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In-Hospital Cardiac Arrest – Are We Overlooking a Key Distinction?

Ari Moskowitz, MD¹, Mathias J. Holmberg, MD^{2,3}, Michael W. Donnino, MD^{1,2}, and Katherine M. Berg, MD¹

¹Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA

²Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA

³Research Center for Emergency Medicine, Department of Clinical Medicine, Aarhus University Hospital, Denmark

Abstract

Purpose of Review—To review the epidemiology, peri-arrest management, and research priorities related to In-Hospital Cardiac Arrest (IHCA) and explore key distinctions between IHCA and Out-of-Hospital Cardiac Arrest (OHCA) as they pertain to the clinician and resuscitation scientist.

Recent Findings—IHCA is a common and highly morbid event amongst hospitalized patients in the United States. As compared to patients who experience an OHCA, patients who experience an IHCA tend to have more medical comorbidities, have a witnessed arrest, and be attended to by professional first responders. Further, providers resuscitating patients from IHCA commonly have access to tools and information not readily available to the OHCA responders. Despite these differences, society guidelines for the peri-arrest management of patients with IHCA are often based on data extrapolated from the OHCA population. To advance the care of patients with IHCA, clinicians and investigators should recognize the many important distinctions between OHCA and IHCA.

Summary—IHCA is a unique disease entity with an epidemiology and natural history that are distinct from OHCA. In both research and clinical practice, physicians should recognize these distinctions so as to advance the care of IHCA victims.

Keywords

Cardiac Arrest; Practice Guideline; Ultrasound; Extra Corporeal Membrane Oxygenation; Induced Hypothermia

Corresponding Author: Katherine M. Berg, MD, Beth Israel Deaconess Medical Center, Division of Pulmonary, Critical Care, and Sleep Medicine, 330 Brookline Ave, Boston, MA, 02215, Phone: (617) 667-5864, kberg@bidmc.harvard.edu.

Conflicts of Interest:

Dr. Moskowitz, Dr. Berg and Dr. Donnino hold volunteer roles at the American Heart Association. Dr. Berg and Dr. Donnino hold volunteer positions at the International Liaison Committee on Resuscitation.

Introduction: In-Hospital Cardiac Arrest – a Dangerous but often Overlooked Disease

Periodically, the American Heart Association (AHA) publishes updated guidelines for cardiopulmonary resuscitation (CPR) and Emergency Cardiovascular Care. These guidelines are based on careful weighing of the evidence, with new studies being incorporated into the growing body of knowledge that informs management decisions.(1) The European Resuscitation Council (ERC) and other international councils follow a similar practice, with each organization also receiving guidance from Consensus on Science with Treatment Recommendations statements issued by the International Liaison Committee on Resuscitation (ILCOR).(2) With each cycle, the lack of data on in-hospital cardiac arrest (IHCA) is highlighted. The IHCA and out-of-hospital cardiac arrest (OHCA) populations are quite different, but in the absence of IHCA-specific literature we often extrapolate from the OHCA evidence. Even when guideline statements have been published for IHCA, they differ very little from those for OHCA.(3) As our population of hospitalized patients becomes increasingly complex and new technologies become available, the epidemiological and management differences between IHCA and OHCA are becoming more pronounced. Although the foundational elements of good quality CPR and early defibrillation for shockable rhythms almost assuredly benefit all patients with cardiac arrest, other aspects of care may be more applicable or unique to IHCA. These aspects are often included in published guidelines but are rarely incorporated into the algorithms used by the bedside clinician when faced with a cardiac arrest at 3am. In the current manuscript, we present a few areas of emerging science or controversy in IHCA which either potentially warrant more prominent placement in clinical guidelines or further research to determine the best approach.

Cardiac Arrest in the Intensive Care Unit – Targeting Physiologic Parameters during Cardiopulmonary Resuscitation

Cardiac arrest in the intensive care unit (ICU) accounts for the majority of IHCA events occurring in the United States.(4, 5) Over time, the proportion of IHCA occurring in the ICU has increased, potentially due to hospitals concentrating sicker patients in the ICU. While rates of hospital survival have improved over time amongst patients who experience IHCA on the ward and in the ICU, the rate of improvement for ICU arrests has been less pronounced.(4)

Patients who arrest in the ICU are highly monitored and likely to have advanced hemodynamic monitoring devices already in place at the time of the arrest. Although the use of pulmonary artery catheters has decreased, they are employed in ~5% of ICU patients.(6) These patients often have higher severity-of-illness scores (7) and may be more likely to suffer an IHCA. Arterial catheters and central venous catheters are used in upwards of 30% of ICU patients.(6)

While a majority of IHCAs occur in the ICU, and many patients have indwelling catheters at the time of arrest, there is little guidance for how these tools should be utilized in the intra-

arrest period. Evidence has suggested, for instance, that myocardial blood flow (driven by coronary perfusion pressure) and cardiac output during chest compressions are strong predictors of return of spontaneous circulation (ROSC).(8) In addition, studies in animal models have found that targeting higher blood pressure or coronary perfusion pressure during CPR improves survival.(9, 10) Most recently, in a pediatric ICU setting, patients who suffered IHCA and had invasive arterial monitoring at the time of arrest were more likely to survive with good neurologic outcome if the diastolic blood pressure was maintained above 25mmHg during CPR.(11) Utilizing arterial lines to target a certain blood pressure during CPR is not, however, a practice that has reached the bedside routinely, in spite of this emerging research. Whether this is a missed opportunity, when these lines are already in place, warrants consideration.

Beyond monitoring physiologic targets during chest compressions, invasive arterial and pulmonary artery catheters may allow for earlier identification of ROSC and therefore earlier termination of unnecessary chest compressions or administration of vasoactive medications. Prior work suggests that many providers may inappropriately continue CPR even when a pulse is detected if that pulse check is done prior to the requisite two minutes of CPR after a shock/drug administration.(12) In our experience, this confusion can persist even in the presence of an arterial line showing a pressure tracing indicating ROSC.

The most recent 2015 AHA guidelines indicated that the use of physiologic parameters when possible to guide CPR may provide valuable information about the patient, although exactly how to incorporate this information into the flow of the arrest algorithm is not as well-defined and the overall supporting evidence was acknowledged to be poor.(13) Clearly there is a knowledge gap in the evidence base when it comes to patients who suffer IHCA in the ICU with advanced monitoring devices in place. Future research endeavors should focus on the unique population of patients who experience IHCA in the ICU to inform more tailored guideline recommendations and treatment algorithms.

Point of Care Ultrasound during Cardiopulmonary Resuscitation

In recent years, the wide availability of point-of-care ultrasound (POCUS) technology has contributed to an increasing use of bedside ultrasound during cardiac arrest.(14) POCUS during resuscitation has been suggested to identify underlying otherwise occult etiologies of arrest (e.g. cardiac tamponade) (15–19) and to help with intra-arrest prognostication when used to detect spontaneous cardiac movement (20–24). In one small randomized trial assessing the effect of POCUS on outcome of ACLS, investigators found no improvement in rates of ROSC, but this study was underpowered and limited by concerns about design.(25)

The most recent AHA guidelines provide a class IIb, level of evidence C recommendation for the use of ultrasound as an adjunct to standard patient evaluation if a qualified sonographer is present.(13) This recommendation comes on the basis of a review performed by ILCOR which found inadequate evidence to support/refute the use of POCUS. (26) Notably, one recent study found that the use of bedside ultrasound during resuscitation increased the duration of pulse-checks to nearly double that recommended in society guidelines, raising concerns about safety.(27) To decrease the likelihood of chest

compression interruptions, while maintaining the ability to identify potentially reversible causes of arrest, some have suggested the use intra-arrest transesophageal ultrasound.(17, 28)

Although POCUS is conceivably more readily available in the inpatient setting, the large majority of studies have been carried out in the emergency department and pre-hospital setting, with strikingly few studies exploring its use in IHCA populations where causes of arrest and POCUS availability may differ.(29, 30) The two studies we identified focusing specifically on IHCA patients were both small and largely qualitative in nature.(30, 31) Additional investigation is needed in this area so as to provide guidance to ACLS practitioners caring for IHCA patients.

Extra-Corporeal Cardiopulmonary Resuscitation

With advancing technology, the availability and use of extra-corporeal membrane oxygenation (ECMO) and extra-corporeal cardiopulmonary resuscitation (ECPR) has dramatically increased over the past decade.(32, 33) ECPR is defined as the implementation of extra-corporeal membrane circulation during cardiac arrest refractory to conventional CPR to temporarily support perfusion. Given that many IHCA events occur at tertiary hospitals with access to ECMO technology, there is an urgency to develop guidelines surrounding the use of ECPR during IHCA.

In 2015, ILCOR performed an evidence review comparing ECPR to conventional CPR which identified a number of reviews, case reports, and observational studies on the topic. Notably, of the observational studies reviewed, most focused on the IHCA population—a unique occurrence in cardiac arrest investigations.(26) The reported results of ECPR in IHCA are mixed and dependent on the selected patient population and specific setting. Some studies suggest a mortality benefit of ECPR compared to conventional CPR (34) or historic controls (35), and other studies suggest no benefit of ECPR.(36) The heterogeneity of the available studies and the complexity of deploying ECPR make the results difficult to interpret, although the use of ECPR is likely to be most beneficial in patients with very high expected mortality.

On the basis of these studies and the ILCOR evidence review, the 2015 AHA guidelines provide a class IIb, level of evidence C recommendation for the use of ECPR in select patients when local expertise is available and the cause of arrest is potentially reversible with short-term mechanical support.(13) Balancing the expense and complexity of ECPR in IHCA (37) against what appears to be a survival benefit (at least in populations with very high expected mortality) will be challenging for centers in the near future. This is an area in which additional research into patient selection and resource allocation is needed so as to best apply this expanding technology.

Timing of Intra-Arrest Interventions

Data on most intra-arrest interventions derive from OHCA settings, where delivery times depend on ACLS provider response times. For IHCA, the delivery of epinephrine for non-shockable rhythms occurs most often within 5 minutes, compared to nearly 20 minutes in

OHCA, see Figure.(38–41) In OHCA with shockable rhythms, anti-arrhythmic drugs are often first provided 20 minutes after arrest, whereas delivery in IHCA is likely much more rapid.(39, 42) These differences may have substantial impact as evidence suggests that the efficacy of intra-arrest medications may be time-dependent.(42) Similar concerns arise when evaluating defibrillation strategies.(43) For example, providing 2 minutes of CPR between the first and second shock might be beneficial in OHCA with long downtimes, but less helpful for a witnessed IHCA with very short no-flow periods. These questions remain not only unanswered but often unasked, and current management algorithms suggest the same strategy for both OHCA and IHCA.(13) Future research should consider how the arrest setting affects timing of interventions, and whether the cardiac arrest algorithms for IHCA should be distinct from OHCA where timing of interventions differs substantially.

Targeted Temperature Management

The optimal approach to temperature management after cardiac arrest has become more controversial in recent years following a 2013 trial showing that there was no difference in outcome when using 33°C or 36°C.(44) Based on this and earlier controlled studies, ILCOR advised that clinicians target a temperature between 32–36°C after ROSC.(13, 44–47) Although strongly recommended for shockable OHCA, targeted temperature management (TTM) is only suggested for IHCA due to a lack of high-quality evidence in this patient population. No randomized controlled trial has ever been done to investigate the effect of TTM after IHCA. Two observational studies, both using the same national registry, found approximately 2–6% of IHCA patients receive TTM, although the reasons why patients received TTM or did not were not clear.(48, 49) Investigators did not find that TTM was associated with benefit in IHCA, but these studies were significantly limited by being unable to determine which patients were following commands after ROSC, a variable that influences both whether TTM is undertaken and outcome. A possible explanation for the worse outcomes associated with TTM in one study is, therefore, that they had worse neurologic status to begin with.(50)

Although the existing data are insufficient to conclude that TTM is not beneficial in the IHCA population, whether there is risk from TTM after IHCA is also unclear. The original OHCA randomized trials in 2002 reported trends towards increased pneumonia and sepsis in patients treated with mild hypothermia,(45, 46) although overall outcomes were still improved. Observational studies have supported these findings of increased infection, (51, 52) but whether these effects are significant or alter outcomes in the IHCA population remains unknown. Similarly, coagulopathy and hemodynamic instability are theoretical concerns at some levels of hypothermia, but in the OHCA population these effects have been found to be minor and outweighed by the benefit of TTM. Sepsis, respiratory failure and coagulopathy, however, are all common in the IHCA population even before the arrest occurs, and cooling may exacerbate these physiologic derangements more than in OHCA. The lack of conclusive evidence of benefit/harm may have contributed (along with heterogeneity in patient populations and immediate arrest outcomes) to the striking inconsistency in the use of TTM for IHCA, from 0% at some centers to ~75% at our own center.(49) This is a resource-intensive treatment, and further research to determine its effectiveness for IHCA patients is much needed.

Who are we resuscitating, and who should we be?

Cardiac arrest research, with the exception of cardiac arrest prevention, excludes those patients who have a pre-existing “do-not-resuscitate” (DNR) order. These patients have self-identified as patients on whom CPR should not be performed and are thus not included in cardiac arrest registries or clinical trials. There is, however, significant variability in attitudes toward end-of-life care, both among patients and among providers. This variability may lead to some patients receiving CPR while others with similar comorbidities and acuity of illness are made DNR and are thus not included in our assessments of IHCA incidence and outcomes. The AHA addresses this issue to some degree in their 2013 statement on IHCA, stating that even the incidence of IHCA is hard to determine because so much of what is recorded depends on code status, and code status depends on both patient/family preference and the culture of the admitting institution.(3)

Some of this variability may stem from the fact that decisions on whether or not to undergo CPR are often made by patients/families with little guidance or preparation, which may lead to confusion. One study found that 20% of patients with a DNR order in place actually wanted a time-limited trial of CPR when given hypothetical scenarios.(53) A large body of data from La Crosse, Wisconsin (USA), where there has been an ongoing project for decades aimed at getting all residents to complete an advanced directive, has shown that many patients prefer to limit aggressiveness as they get sicker. The La Crosse program has led to more patients documenting that they choose to have aggressive care withheld as they are nearing death, and more chronically-ill patients documenting a DNR order.(54) The leaders of that project have reported decreasing incidence of CPR attempts in patients over 65 and a significant improvement in survival in this age group when CPR is attempted, suggesting that patients who are choosing to undergo CPR if an arrest occurs are more likely to benefit.(55) Improving goals of care conversations to shrink the communication gap between physicians and patients and optimize decision-making regarding when CPR is appropriate is of paramount importance.

Discussion/Conclusion

Although cardiac arrest is common and highly morbid, funding for research into cardiac arrest prevention and treatment lags far behind other disease processes per annual death.(56) The complexity of conducting clinical trials in this patient population cannot be overstated, and may contribute to the relatively small number of investigators actively engaged in the field. Judging from our own knowledge of current trials and from the cardiac literature to-date, only a small fraction of this work is being done on IHCA. As detailed in this review, IHCA is a distinct disease entity separate from OHCA with unique challenges and opportunities. At present, however, published guidelines often do not distinguish between OHCA and IHCA in making recommendations regarding cardiac arrest resuscitation and post-ROSC care. Given the distinct characteristics of IHCA, we believe that care of these patients can be advanced through more dedicated research and guideline development targeted specifically at this population.

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Key Points

1. In-hospital cardiac arrest is a common and highly morbid disease entity.
2. In-hospital cardiac arrest is a unique disease entity that affects a patient population that is distinct from those who experience out-of-hospital cardiac arrest and is attended to by professional first responders access to tools and information not readily available in the out-of-hospital setting.
3. Given differences between in-hospital and out-of-hospital arrest that transcend ‘arrest location,’ future research and guideline development should consider in-hospital cardiac arrest a unique disease entity and better customize care for victims.
4. Deciding who to resuscitate from in-hospital cardiac arrest is a complex question requiring a number of social, economic, and medical considerations. Additional investigation is needed regarding shared decision making around the question ‘do not resuscitate.’

Figure 1.
Timing of Intra-arrest Interventions in Out-of-Hospital Cardiac Arrest (OHCA) vs. In-hospital Cardiac Arrest (IHCA)