Special Populations: Cardiac Arrest

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Introduction

Cardiac arrest (CA) is unlike any other medical condition. Patients presenting in the absence of native cardiac function, by definition, have minimal perfusion to vital organs without any assurances of return of spontaneous circulation (ROSC). The role of the emergent vascular access provider in treating this condition is therefore to *establish vascular access for the purpose of introducing medications into the circulation that will stimulate the resumption of native cardiac activity while supporting continued organ perfusion*. Timing is key for this intervention. Delayed administration of the necessary medications and fluids required for adequate organ perfusion will likely lead to worse outcomes for these patients. This chapter will address some of the common obstacles that prevent emergent vascular access in patients experiencing cardiac arrest, including solutions to these obstacles. Providers should prioritize the rapid establishment of a vascular access device (VAD) for these patients, *assuming that early access is always preferred to delayed or deferred access*. Providers should recognize that delays in obtaining vascular access for patients experiencing cardiac arrest directly contributes to increased mortality and morbidity for these patients.

Cardiac arrest can affect patients of any age, race, gender, or ethnicity, in any location, and at any time. As reported by the American Heart Association (AHA) Advanced Cardiovascular Life Support (ACLS) guidelines, approximately 356,000 incidences of out-of-hospital cardiac arrest (OHCA) were reported in the United

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States in 2018, with only about 10.4% of these patients surviving to hospital discharge [1]. The likelihood of permanent brain and other irreversible organ damage increases with extended duration of reduced organ perfusion following cardiac arrest. Therefore, decreasing the time between onset of cardiac arrest and the initiation of external chest compressions is essential to the appropriate management of cardiac arrest. A high priority is also placed on obtaining immediate vascular access, as the prompt administration of vasopressors and other medications following OHCA appears to improve patient survival when compared to chest compressions alone [1–3].

Pathophysiology of Cardiac Arrest

The heart is the central organ of blood flow. Its primary function is to circulate blood throughout the body. Blood is collected through the venous system and deposited in the right atrium and then into the right ventricle, where it is pushed through the lungs, where oxygenation of the blood occurs. In the lungs, carbon dioxide is removed and oxygen is bound. Oxygenated blood is then deposited in the left atrium before traveling to the left ventricle, where it is pumped into the arterial system to provide oxygenation to the body's tissues. This pumping action is essential to survival. During cardiac arrest, the heart stops effectively pumping oxygenated blood, which leads to hypoxemia as vital organs are deprived of oxygenated blood flow. Oxygen deprivation leads to injury to the brain, kidneys, heart, and other vital organs.

As depicted in Fig. 9.1, patients may have regular, organized cardiac rhythm prior to the precipitating event (e.g., acute myocardial infarction or acute respiratory arrest) that leads to cardiac arrest. However, following this precipitating event, most patients will experience a predictable stage-wise decompensation in cardiac function, progressing from an organized dysrhythmia (e.g., ventricular tachycardia, or VT) into a disorganized rhythm (e.g., ventricular fibrillation, or VF). Once the dysrhythmia has adequately disrupted the heart's ability to contract in an organized fashion, the patient's pulse will begin to disappear. By the time that the patient is experiencing ventricular fibrillation, the pulse is typically absent. However, the pulse can already be absent in the VT phase, and this is referred to as pulseless

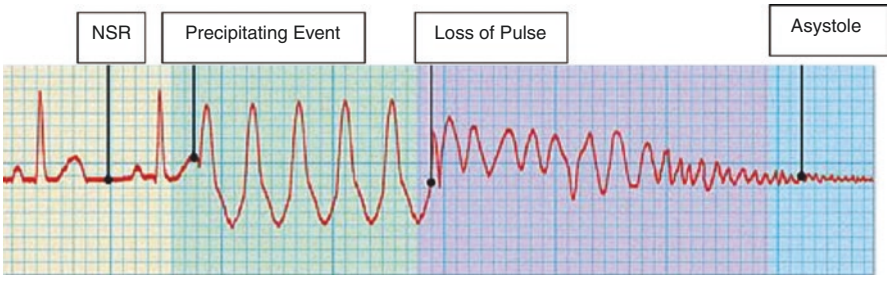

Fig. 9.1 Progression of life-threatening dysrhythmias following cardiac arrest

ventricular tachycardia (pVT). Patients who have pVT/VF are generally very responsive to electrical defibrillation, so these rhythms are categorized as "shockable rhythms." Patients who present with a shockable rhythm as their initial cardiac rhythm will generally have a better prognosis than patients who present with a non-shockable rhythm (e.g., asystole or other pulseless rhythms) [4]. A table of the shockable and non-shockable cardiac rhythms is presented in Fig. 9.2.

Torsades de pointes (TdP) is a specific type of polymorphic ventricular tachycardia seen in patients with a long QT interval. This phrase translates from the French as, "twisting of the points." It is characterized by rapid, irregular QRS complexes, which appear to be twisting around the electrocardiogram (ECG) baseline, as shown in Fig. 9.3. This specific form of VT may respond favorably to magnesium sulfate infusion, which is why it is important that the emergency care provider recognize it.

The *presence or absence of a palpable pulse* is the most important finding in the management of OHCA patients. The absence of a pulse mandates immediate recognition and action, as does the return of a pulse when management is ultimately successful. It should be noted that the "pulse" referenced here is a detectable arterial pulse using the provider's hands. Thus, patients may be experiencing some degree of organized cardiac contraction (e.g., cardiac activity on ultrasound) even when a pulse is absent. Similarly, the patient may have a normal sinus rhythm (NSR) or other organized cardiac rhythms without a pulse – this is called pulseless electrical activity (PEA). Although PEA is often portrayed as a pulseless sinus rhythm, it can be any non-shockable rhythm. All non-shockable pulseless rhythms are treated the same, unless there is evidence of organized cardiac contraction or forward flow on ultrasound imaging.

Although cardiopulmonary resuscitation (CPR) has been the subject of aggressive research since the 1950s, modern resuscitation theory is largely built upon the "three-phase" model introduced by Weisfeldt in 2002 [5]. This model for our understanding of the pathophysiology of cardiac arrest begins at ventricular fibrillation

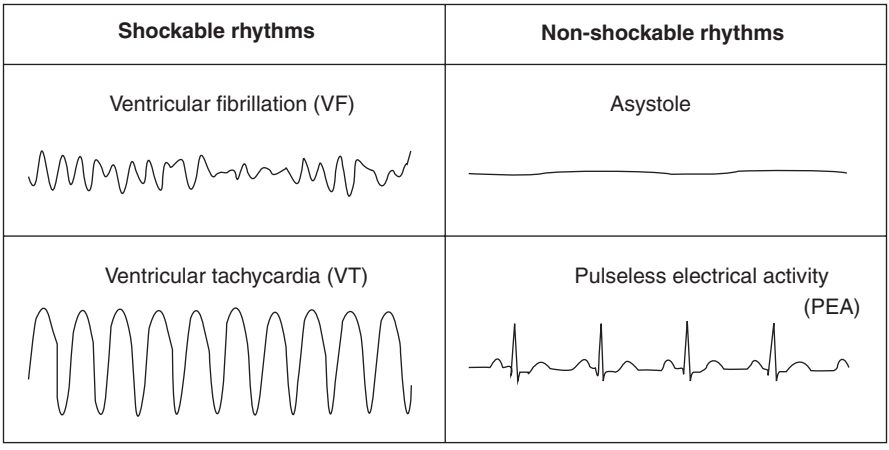

Fig. 9.2 Shockable and non-shockable cardiac rhythms associated with cardiac arrest

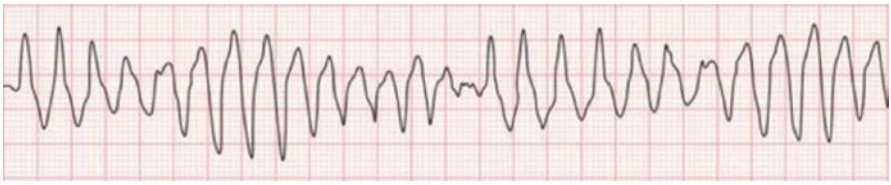

Fig. 9.3 *Torsades de pointes* (polymorphic VT) waveform

(VF) and pulseless ventricular tachycardia (pVT), soon followed by three discrete time periods or phases following the moment of cardiac arrest (i.e., when systemic perfusion is lost). The "electrical" *phase* begins at the precise moment of cardiac arrest and lasts about 5 minutes [5]. During this initial phase, immediate electrical defibrillation should be the priority for emergency providers, and survival appears to be very good (about 60%) for patients in this phase who are treated promptly with defibrillation. Those patients who are not adequately defibrillated within the first 5 minutes following cardiac arrest will progress to the "circulatory" *phase*, which appears to begin 5–10 minutes after the onset of VF. Patients who present during this second phase will require a brief period (e.g., 1–3 minutes) of aggressive chest compression to restore circulation prior to defibrillation attempts. In this phase, the blood remains adequately oxygenated with a tolerable acid-base balance, permitting stabilization of the myocardium with restoration of blood flow to the coronary arteries through chest compressions alone. Unfortunately, very few cardiac arrest patients present to the emergency provider within 10–15 minutes following the onset of cardiac arrest. Consequently, most patients who present to the emergency department have already entered the third phase, the so-called "metabolic" phase, before receiving any specific intervention. Patients in the metabolic phase of cardiac arrest may require drug administration to restore homeostasis, especially correction of metabolic acidosis (with sodium bicarbonate) and other pharmacologic measures, including epinephrine infusion, to restore homeostasis. Chest compressions and electrical defibrillation alone cannot restore native cardiac function for patients presenting in the metabolic phase. These patients invariably appear to require vascular access for the infusion of medications to restore biochemical homeostasis before traditional measures can succeed. Unfortunately, the vast majority of patients treated for cardiac arrest are first encountered by medical providers in the metabolic phase. In this phase, vascular access is an even higher priority, since these patients are unlikely to survive without the administration of resuscitative medications.

Weisfeldt's three-phase model helps to explain why patients presenting to the emergency care provider with an initially shockable rhythm have a three times higher survival rate (37%) than patients presenting with asystole or PEA (12%) [4]. This differential is likely due to the fact that patients presenting with VT/VF are in an earlier phase of their disease process. Unfortunately, delayed reperfusion following ischemic injury leads to metabolic acidosis and a higher concentration of pro-inflammatory mediators, which will prevent epinephrine and other cardioactive/

vasoactive medications from working. In vitro studies with myocardial cells suggest that delayed reperfusion worsens outcomes [6, 7]. Thus, the timing of vascular access and medication infusion are paramount to patient survival, as most patients presenting to emergency care providers have already progressed to the metabolic phase of injury. Minutes wasted by failed vascular access attempts readily translate to decreased survival for cardiac arrest patients.

In the 1970s, approximately 60% of all OHCA patients treated in the United States presented with VF/VT, but this proportion has declined to only 25–30% over the last few decades [8]. The cause of this change is unclear and may be due to reporting bias or to later (i.e., more advanced) presentations for out-of-hospital cardiac arrest patients. Whatever the cause, almost three-fourths of OHCA patients receiving care in the United States today present with asystole or PEA (e.g., non-shockable rhythms) as the initial documented cardiac rhythm. Since these patients are presenting in the metabolic phase of cardiac arrest, these patients will not respond favorably to defibrillation and chest compressions alone. Patients with OHCA require immediate intervention (including the infusion of medications) to stabilize their condition, and their likelihood of survival decreases with increasing delay from time of arrest to time of first intervention. Assuming that present trends continue, we suggest that emergent vascular access will play an increasingly important role in the care of OHCA patients into the future.

Many other outcomes are important in the setting of cardiac arrest, beyond mere survival. It has been well-established that OHCA patients have a very low rate of survival-to-hospital discharge. Only about 30% of subjects presenting with VT/VF survive to hospital discharge, and this percentage is much lower for those presenting in PEA or asystole (e.g., 2–5%) [8]. Although it has recently been suggested that epinephrine infusion may not improve survival to hospital discharge following OHCA [9], there seems to be consensus within the medical literature that some medications are needed to supplement the effects of high-quality CPR and early defibrillation, even if the optimal medications and doses are not yet understood. Even if epinephrine is ultimately demonstrated to not be the optimal resuscitative medication, it is still likely that most patients presenting to the emergency care provider during the metabolic phase of cardiac arrest will still require some medication or fluid to aid in the restoration of metabolic homeostasis. As more effective medications are discovered to treat cardiac arrest, immediate vascular access will undoubtedly remain an essential requirement for patient survival [10].

In 1991, the AHA introduced the "Chain of Survival" model, meant to guide the effective and efficient treatment of cardiac arrest [11]. This model was originally intended for use by emergency medical services (EMS) but has subsequently been adapted to apply to all healthcare providers who treat cardiac arrest patients. The Chain of Survival includes five time-sensitive and co-dependent factors, including early vascular access, early CPR, early defibrillation, early ACLS, and early post-resuscitative care, as described in Table 9.1.

The first goal of ACLS intervention is to restore native cardiac function, generally referred to as return of spontaneous circulation (ROSC). The *achievement of ROSC*

Table 9.1 The American Heart Association (AHA) "Chain of Survival" [11]

Early access	All pre-EMS arrival efforts of care. This includes identifying the event as "sudden cardiac death" (SCD) and initiating emergency medical protocols
Early CPR	Initiation of immediate cardiopulmonary resuscitation
Early defibrillation	Electrical shock to restore spontaneous heart rhythm (if the patient presents with a "shockable rhythm")
Early ACLS	Drug therapies and airway management intended to achieve spontaneous heart rhythm
Early post-resuscitative care	To restore and conserve cognitive function and prevent secondary organ damage

may be considered to be an essential first step toward restoring homeostasis and organ perfusion. However, ROSC can be short-lived, especially if the underlying cause of the cardiac arrest is not adequately corrected. Therefore, transient ROSC may not necessarily be associated with improved survival or other important clinical outcomes. While minimal organ perfusion may be provided with external chest compressions, patients cannot survive without eventually realizing ROSC. It is imperative that organ perfusion be restored as soon as possible following cardiac arrest, and perfusion to the vital organs must be maintained to prevent necrotic tissue damage.

As transient ROSC appears to have limited clinical value, sustained ROSC should be the provider's initial goal during the earliest stages of OHCA resuscitation. We suggest that *sustained ROSC* (commonly defined as lasting >20 minutes) represents a more clinically relevant outcome for cardiac arrest patients than transient ROSC. Consequently, any intervention that is associated with sustained ROSC should be valued above interventions that produce a more transient ROSC. While interventions associated with sustained ROSC may not ultimately be associated with improved survival-to-hospital discharge, achievement of sustained ROSC is at least a marker that should be considered evidence of improved outcome as compared to unsustained ROSC. Clearly, *survival-to-hospital discharge with good neurological outcome* is the gold standard for a favorable cardiac arrest outcome. However, this outcome depends upon myriad factors beyond the control of the vascular access provider, including decisions about goals of care and withdrawal of care that may be made days or weeks after successful ROSC. We suggest that the emergency vascular access provider should prioritize the realization of sustained ROSC above other outcomes in the emergent setting, understanding that this outcome does not necessarily translate to improved long-term survival.

Consequently, we suggest that *the goal of the emergency vascular access provider should be to provide emergent vascular access leading to sustained ROSC for out-of-hospital cardiac arrest patients*, understanding that more ambitious outcomes may be, at least in part, dependent upon subsequent management by the inpatient team. Restoring native cardiac function appears to be an essential first step toward enabling survival-to-hospital discharge with good neurologic function. Unfortunately, whether this gold standard outcome is actually realized relies upon many decisions and events that extend well beyond the scope of the frontline vascular access provider.

Medications in Cardiac Arrest

Understanding that early medication administration is not guaranteed to elicit improved outcomes for patients, responsibility for establishing the earliest possible vascular access should remain a priority for emergency care providers treating patients in cardiac arrest. Many routes for possible medication infusion are available to the emergency care provider, and these will be discussed in later portions of this chapter. In this section, we will discuss the potential roles of various medications currently recommended by the AHA for the restoration of metabolic homeostasis following cardiac arrest. These medications include *epinephrine*, *amiodarone*, *lidocaine*, *magnesium sulfate*, and *sodium bicarbonate* and are listed in Table 9.2. Current ACLS recommendations do not require dosing adjustment according to route of administration, and all of these medications can be given by the intraosseous (IO), peripheral intravenous (PIV), or central venous catheter (CVC) routes.

Table 9.2 Medications recommended by Advanced Cardiac Life Support (ACLS) guidelines for the management of OHCA [12, 13]

Drug	Indication	Drug class	Mechanism	Dosing
Epinephrine	Pulseless arrest	α-adrenergic agonist	Vasoconstriction (increases venous return and preload)	1 mg every 3–5 minutes
Vasopressin	Pulseless arrest	Non-adrenergic vasoconstrictor	Vasoconstriction (increases venous return and preload)	40 units to *replace* the first or second dose of epinephrine, one time only
Amiodarone	Refractory or recurrent lethal arrhythmia	Non-selective cation blocker (Class III-A recommendation)	Sodium, potassium, and calcium channel antagonism (anti-arrhythmic properties)	300 mg bolus followed by 150 mg 3–5 minutes later
Lidocaine	Refractory or recurrent lethal arrhythmia	Anti-arrhythmic (Class II-B recommendation)	Sodium channel blocker (anti-arrhythmic properties)	1–1.5 mg/kg (increase dosage by 0.5 mg/kg in 5-minute intervals until a max dose of 3 mg/kg is reached)
Magnesium sulfate	Hypomagnesemia or *torsade de pointes* cardiac arrest	Electrolyte supplementation/ anti-arrhythmic (Class II-B recommendation)	Sodium and potassium transport co-factor (anti-arrhythmic properties)	1–2 gm bolus diluted via 10 mL D_5W
Sodium bicarbonate	Metabolic acidosis	Alkalizing agent (Class III recommendation)	Increases blood pH (reduces acidosis)	1 mEq/kg

Generally, resuscitation drugs should be delivered within the first 10 seconds of a new round of CPR [12, 13]. Due to reduced cardiac output and the inefficiency of venous return during cardiac arrest, resuscitative medications may require up to 90–120 seconds to reach central circulation, depending upon the route of administration.

Epinephrine (Adrenaline)

The early administration of epinephrine for the treatment of cardiac arrest has been shown to increase the likelihood of achieving ROSC, although it may not lead to improved 30-day outcomes [14]. Nonetheless, epinephrine is currently recommended as a first-line medication to stimulate ROSC in patients presenting with a non-shockable rhythm (Class 1 recommendation) in the most recent AHA guidelines update [13]. Despite widespread adoption of the use of epinephrine to treat cardiac arrest, the dosing, timing, and frequency of epinephrine administration for cardiac arrest remain controversial. Although high-dose (e.g., 5–10 mg) bolus doses of epinephrine have been recommended in the past, the current recommendation is for epinephrine to be provided in aliquots of 1 mg every 3–5 minutes [13].

There is evidence in a canine model that subsequent doses of epinephrine exert a lessening effect on myocardial contractility without diminishing the drug's effect on arterial blood pressure. This phenomenon is termed "differential tachyphylaxis" and may have implications for the use of epinephrine in the treatment of cardiac arrest [15]. The potential benefit of epinephrine infusion appears to be integrally linked to the timing of its administration. In a rat model, one study showed that 100% of subjects survived if CPR was initiated within 2 minutes of cardiac arrest, regardless of the use of epinephrine. However, when CPR was 6 minutes after cardiac arrest, only 32% of subjects achieved ROSC with compressions alone, while 81% of subjects receiving epinephrine achieved ROSC [16].

While epinephrine use does appear to increase the rate of ROSC in cardiac arrest patients presenting with unshockable rhythms, this benefit may not universally translate to improved survival-to-hospital discharge, favorable neurologic outcomes, or other desirable outcomes. In 1998, the OTAC Study Group reported an association between the use of epinephrine and increased mortality for in-hospital cardiac arrest (IHCA) patients, although this study excluded anyone who presented more than 15 minutes after the onset of cardiac arrest, and the mean time from onset of CPR to first dose of epinephrine was more than 5 minutes (5.14 ± 6.9 min) even in those who survived to 1 hour [17]. In fact, the authors found similar poor outcomes for all of the other studied ACLS drugs (i.e., atropine, bicarbonate, calcium, lidocaine, bretylium) [17]. It seems unlikely that these results can be directly translated to an out-of-hospital cardiac arrest population, especially when the "down time" (i.e., time from the onset of cardiac arrest to the initiation of chest compressions and other interventions) is unknown.

Results from the PARAMEDIC-2 trial suggest that the use of epinephrine in OHCA patients leads to improved ROSC and 30-day survival (when compared to

placebo) but is not associated with improved survival with favorable neurologic outcomes, since more survivors from the epinephrine group in this study experienced severe neurologic impairment [3]. Thus, it seems that epinephrine has a time-dependent effect, with little benefit seen in the first few minutes following cardiac arrest, followed by a period of unknown duration in which it may increase the likelihood of ROSC but may not offer long-term survival benefit or increase the likelihood of survival with a favorable neurologic outcome. It remains to be discovered whether the unfavorable outcomes associated with the use of epinephrine in OHCA are related to uncorrectable ischemic injuries or, perhaps more likely, are due to inadequacies in current post-cardiac arrest management.

While the importance of epinephrine infusion to realization of ROSC appears to be increased with prolonged durations of cardiac arrest, a paradoxical myocardial epinephrine response also appears to exist, with epinephrine infusion given later in the treatment of OHCA also contributing to greater post-ROSC myocardial suppression [16].

In his original investigation of the IO route for epinephrine administration in animal models, Macht noted that aqueous solutions of epinephrine were absorbed just as quickly via IO as PIV routes. Effects on heart rate and blood pressure were also similar in duration. However, suspensions of epinephrine in oil showed a significantly longer duration of pressor effect. He speculated that these oil emulsions remained in the marrow for a long time and "act as reservoirs for a drug that is slowly liberated and dispensed by the oil." [18]

Spivey and colleagues [19] observed that IO epinephrine at standard IV doses (0.01 mg/ kg) had no significant effect on diastolic or mean blood pressure in an anaesthetized swine model. Higher doses (0.1 mg/kg) produced a more pronounced effect on blood pressure. One recent study showed that early IO epinephrine leads to better neurological outcomes than delayed IV epinephrine in a swine model of prolonged ventricular fibrillation [20].

Although studies in human subjects are lacking, animal models have been developed which appear to suggest a difference in the timing and maximum concentration of epinephrine realizable from PIV versus IO infusion of epinephrine. While no difference has been shown between the appearance of epinephrine administered via sternal IO and PIV into the central circulation, tibial IO delivery of the drug appears to be delayed when compared to these more proximal infusion sites [21]. Furthermore, the maximum concentration of epinephrine realized with IV infusion of 1 mg epinephrine appears to be 5.87 and 2.86 times greater than with tibial IO and sternal IO infusion, respectively [21]. The results of this and other studies suggest that larger doses of epinephrine may be warranted with IO infusion [22], although current ACLS recommendations assume that the 1 mg IO dose is equivalent to the 1 mg IV dose.

Vasopressin

This medication is recommended as an alternative vasopressor to epinephrine, currently recommended to replace the first or second dose of epinephrine.

Amiodarone

During resuscitative efforts, amiodarone may terminate lethal arrhythmias unresponsive to high-quality CPR and electrical defibrillation. In two randomized, double-blind, placebo-controlled trials – the ARREST [23] and ALIVE trials [24] – amiodarone demonstrated improved survival-to-hospital admission when compared to lidocaine and placebo, respectively, for the use of shock refractory ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT) in OHCA. Although these trials did not show improvement in favorable neurological outcome or survival-to-hospital discharge, they were not powered to assess for these outcomes.

One recent secondary analysis of a randomized, placebo-controlled trial of antiarrhythmic drug infusion to terminate shock-refractory VF/pVT in the prehospital setting suggested improved hospital discharge survival and other important clinical outcomes among patients who received IV amiodarone or lidocaine, when compared to those who received IO infusion of the same dose of medication [25]. Of note, the vast majority of subjects in this study received tibia 1 IO cannulation, and all subjects received standard drug dosing regardless of route of infusion.

Lidocaine

Lidocaine has not been shown to be associated with improved neurological outcomes or survival in OHCA due to refractory ventricular fibrillation or pulseless VT, when compared to amiodarone or placebo [23]. However, it may be considered if amiodarone is not available.

Magnesium Sulfate

The use of magnesium sulfate for the treatment of a presenting *torsades de pointes* rhythm has been shown to be effective, as reported in two trials [26, 27]. However, the routine administration of magnesium sulfate during cardiac arrest is not recommended unless this cardiac rhythm is identified.

Sodium Bicarbonate

Sodium bicarbonate may help to restore metabolic homeostasis by reducing the metabolic acidosis caused by inadequate peripheral blood flow during cardiac arrest. Analysis of results from the Brain Resuscitation Clinical Trial III showed that earlier and more frequent use of sodium bicarbonate was associated with higher rates of early resuscitation and better long-term outcomes [28]. Early restoration of oxygen content, tissue perfusion, and cardiac output with a combination of high-quality chest compressions and effective ventilation may also help to restore the acid-base imbalance. However, providers should be aware that high-quality chest

compressions alone only achieve a blood pressure about one-third of the native blood pressure, and this may be inadequate to ensure optimal perfusion of the vital organs. Thus, even patients receiving appropriate optimal chest compressions may not realize normalization of their blood acid-base balance with external cardiac compressions alone.

While normal blood pH is between 7.35 and 7.45, cardiac arrest patients often present with profound acidosis (pH < 7.35). Depending upon the etiology of the cardiac arrest, the acidosis could be due to respiratory causes (e.g., hypoventilation with carbon dioxide retention), metabolic causes (e.g., lactic acid accumulation due to hypoxic shunting toward anaerobic metabolism), or both. Unfortunately, profound acidosis (pH < 6.80) causes severe direct myocardial depression [29] and limits the ability of epinephrine to increase myocardial contractile force [15]. In fact, the effect of exogenous (and likely endogenous) epinephrine on contractile force becomes progressively worse as the pH descends [15]. Thus, reversing acidosis early in the course of the patient's management should be a goal of early cardiac arrest resuscitation. Although sodium bicarbonate infusion can increase the pH transiently, permanent correction of the acidosis will depend on a variety of factors, including ROSC, the restoration of adequate intravascular fluid volume, reversal of carbon dioxide retention, and correction of ongoing tissue ischemia.

Intravenous fluids (e.g., lactated Ringer's or normal saline solution) should also be considered a medication for purposes of OHCA management, as patients with hypovolemia may require rehydration in order to restore homeostasis. It is also likely that IV fluids help to restore normal acid-base balance, thereby improving the serum pH and increasing the likelihood that exogenous epinephrine and other cardioactive medications are able to exert their effects.

Several pharmacokinetic studies in animal models have shown that medications given via IO had the same efficacy as medications given with the IV route [30]. However, other studies have suggested that epinephrine dosing may need to be higher with IO infusion than with PIV infusion [19]. Whatever the proper dose, many previous studies have suggested efficacy for the IO infusion of epinephrine [31–40].

Other medications that have been given via the IO route for the treatment of cardiac arrest include *atropine* [32, 33, 35, 36, 39], *calcium chloride* [34, 35, 38], *dextrose* [35], and *lidocaine* [35, 37].

Location Matters

Burgert et al. conducted a randomized study to assess pharmacokinetics of epinephrine administered using tibial IO, sternal IO, and peripheral IV in a porcine model of cardiac arrest [21]. This group found that the more distal the insertion site, the slower the epinephrine reached maximum concentrations. Similarly, Vorhees et al. found in a dog CPR model that there is extensive central blood flow redistribution during CPR, resulting in significant reductions in arterial blood flow to the abdominal organs [41]. Extrapolating these findings to the extremities of man, one would

expect that perfusion to the distal parts of the extremities (especially the lower extremities) should be lower (with less venous return) than the more proximal portions of the extremities. In other words, the closer a VAD is placed to the heart and central vessels, the more medication will likely find its way to the heart. It has been well-established that cardiac output and resulting systolic blood pressure are only about *one-third* of normal levels during CPR [42, 43]. Thus, peripheral veins (and the IO spaces drained by them) are likely to be poorly perfused with reduced venous return during CPR. This disadvantage is likely progressively worsened as the insertion site is moved more distally from the central circulation.

Previous studies performed on human subjects echo these findings from animal studies. In one study comparing peripheral to central venous infusion of Cardio-Green® dye in adult human cardiac arrest victims undergoing CPR, the authors sampled blood from the right femoral artery every 30 seconds during 5 minutes of closed chest compressions [44]. They found that dye injections given through an antecubital PIV were associated with no dye appearance at the femoral artery until more than 60 seconds after infusion. In fact, the concentration of dye recovered following antecubital PIV infusion was negligible even at the conclusion of the 5-minute study period. Conversely, the concentration of dye noted 30 seconds after central venous infusion was four times greater than the highest concentration ever achieved following PIV infusion [44]. These findings led the study authors to conclude that central venous infusion of ACLS medications is far superior to PIV infusion, suggesting that central venous access should be the standard of care for CA management. However, since the blood sampling site in this study was located at the femoral artery (well below the diaphragm), the lack of dye appearance in the PIV samples may represent the combined effect of impaired venous return from the upper extremity as well as impaired perfusion of the lower extremities during CPR.

Selection of Vascular Access Device

The current ACLS guidelines for the establishment of emergent vascular access for OHCA patients appears to be based primarily upon anecdotal evidence, with PIV access prioritized as the gold standard for immediate access, as “the pharmacokinetic properties, acute effects, and clinical efficacy of emergency drugs have primarily been described when given intravenously” [1]. This seemingly historical basis for the preference of PIV infusion of medications, combined with conflicting evidence on the equivalency of IO versus PIV infusion dosing, has led to significant disagreement within the scientific community on whether or not IO infusion is truly equivalent to IV dosing of commonly utilized OHCA medications.

In the absence of adequate conflicting evidence, the IO infusion of equivalent doses of resuscitative medications has been endorsed, “if attempts at intravenous accesss are unsuccessful or not feasible” [1]. But this guidance fails to provide the emergent vascular access specialist with usable guidance on precisely when and how IO or other alternative vascular access methods should be utilized when PIV access appears to be unobtainable. At present, emergent vascular access specialists

Table 9.3 Comparison of different VADs commonly used for OHCA management

	PIV	CVC	IO
Insertion	Varying degree of difficulty	Time-consuming; may require advanced level provider	Rapid, simple insertion
Medication Delivery	All ACLS meds	All ACLS meds	All ACLS meds
Dosing	Standard	Standard	Presumed standard
Duration of use	Long term	Long term	Short term (<48 hrs)
Representative Complications	Delayed placement, extravasation	Delayed placement, pneumothorax, hematoma, arterial placement	Dislodgement, extravasation

are left to decide for themselves when this apparent threshold marking the inability to obtain PIV access has been realized.

Despite this lack of guidance, we suggest that many factors should be taken into account during the selection of a VAD for OHCA management. These factors include *speed* of placement, anticipated *success* of placement, likely *complications*, *adequacy* of the line for present and *future vascular access needs*, and potential need for *dosing adjustments*. Table 9.3 provides a brief comparison of the various VAD options available to the emergency care provider when establishing emergent vascular access for OHCA.

Speed of Access

The first priority to consider in selecting a VAD for OHCA is how quickly the provider can achieve successful placement. When feasible, it is suggested that *multiple care providers attempt VAD placement simultaneously* on the same patient. Although this approach may be more labor-intensive, a simultaneous collateral approach to obtaining vascular access is likely to yield useable vascular access more rapidly than a linear single-provider technique. This competitive approach may also yield multiple useable VADs for the patient, allowing the delivery of multiple drugs or fluid boluses simultaneously. In general, IO access appears to be most rapidly accomplished in the setting of OHCA management, requiring less than 2 minutes, as compared to PIV or CVC placement [24, 45, 46].

First-Attempt Success Rates

A randomized, controlled trial comparing the effectiveness of PIV with proximal tibial IO (PTIO) and proximal humeral IO (PHIO) insertion demonstrated that PTIO insertion is more likely to be successful on the first attempt (91% PTIO, 51% PHIO, 43% PIV) with time to successful placement significantly shorter for this approach (4.6 min, versus 7.0 min for PHIO, and 5.8 min with PIV) [47]. However, utilizing current ACLS guidelines for medication dosing, patients who receive a

PIV versus an IO insertion appear to be more likely to achieve ROSC (55.5% vs. 43.6%, $p < 0.001$) and likely have improved survival-to-hospital discharge rates (22.8% vs. 14.9%, $p = 0.003$) when compared to those who receive PTIO insertion [48]. Thus, the clinical benefits of improved first-attempt success rates for PTIO insertion may be compromised by the apparent reduced efficacy of standard IV/IO dosing for resuscitative medications.

Future Directions for OHCA Research

The urgent need for head-to-head prospective comparisons between PIV and IO access for OHCA patients cannot be overstated. At present, guidelines for the establishment of vascular access in OHCA appear to be based almost entirely upon anecdotal and profoundly limited data. Prospective studies comparing important clinical outcomes for patients randomized to PIV or IO at the time of prehospital or early emergency department presentation for OHCA will be required to clearly identify any potential advantage to one vascular access technique or another. Considering the conflicting evidence that exists for the equivalency of PIV and IO dosing, additional research is also needed to determine if IO dosing should reasonably be assumed to be equivalent to PIV dosing. Current evidence suggests consistently that IO dosing may need to be greater than PIV dosing, especially if providers wish to continue utilizing subdiaphragmatic IO insertion sites. The importance of simultaneous crystalloid fluid infusion during OHCA resuscitation to improve the circulation of medications infused from the lower extremities also appears to be warranted. We suggest that supradiaphragmatic (i.e., humeral, sternal) IO insertion sites should be prioritized in such studies and that they should be compared with upper extremity PIV insertion sites.

An Algorithmic Approach to VAD Placement for OHCA

Given the relative dearth of clear guidance on the timing and preference of vascular access techniques currently offered by authorities on the topic, the emergency vascular access specialist is left, to some degree, to weigh the relative indications and contraindications of each vascular access technique on its own merits with each vascular access episode. *Peripheral intravenous access appears to be the optimal form of vascular access, when it is viewed to be readily available and adequate for therapy by the provider*. That said, the provider must determine for him or herself whether PIV access is actually feasible, and this assessment appears to depend upon a myriad of considerations. Given the immediate need for vascular access in the setting of OHCA, we propose that the inability to immediately (e.g., within 30 seconds) achieve PIV access should imply the need to consider IO insertion, preferably at the proximal humeral or sternal IO insertion site. Proximal tibial IO insertion (or other lower extremity IO insertion sites) should be considered suboptimal to more proximal IO insertion sites and should only be considered when more proximal IO or PIV insertion sites are not felt to be available for cannulation.

Conclusions

Out-of-hospital cardiac arrest is a unique clinical condition, which requires careful attention to the need for immediate vascular access to allow for stabilization and resuscitation of the patient. Although current ACLS recommendations do not provide adequate guidance for VAD selection in this context, the peripheral intravenous route is currently endorsed as the gold standard for emergent vascular access with OHCA. When PIV access is not felt to be immediately available, other forms of vascular access, including IO and CVC placement, should be considered. Dosing considerations remain unclear, especially whether IO dosing is truly equivalent to PIV dosing for commonly utilized resuscitative medications. Future prospective research comparing IO to PIV cannulation in the prehospital and early emergency department setting is needed to determine whether the route of vascular access selected for OHCA management is likely to influence important clinical OHCA outcomes.

Key Points

- The gold standard technique for obtaining emergent vascular access in the setting of OHCA remains peripheral intravenous cannulation.
- Intraosseous cannulation should be considered when PIV cannulation is deemed to be inadequate or unavailable by the emergency care provider.
- Current IO dosing may be inadequate, when compared to standard PIV dosing, at achieving adequate serum concentrations of epinephrine and other commonly used medications.
  - Cardiac arrest management is highly time-sensitive, underscoring the need for early and rapid venous access.
  - Sternal and proximal humeral IO catheters provide superior access to the central circulation during cardiac arrest, when compared to peripheral (e.g., tibial) IO access sites.
  - Volume infusion of crystalloid fluids with pressure bag likely improves the delivery and distribution of resuscitative medications during cardiac arrest, especially when introduced via the IO or PIV route.
- Emergent vascular access providers should utilize their own clinical acumen in assessing the need for PIV versus other forms of vascular access in the treatment of OHCA.

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