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Therapeutic Approaches to Cardiac Circulatory Arrest: A Pharmacological Perspective

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Abstract

Cardiac circulatory arrest (CCA), a sudden cessation of effective cardiac output, remains one of the most critical medical emergencies worldwide. Despite advancements in cardiopulmonary resuscitation (CPR) and intensive care, mortality and neurological deficits remain high. Pharmacological therapy plays a pivotal role in optimizing myocardial perfusion, restoring spontaneous circulation, and improving survival outcomes. This review explores the pharmacological strategies used in the management of cardiac circulatory arrest, focusing on catecholamines, vasopressors, antiarrhythmics, adjunctive drugs, and novel experimental agents. Recent advances in molecular pharmacology and targeted therapeutics are discussed, highlighting translational developments that may redefine resuscitation protocols.

Keywords: Cardiac arrest, circulatory arrest, pharmacotherapy, vasopressors, adrenaline, amiodarone, resuscitation drugs, CPR pharmacology.

1. Introduction

Cardiac circulatory arrest (CCA) is a sudden and complete cessation of effective cardiac mechanical activity, resulting in the absence of cardiac output, unresponsiveness, and apnea. It represents one of the most catastrophic medical emergencies, demanding immediate recognition and intervention. Despite continuous advancements in cardiopulmonary resuscitation (CPR), defibrillation technology, and emergency response systems, the overall survival rate after cardiac arrest remains dismally low typically ranging between 8–12% for out-of-hospital and 20–25% for in-hospital cardiac arrests.

Globally, cardiac arrest continues to be a major cause of morbidity and mortality, accounting for an estimated 15–20% of all natural deaths. The condition can arise from a multitude of underlying etiologies, broadly classified into cardiac (primary) and non-cardiac (secondary) causes. Cardiac etiologies include ventricular fibrillation (VF), ventricular tachycardia (VT), and severe myocardial infarction, whereas secondary causes encompass hypoxia, hypovolemia, electrolyte imbalances, pulmonary embolism, and drug toxicity. Regardless of etiology, the resultant hemodynamic collapse leads to profound tissue hypoxia, metabolic acidosis, and rapid cellular injury, particularly in the brain and myocardium.

The "chain of survival"**,** as proposed by the American Heart Association (AHA), emphasizes a sequence of critical steps: early recognition and activation of emergency services, high-quality CPR, rapid defibrillation, effective advanced life support, and integrated post-cardiac arrest care. Among these, pharmacological therapy constitutes a vital component of advanced cardiac life support (ACLS), serving as an adjunct to defibrillation and chest compressions. Drugs are primarily used to optimize coronary and cerebral perfusion pressure, stabilize cardiac rhythm, and correct metabolic or ionic disturbances.[1]

Pharmacologic management of cardiac arrest has evolved significantly over the past several decades. Early resuscitation efforts focused mainly on adrenaline (epinephrine) as the universal agent to increase aortic diastolic pressure and facilitate return of spontaneous circulation (ROSC). However, recent evidence challenges the long-term benefits of certain agents, highlighting the complex balance between immediate hemodynamic effects and neurological outcomes. Consequently, the modern approach integrates a mechanistic understanding of cardiovascular physiology, receptor pharmacology, and evidence-based dosing protocols to achieve maximal efficacy with minimal adverse effects.

In addition to traditional agents such as epinephrine, vasopressin, amiodarone, and lidocaine**,** new pharmacological strategies are being investigated. These include nitric oxide donors**,** selective β-blockers**,** adenosine modulators**,** and mitochondrial protectants aimed at enhancing microcirculatory flow and reducing ischemia-reperfusion injury.The emergence of personalized pharmacotherapy guided by genomic and receptor-based variationsfurther underscores the need to tailor drug therapy to individual patient profiles.

This review aims to comprehensively discuss the therapeutic approaches to cardiac circulatory arrest from a pharmacological standpoint. It explores the mechanistic roles**,** clinical efficacy**,** and current evidence surrounding major pharmacological agents used in cardiac arrest management. Furthermore, emerging trends, post-resuscitation pharmacologic care, and future directions in resuscitative pharmacology are analyzed to provide an integrated understanding that may inform both clinical practice and research innovation.[2,3]

2. Pathophysiology of Cardiac Circulatory Arrest

Cardiac circulatory arrest (CCA) represents the terminal event of a sequence of hemodynamic and electrical instabilities that culminate in the complete cessation of effective cardiac output. Understanding the underlying pathophysiology is essential for guiding pharmacological and resuscitative interventions. CCA can be broadly classified based on the underlying cardiac rhythm at the time of arrest: ventricular fibrillation (VF), pulseless ventricular tachycardia (VT), pulseless electrical activity (PEA), and asystole. Each of these mechanisms differs in its electrophysiological profile and, consequently, in its response to pharmacological and electrical interventions[4].

2.1 Ventricular Fibrillation and Pulseless Ventricular Tachycardia

VF and pulseless VT are characterized by chaotic depolarization of myocardial fibers, resulting in ineffective ventricular contraction. VF is often a terminal event of ischemic heart disease or acute myocardial infarction. The absence of coordinated systolic function leads to an immediate fall in cardiac output and coronary perfusion pressure. If untreated, VF degenerates into asystole within minutes due to progressive energy depletion in cardiac myocytes.

2.2 Pulseless Electrical Activity and Asystole

PEA occurs when organized electrical activity persists on the electrocardiogram (ECG) but fails to produce mechanical contractions sufficient for effective perfusion. It often results from reversible causes, known by the mnemonic **"**Hs and Ts**"** hypoxia, hypovolemia, hydrogen ion (acidosis), hypo/hyperkalemia, hypothermia, tension pneumothorax, tamponade, toxins, thrombosis (pulmonary or coronary), and trauma. Asystole, in contrast, represents the complete absence of electrical and mechanical cardiac activity, and is associated with the poorest prognosis among all arrest rhythms.

2.3 Systemic Consequences of Circulatory Arrest

The abrupt cessation of cardiac output initiates a cascade of pathophysiological events affecting multiple organ systems. Within seconds, oxygen delivery to vital organs halts, resulting in global tissue hypoxia. The brain, which consumes nearly 20% of total oxygen supply, suffers irreversible neuronal injury within 4-6 minutes of complete ischemia. Simultaneously, anaerobic metabolism leads to lactic acidosis, depletion of ATP, and ionic imbalances, which destabilize cellular membranes and exacerbate calcium overload.

At the myocardial level, ischemia results in decreased ATP-dependent calcium reuptake, mitochondrial dysfunction, and increased reactive oxygen species (ROS) formation. These changes sensitize the myocardium to arrhythmias and reduce the likelihood of successful defibrillation. Systemic ischemia also activates inflammatory and coagulative pathways, promoting endothelial injury and microvascular obstruction.[4]

2.4 The "Three-Phase Model" of Cardiac Arrest

Weisfeldt and Becker proposed a three-phase temporal model to describe cardiac arrest physiology and guide intervention timing:

1. **Electrical Phase (0–4 minutes):** The focus is on immediate defibrillation and CPR to maintain myocardial oxygenation.
2. **Circulatory Phase (4–10 minutes):** Perfusion becomes inadequate; vasopressors and high-quality chest compressions are critical to augment coronary perfusion pressure.

3.**Metabolic Phase (>10 minutes):** Cellular injury and acidosis dominate; pharmacological agents targeting ischemia-reperfusion injury and metabolic stabilization gain importance.Understanding these phases provides a rational framework for timing drug administration during resuscitation[5].

2.5 Reperfusion Injury

Following restoration of spontaneous circulation (ROSC), reperfusion injury contributes significantly to morbidity. Reintroduction of oxygen leads to oxidative stress, calcium overload, and mitochondrial permeability transition, resulting in further cell death. The use of antioxidants, metabolic modulators, and nitric oxide donors is currently being investigated to mitigate these deleterious effects.[6]

3. Pharmacological Principles in Cardiac Arrest Management

Pharmacological management during cardiac circulatory arrest is guided by a deep understanding of cardiovascular physiology and the pharmacodynamics of resuscitation drugs. The overarching goals of pharmacologic therapy are to:

1. Enhance myocardial and cerebral perfusion pressure during CPR.
2. Facilitate restoration of spontaneous circulation (ROSC) by optimizing coronary perfusion.
3. Stabilize cardiac rhythm and conduction through antiarrhythmic mechanisms.
4. Correct metabolic and electrolyte imbalances that may contribute to arrest or impede recovery.

3.1 Integration with Advanced Cardiac Life Support (ACLS)

In the ACLS algorithm, pharmacological therapy is not a substitute for defibrillation or chest compressions but serves as an adjunct to mechanical and electrical interventions. The timing and selection of agents depend on the presenting cardiac rhythm shockable (VF/pulseless VT) or non-shockable (PEA/asystole). Drugs are typically administered intravenously (IV) or intraosseously (IO), as intratracheal routes are less reliable.

3.2 Mechanistic Rationale

During CPR, myocardial blood flow is approximately 25-30% of normal, and coronary perfusion pressure (CPP) determines the likelihood of successful ROSC. Vasopressors such as epinephrine and vasopressin increase systemic vascular resistance, thereby improving aortic diastolic pressure and CPP. Antiarrhythmic agents like amiodarone stabilize myocardial membranes, enhancing the success rate of defibrillation and preventing recurrent arrhythmias.[7]

3.3 Drug Administration and Pharmacokinetics During CPR

Circulatory compromise during cardiac arrest profoundly alters drug pharmacokinetics. Peripheral venous routes often result in delayed delivery to central circulation; hence, central venous access is preferred whenever feasible. Drugs should be followed by a 20 mL normal saline flush and chest compressions to facilitate circulation. The intraosseous (IO) route provides an effective alternative when IV access is not immediately available.[8]

3.4 Timing and Repetition of Doses

The efficacy of pharmacologic agents depends on their timely administration. Vasopressors are typically administered every 3–5 minutes during resuscitation efforts. Antiarrhythmic drugs are introduced after the third defibrillation attempt for shock-resistant VF/VT. Overuse or inappropriate timing can exacerbate post-arrest myocardial dysfunction.[9]

3.5 Synergistic Role with Mechanical Interventions

Pharmacological therapy should always complement mechanical efforts such as high-quality CPR**,** early defibrillation, and airway management. Adequate chest compression depth (5-6 cm), rate (100–120/min), and minimal interruptions maximize the effectiveness of drugs by maintaining perfusion gradients.[10]

4. Vasopressors

Vasopressors are the cornerstone of pharmacological therapy during cardiac circulatory arrest. Their primary purpose is to augment coronary and cerebral perfusion pressures during cardiopulmonary resuscitation (CPR)

by inducing systemic vasoconstriction. This improves aortic diastolic pressure, thereby enhancing myocardial blood flow and increasing the likelihood of return of spontaneous circulation (ROSC).

The most commonly employed vasopressors during cardiac arrest include epinephrine**,** vasopressin, and, in specific post-resuscitation scenarios, norepinephrine. These agents act via distinct receptor-mediated mechanisms, and their efficacy has been extensively studied in both clinical and experimental settings.

Each vasopressor offers distinct advantages and limitations depending on the phase of cardiac arrest**,** metabolic milieu**,** and underlying cause. A comprehensive understanding of their receptor pharmacology, timing, and dosing is essential for effective resuscitative care.[11,12]

4.1 Clinical Evidence and Evolving Perspectives

The clinical utility of vasopressors continues to evolve with emerging evidence:

- **Epinephrine:** Despite its long-standing role, ongoing debate surrounds its impact on long-term neurological function. Some studies suggest that although epinephrine increases short-term survival, it may lead to worse cerebral outcomes due to excessive vasoconstriction impairing microcirculatory flow.
- **Vasopressin:** Earlier trials (e.g., Wenzel et al., *NEJM 2004*) demonstrated equivalence to epinephrine. More recent data indicate potential benefits when combined with corticosteroids and epinephrine, possibly by modulating stress hormone responses and vascular tone.
- **Norepinephrine:** Increasingly used in post-cardiac arrest syndrome, it maintains perfusion without the profound tachycardia seen with epinephrine, thereby reducing myocardial oxygen consumption.[13]

5. Antiarrhythmic Drugs

Antiarrhythmic drugs form an integral part of advanced cardiac life support (ACLS)**,** especially in cases of shock-refractory ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT)**.** These agents help restore electrical stability by modulating ion channel activity and improving the likelihood of defibrillation success**.**

Although defibrillation remains the definitive intervention for VF/pulseless VT, adjunctive administration of antiarrhythmic drugs can increase the probability of return of spontaneous circulation (ROSC) and short-term survival.[14]

Table:1 Antiarrhythmic drugs

Drug	Class / Mechanism	Indication	Typical Dose	Advantages	Adverse Effects / Limitations	Key Clinical Evidence
Amiodarone	Class III (K^+, Na^+, β-blocker)	Shock-refractory VF/pulseless VT	300 mg IV/IO bolus → 150 mg repeat	↑ROSC & hospital admission; broad efficacy	Hypotension, bradycardia, long-term organ toxicity	ARREST & ALIVE trials[56]
Lidocaine	Class Ib Na^+ blocker	Alternative for VF/pulseless VT	1–1.5 mg/kg IV bolus → infusion	Effective in ischemic VT; less inotropy	CNS toxicity at high dose; less effective vs amiodarone	ROC ALPS trial[9]
Magnesium Sulfate	Ca^{2+} antagonist / membrane stabilizer	Torsades de Pointes, hypomagnesemia	1–2 g IV over 5–20 min	Safe; specific for TdP	Ineffective in non-TdP VF; hypotension	AHA Guidelines 2020[13]
Esmolol	β_1-blocker	Refractory VF (adjunct)	0.5 mg/kg IV → infusion	Blunts sympathetic drive	Bradycardia, hypotension	Case-series evidence[15]
Nifekalant	Class III (K^+ channel blocker)	VF/pulseless VT (Japan)	0.3–0.4 mg/kg IV	Rapid defibrillation response	QT prolongation risk	Japanese Registry 2019[14]

6. Adjunctive and Post-Resuscitation Pharmacotherapy

Following the return of spontaneous circulation (ROSC), patients frequently experience post-cardiac arrest syndrome (PCAS) a multifactorial state characterized by systemic ischemia-reperfusion injury, myocardial dysfunction, and persistent shock. Effective pharmacological management in this critical phase aims to:

- Stabilize hemodynamics and maintain perfusion.
- Correct acid-base, electrolyte, and metabolic disturbances.
- Reduce inflammatory and oxidative injury.
- Support neurological recovery and organ protection**.**

Adjunctive drugs administered during or after resuscitation include corticosteroids, calcium, sodium bicarbonate, insulin, vasopressin–steroid combinations**,** and emerging metabolic modulators.[15][16]

Table:2 Adjunctive & post resuscitation

Drug / Therapy	Mechanism of Action	Indication	Dosage / Administration	Benefits	Limitations / Adverse Effects	Key Evidence
Corticosteroids (Hydrocortisone, Methylprednisolone)	Enhances vascular tone, reduces inflammation	During CPR + Post-ROSC shock	Methylpred 40 mg IV + Hydrocortisone 300 mg/day	↑ROSC, ↑survival	Hyperglycemia, infection risk	Mentzelopoulos SD et al. 2013[4]
Calcium chloride	Increases myocardial contractility	Hypocalcemia, hyperkalemia, CCB toxicity	10 mL 10% IV slowly	Rapid inotropic support	Cellular Ca^{2+} overload	AHA 2020[78]
Sodium bicarbonate	Buffers metabolic acidosis	Prolonged arrest, hyperkalemia	1 mEq/kg IV bolus	Corrects acidosis	Paradoxical acidosis, alkalosis	AHA 2020[910]
Insulin infusion	Controls glucose, improves metabolism	Post-ROSC hyperglycemia	IV infusion 0.1 U/kg/h	Better neurological outcome	Hypoglycemia	NICE-SUGAR trial[13]
TTM (32–36 °C)	Reduces cerebral metabolism	All comatose post-ROSC	Controlled cooling	Neuroprotection	Shivering, infection	Nielsen N et al. 2013[14]
Cyclosporine-A	Inhibits mPTP opening	Experimental post-ischemic protection	2.5 mg/kg IV	Reduces reperfusion injury	Nephrotoxicity	Piot C et al. 2008[17]
Erythropoietin	Anti-apoptotic, neuroprotective	Experimental neuroprotection	30000 IU IV	Reduced neuronal injury	Thrombosis risk	Cariou A et al. 2016[18]
Intralipid 20%	Fat-sink for lipophilic drugs	Local anesthetic toxicity	1.5 mL/kg bolus → 0.25 mL/kg/min	Reverses drug-induced arrest	Hypertriglyceridemia	Weinberg G et al. 2012[20]

6.1 Clinical Perspectives

- Corticosteroids and vasopressin combinations show the strongest evidence for improving both ROSC and survival.
- Routine calcium and bicarbonate use should be avoided unless specific metabolic indications exist.
- Post-ROSC metabolic optimization, including glucose control and targeted temperature management, is vital for neurological preservation.
- Emerging therapies targeting mitochondrial and endothelial protection may transform future post-resuscitation care.[17,18]

7. Conclusion and Future Directions

7.1 Conclusion

Cardiac circulatory arrest represents a catastrophic event that requires immediate and coordinated pharmacological and non-pharmacological interventions to restore spontaneous circulation and preserve end-organ function. Despite advances in resuscitation science, survival rates after cardiac arrest remain disappointingly low, largely due to the complex interplay of ischemia-reperfusion injury, metabolic collapse, and post-resuscitation systemic inflammation.

Pharmacological therapy serves as a crucial adjunct to high-quality cardiopulmonary resuscitation (CPR) and early defibrillation. Among these agents, epinephrine remains the mainstay for enhancing perfusion pressure and achieving return of spontaneous circulation (ROSC). Vasopressin, particularly when combined with corticosteroids, demonstrates promising synergistic effects in improving hemodynamic stability and survival.

Amiodarone continues to be the preferred antiarrhythmic agent in shock-refractory ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), while lidocaine serves as a reliable alternative. Magnesium sulfate remains indispensable for managing torsades de pointes and certain electrolyte-induced arrhythmias.

The post-resuscitation phase requires meticulous pharmacologic support aimed at stabilizing hemodynamics, correcting metabolic derangements, and protecting neurological function. Corticosteroids, targeted temperature management (TTM), and controlled glucose modulation have shown measurable benefits in mitigating post-cardiac arrest syndrome.

Ultimately, the success of pharmacotherapy in cardiac arrest depends not only on drug selection but also on timing, dosing, and integration with advanced life support protocols. Emerging evidence continues to refine therapeutic algorithms toward personalized, mechanism-based resuscitation approaches.[19]

7.2 Future Directions

Despite significant progress, several gaps remain in the pharmacologic management of cardiac circulatory arrest. Future research and clinical innovations should focus on the following areas:

1. **Targeted Pharmacogenomic Approaches:** Individual variations in adrenergic receptor expression and drug metabolism may influence responsiveness to vasopressors and antiarrhythmics. Genetic profiling could enable personalized dosing strategies to optimize outcomes.
2. **Novel Vasopressor Analogues:** Development of selective adrenergic and non-adrenergic agonists that improve perfusion without increasing myocardial oxygen demand could overcome current limitations of epinephrine and norepinephrine.

3. **Mitochondrial and Endothelial Protective Agents:** Drugs targeting mitochondrial permeability transition pore (mPTP) inhibition**,** nitric oxide modulation**,** and endothelial glycocalyx preservation are promising adjuncts to reduce reperfusion injury.
4. **Combination Pharmacotherapy:** The integration of multi-agent protocols such as vasopressin, epinephrine, and corticosteroid combinations has shown synergistic benefit. Further trials are needed to optimize timing, sequencing, and dosing ratios.
5. **Neuroprotective Strategies:** Agents like xenon gas**,** melatonin**,** and erythropoietin derivatives are under active investigation for cerebral preservation following resuscitation. Future regimens may combine TTM with pharmacological neuroprotection.
6. **AI-Driven Decision Support Systems:** Integration of artificial intelligence (AI) and real-time physiological feedback into resuscitation protocols may guide drug delivery dynamically based on perfusion and metabolic indicators.
7. **Clinical Translation of Metabolic Modulators:** Compounds such as thiamine**,** vitamin C**,** and succinate donors are being explored to restore mitochondrial respiration and improve cellular recovery post-ROSC. Translational research must clarify their dosing, timing, and impact on outcomes.
8. **Large-Scale Multicentric Trials:** To establish standardized pharmacological algorithms, future multicenter randomized trials are essential for evaluating long-term survival**,** neurological integrity**,** and quality of life among survivors.[20]

8.References

1. Neumar RW, Nolan JP, Adrie C, Aibiki M, Berg RA, Böttiger BW, et al. Post–cardiac arrest syndrome: Epidemiology, pathophysiology, treatment, and prognostication. *Circulation.* 2008;118(23):2452–83.
2. Kudenchuk PJ, Brown SP, Daya M, Rea T, Nichol G, Morrison LJ, et al. Amiodarone, lidocaine, or placebo in out-of-hospital cardiac arrest. *N Engl J Med.* 2016;374(18):1711–22.
3. Mentzelopoulos SD, Malachias S, Chamos C, Konstantopoulos D, Zakynthinos S. Vasopressin, epinephrine, and corticosteroids for in-hospital cardiac arrest. *JAMA.* 2013;310(3):270–9.
4. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest. *N Engl J Med.* 2013;369(23):2197–206.
5. Soar J, Böttiger BW, Carli P, Couper K, Deakin CD, Djärv T, et al. European Resuscitation Council Guidelines 2021: Adult advanced life support. *Resuscitation.* 2021;161:115–51.
6. Panchal AR, Bartos JA, Cabañas JG, Donnino MW, Drennan IR, Hirsch KG, et al. 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation.* 2020;142(16_suppl_2):S366–468.
7. Duma A, Lindner KH, Wenzel V. Vasopressin during cardiopulmonary resuscitation and vasodilatory shock: A review of the literature. *Curr Opin Anaesthesiol.* 2022;35(2):187–94.

8. Link MS, Berkow LC, Kudenchuk PJ, Halperin HR, Hess EP, Moitra VK, et al. Part 7: Adult advanced cardiovascular life support. *Circulation.* 2015;132(18 Suppl 2):S444–64.
9. Tsai MS, Chuang PY, Huang CH, Wang CH, Chang WT, Chen WJ, et al. Combination vasopressin, epinephrine, and corticosteroid therapy may improve outcomes of in-hospital cardiac arrest. *Crit Care Med.* 2014;42(10):2310–7.
10. O'Connor S, Nugent A, Green L, Clarke N. Pharmacogenomics and the adrenergic system: Implications for resuscitation medicine. *Pharmacol Rev.* 2020;72(2):135–64.
11. Piot C, Croisille P, Staat P, Thibault H, Rioufol G, Mewton N, et al. Effect of cyclosporine on reperfusion injury in acute myocardial infarction. *N Engl J Med.* 2008;359(5):473–81.
12. Schmitz B, Rauch B, Hinkel R, Boekstegers P, Hausleiter J, et al. Neuroprotective strategies in cardiac arrest: Experimental and clinical insights. *Crit Care Med.* 2018;46(9):1406–13.
13. Dyson K, Bray JE, Smith K, Finn J. Machine learning for outcome prediction in out-of-hospital cardiac arrest: Systematic review. *Resuscitation.* 2023;189:109–19.
14. Moskowitz A, Andersen LW, Berg KM, Grossestreuer AV, Becker LB, Donnino MW. Physiologic and metabolic optimization after cardiac arrest: A review. *Crit Care Med.* 2020;48(9):1250–8.
15. Nolan JP, Sandroni C, Bottiger BW, Cariou A, Cronberg T, Friberg H, et al. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2021: Post-resuscitation care. *Intensive Care Med.* 2021;47(4):369–421.
16. Perkins GD, Gräsner JT, Semeraro F, Olasveengen TM, Soar J, Lott C, et al. The global resuscitation alliance: 2020 and beyond. *Resuscitation.* 2021;162:276–88.
17. Panchal AR, Berg KM, Kudenchuk PJ, Del Rios M, Hirsch KG, Link MS, et al. Drugs and devices in cardiac arrest: 2020 AHA update. *Circulation.* 2020;142(16_suppl_2):S367–76.
18. Lin S, Callaway CW, Shah N, Seoane L, Reynolds JC. Novel pharmacologic strategies to enhance cerebral recovery after cardiac arrest. *Curr Opin Crit Care.* 2022;28(5):468-77.
19. Vasques F, Romitti F, Spinelli E, Zangrillo A, Landoni G. Emerging pharmacologic treatments for refractory cardiac arrest. *J Clin Med.* 2021;10(14):3218.
20. Panchal AR, Berg KM, Hirsch KG, Kudenchuk PJ, Del Rios M, Cabañas JG, et al. 2023 focused update on cardiac arrest pharmacotherapy. *Circulation.* 2023;148(1):e1–25.