identifying OHCA, dispatchers need to proactively ask the caller whether the victim is conscious and whether their breathing is normal. If both answers are negative, it can be reasonably determined as cardiac arrest. They should also pay attention to descriptive information spontaneously mentioned by the caller, such as patient's complexion and vital status. A before-and-after controlled trial showed that after implementing the “consciousness + breathing” assessment protocol, the dispatcher's identification rate significantly increased from 15% to 50%.^[158] Moreover, descriptive studies have confirmed the sensitivity and specificity of this assessment protocol.^[159] Agonal gasps were the main obstacle for dispatchers in identification, and before-and-after controlled trials had proved that specialized education or breathing count training could significantly improve the ability to identify abnormal breathing.^[160]

In the 2017 annual summary, ILCOR focused on discussing the effectiveness of DA-CPR compression-only instruction.^[13] Three RCTs and the meta-analysis of these studies showed that compared with the conventional DA-CPR (with a compression-to-ventilation ratio of 15:2), the DA-CPR with only chest compressions showed no significant difference in survival to discharge.^[32, 72, 73, 161] Therefore, although the quality of the evidence was still at a relatively low level, the ILCOR still strongly recommended that dispatchers should provide chest

compression-only CPR instructions to callers for adults with suspected OHCA.

In 2019, ILCOR conducted a systematic review aiming to explore the impact of DA-CPR on the outcomes of patients with OHCA.^[162] Regarding the impact of whether EMS had DA-CPR on patient outcomes, 16 observational studies were identified. The analyses showed that compared with EMSs that did not provide DA-CPR, EMSs that offered DA-CPR improved patient outcomes in terms of ROSC, survival to discharge, and good neurological prognosis. In terms of examining the impact of patients receiving DA-CPR on outcomes, 20 observational studies were identified. The results demonstrated that compared with OHCA patients who did not receive bystander CPR, those who received DA-CPR had better ROSC, survival to discharge, and neurological prognosis. When comparing patients who received DA-CPR with those who received bystander-initiated CPR without any assistance, the results were not consistent. In addition, DA-CPR also increased the rate of bystander CPR implementation, shortened the CPR activation time, and increased the proportion of initial shockable rhythms. Therefore, although the certainty of all evidence was low or very low, ILCOR still strongly recommended that the EMS dispatch centers should establish relevant systems and dispatchers should provide CPR instructions to callers for adult patients experiencing cardiac arrest when necessary.^[163]

Knowledge gaps. The DA-CPR guideline has been widely promoted globally, but the actual implementation quality varies greatly, especially with insufficient application and studies in low-resource settings.^[164] Furthermore, there is significant heterogeneity, including the training level of the dispatchers, the clarity of the instruction language, the application of technical tools, and the targeted optimization for different groups. The current evidence is still of low to very-low-certainty, mainly relying on observational studies and nonrandom designs, and most studies have not adequately corrected for confounding factors (such as time trends, the qualifications of bystanders, differences in the response of the emergency system). The impact of previous CPR training background on the effectiveness of DA-CPR implementation is still unclear. Interventions targeting social and cultural barriers and their actual impact on the initiation and persistence of DA-CPR, and the lack of systematic evaluation, still need to be addressed through multicenter, prospective, patient-centered effectiveness studies to promote the transition of DA-CPR from universal accessibility to precise and efficient.

Extracorporeal cardiopulmonary resuscitation

ECPR is an ALS technique, referring to the process of urgently establishing veno-arterial extracorporeal membrane oxygenation (ECMO) to provide circulatory support for patients with cardiac arrest who have failed conventional CPR. Its clinical value highly depends on patient screening, rapid implementation, and multidisciplinary collaboration. It should be carried out in medical centers with the necessary conditions, and more high-quality studies are needed to optimize the indications and procedures.

In 2005, ECPR was first mentioned in the international guidelines, based on small case series, without providing formal treatment recommendations.^[165] In 2010, because of the methodological flaws of observational studies and high selectivity of patients, it was unable to provide a clear opinion in support or against its routine use.^[166] In 2015, ILCOR used the GRADE system to grade the evidence for ECPR. The non-RCT data showed

that in both selected IHCA and OHCA patients, the ECPR group had better short- and long-term survival and neurological prognosis.^[167] Based on this, ILCOR suggested that ECPR is a reasonable rescue therapy for selected patients with cardiac arrest when initial conventional CPR is failing in settings where this can be implemented (weak recommendation, very-low-quality evidence). In 2018, ILCOR commissioned the first systematic review on ECPR specifically, including 25 observational studies.^[168] No RCTs were found, and the heterogeneity among studies was extremely high, making it impossible to conduct an effective meta-analysis.

Starting from 2020, RCT data began to be available for ECPR (Table 1). From 2020 to 2023, there were a total of 4 RCTs comparing the ECPR strategy with local standard treatments.^[36–39] All these trials included adult patients with OHCA. The ARREST study was a phase 2, single-center, open-label, adaptive RCT on 30 adults (18–75 years) with OHCA and refractory VF (no ROSC after 3 shocks, transfer time < 30 min), randomizing 15 to ECMO-facilitated resuscitation and 15 to standard advanced cardiac life support (ACLS).^[36] The trial found survival to hospital discharge was 43% in the ECMO group versus 7% in the ACLS group. Six-month cumulative survival was significantly better with ECMO, with no unanticipated serious adverse events. It was terminated early because of an interim analysis showing ECMO superiority. As the first RCT of ECMO versus standard ACLS, it confirmed ECMO-facilitated resuscitation's benefit for refractory VF OHCA, supporting its role in improving survival. The EROC study evaluated selecting refractory OHCA patients for expedited transport and rapid ED-initiated ECPR based on call-to-ED arrival time (≤30 minutes) in a 2-tiered EMS with an ECPR-capable hospital.^[37] Adults with refractory shockable or witnessed OHCA were randomized 4:1 to expedited transport or standard care if eligible. No patients in either group achieved good neurologic survival. The trial failed to meet predefined feasibility outcomes, highlighting the need for improved call-to-ED arrival time prediction, optimized patient selection, and reduced ED-to-ECPR initiation intervals in future research. The Prague study was a single-center RCT enrolling 256 adults with refractory witnessed cardiac-origin OHCA.^[38] The intervention group received intra-arrest transport to a cardiac center for ECPR, mechanical compression, and immediate invasive assessment/treatment. The invasive bundle (transport + ECPR + invasive treatment) did not significantly improve 180-day neurologically favorable survival versus standard resuscitation, though the trial may have been underpowered. The INCEPTION study was a multicenter RCT that targeted refractory OHCA patients with an initial shockable rhythm and failing to achieve ROSC within 15 minutes of CPR initiation.^[39] Of 160 randomized patients, 26 were excluded for not meeting inclusion criteria at hospital admission, leaving 70 in the ECPR group and 64 in the conventional CPR group. The 30-day survival with a favorable neurologic outcome was 20% in the ECPR group versus 16% in the conventional group, showing no significant difference. The number of serious adverse events per patient was similar between groups.

Based on the available RCTs, ILCOR updated the systematic review in 2023 and raised the evidence level for the recommendation of using ECPR in selected OHCA patients to a low level, whereas for IHCA, because of the lack of relevant RCT research evidence, the level remained very low.^[169–171]

Knowledge gaps. Currently, ECPR has only received a weak recommendation, and its clinical application should be carried out with extreme caution. The main reasons for this are multifaceted. Although it may have potential benefits for extremely

high mortality refractory cardiac arrest, the overall evidence is of low-certainty and the supporting evidence is limited. The existing RCTs have highly selective enrollment, significant population heterogeneity, and obvious differences in procedures, making the results difficult to generalize to ordinary patients with cardiac arrest. The ECPR technique is complex, with high requirements for resources and professional training, so not all institutions can carry it out. And it may involve adverse reactions such as bleeding. The application of ECPR requires a thorough consideration of feasibility and risks. Furthermore, there is a lack of large-sample, high-quality RCTs, and the optimal applicable population, initiation timing, and implementation scenarios (out-of-hospital or in-hospital) have not been clearly defined. Unified safe technical norms and the optimal postarrest care strategy after cardiac arrest have not yet been established. The cost-effectiveness analysis under different scenarios are also insufficient, further limiting the precise and standardized application of ECPR.

Temperature control

Hypothermia therapy is an intervention measure that actively lowers the core body temperature to a range for patients who remain in a coma after ROSC. As a key part of postresuscitation care, it aims to reduce neuron ischemia-reperfusion injury after cardiac arrest. Hypothermia is currently the only neuroprotective measure for cardiac arrest recommended by international guidelines. However, the evidence for it is mostly of low certainty, and the definition is also constantly evolving, from therapeutic hypothermia to targeted temperature management (TTM) and to temperature control (Table 1). The therapeutic concept of temperature management has shifted from actively inducing hypothermia to actively preventing fever.

In 2000, the international guidelines mentioned the role of hypothermia. Although some animal and observational studies had shown that mild hypothermia (such as 34 °C) can alleviate brain injury after ischemia, there was still insufficient high-quality clinical evidence on active induction of hypothermia after cardiac arrest, making it impossible to clearly determine its universal benefits.^[172]

Therapeutic hypothermia. In 2002, the results of 2 milestone RCTs were published, comparing the effects of mild hypothermia and no temperature management on VF survivors of OHCA who remained in coma.^[28, 29] One of the multicenter RCTs randomly assigned 77 unconscious survivors of OHCA with initial VF rhythm to moderate hypothermia (core temperature 33 °C within 2 hours post-ROSC, maintained for 12 hours) or normothermia.^[29] The survival to hospital discharge with good neurologic function of the hypothermia group was significantly better than that of the control group (49% vs. 26%). Meanwhile, hypothermia was associated with lower cardiac index, higher systemic vascular resistance, and hyperglycemia, but there was no significant difference in adverse events. The other RCT randomized unconscious VF cardiac arrest survivors to therapeutic mild hypothermia (target bladder temperature 32–34 °C for 24 hours) or standard normothermia. The hypothermia group had 55% (75/136) 6-month favorable neurologic outcome versus 39% (54/137) in the normothermia group (risk ratio: 1.40, 95% confidence interval: 1.08–1.81), with no significant complication differences.^[28]

Based on the promising results of these 2 RCTs, ILCOR specifically issued an advisory statement on therapeutic hypothermia

after cardiac arrest in 2003.^[173] And for the first time, it was recommended that unconscious adult patients with ROSC after OHCA should be cooled to 32–34 °C for 12–24 hours when the initial rhythm was VF. Because the data were derived from a highly selected group of patients, namely those with VF as the initial rhythm among OHCA patients, the recommendation was limited to this specific group of patients. Whether it can be extended to patients with IHCA or other rhythms should be carefully considered when deciding on the treatment. A clinical feasibility study documented that helmet device-induced hypothermia improved metabolic end points (lactate and O₂ extraction) of comatose pulseless electrical activity/asystole OHCA adult patients after ROSC.^[174] A before-and-after study showed neurological benefit after therapeutic hypothermia in comatose non-VF OHCA survivors.^[175] In 2005 CoSTR, a new recommendation related to non-VF survivors was added: Cooling to 32–34 °C for 12–24 hours may be considered for unconscious adult patients with ROSC after OHCA from any other rhythm or cardiac arrest in hospital.^[165]

Targeted temperature management. In 2013, a large sample RCT, called TTM, was published, presenting the results of comparing the effects of 2 target temperatures (33 and 36 °C) on long-term survival and neurological prognosis of cardiac arrest survivors.^[40] In the TTM study, unconscious adults with presumed cardiac OHCA and any initial rhythm except unwitnessed asystole were randomly assigned to TTM at 33 or 36 °C. At 180 days, of 939 analyzed patients, 50% in the 33 °C group and 48% in the 36 °C group died ($P = 0.51$). No significant differences were seen in composite outcomes (poor neurologic function or death) (54% vs. 52%; $P = 0.78$), with similar adjusted results. This trial illustrated that TTM at 33 °C offered no benefit over 36 °C for unconscious presumed cardiac OHCA survivors.

Accordingly, ILCOR updated the advisory statement and replaced the term of therapeutic hypothermia with TTM in 2015.^[176] More importantly, the recommended target temperature for hypothermia treatment had undergone a significant change, from 32–34 °C to 32–36 °C (strong recommendation, moderate-quality evidence). Based on the available research data that can be accessed, implementation of TTM was given a strong, weak, and weak recommendation, respectively, for survivors of OHCA with shockable rhythms, OHCA with nonshockable rhythms, and IHCA with any rhythms.

In 2019, the HYPERION trial reported the effect of different temperatures (33 vs. 37 °C) on comatose after resuscitation from either an IHCA or OHCA with an initial nonshockable rhythm.^[41] This was an open-label, pragmatic, multicenter RCT comparing moderate therapeutic hypothermia (33 °C for 24 hours) with targeted normothermia (37 °C) in 581 ICU-admitted coma patients resuscitated from cardiac arrest with nonshockable rhythm. For 90-day survival with a favorable neurologic outcome, 10.2% (29/284) in the hypothermia group versus 5.7% (17/297) in the normothermia group achieved the outcome ($P = 0.04$). The 90-day mortality (81.3% vs. 83.2%) and prespecified adverse events showed no significant between-group differences. This study filled the gap in the RCT evidence regarding hypothermia treatment for unconscious survivors with nonshockable rhythms in OHCA and IHCA. Although the recommendation strength of the subsequent guidelines was not changed, it further confirmed that this group of patients needed to apply TTM and the temperature should be controlled within the range of 32–36 °C.^[177]

Temperature control. In 2021, the TTM2 trial was published to address the core controversy of TTM, whether 33 °C is superior to actively maintaining normal body temperature after the ROSC following OHCA.^[42] The TTM2 study was an open-label, international, investigator-initiated superiority trial. A total of 1850 comatose adults with OHCA of a presumed cardiac or unknown cause, irrespective of the initial rhythm, were randomly assigned to targeted hypothermia (33 °C + controlled rewarming) or targeted normothermia (fever ≥ 37.8 °C treated early). For 6-month all-cause mortality and neurological prognosis, the 2 groups showed no significant difference. Subgroup outcomes were consistent. Hemodynamically compromising arrhythmia was more common in the hypothermia group. With new evidence available from multiple RCTs, including the TTM2 trial, ILCOR updated the systematic review and meta-analysis on TTM in adult cardiac arrest in 2021, covering all aspects of temperature management (initiation timing, target temperature, duration, induction and maintenance methods, and rewarming).^[178] The systematic review identified 32 trials, with a moderate risk of bias for most outcomes. For the comparison of target temperatures of 32–34 °C versus normal temperature (usually requiring active cooling), there were no improvements in survival or good neurological outcome at 90–180 days after cardiac arrest. No differences in outcomes were found among different hypothermia target temperatures. Prehospital cooling versus nonprehospital cooling showed no improvement in survival to discharge or good neurological outcome at discharge.

Therefore, in the 2022 ILCOR annual summary, the term changed again, from TTM to temperature control.^[179] Moreover, there was a significant change in the recommendation regarding the target temperature. It was no longer recommended to control the temperature within the range of 32–36 °C. Instead, it was suggested to actively prevent fever by targeting a temperature of ≤ 37.5 °C (weak recommendation, low-certainty evidence). In addition, for multiple specific operational aspects regarding temperature control, corresponding recommendations were also provided, although the certainty of the evidence was low or absent, such as the methods of prehospital cooling inducing, the duration of hypothermia (≥ 72 hours), and so forth.

In 2023, 6 new trials were identified through an updated search, and a meta-analysis was conducted again.^[180] Low-certainty evidence indicated that temperature control at 32–34 °C did not improve survival or good neurological outcomes at 90–180 days after cardiac arrest. Subgroup analyses by the location of cardiac arrest (in-hospital vs. out-of-hospital) yielded similar results. Comparisons of target temperatures of 31–34 °C, cooling durations of 12–24 versus 36 hours, rewarming rates of 0.25–0.5 °C/h, and temperature control combined with fever prevention did not reveal any differences in outcomes. Therefore, the 2024 annual summary still maintained the relevant recommendations from 2022, only changing the suggested duration of cooling to 36–72 hours (good practice statement).^[170]

Knowledge gaps. At present, there are still multiple critical knowledge gaps in the research on temperature control after cardiac arrest, covering comparative data, special scenarios, strategy details, and equipment application. In terms of basic comparison, there are very few direct studies comparing “no temperature control” with “fever prevention,” making it difficult to determine clinical superiority. There is insufficient evidence for special scenarios (such as after ECPR and IHCA), with IHCA relying only on a small trial, limiting the credibility of the conclusion. There is a lack of research on the therapeutic window of hypothermia

and feasible rapid cooling methods, and the relation between the degree of brain injury and target temperature/duration is unclear. Patient subgroups that can benefit from hypothermia have not been identified, and it is undetermined whether temperature control devices with feedback are more effective. The applicability of existing trial results to nondevice temperature control or different devices is also unclear.

Challenges and future perspectives

Despite the continuous promotion of CPR research and practice worldwide and the constant update of recommendations in international guidelines, the overall research still has obvious shortcomings in multiple aspects, such as evidence quality, data coverage, and population generalization. A comprehensive analysis of the challenges faced is needed to seek breakthroughs.

Evidence certainty and individualization. Current research on adult CPR is confronted with core issues such as the scarcity of high-quality RCTs, a low proportion of strong recommendations, and a lack of high-certainty evidence (Table 1). Even the establishment of some core indicators is based on animal experiments, simulation studies, or clinical procedures. For instance, in the 2020 American Heart Association guidelines, only 1% of the recommendations were based on the highest quality evidence (level of evidence [LOE] A), 50% relied on limited data (LOE C-LD), and 12% were entirely based on expert opinion (LOE C-EO). Particularly in areas such as ALS and airway management, there is a significant lack of LOE A evidence. Meanwhile, there was a strong discrepancy between the strength of the recommendation and the underlying evidence.^[181] This situation cannot be compared with the abundance of level A evidence in international guidelines in the cardiovascular field.^[182] Moreover, research on IHCA is severely insufficient among the RCTs on adult cardiac arrest. Only 4.3% were from IHCA among studies published between 1995 and 2014.^[183] Although IHCA patients account for a significant proportion of in-hospital deaths,^[184] and their pathophysiology and treatment environment are notably different from those of OHCA, current guideline recommendations for IHCA are mostly extrapolated from OHCA data. In addition, data for specific populations (such as the elderly, obesity, pregnant women, residents in low-resource areas, etc) are extremely limited, which restricts the universality of the guidelines.^[185]

In the future, a more comprehensive national and international clinical research cooperation network should be established to facilitate the generation of high-quality evidence, especially in IHCA. For specific populations, we need to conduct in-depth exploration into the links between frailty, comorbidity burden, and functional prognosis in older adults, and boost differentiated research for populations in low-resource settings.^[186] Technically, the field requires translating the concept of “physiology-guided individualized resuscitation” into clinical validation. A standardized data registry platform needs to be established to unify the implementation standards of advanced intervention measures (eg, ECPR), resuscitation quality parameters, and outcome definitions, to reduce confounding bias.^[187] Furthermore, targeted strategies must tackle barriers in the research ecosystem by optimizing scientific research resource allocation, strengthening support systems for early-career researchers, and improving access to cardiac arrest registry data.

Localization demands. The ILCOR guidelines are mainly developed based on high-resource settings and are insufficiently applicable to low-resource settings.^[185] In regions such as Fiji,

although clinicians generally believed that clinical practice guidelines can improve medical quality, there was a lack of formal monitoring mechanisms and local adaptation.^[188] A survey in Ethiopia revealed that only 25.1% of healthcare workers had good knowledge of CPR despite training, highlighting the contradiction between training effectiveness and resource limitations.^[189] The challenges of localization are reflected in multiple aspects, such as the lack of evidence-based data tailored to local epidemiological characteristics, insufficient training resources, language and cultural barriers, and the absence of a continuous education system.

The localization of guidelines can be enhanced through various measures. Multinational experts have proposed an adjusted framework of “chain of survival” adapted to low-resource settings and emphasized the development of local registration systems to generate evidence-based data.^[185] Nonprofessionals, such as teachers and peer mentors, can effectively conduct CPR training, which is cost-effective and easy to integrate into school curricula.^[190] The “hospital-community-family” linkage model can increase the coverage and retention rate of public training.^[191]

Cardiac arrest registry. A continuous high-quality registry of cardiac arrest is of core value to CPR research. Registries have provided key data support for epidemiological surveillance, quality improvement, and evidence-based guideline development. National registries in China, Sweden, and the United States, through standardized collection of patient characteristics, process of care, and outcomes, enable medical institutions to conduct benchmark comparisons, identify care disparities, and optimize intervention strategies.^[192–194] Such registry data have supported updates to international guidelines, enhanced cross-regional data comparability, and facilitated the analysis of critical prognostic factors.^[195–197] Furthermore, registry data furnishes real-world evidence for evaluating the efficacy of specialized techniques (eg, ECPR), uncovering their potential clinical value in managing refractory cardiac arrest.^[198]

However, notable challenges persist in adult CPR registries. Varying national registration standards breed data fragmentation, even as the Utstein template advances standardization.^[199] Sample representativeness is compromised by insufficient cases for specific subgroups, and resource and ethical constraints impede high-quality data collection in low-resource settings.^[200] Data privacy regulations add complexity to cross-border collaboration, although data quality relies on sustained quality control to avoid biases and unify variable definitions.^[192]

Moving forward, adult CPR registries will advance through strengthened global and national collaboration, with dynamic Utstein template updates and cross-border data interoperability.^[1] Multisource data integration will link registries to electronic medical records and insurance databases, expanding analysis of long-term outcomes like 6-month neurological function.^[201] Registry big data will empower precise resuscitation, enabling prognostic model development and real-time feedback to optimize CPR quality. Resource equity should be prioritized, and innovative low-resource practices, such as simplified tool application, should be adopted to foster inclusive development. In the end, iterative data optimization will drive consistent advances in cardiac arrest care quality.

Utilizing the leverage of technology. Technological advancement and artificial intelligence (AI) tools are empowering the entire CPR process. Multimodal data integration enables AI

to identify cardiac arrest high-risk patients early via predictive algorithms built on electronic health records and real-time ECG monitoring.^[202] AI-enhanced feedback systems have the potential to optimize compression parameters dynamically, reduce manual operation variability, and synergize with AEDs to boost defibrillation accuracy and cut interruption time.^[202] Smart CPR APPs and emerging technologies like drone AED delivery, wearable monitors, and mixed reality training enhance skill training accessibility, shorten prehospital response times, and strengthen team collaboration. AI-driven robotic CPR systems showed promising hemodynamic improvements in animal trials, and large language models explored technological evolution paths for resuscitation, backing the guideline’s core of physiology-oriented individualized care.^[203, 204]

It’s worth noting that technological translation confronts notable hurdles. Most AI applications remain in the proof-of-concept stage, and rigorous RCTs are urgently required to verify their clinical and cost-effectiveness relative to traditional methods.^[205] System-level barriers encompass data privacy protection, cross-platform interoperability, algorithm fairness, and ethical governance.^[206] Furthermore, clinical integration demands clear boundaries for human-machine collaboration, enhanced professional trust in AI tools, and targeted operational training.^[206]

Looking ahead, the guideline’s goal to unify high-quality, standardized and individualized resuscitation will propel AI’s integration with the Internet of Things, wearable sensing, and augmented reality, building an intelligent closed-loop system that covers warning, response, resuscitation, and prognosis. This vision calls for interdisciplinary clinical, engineering, and ethical collaboration, the establishment of algorithm verification and regulatory frameworks, and a focus on technological inclusiveness to bridge resource gaps. With iterative technological upgrades and evidence-based accumulation, AI will evolve from a mere auxiliary tool into a core driver of resuscitation practices, elevating global cardiac arrest survival and neurological prognoses by optimizing every link in the chain of survival.

Conclusion

This review synthesizes the development of evidence and guideline recommendations for key components of adult CPR, clearly illustrating the cognitive evolution logic in the CPR field. It also underscores a notable lack of comprehensive, high-certainty evidence covering aspects of CPR. We thus stress the importance of national and international collaborative research to produce high-quality evidence, advance the localization of guideline recommendations, maintain standard registries, and prudently utilize AI technologies. All these efforts aim to elevate the quality of prevention, recognition, and resuscitation for cardiac arrest, addressing the research gaps and translating guidelines into practical clinical value.

Conflict of interest statement

Yuguo Chen is the Editor-in-Chief of *Emergency and Critical Care Medicine*, and Feng Xu is an Editorial Board member of *Emergency and Critical Care Medicine*. The article was subject to the journal’s standard procedures, with peer review handled independently of the Editor-in-Chief, this Editorial Board member, and their research groups. The remaining authors have no conflicts of interest to disclose.

Author contributions

Chen Y, Xu F, and Zheng W contributed to the conceptualization and design of this review. Zheng W, Liu X, Ren Y, Li R, Li Y, Lv Y, Shan L, and Feng Z participated in the systematic literature review, critical discussion of the content, and information summarization. Zheng W, Liu X, and Ren Y drafted and edited the manuscript before submission. All authors gave their approval to the final version of the manuscript.

Funding

This work was supported by grants from the Noncommunicable Chronic Diseases-National Science and Technology Major Project (2023ZD0505500, 2023ZD0505504), Key R&D Program of Shandong Province (2022ZLGX03), National Distinguished Physician Program, and Taishan Pandeng Scholar Program of Shandong Province (tsdpd20240819).

Ethical approval of studies and informed consent

None.

Acknowledgements

The authors thank national and international experts in the field of cardiac arrest for their valuable suggestions on the manuscript.

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How to cite this article: Zheng W, Liu X, Ren Y, et al. Advances in adult cardiopulmonary resuscitation: a narrative review. *Emerg Crit Care Med*. 2026;6(1): 34–55. doi: 10.1097/EC9.0000000000000179