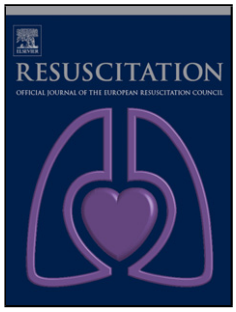

Cardiac Arrest: An Interdisciplinary Review of the Literature from 2018

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Cardiac Arrest: An Interdisciplinary Review of the Literature from 2018

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The Interdisciplinary Cardiac Arrest Research Review (ICARE) group members who contributed to this manuscript are listed in Appendix A.

ABSTRACT

Objectives: The Interdisciplinary Cardiac Arrest Research Review (ICARE) group was formed in 2018 to conduct a systematic annual search of peer-reviewed literature relevant to cardiac arrest (CA). The goals of the review are to illustrate best practices and help reduce knowledge silos by disseminating clinically relevant advances in the field of CA across disciplines.

Methods: An electronic search of PubMed using keywords related to CA was conducted. Title and abstracts retrieved by these searches were screened for relevancy, separated by article type (original research or review), and sorted into 7 categories. Screened manuscripts underwent standardized scoring of overall methodological quality and importance. Articles scoring higher than 99 percentiles by category-type were selected for full critique. Systematic differences between editors and reviewer scores were assessed using Wilcoxon signed-rank test.

Results: A total of 9119 articles were identified on initial search; of these, 1214 were scored after screening for relevance and deduplication, and 80 underwent full critique. Prognostication & Outcomes category comprised 25% and Epidemiology & Public Health 17.5% of fully reviewed articles. There were no differences between editor and reviewer scoring.

Conclusions: The total number of articles demonstrates the need for an accessible source summarizing high-quality research findings to serve as a high-yield reference for clinicians and scientists seeking to absorb the ever-growing body of CA-related literature. This may promote further development of the unique and interdisciplinary field of CA medicine.

MeSH Keywords: Heart Arrest, Out-of-Hospital Cardiac Arrest, Cardiopulmonary Resuscitation, Epidemiology, Emergency Medical Services, Sudden Cardiac Death,

INTRODUCTION

An individual of any age may suffer a cardiac arrest (CA) without warning [1]. The 2018 AHA guidelines defines CA as “the cessation of cardiac mechanical activity, as confirmed by the absence of signs of circulation”[2]. The etiology of CA can be broadly categorized to cardiac vs. non-cardiac [3]. The precise estimation of the overall CA incidence is difficult, as epidemiologic reports often comprise CA subtypes according to location of occurrence (in-hospital or out-of-hospital), Emergency Medical Services (EMS) involvement, etiology, and age groups. In addition,

the lack of a comprehensive and uniform national or international standardized repository of data in CA further challenges an accurate epidemiologic appraisal.

OHCA accounts for over 350,000 deaths in the United States annually [4], and continues to be a major public health challenge worldwide. Despite advances in resuscitation and critical care medicine, large variation in cardiac arrest survival rates exists at community, national, and global levels [5, 6].

Recognizing the need for a concise and accessible literature source to disseminate the findings on the growing knowledge in the CA field, the Interdisciplinary Cardiac Arrest Research Review (ICARE) Group was created in 2018 with the goals of disseminating evidence on best practices, stimulating further research lines, and promoting team science with a transdisciplinary approach to the field of CA medicine. This work was inspired by the success of Global Emergency Medicine Literature Review (GEMLR) initiative [7] in facilitating awareness of research published in relation to global health.

This review gathers summary of articles from multiple sources in a systematic fashion, presenting the ones chosen as having specific relevance or value to the different CA domains after a structured review process and involves the input from clinicians from multiple disciplines. Unlike a formal systematic review or meta-analysis that appraises the literature based on a specific research question, the scope of this review is to summarize the yearly updates on high-quality CA research. The intent of the ICARE review is to serve as a resource both for practitioners caring for CA patients as well as academic researchers.

METHODS

Our procedures were largely influenced by GEMLR's reproducible methodology. The ICARE working group comprised 28 reviewers, 10 editors, and 4 editorial board members from multiple disciplines and educational backgrounds in the field of CA medicine and underwent a rigorous selection process. The editors are practicing clinicians and scientists actively involved in the CA field. The detailed protocol used by the ICARE group is available as **Supp. 1**.

Literature search

Publications pertaining to CA were searched on PubMed in two phases: the first included publications between January and May, and the second phase between June and December 2018.

All publications with an 'Electronic Date of Publication' (if applicable) or 'Print Date of Publication' (if applicable) in 2018 were included. The search terms used are listed in **Table 1**. Only articles published in English were selected. Publications that were news articles, editorials, case reports, commentaries, and letters to the editor were excluded. The full MEDLINE search query is presented in **Supp. 2.**

Article Screening

The titles and abstracts of articles identified during the literature search were screened by the technical and assistant technical editor based on their relevance to the field of CA. Full texts of selected articles were classified as either Original Research (OR) or Review (RE) according to the study design. The boundaries of the field of CA medicine are not clearly defined; for the purpose of this review we created seven categories through a consensus process: Epidemiology & Public Health (EPH), Prehospital Resuscitation, Technology & Care Processes (PRE), In-Hospital Resuscitation & Post-Arrest Care Processes (IN), Prognostication & Outcomes (PRO), Pediatrics (PED), Basic Science & Pharmacology (BSP), and Interdisciplinary Guidelines & Reviews (GL).

Article Scoring

Using a predefined scale according to the study type (OR versus RE), each article was scored by two independent and blinded reviewers across five separate categories; these included article's clarity, design, ethics, importance, and impact. Total scores ranged between 0-22 (**Table 2** displays OR scoring scale, and **Table 3** scoring scale for RE articles). These scales were created to identify articles with a robust methodology and high importance to the field of CA. For quality assurance, 30-40 articles in each category were scored twice (one reviewer, one editor). Systematic differences in scores between editor and reviewer were assessed using Wilcoxon signed-rank test.

Full Article Review

Articles scoring higher than 99 percentiles by category and type were chosen for a full review. Reviewers then summarized selected articles encompassing the objective, key findings, as well as strengths and limitations of each study. Subsequently, editors reviewed summaries for content, accuracy, and style according to each category.

RESULTS

The screening, scoring, and full article review process is presented in **Figure 1**. A total of 9119 articles were identified and after removal of duplicates and those not relevant to CA; 1214 articles were categorized and underwent full review. Inter-rater reliability between the screening editors revealed a Cohen's kappa score of 0.90 (95% CI: 0.87 – 0.94). Article scoring statistics for each article category are summarized in **Table 4**. Eighty articles were selected for a full summary and critique; of these, 52 (65%) were OR articles. Twenty five percent of summarized articles were in the PRO category and 17.5% in EPH. No significant differences between editor and reviewer scoring were found. Editor and Reviewer scoring evaluations of the included articles are available as **Supp. 4** (Original Research Articles) and **Supp. 5** (Review Articles).

DISCUSSION

Full summaries and critique of the top scoring CA articles of 2018 identified by our review are available as **Supp. 3.** Below, we highlight the critical findings of our top-scoring articles.

Epidemiology & Public Health (EPH)

Four of the RE articles in this category were systematic reviews and meta-analyses of clinical conditions that were associated with an increased incidence of CA[8-11]. Alba et al. [12] reported on the incidence of CA in heart transplant patients. Alqahtani et al. [9] reported on regional variation in incidence and outcomes of overdoses related-CA, however when compared to non-overdose CA patients, overdose patients were more likely to survive to discharge. The other two reviews identified the association of certain cardiac conditions with CA-related death [10, 11]. There was a significant association between atrial fibrillation and CA-related death. A systematic review and meta-analysis by Nalliah et al. [11] demonstrated that mitral valve prolapse was observed in 11.7% of CA patients with undetermined cause of death.

Cavacanthi et al. [13] reviewed implantable cardiac defibrillator placement in patients with nonischemic cardiomyopathy and reported a significant reduction in all-cause mortality and arrhythmia-related deaths. In the general, adult population, Kenttä et al. demonstrated that a novel electrocardiographic marker, T-wave area dispersion, was independently predictive of sudden cardiac death (4.6-fold increase in adjusted risk).

Two studies focused on one of the important links in the 'chain of survival': effective CPR. Lockey et al.'s [15] review found an association between Advance Cardiac Life Support trained rescuers and return of spontaneous circulation (ROSC) and survival to hospital discharge. In a randomized clinical trial (RCT) comparing self-trained Basic Life Support and facilitator-led training, Pederson et al. [16] demonstrated that at 3 months, the self-trained group had adequate retention of skills, but there was a significant decrease in the percentage of correct compressions in the facilitator-led group. Early and effective CPR can improve CA outcomes and encouraging self-training of CPR may allow for more members of the community to be trained. Groups previously trained by facilitators may benefit from a re-evaluation of skills, and possibly retraining.

Prehospital Resuscitation, Technology & Care Processes (PRE)

The first link in the 'chain of survival' involves early recognition of a CA event and early access to emergency response services. Eleven of the top-scoring articles were PRE articles. A systematic review by Song et al. [17] demonstrated again that bystander CPR was associated with increased rates of survival. This is important to highlight as in 2017, only 46% of patients who had CA outside the hospital received bystander CPR, and the outcomes for women remain disproportionally worse than men [18]. In a simulation study, Birkun et al. [19] demonstrated that pre-recorded instructional audio is not inferior to dispatcher-assisted CPR when it comes to assisting untrained rescuers to perform compression-only CPR. This is an important finding that may lead to improving access to CPR instructions in areas where trained dispatchers may not be readily available or when there is a language barrier between dispatcher and caller.

2018 saw the publication of several major prehospital airway studies. In a prospective RCT by Benger et al. [20] and a systematic review and meta-analysis by White et al. [21], no significant outcome differences were found in pre-hospital use of supraglottic airway vs. tracheal intubation; however in a multicenter RCT by Wang et al. [22], initial use of supraglottic airways (laryngeal tube) by prehospital personnel in CA patients was associated with higher survival rates at 72 hours. The latter finding may be partly explained by the decrease in multiple attempts at endotracheal intubation, tube misplacement, and interruption of CPR when using a supraglottic airway.

In a meta-analysis comparing CA patient outcomes when transported to cardiac resuscitation centers vs. non-cardiac resuscitation centers, Lipe et al. [23] showed increased odds

ratios of both survival and survival with good neurologic outcome when transported to specialized centers.

In an RCT by Jabre et al. [24] assessing the noninferiority of bag-mask ventilation (BMV) against endotracheal intubation (ETI), no statistical difference in survival to 28 days between the groups was found. Emergency physicians supervised airway intervention and performed ETI. Nonetheless, a 2-fold increase of aspiration in the BVM group compared to the ETI group was reported, suggesting an important adverse risk in using BVM compared to ETI during initial airway management.

In-Hospital Resuscitation & Post-Arrest Care Processes (IN)

The majority of articles scored highly in this category are OR articles (80%). The use of therapeutic hypothermia (TH) in CA is a concept that has existed since the 1950s[25], and has reemerged in the early 2000s. Four articles in the IN category studied the effects of TH in CA. In a swine study, Xu et al. [26] showed that rapid esophageal cooling led to decreased cardiac and neurological injuries, implying the significance of time to target temperature in decreasing tissue injury after CA. The FROST-I, a multicenter, international, RCT, studied the effectiveness of different temperatures in the range of 32-34 ℃ and found no clinically significant differences in neurological outcomes [27]. One of the complications associated with TH is coagulopathy. This was investigated in a single-center RCT by Jeppesen et al.[28], demonstrating that platelet aggregation was abnormal in OHCA patients independent of the patient's core temperature, but that there was no statistically significant difference related to the duration of targeted temperature management (TTM), and the degree of reduction in platelet aggregation was likely to be clinically insignificant. The effect of TTM on biomarkers of prognostication was studied by Duez et al.[29] in a multicenter RCT, and the group found that the duration of TTM post-CA (24 vs. 48 hrs) did not affect levels or prognostic performance of neuron-specific enolase (NSE) and protein S100B.

Post-resuscitation efforts involve optimizing multiple organ systems with the goal of decreasing further neurological injury. In a multicenter RCT by Jakkula et al.[30] studying the effect of low-normal vs. high-normal mean arterial pressure (MAP) post-CA showed no statistical significance in NSE and S100B (surrogate biomarkers of hypoxic-ischemic brain injury) or troponin (surrogate marker of cardiac injury) levels, duration of intensive care or mechanical ventilation, 30-day mortality, or functional status at hospital discharge and at 6 months. A

systematic review with a meta-analysis studying survival in OHCA with early use of coronary angiography observed statically significant improvement in short and long-term survival rates, as well as neurological outcomes in patients who underwent early coronary angiography [31].

Basic Science & Pharmacology (BSP)

Nine top-scoring studies were selected in the BSP category. Six of the 7 included OR articles involved the use of an animal model, such as rats, mice, swine, and porcine. Two ORs studied pharmacologic interventions that would improve outcomes post-arrest. Wallisch et al.[32] studied the therapeutic potential for reducing acute cerebral edema in a pediatric CA model and demonstrated that AER-271, an AQP4 (a water channel protein responsible for fluid transport in the cortex) antagonist may facilitate fluid reabsorption after CA, thereby mitigating ischemia-induced edema. Previous studies demonstrated improved survival in patients treated with neuromuscular blockade (NMB) infusion who underwent TTM; however, a study by Byung Kook et al. [33], refuted this finding. In an open-labeled multicenter RCT conducted in South Korea to investigate outcomes in CA patients undergoing TTM who were treated with NMB infusion for the prevention of shivering, the authors found no difference in survival or neurological outcome at hospital discharge, ICU and hospital LOS, or changes in PaO2/FiO2 ratios.

Antipsychotics and antidepressants can affect cardiac conduction at different phases of the cardiac action potential. In a review by Sicouri et al.[34], the mechanisms by which patients are vulnerable to deadly arrhythmias by the administration of QT-prolonging medications are discussed, including how such medications can unmask Brugada syndrome in patients who have channelopathies. In another review paper, Jou et al.[35] discusses the role of inflammatory cytokines in CA and post-CA physiology, highlighting potential therapeutic targets. Tahsili-Fahdan et al.[36] reviews the pathophysiology of brain ischemia-reperfusion injury that occurs post-CA and the role that TTM plays in mitigating these effects.

Traumatic arrests have the lowest recovery rates of all cardiac arrests. In a study by Anderson et al. [37], using swine models of traumatic arrests show improved outcomes with chest compressions focused over the left ventricle.

Three studies evaluated post-arrest therapies that improve neurological outcomes. Babini et al.[38] looked into the effect of hypercapnia on cerebral perfusion, which has been linked to better outcomes. They demonstrated that in swine models of VF arrest, mild hypercapnia resulted

in less neuronal degeneration but had similar short-term neurological outcomes as normocapnic states. Similarly, Byunghuym et al.[39] demonstrated that rats undergoing vagus nerve stimulation following resuscitation may have increased cerebral blood flow and improved neurological recovery. In a study researching novel therapeutic interventions that prevent ischemic reperfusion brain injury post-CA, Hayashida et al.[40] demonstrate that S-nitrosoglutathione reductase inhibition in murine models of CA provided a protective mechanism and prevented worsening of injury by alternatively enhancing protein S-nitrosylation. They further evaluated the activity of S-nitrosoglutathione reductase where levels were significantly increased in convenience samples collected from post-CA patients.

Prognostication & Outcomes (PRO)

Prognostication & Outcomes category had the highest number of top-scoring articles. None of the currently used neurological predictors are 100% specific, which is why current guidelines recommend using a multimodal approach and that prognostication be delayed up to 72 hours post-ROSC [41]. Tong et al.[42] reported on earlier vs. delayed prognostication in an observational cohort, and were unable to establish an optimal time window for neuroprognostication following CA.

Bevers et al. [43] in a retrospective observational study of a prospective cohort of CA patients treated with TTM at a single center sought to determine the prognostic value of using a combination of clinical exam, MRI, and EEG findings to predict the outcome. Another modality that may be used to assist with predicting outcomes is the critical care illness scores which have been successfully used in disease processes such as sepsis. Isenschmid et al. [44] attempted to study the performance of clinical scores in predicting mortality and neurological outcome and observed that each score type had varying sensitivity and specificity when it came to predicting in-hospital mortality, neurological outcome at discharge, and mortality at 30 days. Their study demonstrated that scores designed specifically for CA patients (CAHP and OHCA) performed better when compared to traditional ICU scores (APACHE II and SAPS II)

Scarpino et al. [45] employed a multimodal approach of neurophysiological and neuroradiological studies to predict outcome within 24 hours of arrest in a cohort less impacted by the self-fulfilling prophecy bias. EEG, somatosensory evoked potentials, and head computed tomography (CT) were sensitive and specific in predicting poor outcome post-CA. The prognostic

value of the neurological exam in in-hospital and OHCA patients treated with TTM was explored by Matthews et al. [46].

Nagaraj et al. [47] sought to revise the Cerebral Recovery Index, a group of quantitative EEG measurements. Another quantitative study that scored highly in the prognostic category was the use of a quantitative pupillometry in a multimodal approach to predict post-arrest outcomes [48].

Biomarkers are emerging as potential prognostic tools in CA medicine. Isenschmid et al. [49] analyzed the predictive value of biomarkers of distinct pathways within the post-CA syndrome: cardiac dysfunction, systemic inflammatory response, and shock. Although the authors demonstrated that the biomarker levels reflected the severity of the post-CA syndrome, Pekkarinen et al. [50] analyzed biomarkers of hemodynamic instability and demonstrated that in post-CA patients levels of procalcitonin at admission predicted low MAP during the initial 48 hrs. The ideal MAP targets post-arrest have not been defined yet, and its prognostic value is unclear. Grand et al. [51] identified risk factors that are associated with lower MAP after CA.

The only serum biomarker currently approved for prognostication after CA is NSE [52], a protein found in neuronal cell bodies and axons. Moseby-Knappe et al. [53] demonstrated that neurofilament light-chain (NFL), a protein that is part of the neuronal cytoskeleton, demonstrated prognostic value superior to NSE, and NFL also outperformed all single neuroprognostic modalities recommended by current guidelines. Its predictive value further increased when combined with other clinical variables and neurological exams.

Na et al. [54] performed a meta-analysis of the utility of gray matter to white matter ratio in the initial head CT at predicting neurological outcome and found that basal ganglia gray to white matter ratio had the highest accuracy at predicting outcome.

There is a paucity of long-term follow-up studies on CA patients. In a study by Agarwal et al. [55], the group retrospectively assessed determinants of long-term outcomes in a group of CA survivors that were prospectively enrolled and demonstrated that discharge status did not always correlate with long-term neurological recovery (CPC at 1 year).

Optimizing post-CA care includes preventing extreme variations in vital signs [56]. An ad hoc analysis of a prospective, multicenter Japanese database on comatose patients that received therapeutic hypothermia for 72 hours post-OHCA was assessed to see if variations in heart rate could yield prognostic information. Patel et al.'s [57] meta-analysis of 16 studies demonstrated

that intra-arrest hyperoxia was associated with improved survival, whereas post-arrest hyperoxia was associated with higher mortality. Although only two studies examined intra-arrest PaO2 level and 14 studies examined post-arrest hyperoxia with variable time points of PaO2 sampling, this review highlights an important variable that should be closely monitored in CA patients.

The appropriate use of extracorporeal cardiopulmonary resuscitation (ECPR) in post-arrest patients is still being established and two retrospective studies assessed the use of ECPR and outcome prognostication. Otani et al. [58] demonstrated that low flow times were associated with favorable outcomes in ECPR patients and Mandigers et al. [59] demonstrated how ECPR may improve survival in CA due to massive pulmonary embolism. These studies' largest limitation is that they represent a highly selected cohort, as not all post-CA patients meet criteria for ECPR.

Laboratory studies may be used to aid in outcome prediction. Fibrinolysis has been associated with increased mortality in critically ill trauma or septic patients, and in a study by Buchtele et al. [60], increased markers of fibrinolysis on admission with a maximum lysis value on thromboelastometry of >20% was suggestive of a predictor of poor outcome in OHCA survivors. In a retrospective study, Fontana et al. demonstrated that a higher red blood cell distribution width post-CA may be a marker of chronic organ dysfunction and is associated with poor neurological outcome at 3 months.

Elmer et al. [61] reports that the direct transport or early transfer of patients with OHCA to a regional CA center is associated with improved prognosis

Pediatrics (PED)

Seven articles were chosen for the pediatrics category, six of which were OR. A majority of the studies looked into CPR technique and quality[62-65]. In a prospective RCT, Cheng et al. showed that the inclusion of a CPR coach in the resuscitation teams using a feedback defibrillator yielded a statistically significant improvement in excellent CPR delivery. Jung et al. [64] conducted a mannequin study comparing the effectiveness of three different chest compression techniques for the single rescuer in infant CA. This included a novel "knocking fingers" technique designed to reduce operator fatigue and interruptions, while still providing adequate chest compressions and ventilation. Lin et al. [63] showed better retention of BLS knowledge and CPR skills by participants who received monthly practice and feedback. Assessing various elements of CPR quality in IHCA in pediatric patients sub-grouped by age using a feedback monitor-

defibrillator in a retrospective, multi-center observational study, Niles et al. (63) showed that overall compliance was poor, and in particular, chest compression depth in infants.

The single RE article that was top-scoring in the pediatric category was the 2018 update to the PALS guideline released by the AHA following the Pediatric Task Force of the International Liaison Committee on Resuscitation (ILCOR), which reviewed a single article demonstrating a significant increase in ROSC, yet no difference in survival, with lidocaine compared to amiodarone for in-hospital ventricular fibrillation or pulseless ventricular tachycardia arrest[66].

Two OR studies evaluated pediatric post-CA care. Yunge et al. [67] studied the effects of automated, servo-control vs. non-servo-controlled TTM in an international multicenter study. They found that although the automated methods were more accurate, use of cooled IV fluids, ice packs, and adjusting the environmental temperature did not change complication rates, survival to discharge, or outcomes at 6 months.

Meert et al.'s [68] prospective study of the neurobehavioral outcomes of pediatric IHCA patients, who received ECPR in 37 pediatric ICUs in North America and the UK, helps elucidate ECPR efficacy in primarily post-cardiac surgery patients.

Interdisciplinary Guidelines & Reviews (GL)

Guidelines help standardize CA management and identify important areas that need further research or quality improvement. Ten reviews scored highly in the interdisciplinary guidelines and reviews category. A French expert panel conducted a systematic review of current literature and came up with a consensus statement regarding the use of TTM in the ICU making 30 recommendations regarding patients that should undergo TTM, method of cooling, and populations that do not benefit from TTM[69]. Karcioglu et al.[70] reviewed safety and adverse effects associated with TTM to help maximize the benefit of TTM following CA. In another systematic review and meta-analysis, a sudden cardiac death risk stratification tool developed for patients with hypertrophic cardiomyopathy (HCM Risk-SCD) was analyzed to determine if patients were being optimally selected for implantable cardiac defibrillator placement. The authors found that patients with hypertrophic cardiomyopathy identified as low-risk (implantable cardiac defibrillator not recommended) by the tool had a much lower (1%) rate of sudden cardiac death compared to the previously predicted rate of 4%[71].

Madder et al.[72] reports on the use of a multidisciplinary approach to maximize

neurological recovery while minimizing secondary brain injury with examples of evidence-supported therapies and care bundles that are associated with improved outcomes.

Kitamura et al.[73] reviews the first 18 months of a national OHCA registry in Japan, that includes both pre- and in-hospital treatments received by all patients, and their neurological function at 1 month. This database is unique because it continues to collect data on interventions received after hospital admission.

The variability of outcomes used in CA literature makes it difficult to compare findings from one study to another. Haywood et al.[74] have sought to identify the core set of outcome measures that should be used to facilitate and optimize comparisons across studies

CA studies are prone to bias due to difficulties with enrolling patients during the acute resuscitation phase. In a review that summarizes evidence from Cochrane Systematic Reviews, Pacheco et al. discusses interventions that positively affect CA outcomes[75].

In a statement from the AHA, Cheng et al.[76] review optimal strategies for learning that can be translated into effective practice and suggest new practice models that may be more effective at maximizing retention of knowledge needed in a high-stress resuscitation situation.

With more easy access to commercial air travel, the likelihood of an in-flight CA and performing in-flight CPR is increasing. Hinkelbein et al. [77] provide guidance on how to effectively attempt resuscitation of a CA patient while in-flight.

LIMITATIONS

The 2018 Interdisciplinary Cardiac Arrest Research Review has several limitations. First, the conclusions presented in this review are not designed to change professional practice. The aim of this literature review is to highlight the breadth of articles published in the field of CA medicine and demonstrate the current state of this growing area of critical care research on an annual basis. An intrinsic shortcoming of this approach is that it does not allow to provide extensive context, such as historical comparison, or to account for differences in systems of care. To address this concern, we provide article summaries and commentaries for additional context in Supp. 3. Second, while the methodology used to screen, score and select articles is designed to capture the most relevant published research in the field of CA medicine, it is likely that this process still omits some high-quality publications that deserve attention. Nonetheless, the methods used in this review has been adapted from another well-established literature review. Lastly, in order to remain

objective in this literature search, this review did not include letters to the editor, commentaries, and other editorials that may provide important context to the selected articles.

CONCLUSION

In its first year, the Interdisciplinary Cardiac Arrest Research Review screened more than a thousand articles related to CA and, after a rigorous scoring process, fully summarized 80 articles in seven different categories. This year's top-scoring articles were focused on prognostication and outcomes post-CA. The total number of articles relevant to CA demonstrate the need for an accessible guide that summarizes findings of quality research articles to serve as a reference for clinicians and scientists, given the challenge to monitor the growing body of CA literature. ICARE's goal is to further the development of the unique and interdisciplinary field of CA medicine.

Conflicts of Interest: None to declare

APPENDIX

Appendix A: Interdisciplinary Cardiac Arrest Research Review (ICARE) 2018 Managing Editors, Editors, and Reviewers

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LIST OF TABLES AND FIGURES

Table 1: Search Terms for PubMed Search

Table 2: Scoring of Original Research (OR) Articles

Table 3: Scoring of Review (RE) Articles

Figure 1: Flowchart of screening and scoring process

Table 4: Summary Statistics of Reviewer Scoring by Category and Article Type

Table 5: Interdisciplinary Cardiac Arrest Research Review 2018 Articles

SUPPLEMENT

Supp. 1: The ICARE protocol with detailed methods

Supp. 2: Consolidated MEDLINE Search Query

Supp. 3: Full Article Summaries for 2018 ICARE

Supp. 4: Reviewer and Editor Scores for Evaluated Review Articles

Supp. 5: Reviewer and Editor Scores for Evaluated Original Research Articles

Figure 1: Flowchart of screening and scoring process

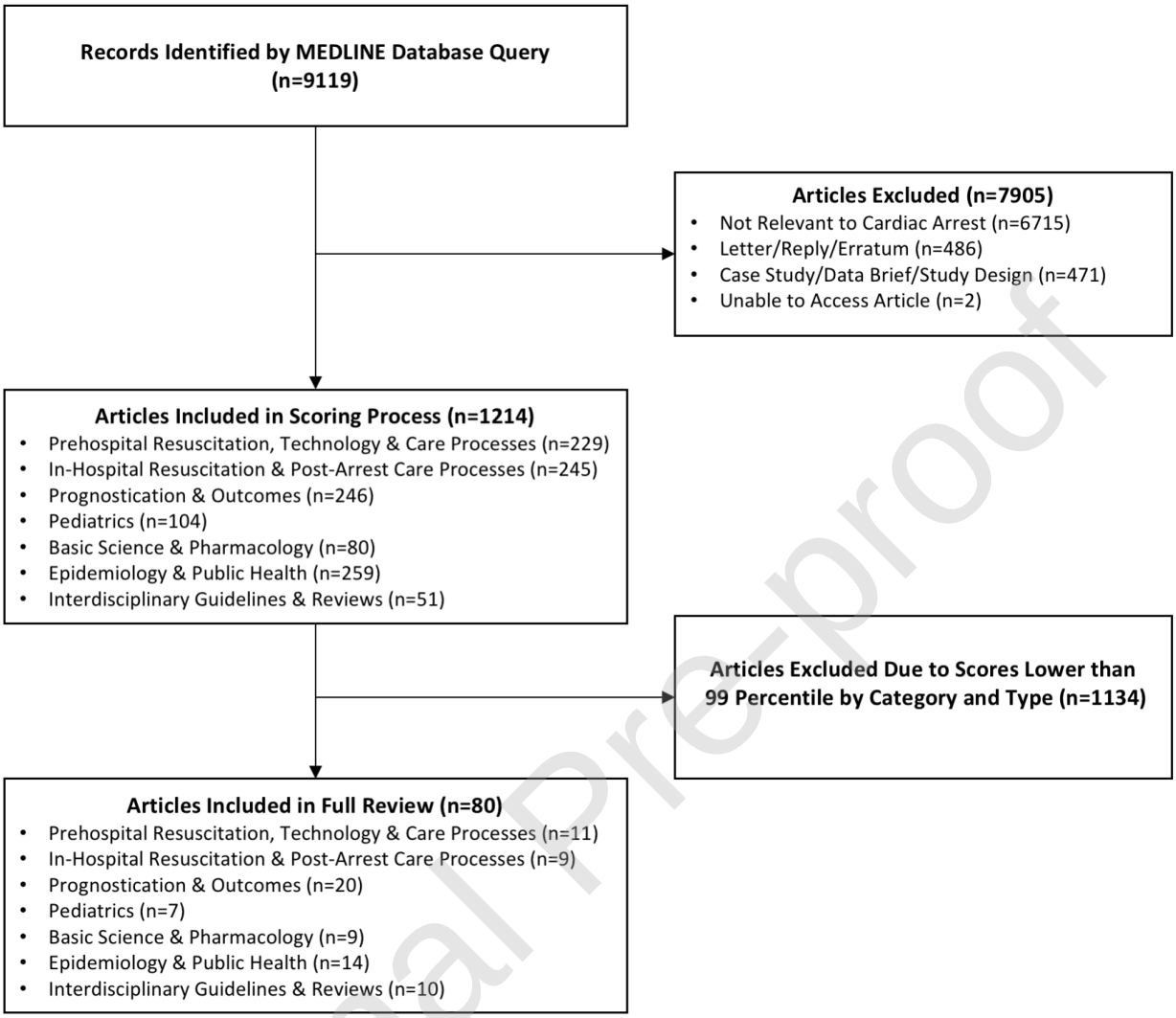

Table 1: Search Terms for PubMed Search

Cardiac Arrest Search Terms
Heart Arrest [MeSH]
Heart Arrest
Cardiac Arrest
Heart Attack
Cardiac
Arrest, Cardiac
Cardiopulmonary Arrest
Ventricular Tachycardia

Table 2: Scoring of Original Research (OR) Articles

Quality Measure	Question		Points
Design A	*Select One*	Descriptive studies (including case studies and case series, natural observation studies and descriptive surveys)	1 *-or-*
		Correlation studies (case control studies, prospective observational studies, retrospective studies)	2 *-or-*
		Non-randomized or non-blinded experimental studies	3 *-or-*
		Randomized, blinded experimental studies	4
B	Study design is appropriate to answer the authors' hypothesis.		1
C	Correct statistical tests are used to analyze the data.		1
D	Results are presented accurately and without bias.		1
E	Limitations are clearly described, and the conclusions are supported by data.		1
Design Total	8 / Out of max score 8		
Ethics A	The study was approved by an institutional review board (IRB)/institutional animal use and care committee, ethics committee, community group, as required by local laws.		2
B	Informed consent was obtained or consent was waived by the IRB (*give point if not applicable, e.g., animal study*).		1
C	The authors declare their conflicts of interest or declare that none exist.		1
Ethics Total	4 / Out of a max of 4		
Importance A	The study results are not specific to one certain patient population but are broadly generalizable to a variety of settings.		2
B	The topic being studied is an important one, in that it advances the field of cardiac arrest research or care.		2
C	The study is clearly relevant to the realm of cardiac arrest research or care.		1
Importance Total	5 / Out of a max of 5		
Impact A	The findings or recommendations of this study may be feasibly implemented by practitioners* of cardiac arrest care.		2
B	Practitioners* would likely change their practice if they were aware of this study.		2
C	The authors of this study raise interesting questions that may stimulate further research.		1
Impact Total	5 / Out of a max of 5 *Practitioner: reader practicing in the category of the article (physician, epidemiologist, pharmacist etc.)		

Table 3: Scoring of Review (RE) Articles

Quality Measure	Question	Points
Clarity A	The review has a clearly stated hypothesis or purpose.	2
B	The authors provide sufficient background to put the results of the review into context.	1
C	The review can be understood by someone with general medical or public health training.	1
D	The authors use clear language and appropriate graphs, tables, and figures throughout the article.	1
Clarity Total	5 / Out of max score 5	
Design A	This is a formal meta-analysis or a systematic review that only includes studies with a control group.	3
B	There is a clear, reproducible method for the selection of studies included in this review.	2
C	Articles for this review were selected by at least two authors blinded to each other's selection.	1
D	The data was aggregated and/or analyzed appropriately.	1
Design Total	7 / Out of max score 7	
Importance A	The review is not specific to one certain patient population but is broadly generalizable to a variety of settings.	2
B	The topic being reviewed is an important one, in that it advances the field of cardiac arrest research or care.	2
C	This is clearly relevant to the realm of cardiac arrest research or care.	1
Importance Total	5 / Out of max score 5	
Impact A	The findings or recommendations of this review appear to have applicability towards improving cardiac arrest research or care.	2
B	Practitioners* would likely change their practice if they were aware of this review.	2
C	The authors of this review raise interesting questions that may stimulate further research.	1
Impact Total	5 / Out of max score 5 *Practitioner: reader practicing in the category of the article (physician, epidemiologist, pharmacist etc.)	

Table 4: Summary Statistics of Reviewer Scoring by Category and Article Type

	Original Research (OR)		Review (RE)	
Article Category	Count (%)	Median (IQR)	Count (%)	Median (IQR)
Basic Science & Pharmacology (BSP)	70 (7.0)	12 (11 - 18)	10 (4.5)	13 (7 - 15)
Epidemiology & Public Health (EPH)	207 (20.8)	12 (11 - 18)	52 (23.6)	17 (13 - 19)
Prehospital Resuscitation, Technology & Care Processes (PRE)	192 (19.3)	12 (10 - 16)	37 (16.8)	14 (12 - 18)
In-Hospital Resuscitation & Post-Arrest Care Processes (IN)	208 (20.9)	12 (10 - 16)	37 (16.8)	15 (7 - 19)
Prognostication & Outcomes (PRO)	220 (22.1)	12 (11 - 12)	26 (11.8)	15.5 (13 - 18)
Pediatrics (PED)	97 (9.8)	12 (11 - 16)	7 (3.2)	16 (12 - 19)
Interdisciplinary Guidelines & Reviews (GL)	---	--- ---	51 (23.2)	15 (13 - 20)
Totals	994 (100.0)	12 (11 - 16)	220 (100.0)	15 (13 - 19)

Table 5: Interdisciplinary Cardiac Arrest Research Review 2018 Articles

Category	First Author	Title	Journal	Type	Summary
Prehospital Resuscitation, Technology & Care Processes	Belletti A	Vasopressors During Cardiopulmonary Resuscitation. A Network Meta-Analysis of Randomized Trials.	Crit Care Med	RE	In a comparison of vasopressors administered in the setting of cardiac arrest, epinephrine and vasopressin may result in an increased rate of survival, increased likelihood of ROSC and improved neurologic outcomes.
	Benger JR	Effect of a Strategy of a Supraglottic Airway Device vs Tracheal Intubation During Out-of-Hospital Cardiac Arrest on Functional Outcome: The AIRWAYS-2 Randomized Clinical Trial.	JAMA	OR	No statistically significant difference in functional outcome was identified between pre-hospital supraglottic airway vs endotracheal intubation provided by paramedics for out-of-hospital cardiac arrest.
	Birkun A	Pre-recorded instructional audio vs. dispatchers' conversational assistance in telephone cardiopulmonary resuscitation: A randomized controlled simulation study.	World J Emerg Med	OR	Pre-recorded instructional audio is no less effective than dispatcher-assisted CPR in assisting untrained rescuers to perform compression-only resuscitation in a simulation setting.
	Deakin C	Can rescuers accurately deliver subtle changes to chest compression depth if recommended by future guidelines?	Resuscitation	OR	Although able to detect subtle changes to chest compression depths, rescuers are still not able to meet the recommended depth for optimal chest compressions.

	Hyun S	Effect of knee positions on cardiac compression variables in cardiopulmonary resuscitation of rescuer; Manikin study.	J Exerc Rehabil	OR	Researchers compared compression forces generated by participants performing CPR in two different positions: with knees on ground at 50 cm from the point of compression, versus knees on ground at 23.3 cm from point of compression. The closer position is associated with higher compression and faster compression release.
	Jabre P	Effect of Bag-Mask Ventilation vs Endotracheal Intubation During Cardiopulmonary Resuscitation on Neurological Outcome After Out-of-Hospital Cardiorespiratory Arrest: A Randomized Clinical Trial.	JAMA	OR	The study assessed if bag-mask ventilation (BMV) was non-inferior to endotracheal intubation (ETI) during cardiopulmonary resuscitation (CPR), using survival with favorable neurological function at 28 days as a primary outcome. No statistical difference was determined, although aspiration was increased in the BMV group.
	Lipe D	Do Out-of-Hospital Cardiac Arrest Patients Have Increased Chances of Survival When Transported to a Cardiac Resuscitation Center?	J Am Heart Assoc	RE	Meta-analysis of randomized controlled trials and observational studies of survival and neurological outcomes following out-of-hospital cardiac arrest (OHCA) patient transport to cardiac resuscitation centers vs non-cardiac resuscitation centers showing increased odds ratios of both survival and survival with good neurologic outcome when transported to specialized centers.

	Perkins G	A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest.	N Engl J Med	OR	In a large double blinded, randomized controlled trial in the United Kingdom, researchers found that paramedic use of epinephrine in out-of-hospital cardiac arrest (OHCA) resulted in a higher rate of 30-day survival than the use of placebo, however, there was no improvement in favorable neurologic outcome. There was a higher percentage of survivors with severe neurologic impairment in the epinephrine group than in the placebo group.
	Song J	The effect of bystander cardiopulmonary resuscitation on the survival of out-of-hospital cardiac arrests: a systematic review and meta-analysis.	Scand J Trauma Resusc Emerg Med	RE	A meta-analysis examining the effect of bystander cardiopulmonary resuscitation (BCPR) on out-of-hospital cardiac arrest patients found increased rates of survival in patients receiving BCPR, especially in those with an initial shockable rhythm.
	Wang H	Effect of a Strategy of Initial Laryngeal Tube Insertion vs Endotracheal Intubation on 72-Hour Survival in Adults With Out-of-Hospital Cardiac Arrest: A Randomized Clinical Trial.	JAMA	OR	Initial use of supraglottic airways rather than endotracheal tubes by advanced-level Emergency Medical Services personnel in out of hospital cardiac arrest is associated with increased 72-hour patient survival.
	White L	Advanced airway management in out of hospital cardiac arrest: A systematic review and meta-analysis.	Am J Emerg Med	RE	In a meta-analysis, no difference in survival or neurologic outcomes following use of supraglottic airway device vs tracheal intubation was found.

In-Hospital Resuscitation & Post-Arrest Care Processes	Duez C	Neuron-specific enolase and S-100b in prolonged targeted temperature management after cardiac arrest: A randomised study.	Resuscitation	OR	Duration of targeted temperature management (TTM) after cardiac arrest does not affect neuron-specific enolase (NSE) and protein S-100b levels nor their prognostic performance.
	Jakkula P	Targeting low-normal or high-normal mean arterial pressure after cardiac arrest and resuscitation: a randomised pilot trial.	Intens Care Med	OR	There was no statistically significant difference in neuron specific enolase (NSE) levels at 48 hours when targeting low-normal or high-normal mean arterial pressure after cardiac arrest.
	Jeppesen A	Platelet aggregation during targeted temperature management after out-of-hospital cardiac arrest: A randomised clinical trial.	Platelets	OR	Platelet aggregation is below the normal range in patients after out-of-hospital cardiac arrest (OHCA); targeted temperature management (TTM), regardless of duration, induces a further slight reduction in platelet aggregation that is small and likely clinically insignificant.
	Khera R	Early coronary angiography and survival after out-of-hospital cardiac arrest: a systematic review and meta-analysis.	Open Heart	RE	The use of early coronary angiography in patients with out-of-hospital cardiac arrest (OHCA) can improve patient survival and neurological outcome.
	Lopez-de-Sa E	A multicentre randomized pilot trial on the effectiveness of different levels of cooling in comatose survivors of out-of-hospital cardiac arrest: the FROST-I trial.	Intens Care Med	OR	The use of different temperatures in the range of 32-34 ℃ in targeted temperature management (TTM) in out-of-hospital cardiac arrest (OHCA) is not associated with clinically significant neurological outcomes.

	Mentzelopoulos S	Exposure to Stress-Dose Steroids and Lethal Septic Shock After In-Hospital Cardiac Arrest: Individual Patient Data Reanalysis of Two Prior Randomized Clinical Trials that Evaluated the Vasopressin-Steroids-Epinephrine Combination Versus Epinephrine Alone.	Cardiovasc Drugs Ther	OR	Stress-dose steroids during and/or after cardiopulmonary resuscitation (CPR) are associated with lower risk of post-resuscitation mortality from septic shock.
	Welsford M	Does Early Coronary Angiography Improve Survival After out-of-Hospital Cardiac Arrest? A Systematic Review With Meta-Analysis.	Can J Cardiol	RE	Based on a meta-analysis of 23 non-randomized studies, the authors found that early coronary angiography (CAG) resulted in statistically significant improvement in short-term (to discharge or 30 days) and long-term (1-5 years) survival in patients who achieved return of spontaneous circulation (ROSC) after out of hospital cardiac arrest (OHCA).
	Xu J	The Effects of the Duration of Aortic Balloon Occlusion on Outcomes of Traumatic Cardiac Arrest in a Porcine Model.	Shock	OR	Aortic balloon occlusion for 30 minutes during traumatic cardiac arrest, as compared to 60 minutes of occlusion or no occlusion, was associated with improved resuscitation and neurological outcome in a pig model.
	Xu J	Faster Hypothermia Induced by Esophageal Cooling Improves Early Markers of Cardiac	J Am Heart Assoc	OR	Novel esophageal cooling after cardiac arrest that may lead to decreased secondary organ injuries via faster

		and Neurological Injury After Cardiac Arrest in Swine.			cooling rates as demonstrated in this swine model.
Prognostication & Outcomes	Agarwal S	Determinants of Long-Term Neurological Recovery Patterns Relative to Hospital Discharge Among Cardiac Arrest Survivors.	Crit Care Med	OR	Determining factors associated with persistently poor or worsening neurologic recovery at 1 year after cardiac arrest in relationship to hospital discharge status include older age and Hispanic background; disposition to home without requirement of services or to acute rehab is associated with favorable recovery pattern.
	Bevers M	Combination of Clinical Exam, MRI and EEG to Predict Outcome Following Cardiac Arrest and Targeted Temperature Management.	Neurocrit Care	OR	A multimodal model including motor response on clinical exam and MRI and EEG findings has high sensitivity and specificity for predicting good clinical outcome in cardiac arrest patients treated with targeted temperature management.
	Buchtele N	Increased Fibrinolysis as a Specific Marker of Poor Outcome After Cardiac Arrest.	Crit Care Med	OR	Increased fibrinolysis makers on admission with a maximum lysis above 20% may be a promising predictor of poor outcome in out-of-hospital cardiac arrest survivors.
	Elmer J	Long-Term Outcomes of Out-of-Hospital Cardiac Arrest Care at Regionalized Centers.	Ann Emerg Med	OR	Direct transport or early transfer of patients resuscitated from an out-of-hospital cardiac arrest to a regional cardiac arrest center appears to be associated with an improved prognosis.
	Fontana V	Can red blood cell distribution width predict	Minerva Anestesiol	OR	High red blood cell distribution width after cardiac arrest may be a marker of

		outcome after cardiac arrest?			chronic organ dysfunction and is associated with an unfavorable neurologic outcome at 3 months.
	Grand J	Mean arterial pressure during targeted temperature management and renal function after out-of-hospital cardiac arrest.	J Crit Care	OR	Higher mean arterial pressure targets may be beneficial for improved kidney function and reduced risk for renal replacement therapy in out-of-hospital cardiac arrest patients. Older individuals and those with cardiac dysfunction are more likely to have lower mean MAP during TTM.
	Inoue A	The Impact of Heart Rate Response During 48-Hour Rewarming Phase of Therapeutic Hypothermia on Neurologic Outcomes in Out-of-Hospital Cardiac Arrest Patients.	Crit Care Med	OR	Heart rate rising during the rewarming phase of therapeutic hypothermia may suggest a potential for favorable neurologic outcome following cardiac arrest.
	Isenschmid C	Routine blood markers from different biological pathways improve early risk stratification in cardiac arrest patients: Results from the prospective, observational COMMUNICATE study.	Resuscitation	OR	The use of combined serum biochemical reflective of post-cardiac arrest syndrome severity holds promise in outcome prediction following cardiac arrest.
	Isenschmid C	Performance of clinical risk scores to predict mortality and neurological outcome in cardiac arrest patients.	Resuscitation	OR	OHCA, CAHP, APACHE II and SAPS II scores are acceptable predictors of in-hospital mortality and short-term neurologic outcome following cardiac arrest.

	Mandigers L	Survival and neurological outcome with extracorporeal cardiopulmonary resuscitation for refractory cardiac arrest caused by massive pulmonary embolism: A two center observational study.	Resuscitation	OR	Extracorporeal cardiopulmonary resuscitation may lead to improved survival in cardiac arrest due to massive pulmonary embolism.
	Marume K	Mortality and Sudden Cardiac Death Risk Stratification Using the Noninvasive Combination of Wide QRS Duration and Late Gadolinium Enhancement in Idiopathic Dilated Cardiomyopathy.	Circ Arrhythm Electrophysiol	OR	Propensity score-matching patient population cohorts were analyzed to better determine 5-year cardiac event rate, such as all-cause death and other composite arrhythmic events such as SCD or aborted SCD. Taken together, this finding provides initial evidence for the reclassification of all-cause death risk due to a cardiac-related event.
	Matthews E	Prognostic Value of the Neurological Examination in Cardiac Arrest Patients After Therapeutic Hypothermia.	Neurohospitalist	OR	The algorithmic timeline of neurological examination in post-arrest patients following therapeutic hypothermia should be delayed due to confounding variables of sedation and low temperatures.
	Moseby-Knappe M	Serum Neurofilament Light Chain for Prognosis of Outcome After Cardiac Arrest.	JAMA Neurol	OR	Serum neurofilament light chain is highly predictive of poor outcome following cardiac arrest and is a promising biomarker to be incorporated in multimodal neuroprognostication algorithms.

	Na M	Gray matter to white matter ratio for predicting neurological outcomes in patients treated with target temperature management after cardiac arrest: A systematic review and meta-analysis.	Resuscitation	RE	Gray matter to white matter ratio in the initial head CT, specifically in the basal ganglia, is a useful predictor of poor neurological outcome after cardiac arrest.
	Nagaraj S	The revised Cerebral Recovery Index improves predictions of neurological outcome after cardiac arrest.	Clin Neurophysiol	OR	Compiled quantitative EEG features in the revised Cerebral Recovery Index score using machine learning shows promise as an early predictor of good and poor neurologic outcome.
	Oddo M	Quantitative versus standard pupillary light reflex for early prognostication in comatose cardiac arrest patients: an international prospective multicenter double-blinded study.	Intens Care Med	OR	The Neurological Pupil index derived from pupillometry shows promise in multimodal outcome prediction of comatose cardiac arrest survivors.
	Otani T	Low-flow time is associated with a favorable neurological outcome in out-of-hospital cardiac arrest patients resuscitated with extracorporeal cardiopulmonary resuscitation.	J Crit Care	OR	Low-flow times are associated with favorable neurologic outcome in ECMO-CPR patients. Up to 20% of patients with low-flow times <58 minutes may achieve a favorable outcome.
	Patel JK	Association between intra- and post-arrest hyperoxia on mortality in	Resuscitation	RE	Intra-arrest hyperoxia is associated with survival whereas hyperoxia in the

		adults with cardiac arrest: A systematic review and meta-analysis.			post-arrest period is associated with lower mortality.
	Pekkarinen PT	Procalcitonin and Presepsin as Prognostic Markers After Out-of-Hospital Cardiac Arrest.	Shock	OR	Admission procalcitonin is a promising marker of hemodynamic instability following cardiac arrest, and is independently associated with long-term outcomes
	Scarpino M	Neurophysiological and neuroradiological multimodal approach for early poor outcome prediction after cardiac arrest.	Resuscitation	OR	In a cohort devoid of withdrawal of life sustaining therapies, early multimodal outcome prediction utilizing EEG, SSEP and CTH was a sensitive and specific method to predict poor outcome following cardiac arrest.
Pediatrics	Cheng A	Optimizing CPR performance with CPR coaching for pediatric cardiac arrest: A randomized simulation-based clinical trial.	Resuscitation	OR	This study examines the impact on the quality of cardiopulmonary resuscitation (CPR) in a simulated pediatric cardiac arrest scenario when including a CPR coach into the resuscitation team.
	Duff JP	2018 American Heart Association Focused Update on Pediatric Advanced Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.	Circulation	RE	An update to PALS algorithm specifically regarding the use of antiarrhythmic drugs in shock refractory VF/pVT in the pediatric population.

	Jung WJ	'Knocking-fingers' chest compression technique in infant cardiac arrest: single-rescuer manikin study.	Eur J Emerg Med	OR	A study of a novel chest compression technique, knocking fingers, for a single rescuer used for infant cardiac arrest compared to two established techniques: two finger and two thumbs.
	Lin Y	Improving CPR quality with distributed practice and real-time feedback in pediatric healthcare providers - A randomized controlled trial.	Resuscitation	OR	When compared to standard BLS training, distributed practice with real-time feedback improved compliance with AHA CPR guidelines after one year.
	Meert K	Extracorporeal Cardiopulmonary Resuscitation: One-Year Survival and Neurobehavioral Outcome Among Infants and Children With In-Hospital Cardiac Arrest.	Crit Care Med	OR	This study analyzes the 12-month survival rate and neurobehavioral outcomes from a population of pediatric patients who suffered in-hospital cardiac arrest and received extracorporeal cardiopulmonary resuscitation (ECPR).
	Niles D	Characterization of Pediatric In-Hospital Cardiopulmonary Resuscitation Quality Metrics Across an International Resuscitation Collaborative.	Pediatr Crit Care Med	OR	This multi-center study from the pediRES-Q Collaborative assessed chest compression (CC) quality in pediatric in-hospital cardiac arrest and found that compliance to the 2015 AHA guidelines for proper rate and depth was poor.
	Yunge M	Effectiveness of Two Targeted Temperature Management Methods After Pediatric Postcardiac Arrest: A	Pediatr Crit Care Med	OR	A study of the feasibility and effectiveness of maintaining targeted temperature control following cardiac arrest with servo-controlled systems

		Multicenter International Study.			compared to non-servo-controlled systems.
Basic Science & Pharmacology	Anderson KL	Left ventricular compressions improve return of spontaneous circulation and hemodynamics in a swine model of traumatic cardiopulmonary arrest	J Trauma Acute Care Surg	OR	Chest compression focused over the left ventricle have improved short-term and 60-min survival as well as hemodynamic variables compared to traditional chest compressions.
	Babini G	Effect of mild hypercapnia on outcome and histological injury in a porcine post-cardiac arrest model.	Resuscitation	OR	Mild hypercapnia results in less neuronal degeneration but similar short-term neurologic outcomes when compared to normocapnia following post-cardiac arrest in porcine models.
	Byunghyun K	Effect of Electrical Vagus Nerve Stimulation on Cerebral Blood Flow and Neurological Outcome in Asphyxial Cardiac Arrest Model of Rats	Neurocrit Care	OR	Vagus Nerve Stimulation during post-resuscitation may increase recovery of cerebral blood flow and enhance neurological recovery in rat models.
	Hayashida K	Improvement in Outcomes After Cardiac Arrest and Resuscitation by Inhibition of S-Nitrosoglutathione Reductase	Circulation	OR	S-nitrosoglutathione reductase inhibition provides a protective mechanism against cardiac arrest-induced brain injury and may prevent worsening of injury by alternatively enhancing protein S-nitrosylation.
	Jou C	The Role of Inflammatory Cytokines in Cardiac Arrest.	Journal of Intensive Care Medicine	RE	Discussion of known cytokine roles in cardiac arrest and post-arrest physiology outlining proposed mechanisms of action and potential therapeutic targets.
	Lee BK	Continuous neuromuscular blockade	Plos One	OR	Continuous neuromuscular blockade infusion as a prophylactic measure to

		infusion for out-of-hospital cardiac arrest patients treated with targeted temperature management: A multicenter randomized controlled trial			prevent shivering is not associated with improved outcomes in patients undergoing temperature targeted management.
	Sicouri S	Underlying the Actions of Antidepressant and Antipsychotic Drugs That Cause Sudden Cardiac Arrest	Arrhythm Electrophysiol Rev	RE	Review of the mechanisms by which antipsychotic and antidepressant medications can cause deadly arrhythmias.
	Tahsili-Fahdan P	Hypothermia and brain inflammation after cardiac arrest	Brain Circ	RE	Review of the pathophysiology and cellular signaling cascades of inflammation and ischemia-reperfusion injury in the brain following cardiac arrest and the role of targeted-temperature management in recovery.
	Wallisch JS	The aquaporin-4 inhibitor AER-271 blocks acute cerebral edema and improves early outcome in a pediatric model of asphyxial cardiac arrest.	Pediatr Res	OR	AER-271, an AQP4 antagonist, has therapeutic potential for reducing acute cerebral edema and improving neurological outcomes after pediatric CA.
Epidemiology & Public Health	Alba A	Incidence and predictors of sudden cardiac death after heart transplantation: A systematic review and meta-analysis.	Clin Transplant	RE	Overall incidence of sudden cardiac death in post-heart transplant patients is 3 times higher than the general population with specific risk factors increasing likelihood of SCD. More studies are needed to help assess which of these patients might benefit from ICD placement.

	Alqahtani S	The incidence and outcomes of out-of-hospital cardiac arrest precipitated by drug overdose: A systematic review and meta-analysis	Resuscitation	RE	This study was a systematic review and meta-analysis to identify studies globally which have recorded the incidence and/or outcomes of adult out-of-hospital cardiac arrests triggered by drug overdose.
	Cartledge S	Understanding patients and spouses' experiences of patient education following a cardiac event and eliciting attitudes and preferences towards incorporating cardiopulmonary resuscitation training: A qualitative study	J Adv Nurs	OR	Cardiac patients and spouses experienced a complex range of emotions following an acute cardiac event and described unmet education and information needs.
	Cavalcanti R	Implantable Cardioverter Defibrillator for the Primary Prevention of Sudden Cardiac Death in Patients With Nonischemic Cardiomyopathy.	Angiology	RE	The aim of this systematic review and meta-analysis of randomized controlled trials was to examine the effectiveness of primary prevention using an implantable cardioverter defibrillator in the population of patients with nonischemic cardiomyopathy.
	Escutnairea J	Traumatic cardiac arrest is associated with lower survival rate vs. medical cardiac arrest – Results from the French national registry	Resuscitation	OR	Survival rates from traumatic OHCA were found to be lower than for medical OHCA in matched cohorts. Despite lower survival, pre-hospital resuscitation efforts for traumatic OHCA were not found to be futile.
	Iglesias D	Analysis of the High-Frequency Content in Human QRS Complexes	Sensors	OR	The use of wavelet transform and analysis of high-frequency content of QRS complexes can be an effective

		by the Continuous Wavelet Transform: An Automatized Analysis for the Prediction of Sudden Cardiac Death			way to distinguish between healthy individuals and SCD patients.
	Kempa M	Polish single-centre follow-up of subcutaneous implantable cardioverter-defibrillator (S-ICD) systems implanted for the prevention of sudden cardiac death	Kardiol Pol	OR	This study describes the experience of a single center in Poland with the use of subcutaneous implantable cardioverter-defibrillator (S-ICD) on patients at risk of sudden cardiac death (SCD) from potentially life-threatening ventricular arrhythmias.
	Kenttä T	Repolarization Heterogeneity Measured With T-Wave Area Dispersion in Standard 12-Lead ECG Predicts Sudden Cardiac Death in General Population.	Circ Arrhythm Electrophysiol	OR	A new electrocardiographic marker, T-wave area dispersion (TW-Ad), measuring repolarization heterogeneity, can identify patients at risk for sudden cardiac death. Specifically, a low TW-Ad in a standard 12-lead resting ECG is highly predictive of SCD in the general population associated with a 4.6-fold adjusted risk for SCD.
	Lockey A	Impact of adult advanced cardiac life support course participation on patient outcomes—A systematic review and meta-analysis	Resuscitation	RE	Rescuer participation in an advanced life support course positively impacts return of spontaneous circulation and 30-day survival of cardiac arrest patients.
	Morand J	Chronic intermittent hypoxia promotes myocardial ischemia-related ventricular	Sci Rep	OR	This study, conducted in rats, demonstrates that chronic intermittent hypoxia is a key risk factor for sudden cardiac death upon myocardial

		arrhythmias and sudden cardiac death			ischemia occurring via sympathoactivation and changes in ventricular repolarization, transmural action potential duration gradient, and endocardial calcium channel expression.
	Nalliah CJ	Mitral valve prolapse and sudden cardiac death: a systematic review and meta-analysis	Heart	RE	This meta-analysis provides indirect evidence of an association of mitral valve prolapse (MVP) due to a high prevalence of MVP in patients with unexplained SCD despite low prevalence in the general adult population. Additionally, pathological characteristics of SCD patients were identified.
	Patel SI	QT prolongation and sudden cardiac death risk in hypertrophic cardiomyopathy	Acta Cardiol	OR	A prolonged QTc interval is an independent risk factor for sudden cardiac death and overall mortality rate in adults with known hypertrophic cardiomyopathy.
	Pederson T	Self-learning basic life support: A randomised controlled trial on learning conditions.	Resuscitation	OR	Self-learning of BLS is not inferior to facilitator-led skills training after three months. Retention of skills, as measured by percentage of correct compressions, is higher in self-taught groups.
	Rattanawong P	Atrial fibrillation is associated with sudden cardiac death: a systematic review and meta-analysis	J Interv Card Electrophysio	RE	AF significantly increased the risk of SCD at a higher proportion when compared with the increased risk of overall mortality.
	Cariou A	Targeted temperature management in the ICU:	Anaesth Crit Care Pa	RE	The article is a consensus statement from a French expert panel concerning

Interdisciplinary Guidelines & Reviews		Guidelines from a French expert panel.			the use of targeted temperature management in critical illness based on a systematic review of current literature.
	Cheng A	Resuscitation Education Science: Educational Strategies to Improve Outcomes From Cardiac Arrest: A Scientific Statement From the American Heart Association.	Circulation	RE	Optimal strategies for learning are needed to enable medical and scientific knowledge to be translated into effective practice.
	Haywood K	COSCA (Core Outcome Set for Cardiac Arrest) in adults: an advisory statement from the International Liaison Committee on Resuscitation	Circulation; Resuscitation	RE	Identification of a core set of outcome measures, and standardization of these measures across cardiac arrest trials, will facilitate comparisons across studies and allow the development of pragmatic efficacy trials
	Hinkelbein J	In-flight cardiac arrest and in-flight cardiopulmonary resuscitation during commercial air travel: consensus statement and supplementary treatment guideline from the German Society of Aerospace Medicine (DGLRM)	Intern Emerg Med	RE	Although rare, in-flight cardiac arrest during commercial air travel, can be exceedingly difficult to treat. Little guidance exists in terms of optimal strategies to manage this high stakes event.
	Karcioglu O	A Systematic Review of Safety and Adverse Effects in the Practice of	Am J Emerg Med	RE	To maximize the benefit of targeted temperature management (32-36 °C) following out-of-hospital cardiac

		Therapeutic Hypothermia.			arrest, the practitioner needs to anticipate and understand the adverse effects and complications that may arise with this procedure.
	Kitamura T	The profile of Japanese Association for Acute Medicine – out-of-hospital cardiac arrest registry in 2014-2015	Acute Med Surg	RE	The profile of Japanese Association for Acute Medicine – out-of-hospital cardiac arrest registry in 2014-2015
	Madder RD	Multidisciplinary Management of the Post-Cardiac Arrest Patient	Cardiol Clin	RE	This review article outlines a "brain-oriented" multidisciplinary approach to post-arrest patient care based on current literature in an effort to maximize neurologic recovery and limit secondary brain injury.
	O'Mahony C	Effectiveness of the 2014 European Society of Cardiology guideline on sudden cardiac death in hypertrophic cardiomyopathy: a systematic review and meta-analysis	Heart	RE	This systematic review and meta-analysis evaluates the accuracy of a previously published risk stratification tool that predicts the probability of sudden cardiac death (SCD) in patients with hypertrophic cardiomyopathy (HCM Risk-SCD). Establishing the validity of the HCM Risk-SCD enables optimal selection of patients for implantable cardiac defibrillator (ICD) placement based on their baseline risk of SCD.
	Pacheco R	What do Cochrane Systematic Reviewers Say about Cardiac Arrest Management	Sao Paulo Med J	RE	Uncertainty exists about the efficacy interventions used to manage sudden cardiac arrest. This review summarizes evidence from Cochrane Systematic Reviews that focus on cardiac arrest and post-arrest care.

	Soar J	2018 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations Summary	Circulation; Resuscitation	RE	The International Liaison Committee on Resuscitation (ILCOR) continuously analyzes peer-reviewed studies on emergency cardiovascular care (ECC) and cardiopulmonary resuscitation (CPR) with the goal of shortening the time interval between publication of evidence and translation into guideline recommendations. This year the utility of antiarrhythmic drugs for refractory ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT) during or immediately after cardiac arrest (CA) was addressed.