When is a Cardiac Arrest Non-Cardiac?

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Abbreviations:
ACLS: Advanced Cardiac Life Support
CPR: cardiopulmonary resuscitation
EMS: Emergency Medical Services
OHCA: out-of-hospital cardiac arrest

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Abstract

Introduction: While the overall survival rate for out-of-hospital cardiac arrest (OHCA) is low, ranging from 5%-10%, several characteristics have been shown to decrease mortality, such as presence of bystander cardiopulmonary resuscitation (CPR), witnessed vs unwitnessed events, and favorable initial rhythm (VF/VT). More recently, studies have shown that modified CPR algorithms, such as chest-compression only or cardio-cerebral resuscitation, can further increase survival rates in OHCA. Most of these studies have included only OHCA patients with "presumed cardiac etiology," on the assumption that airway management is of lesser impact than chest compressions in these patients. However, prehospital personnel often lack objective and consistent criteria to assess whether an OHCA is of cardiac or non-cardiac etiology.

Hypothesis/Problem: The relative proportions of cardiac vs non-cardiac etiology in published data sets of OHCA in the peer-reviewed literature were examined in order to assess the variability of prehospital clinical etiology assessment.

Methods: A Medline (US National Library of Medicine, National Institutes of Health; Bethesda, Maryland USA) search was performed using the subject headings "OHCA" and "Emergency Medical Services" (EMS). Studies were included if they reported prevalence of cardiac etiology among OHCA in the entire patient sample, or in all arms of a comparison study. Studies that either did not report etiology of OHCA, or that excluded all cardiac or non-cardiac etiologies prior to reporting clinical data, were excluded.

Results: Twenty-four studies were identified, containing 27 datasets of OHCA which reported the prevalence of presumed cardiac vs non-cardiac etiology. These 27 datasets were drawn from 15 different countries. The prevalence of cardiac etiology among OHCA ranged from 50% to 91%. No obvious patterns were found regarding database size, year of publication, or global region (continent) of origin.

Conclusions: There exists significant variation in published rates of cardiac etiology among OHCAs. While some of this variation likely reflects different actual rates of cardiac etiologies in the sampled populations, varying definitions of cardiac etiology among prehospital personnel or varying implementation of existing definitions may also play a role. Different proportions of cardiac vs non-cardiac etiology of OHCA in a sample could result in entirely different interpretations of data. A more specific consensus definition of cardiac etiology than that which currently exists in the Utstein template may provide better guidance to prehospital personnel and EMS researchers in the future.

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Introduction

The Utstein guidelines for uniform reporting of out-of-hospital cardiac arrest (OHCA) data require that each case be deemed either "cardiac" or "non-cardiac" in etiology.[1] This is done primarily to allow for separate analysis of cases felt to be "cardiac" in nature, where standard Advanced Cardiac Life Support (ACLS) management is more likely efficacious, and those felt to be "non-cardiac," where management strategies prioritizing ventilation (eg, choking or hanging), antidote therapy (eg, hyperkalemia), or other non-ACLS approaches may be more beneficial. The first branch point of the Utstein reporting template, after the starting point of "Resuscitations Attempted," removes from further consideration all patients deemed to have suffered "non-cardiac" arrests.

According to the 2004 update of the Utstein guidelines, "An arrest is presumed to be of cardiac etiology unless it is known or likely to have been caused by trauma, submersion, drug overdose, asphyxia, exsanguination, or any other non-cardiac cause *as best determined by rescuers*" (emphasis added).[1] While some studies rely on medical examiner determination

of etiology, most Emergency Medical Service (EMS) studies of OHCA simply rely on the field personnel indicating "cardiac" or "non-cardiac" on their patient care reports.

Possible causes of OHCA are myriad. While some may be obvious even to the Basic Life Support responder, it is often difficult for the paramedic or even the receiving emergency physician[2] to pinpoint the etiology of a given cardiac arrest without laboratory tests, imaging, or even an autopsy. It thus seems risky to dichotomize research data, and discard substantial proportions of patients, based on what must frequently be guesswork by field personnel. It is well-established that choice of denominator significantly affects the math involved in examining a given study outcome. Eisenberg noted as early as 1991 that the survival rate reported by one study increases from 16% to 49% by changing the denominator from "all cardiac arrests" to "bystander witnessed with cardiac etiology and on-scene response < 8 minutes."[3] Since many OHCA studies focus on patients with the best chance of survival (cardiac etiology, witnessed, received bystander cardiopulmonary resuscitation [CPR]), systems where higher proportions of patients are deemed "cardiac" will have larger samples to examine, while those where more patients are deemed "non-cardiac" will have more patients removed from their outcomes calculations.

In addition to research implications, there are patient care implications to the accuracy of the determination of etiology. Many cardio-cerebral resuscitation protocols, including the one in use in the EMS system in the USA, have very different approaches to management depending on whether the arrest is deemed by the providers on scene to be cardiac (generally favoring a course of uninterrupted chest compressions and deferred airway management and ventilation) or non-cardiac (in which case traditional 30:2 CPR is typically begun).

To the best of the authors' knowledge, the reporting of OHCA data as "cardiac" vs "non-cardiac" has not been examined in any detail. The purpose of this study was to examine papers reporting on OHCA databases to determine the percentages of cases deemed cardiac vs non-cardiac in order to examine the variation in these proportions. The study hypothesis was that substantial variation would be found, leading to concerns about the validity and usefulness of such reporting.

Methods

Ovid MEDLINE (US National Library of Medicine, National Institutes of Health; Bethesda, Maryland USA) was searched using the terms "OHCA" and "Emergency Medical Services." Papers were included if they reported etiology of OHCA among the entire study sample, or among all arms of a comparison trial. Papers were excluded if they did not report a breakdown of arrest aetiology,[4,5] excluded one (usually non-cardiac) etiology prior to reporting data, or if the dataset overlapped with another dataset included in the study (Figure 1).

The country of origin of each paper was noted, in order to examine the possibility of regional (by continent) variation. The Human Investigations Committee of the Yale University School of Medicine (New Haven, Connecticut USA) determined that this study does not meet the US federal definition of human subjects research, and is thus not subject to institutional review board oversight.

Results

Twenty-four OHCA databases were located that met the inclusion criteria, in 24 papers, with one paper reporting four different databases. The papers originated from 15 different countries and reported on a total of 369,759 OHCA patients.

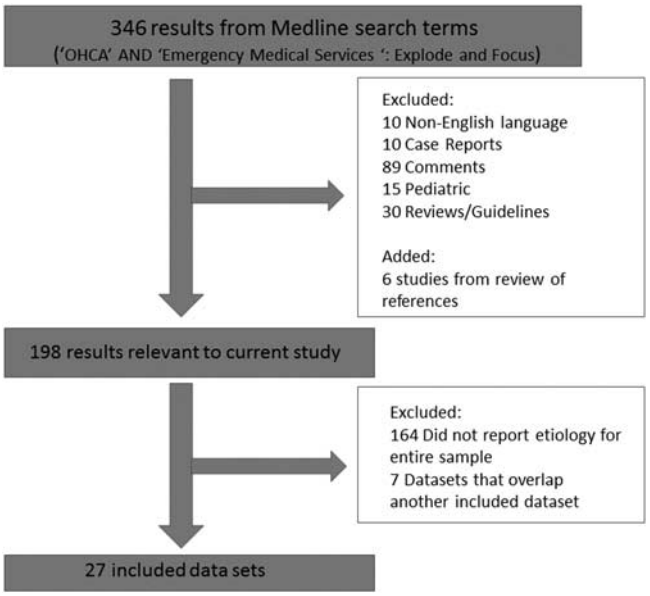

Figure 1. Literature Review Algorithm.
Abbreviation: OHCA, out-of-hospital cardiac arrest.

Overall, the prevalence of cardiac etiology ranged from 50% to 91%. Table 1 shows each of the 27 datasets with the last name of the first author, the nation of origin, the dataset size (total n), and the percentage of cases deemed cardiac. Figure 2 shows the 27 datasets plotted chronologically on the x-axis, with percentage deemed cardiac on the y-axis. Each data point is color-coded by continent, with the relative size of the bubble proportional to the size of the dataset; no obvious visual relationship is noted between dataset size and percentage of arrests deemed cardiac.

Discussion

The Utstein conference in 1990 established several elements of how OHCA is categorized:[6] Was there bystander CPR? Was the etiology cardiac or noncardiac? While most of these items are objective and simple to determine, based on information available to EMS providers on scene, deciding the etiology of a cardiac arrest can be challenging. This survey of the relative proportions of cardiac vs non-cardiac etiology in published data sets of OHCA in the peer-reviewed literature found that the prevalence of cardiac etiology ranged from 50% to 91%.

One possible explanation is that the variation in the relative proportion of cardiac etiology OHCAs is an accurate reflection of variation between the populations sampled. Coronary heart disease, its contributing cardiovascular risk factors, and other arrythmogenic conditions do vary in their prevalence among different populations. These findings show that the degree of variation is similar within regions of the world, as well as between them. Even among samples from within the same nation, Japan, the proportion of OHCAs defined as cardiac varied between 50% and 70%. Thus, it seems more likely that the degree of variation is due to varying interpretations of current definitions: a non-standardized error introduced by the research process.

In a post-hoc analysis, the de-identified database from the Sayre before/after study of 2009[7] was generously supplied by the

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Year[a]	Author	Nation	n	% Cardiac
2014	Wander	US	8626	62%
	Shao	China (PRC)	2421	70%
	Kuo	Taiwan	992	72%
2013	Fothergill	UK	21020	79%
	Ro	Korea	78501	74%
	Nishi	Japan	4338	50%
2012	Wnent	Germany	889	87%
	Tanabe	Japan	138248	58%
	Nurnberger	Austria	1448	85%
	Hiltunen	Finland	671	54%
	Axelsson	Sweden	32341	73%
	Deasy	Australia	33178	73%
2011	Jacobs	Australia	534	91%
	Sladjana	Serbia	591	76%
	Yeeheng	Thailand	73	53%
	Grasner	Belgium	5671	83%
	"	Germany	1882	80%
	"	Spain	955	77%
	"	Holland	2822	90%
2010	Zeitz	Australia	1305	58%
	Do	Denmark	2678	87%
2009	Sayre	US	1859	85%
2008	Nichol	US & Canada	20520	86%
2007	Woodall	Australia	4632	74%
2006	Ong	US	1038	75%
2003	Persse	US	1757	77%
2002	Verbeek	Canada	769	91%

Table 1. Included Datasets

[a] Denotes year of publication; data in most datasets spanned several years.

authors, and enough "cardiac" patients were changed to "non-cardiac" to bring the percentage of "cardiac" etiology patients down from 85% (as published) to 58% (as seen in the largest study, identified in Table 1, by Tanabe et al). This was done by starting at the bottom of each list in the data spreadsheet (the latest patients chronologically) and changing all etiologies from "cardiac" to "non-cardiac" working up the list until the percentage of "cardiac" etiologies dropped to 58%. Survival in the "before intervention" group dropped from 24.6% in Sayre's paper to 18.3% in the revision, and in the "after intervention" group, it increased from 31.2% in Sayre's paper to 33.8% in the revision. This represents a 25.6% relative change in survival for the "before" group (a substantial difference in survival brought on simply by altering the definition of cardiac etiology) and a less substantial 7.6% relative change for the "after" group.

The Utstein template defines cardiac etiology in the negative.[1] An arrest should be classified as cardiac "unless it is known or likely to have been caused by trauma, submersion, drug overdose, asphyxia, exsanguination, or any other non-cardiac cause as best determined by rescuers." This implies that indeterminate cases

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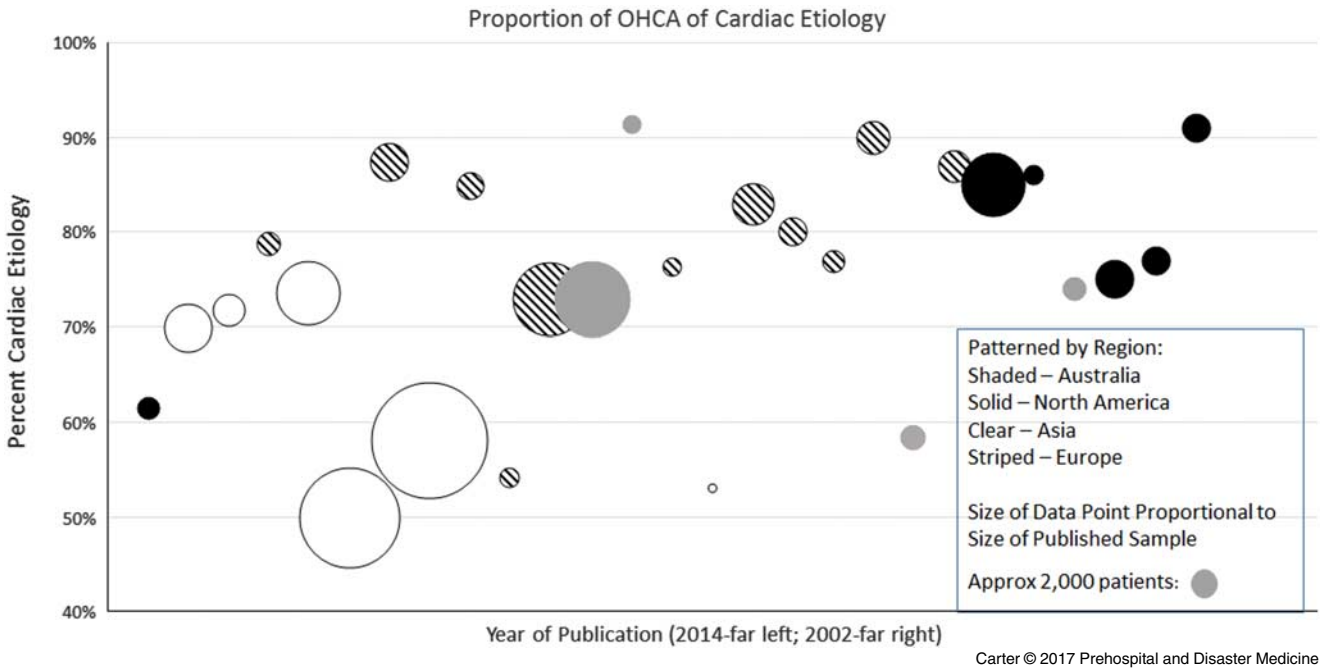

Figure 2. Proportion of OHCA of Cardiac Etiology.
Note: Shows the 27 datasets plotted chronologically on the x-axis, with percentage deemed cardiac on the y-axis. Each data point is patterned by continent, with the relative size of the bubble proportional to the size of the dataset; no obvious visual relationship is noted between dataset size and percentage of arrests deemed cardiac.
Abbreviation: OHCA, out-of-hospital cardiac arrest.

should be considered cardiac etiology. These indeterminate cases are open to various interpretations. Imagine two hypothetical cardiac arrest patients, each found down in their own homes: one, a slim 30-year-old woman; the other, an obese 70-year-old man. In the absence of other past medical history or data available at the scene, the Utstein definition would define both arrests as cardiac etiology. Is it reasonable to assume that responding EMS providers, or even researchers abstracting medical records, would label each patient as cardiac etiology with the same frequency?

Most EMS crew members typically have insufficient evidence at the time of EMS responses to definitively know the etiology of many cardiac arrests. One could list a number of possible cardiac etiologies, including coronary artery disease, congestive heart failure, valvular heart disease, aortic dissection, congenital heart disease, conduction abnormalities, and cardiomyopathies. Each of these categories has any number of possible etiologies; congenital heart disease, for example, could include coronary artery abnormalities, surgically corrected defects (eg, tetralogy of Fallot), hypertrophic cardiomyopathy, Wolff-Parkinson-White syndrome, arrhythmogenic right ventricular dysplasia, and the several cardiac ion channelopathies. This latter category is gaining significant attention as it is becoming recognized that there may be many clinical syndromes other than congenital long QT syndrome and Brugada syndrome that can be attributed to channelopathies.[8,9] There are similarly dozens of non-cardiac etiologies of OHCA, in categories including infectious (sepsis, myocarditis, endocarditis), respiratory (pulmonary embolism, aspiration), immunologic (anaphylaxis, angioedema), toxicologic (both recreational and pharmacologic), electrolyte/metabolic (hyperkalemia, hypocalcemia, metabolic acidosis), and even trauma (hemorrhagic shock, commotio cordis, myocardial rupture).

In these indeterminate cases, where EMS personnel have no reasonable way to determine the underlying pathophysiology of a cardiac arrest, uniform criteria are needed that are consistently applied. Until such criteria are available, full data should be reported on both cardiac and non-cardiac etiology cardiac arrests in peer-reviewed research, rather than removing the presumed non-cardiac cases from further consideration. Those researching OHCA should work to build consensus in order to move towards a revised definition of cardiac arrest etiology, or a more uniform application of existing definitions.

Limitations

It is possible that this search missed one or more papers with other OHCA databases; however, the study objective was not to capture and quantify all such databases, but simply to illustrate the range of percentages of "cardiac" vs "non-cardiac" etiology. Unless a missed database has <50% or >91% of cases deemed "cardiac," the overall findings would be unaffected.

Conclusions

There is substantial variability among cardiac arrests datasets and research publications regarding the percentages of cases deemed to be of "cardiac" vs "non-cardiac" etiology. This has substantial implications for the calculation of survival rates and other research outcomes, as well as clinical practice of OHCA resuscitation.

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