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Rationale and Strategies for Development of an Optimal Bundle of Management for Cardiac Arrest

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Objectives: To construct a highly detailed yet practical, attainable roadmap for enhancing the likelihood of neurologically intact survival following sudden cardiac arrest.

Design, Setting, and Patients: Population-based outcomes following out-of-hospital cardiac arrest were collated for 10 U.S. counties in Alaska, California, Florida, Ohio, Minnesota, Utah, and Washington. The 10 identified emergency medical services systems were those that had recently reported significant improvements in neurologically intact survival after introducing a more comprehensive approach involving citizens, hospitals, and evolving strategies for incorporating technology-based, highly choreographed care and training. Detailed inventories of in-common elements were collated from the ten 9-1-1 agencies and assimilated. For reference, combined averaged outcomes for out-of-hospital cardiac arrest occurring January 1, 2017, to February 28, 2018, were compared with concurrent U.S. outcomes reported by the well-established Cardiac Arrest Registry to Enhance Survival.

Interventions: Most commonly, interventions and components from the ten 9-1-1 systems consistently included extensive public cardiopulmonary resuscitation training, 9-1-1 system-connected smart phone applications, expedited dispatcher procedures, cardiopulmonary resuscitation quality monitoring, mechanical cardiopulmonary resuscitation, devices for enhancing negative intrathoracic pressure regulation, extracorporeal membrane oxygenation protocols, body temperature management procedures, rapid cardiac angiography, and intensive involvement of medical directors, operational and quality assurance officers, and training staff.

Measurements and Main Results: Compared with Cardiac Arrest Registry to Enhance Survival (n = 78,704), the cohorts from the 10 emergency medical services agencies examined (n = 2,911) demonstrated significantly increased likelihoods of return of spontaneous circulation (mean 37.4% vs 31.5%; p < 0.001) and neurologically favorable hospital discharge, particularly after witnessed collapses involving bystander cardiopulmonary resuscitation and shockable cardiac rhythms (mean 10.7% vs 8.4%; p < 0.001; and 41.6% vs 29.2%; p < 0.001, respectively).

Conclusions: The likelihood of neurologically favorable survival following out-of-hospital cardiac arrest can improve substantially in communities that conscientiously and meticulously introduce a well-sequenced, highly choreographed, system-wide portfolio of both traditional and nonconventional approaches to training, technologies, and physiologic management. The commonalities found in the analyzed systems create a compelling case that other communities can also improve out-of-hospital cardiac arrest outcomes significantly by conscientiously exploring and adopting similar bundles of system organization and care. **Key Words:** bundle of care; cardiac arrest; cardiopulmonary resuscitation; emergency medical services; resuscitation centers; sudden cardiac death survival

Sudden cardiac arrest (SCA), particularly out-of-hospital cardiac arrest (OHCA), remains a leading cause of premature death worldwide. Despite widespread community-based bystander cardiopulmonary resuscitation (CPR) training and proliferation of advanced care emergency medical services (EMS) systems, the reported likelihood of survival with favorable neurologic function remains less than 10% in most communities (1). Outcomes are probably even worse among EMS systems not reporting their outcomes, likely reflecting a lack of resources including quality assurance programs that gauge performance or simply not choosing to report dismal outcomes. When prudent data collection programs such as the Cardiac Arrest Registry to Enhance Survival (CARES) registry are introduced, SCA outcomes improve (2, 3).

For decades, consensus-forming groups such as the American Heart Association (AHA) or the International Liaison Committee on Resuscitation (ILCOR) have developed well-promulgated guidelines for implementing both basic and advanced interventions for SCA, emphasizing a judicious "evidence-based" process using published peer-reviewed literature (4, 5). These processes have clear value, but they also have their limitations as well. Evaluated publications can convey conflicting information, involve mixed populations without stratification, routinely possess statistical limitations, or can be confounded by a lack of adherence to intended protocols, all leading to inconclusive findings (6).

Furthermore, in cardiac arrest research, the traditional controlled trials that test the effect of a singular intervention may be one of the main reasons for those misleading or conflicting results and subsequent inconclusive consensus (7). Examining simple binary outcomes though interventional trials (effective or not) has been compromised by the profoundly time-dynamic and multivariable nature of SCA cases. A single intervention (e.g., drug, automated defibrillator) that is highly effective when provided within minutes of a SCA may not be helpful when too many minutes have elapsed. Cardiovascular, pulmonary, and resulting hemodynamic abnormalities can rapidly evolve after SCA onset and those temporal considerations need to be addressed in a multidimensional manner.

In addition, basic CPR itself requires conscientious attention to coordinating multiple interdependent and interactive components (e.g. chest compression rate, depth, recoil, number of interruptions) under different circumstances (8). Likewise, assisted breathing components not only require attention to the frequency, force, and speed of delivery of each breath but also the actual volume and the rapid release of each positive pressure breath once delivered. These ventilatory variables significantly impact circulation and thus the effectiveness of other interventions, including medications, and CPR itself (5, 9, 10). In addition, all of these factors need to be well-controlled and adjusted under certain

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conditions, particularly when flow-enhancing devices are used or when spontaneous circulation or respirations resume (9).

Accordingly, any proscribed ideal target for each of these circulatory and ventilatory components may need to be adjusted and adapted, not only according to the multidimensional and interactive effects of these variables but also according to a myriad of other factors such as time-dependent changes in physiologic conditions and hemodynamics. Such symphonic-like components and movements also require expert conductors who can meticulously anticipate, manage, revise, and adapt a multifaceted, tightly choreographed process instead of employing the same rote fixed protocols and procedures start to finish (11–13).

These complex dynamics over the course of resuscitation efforts may have confounded many of our current "evidence-based" publications, even gold standard clinical trials (10, 14). Specifically, if an otherwise well-designed clinical trial shows a single intervention to be ineffective, that conclusion is likely accurate, but only within the context of that study (10). Experience has now shown investigators that the same intervention might have been demonstrated to be quite effective if it had been introduced using an approach that successfully harmonizes time-appropriate quality CPR performance and/or physiologically sound ventilatory practices (10, 14).

For OHCA, the setting itself may also affect the outcomes. Important variables include the populations served, community residential infrastructure, traffic, geography, climate, dispatch functions, and the frequency and quality of early bystander CPR (bCPR) (15). EMS design alone (system response configuration and resources) can significantly impact the skills of EMS personnel and therefore outcomes (14–17). Receiving facility resources such as extracorporeal membrane oxygenation (ECMO) and percutaneous coronary intervention (PCI) can also influence ultimate outcomes (18). Postresuscitation decision-making (positioning, method/degree of therapeutic cooling, premature withdrawal of support) can all become pivotal considerations as well (19–21).

In essence, many interdependent components forming a longitudinal bundle of management for SCA must be simultaneously optimized, choreographed, and properly implemented with timeappropriate and physiologically driven approaches. Attention to detail must extend from the dispatch center through eventual discharge from the hospital as well as medical follow-up services such as physical and neuropsychiatric rehabilitation (22, 23).

This concept of an interdependent "bundle of care" is not new. Other complex disease conditions also require well-choreographed, multifaceted, interdependent bundles of treatment, not just a single intervention at a time (23). Even the universally recognized metaphor of the "chain of survival" for cardiac arrest (die rettungskette originally described by Fritz Ahnefeld in 1967 [24]) is an early example. Each link in this symbolic chain needs to be present and optimized to enhance survival chances. The common idiom, "only as strong as the weakest link", applies here even more so given the hundreds of links involved.

Recognizing all of these concerns, several dozen resuscitation practitioners from a multitude of nations, specialties, and agencies recently gathered to form an International Resuscitation Collaborative (IRC) to inventory both current and proposed future "best practices" in OHCA management. The group first queried a number of U.S. EMS agencies that had recently reported significant improvements in SCA outcomes and then analyzed each of the them in detail for common elements that could help to summarize and assimilate a potential "work-in-progress" roadmap that might help to create a more optimal bundled approach for OHCA.

The integral intent was to create a user-friendly, reproducible, and attainable practical roadmap built upon state-of-the art evidence and the collective experience of the veteran participants, particularly those well-versed in the budgetary and logistical challenges/pitfalls of implementing new procedures within EMS systems. The process focused on identifying the common synergistic strategies, technologies, and procedures that could be incorporated and well-integrated across the entire spectrum of management, from enhanced dispatch procedures and community-wide initiatives for public involvement to on-scene patient care management and receiving facility interventions.

A basic tenet of validating classic scientific laboratory research is the ability to accurately communicate and reproduce methods from one investigator's laboratory to another's, and, in turn, explicitly reproduce those results. Considering decades of challenges and disappointments posed by traditional clinical trial methodologies, the ultimate purpose here was to construct an alternative approach that could be used to consistently reproduce the research and guide others to enhance neurologically-intact survival following sudden cardiac arrest.

METHODS

Participants

A multidisciplinary collaboration was established by a well-recognized group of cardiologists, emergency and internal medicine physicians, paramedics, and fire rescue leaders in the United States, Canada, and Europe, largely comprised of those who had published or reported new approaches to CPR with associated high rates of resuscitation and neurologically intact survival for both OHCA and in-hospital cardiac arrest. Adopting the moniker, IRC, the majority of the collaborative members have also participated in the processes for developing the related evidence-based management guidelines for the AHA, the European Resuscitation Council, or ILCOR.

Setting

The IRC participants assembled voluntarily, without financial support and sponsorship, in Oakland, CA, in late September 2018 (n = 32) and subsequently in Paris, France, in October 2019 (n = 28). The meeting and invitations to participants were organized and facilitated through the nonprofit organizations, Take Heart America, the French Resuscitation Council, and the Metropolitan EMS Medical Directors Alliance (23).

Prior to their first convocation, a prospective plan was placed into motion in terms of how the evaluation would be conducted and how the IRC participants would report the results. As a first step, the participants prospectively chose to review, analyze, and collate inventories from 10 EMS systems (EMS-10). The

systems chosen were not only those that had reported exceptional improvements in outcomes after introduction of novel or expedited approaches to OHCA care but also those that were able to provide complete process-reporting datasets equivalent to those within the CARES registry (25). The EMS-10 was also derived from 10 geographically diverse U.S. counties including agencies in Alaska, California, Florida, Ohio, Minnesota, Utah, and Washington. Representatives from selected agencies were invited to attend and present their information under the direct scrutiny, interrogatories, and commentaries of the IRC participants.

At both conferences, the prospective plan for the sessions was to first have introductory reports from each system. The introductory comments from participants were delivered in traditional abstract presentation formats later followed by several sessions of modified Delphi roundtables. After detailed inventories of the strategies, interventions, protocols, and procedural approaches, the findings were tabulated to identify commonalities, differences, and complementary elements. Findings were then presented, reviewed, and discussed by IRC members in-person to better delineate and understand the various components identified and, in turn, to create a recommended bundle of management distilled from those discussions.

In contrast to the approach often used by other organizations and the concerns expressed in the Introduction, this deliberative process did not focus on a grading system for any individual intervention. Instead, it focused on distilling the comprehensive inventories derived and tabulated from these high-performance EMS-10 systems. Step 1 was to identify the readily acceptable common elements found in each of these high-functioning systems to create the basic foundation of the proposed bundle of care. Step 2 was to sequentially identify other best practices and innovative procedures from individual systems that were mutually considered to be suitable and complementary additions to the proposed bundle of care roadmap after thoughtfully considering the applicable literature, feasibility, safety, and outcome data. After formulating a comfort level and agreement on those additional components, Step 3 was an additional exercise to identify potential avenues of improvement that could be explored in the future such as prehospital implementation of ECMO, an intervention that has already been introduced into some other agencies, but not among the EMS-10. Of note, training tools, procedural efficiencies, and the impact of resuscitation efforts on personnel were reviewed in great detail. Team-building implementation solutions were also part of the dialogue. Despite numerous academic debates within the deliberations, the interactions were exceptionally congenial with little remaining controversy by the end of the process.

Outcomes Measurements

Although the primary goal of the analysis was to identify the common elements and best practices associated with these highperformance systems, it was recognized that the significant improvements in outcomes originally reported by the EMS-10 were based on historical controls within each of the individual communities. Therefore, for reference purposes, the IRC also obtained and combined the OHCA outcomes during the prior 12-month calendar year (2017, or a more proximate 12-mo period, March 2017 to February 2018). These aggregate 12-month data were then compared with the concurrent (2017) calendar year outcome data reported by the respected CARES project. CARES, a voluntary registry launched as a collaborative effort between the U.S. Centers for Disease Control and Prevention and Emory University, has become a reliable marker of outcomes among many progressive U.S. EMS systems conscientiously monitoring their OHCA outcomes (2).

Data collected and reported through CARES include process data such as the time elapsed from the first call to 9-1-1 (or equivalent) until initiation of basic CPR by first responders or time of return of spontaneous circulation (ROSC) as applicable as well as documentation of whether the OHCA was witnessed and if CPR was performed by bystanders. It also includes what the presenting cardiac rhythm was and, when applicable, the eventual neurologic status using the Cerebral Performance Category (CPC) score at the time of hospital discharge (HD).

The primary analysis reference point for the current evaluation was the mean rate of HD with a favorable neurologic outcome defined as a CPC score of 1 or 2 (HD CPC 1–2) and, secondarily, the frequency of ROSC, regardless of the first recorded cardiac rhythm (2, 23, 26).

Interventions Evaluated

The interventions evaluated are best defined by the in-common elements and components identified among the EMS-10 and reported in the inventories obtained. The in-common practices among those systems were supported by the best available preclinical and clinically relevant evidence. The inventories considered detailed best practices and tools for training and implementing both conventional and novel interventions. However, among participants, the interventions originally assessed within individual systems were considered the most important components when finally examining and tabulating the respective bundles of care that resulted in outcome improvements.

Statistical Analyses

Statistical comparisons between the concurrent CARES and EMS-10 outcomes included two-tailed Fisher exact test and calculations of the odds ratio (OR) with 95% CIs (95% CI). Data are expressed as a mean \pm sD with *p* value of less than 0.05 defining statistical significance.

RESULTS

The location of the analyzed EMS-10 systems and the interventions used in each are shown in **Table 1** and **Figure 1**. Collectively, these agencies provide 9-1-1 responses for residential populations of approximately 4 million persons. A total of 2,911 OHCA patients were treated by the EMS-10 during the respective 12-month analysis periods. Figure 1 includes those interventions deployed by each or all (bolded) of the EMS-10 agencies and their receiving hospitals. Community response components included techniques to increase the frequency of bCPR such as lay rescuer training in schools, just-in-time dispatch-assisted CPR including "no-no-go" dispatch protocols, and smart phone applications (27–30). The mean frequency of bCPR across the 10 systems was 43.7%.

TABLE 1. Outcomes From 10 High-Functioning Emergency Medical Services Systems, Both Individually and Combined, As Compared With Cardiac Arrest Registry to Enhance Survival Outcomes

9-1-1 System Jurisdictions	Total Cases, n	Bystander Cardiopulmonary Resuscitation, %	Return of Spontaneous Circulation (%)	HD, % (n)	HD With CPC 1, 2 (n)	HD With CPC 1, 2 (%)	Utstein 2 Casesª, % (n)
Alameda County, CA	1043	38	33.20	11.3 (118)	85	8.10	48 (20/42)
Anchorage, AK	249	73	37.30	16.1 (40)	39	15.70	32.3 (10/31)
Anoka County, MN	211	31.30	33.60	16.1 (34)	32	15.20	37.5 (7/18)
St. John's County, FL	155	52	46.50	12.9 (20)	17	11	26 (7/27)
Lucas County, OH	510	43.30	31.80	11.6 (59)	43	8.40	37 (15/41)
Minneapolis-St. Paul, MN	387	36.80	47	14.5 (56)	39	10.10	44 (15/34)
Palm Beach County, FL	41	48.80	58.50	12.2 (5)	5	12	25 (1/4)
Rialto, CA	90	41	46	18 (16)	12	12.80	40 (4/10)
Salt Lake City, UT	131	64	44	21 (28)	26	19.80	58 (15/26)
Whatcom County, WA	94	45.70	41.50	19.1 (18)	14	14.90	75 (6/8)
Emergency Medical Services-10	2,911	43.70	37.4	13.5 (394)	312	10.70	41.6 (100/241)
Cardiac Arrest Registry to Enhance Survival ^b	78,704	44.9	31.5	10.4 (8,223)	6,622	8.4	29.2 (2,540/8,689)
p		Nonsignificant	< 0.0001	< 0.0001	0.0002	0.0002	0.0001

CPC = Cerebral Performance Category, HD = hospital discharge.

^aRate of HD with favorable neurologic function among patients with the greatest likelihood of survival, namely those with a witnessed arrest, a first recorded rhythm of either ventricular tachycardia or ventricular fibrillation and those who received bystander cardiopulmonary resuscitation (CPR).

^bCardiac Arrest Registry to Enhance Survival rates of survival to hospital discharge with good neurologic function rates remained constant in 2017 and 2018. Patients with a CPC score of 1 or 2 were considered to have a favorable neurologic outcome. Secondary clinical outcomes included rates of return of spontaneous circulation, overall frequency of hospital discharge, and Utstein 2 Cases. Bystander CPR rates are from 2017. Collective outcome data for the 10 Emergency Medical Services systems are in bold.

In addition to phone applications, other evolving technologies were common as shown in Figure 1 and Supplemental Digital Content 1 (http://links.lww.com/CCX/A314). Supplementary Table 1, a-d (Supplemental Digital Content 1, http://links.lww. com/CCX/A314) displays the key first responder, basic life support, and advanced life support interventions provided on-scene, including the commonality of feedback tools for quality CPR performance. There was in-common practice of applying an impedance threshold device (ITD) whether using a facemask, supraglottic airway, or endotracheal intubation for ventilation (14, 22, 26). As shown in Supplementary Table 1, a-d (Supplemental Digital Content 1, http://links.lww.com/CCX/A314) and Supplemental Digital Content 2 (http://links.lww.com/CCX/A315), the ITD was combined with automated mechanical CPR devices employing an active compression-decompression (ACD) component in eight of the 10 systems (22, 26). Automated CPR was not only used for transport safety but also used during on-scene resuscitation to standardize chest compression rate, depth, and recoil and to better enhance intrathoracic pressure regulation (26, 31, 32). With its ability to generate even more negative intrathoracic pressure during the decompression phase, a manual ACD CPR pump was used prior, or as alternative, to using automated CPR in six of those eight systems (26, 31, 32).

All EMS-10 systems had designated resuscitation centers providing rapid access to PCI and targeted (core) temperature management (TTM) with most centers aiming for 33°C for 24 hours minimally (33). As indicated in the tables, ECMO protocols were commonly used or soon to be implemented in those centers. Three systems had implemented technology to gradually raise the head and thorax to a specified degree during CPR which had consistently augmented local resuscitation rates incrementally (22, 31, 34). Another consistent attribute overall was intensive involvement of medical directors, quality assurance officers, operations chiefs, and training staff.

Stratified by pediatric and adult OHCA, a more comprehensive IRC description of the underlying rationale for any specific individual intervention was detailed within the Supplemental Digital Content 1 (http://links.lww.com/CCX/A314) and Supplemental Digital Content 2 (http://links.lww.com/CCX/A315).

Based upon these inventory analyses and discussions, the IRC assimilated "seven pillars of care" (Fig. 2) to be considered when implementing a more comprehensive resuscitation bundle. Interactions between these seven domains had emerged not only as being quite codependent but also synergistic in terms of improved outcomes (22). Beyond specifying that all core elements be included in the roadmap, the IRC stipulated emphatically that

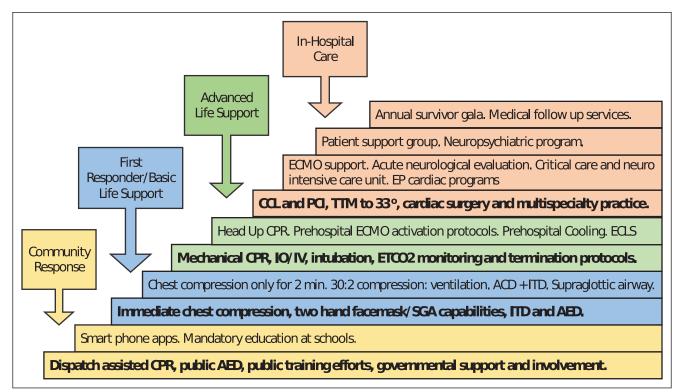


Figure 1. The bundle of care. No single intervention is effective in the treatment of cardiac arrest. Key interventions that are similar across all 10 emergency medical services systems are in *bold*. ACD = active compression decompression, AED = automated external defibrillator, CCL = cardiac catheterization laboratory, CPR = cardiopulmonary resuscitation, ECLS = extracorporeal life support program, ECMO = extracorporeal membrane oxygenation, EP = electrophysiologic programs, ETCo₂ = end-tidal Co₂, IO = intraosseous infusion, ITD = impedance threshold device, PCI = percutaneous coronary intervention, SGA = supraglottic airway, TTM = therapeutic temperature management.

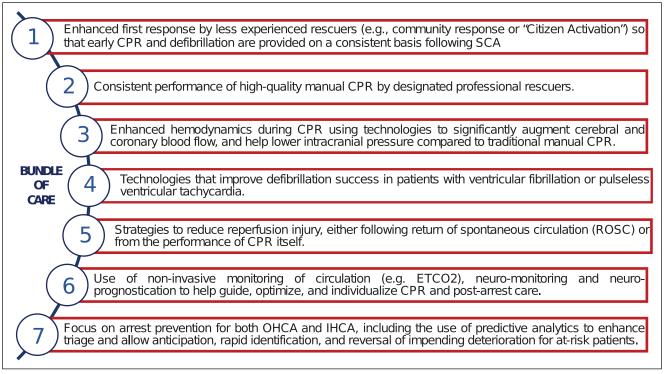


Figure 2. Seven pillars of care. All 10 emergency medical services systems first focused on the rapid delivery of chest compressions and performance of highquality manual cardiopulmonary resuscitation (CPR) by first responders. Several included the use of one or more CPR feedback tools or guides. All of these systems implemented one or more of the recent technology and procedural advances such as expedited dispatch-assisted CPR instructions or smart phone apps, mechanical CPR, active compression decompression CPR, impedance threshold device airway attachments, elevation of the head and thorax during CPR, targeted temperature management strategies, extracorporeal membrane oxygenation CPR, and rapid percutaneous coronary intervention as part of the bundle. $ETCo_2 =$ endtidal Co_9 , IHCA = in-hospital cardiac arrest, OHCA = out-of-hospital cardiac arrest, ROSC = return of spontaneous circulation, SCA = sudden cardiac arrest.

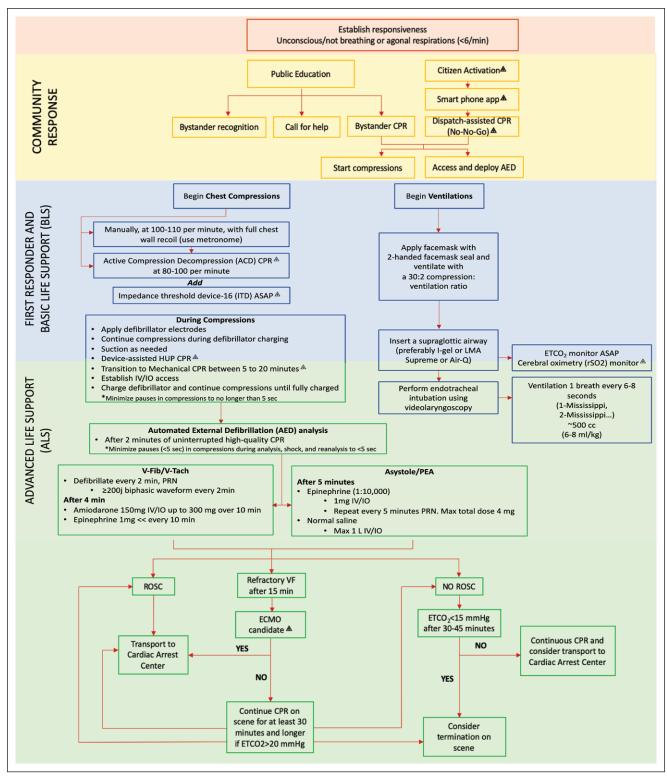


Figure 3. Optimal bundle of care. ^{\triangle}Not currently part of the standard American Heart Association or the International Liaison Committee on Resuscitation. Each intervention requires adequate personnel and, in some cases, special devices and technology. Interventions that may be performed by either basic life support or advanced life support (ALS) personnel are found in bullet points that span both groups of rescuers. ACD = active compression decompression, AED = automated external defibrillator, ASAP = as soon as possible, CPR = cardiopulmonary resuscitation, ECMO = extracorporeal membrane oxygenation, ETCo₂ = end-tidal carbon dioxide, HUP = head up CPR, IO = intraosseous infusion, IV = IV access, ITD = impedance threshold device, LMA = laryngeal mask airway, Max = maximum, PEA = pulseless electrical activity, PRN = *pro re nata*, ROSC = return of spontaneous circulation, rSO₂ = regional oxygen saturation from cerebral oximetry, VF, V-Fib = ventricular fibrillation, V-Tach = ventricular tachycardia.

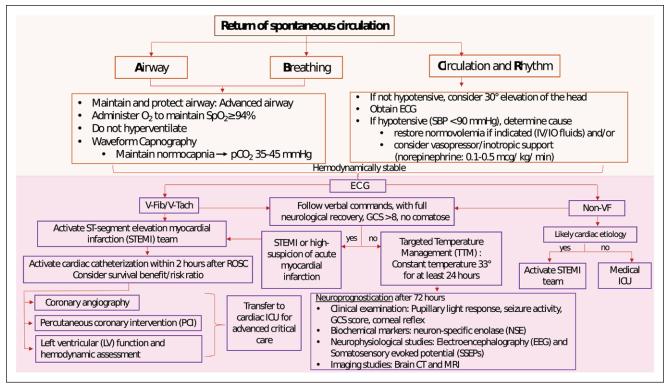


Figure 4. In-hospital cardiac arrest care. ECG = electrocardiogram, EEG = electroencephalography, GCS = Glasgow Coma Scale, IO = intraosseous infusion, IV = IV access, LV = Ieft ventricular, NSE = neuron specific enolase, PCI = percutaneous coronary intervention, ROSC = return of spontaneous circulation, SBP = systolic blood pressure, SpO₂ = oxygen saturation from pulse oximetry, SSEPs = somatosensory evoked potentials, STEMI = ST-segment elevation myocardial infarction, TTM = therapeutic temperature management, VF, V-Fib = ventricular fibrillation, V-Tach = ventricular tachycardia.

the many fine details outlined for training and execution were pivotal to success as was close attention to the less tangible aspects of monitoring and team building (**Figs. 3** and **4**).

In terms of comparative outcomes, the mean ROSC rates for all cases, regardless of presenting cardiac rhythm, ranged from 35% to 40% (Table 1). The overall frequency of HD CPC 1–2 (favorable neurologic outcome), even including the large percentage of patients presenting with asystole, was 10.7% (range 8.1–19.8%), and there were no significant differences identified across the various systems. Stratifying for the bystander-witnessed cases presenting with ventricular fibrillation/ventricular tachycardia (VF/VT) for which a bystander performed basic CPR and/or used an automated external defibrillator, the mean HD CPC 1–2 was 41.6% (range 25–75%).

For comparative reference, mean ROSC and HD CPC 1–2 rates were significantly higher than CARES counterparts (Table 1). Overall, combined mean HD CPC 1–2 frequency was nearly 30% higher in the EMS-10 group (10.7%) versus 8.4% for CARES (p < 0.002; OR = 1.30, 95% CI = 1.159–1.473). For the subgroup of VF/VT bystander-witnessed arrests with bystander intervention, HD CPC 1–2 was 41.6% versus 29.2% in CARES (p < 0.001). The frequencies of bCPR were similar (EMS-10: 43.7% vs CARES: 44.9%) as were all other comparison data reviewed (e.g., age, sex, EMS response intervals).

As a supplemental evaluation, investigators analyzed the annualized cost of adding all of the proposed equipment. The evaluation included a 3-year amortization analysis of the costs for a standard 12-lead monitor-defibrillator with pulse oximetry, ETCO, detectors, and quality CPR monitors, as well as the less conventional adjunct technologies such as automated CPR devices, ACD pumps, the ITD, intraosseous infusion supplies, equipment for device-assisted controlled sequential elevation (DACSE) of the head and thorax during CPR, and the cost of other consumables (e.g., medications, airways, personal protective equipment, electrocardiographic pads, IV fluids). The final amortization, including the cost of the standard monitor-defibrillator, was roughly 13,000 U.S. dollars a year for each response vehicle (ambulance). That figure represents an approximate 1–2% increment in the annual cost of operating an ambulance when one considers the major overriding costs of personnel salary and benefits, the amortized cost of the vehicle itself, and all of the other emergency equipment, supplies, and consumables, including fuel, oxygen, and many levels of disposables.

DISCUSSION

For decades, traditional gold-standard trials testing singular interventions for OHCA have yielded disappointing results. Most of those trials were typically perplexed by the pivotal interactive nature of various interdependent variables. In addition, underrecognized confounding factors such as suboptimal quality of CPR, overzealous positive pressure ventilation, time delays to interventions, and many other systematic factors played large roles (9, 10, 14, 17, 19, 21, 23, 31, 35–38). Low survival rates create further statistical quandaries, especially in essential subgroup analyses. Overall, those trials provided useful observational data collection, but the inherent realities and

limitations of OHCA studies have stymied progress in validating life-saving interventions.

In this current analysis, survival rate improvements were independently reported by 10 independent EMS systems concomitantly introducing an evolving and very similar "bundled" management approach to OHCA. The analysis purposefully involved this selection bias using those systems that had adopted novel approaches and subsequently reported significant and fairly rapid improvements in outcomes. Although the agencies each possessed diverse attributes in terms of agency size, population components, variable response configurations, and geographically diverse jurisdictions, the analyses revealed that, despite these differences, each had adopted similar, comprehensive strategies as reported here and each had similar results. Portfolio inventories consistently featured highly integrated procedural and technological interventions that were physiologically driven and intensely choreographed across the seven pillars of care (12, 19, 20, 23, 26, 28, 31, 39, 40).

The identified elements were largely based on qualityimprovement initiatives independently conducted in each jurisdiction over a short period of time during which the more traditional system factors (%VF/VT, response intervals, early defibrillation) remained largely constant. Although acknowledging the typical limitations of historically controlled observations, the IRC did emphasize that many of the outcome improvements were not only clear and sustained incremental improvements that appeared soon after introducing the new elements, but that they were also considered relatively reproducible findings across these independent and diverse agencies working in parallel of each other.

Beyond attention to the interdependent bundled approach, most improvements had their roots in well-designed preclinical trials and several compelling clinical feasibility/safety studies while also paying close attention to physiologically driven CPR technologies and procedures (22). With the many overlapping common elements, the participating IRC members readily constructed what they believed to be a feasible, relatively inexpensive, and largely reproducible roadmap for improving OHCA outcomes (Figs. 2 and 3).

Most commonly, the majority of these EMS-10 systems had 1) included the use of new technological tools for bCPR and streamlined dispatch procedures (41, 42); 2) introduced the "combination" of an ITD with highly choreographed and closely monitored quality CPR, usually expedited by mechanical CPR devices (10, 14, 26, 39); and 3) they also used designated receiving facilities that provided TTM and rapid access to PCI (18–20, 33). Several systems had yet to implement technologies such as ECMO (in-hospital or prehospital) or DACSE of the head and thorax during CPR (22, 31, 43–47). However, all of the participants, including non-U.S. attendees, clearly indicated intentions to eventually incorporate both of these as well and monitor the outcomes (18, 22).

Many of the proposed technologies and interventions carry fiscal impact in terms of the devices, software, training, and monitoring needs (48). However, it was agreed that the consistent improvements indicated cost-worthiness and the reported subanalysis indicated only a very small incremental increase in the annualized cost of operations.

IRC participants did emphasize that for the proposed bundle of care to be effective (23), it required meticulous attention to detail and conscientious training incorporating procedural efficiencies for rapid and highly choreographed, physiologic sound interventions (14, 23, 31, 38, 49, 50). They also expressed concern for harm if interventions are not implemented correctly. Although positive pressure ventilation can be used to achieve adequate lung inflation (to enhance oxygenation and transpulmonary blood flow during CPR), it can also detrimentally obstruct circulation if provided too frequently (9). Likewise, the ITD can significantly improve survival chances, but only with optimal combinations of minimally interrupted chest compressions (rate, depth, and full chest recoil) properly coordinated with ventilation (14, 17, 31, 36, 38, 39). Conversely, they stressed that using novel procedures with simpler "system-1 thinking" strategies, such as age-based pediatric dosing, will not only expedite delivery of care but will also diminish errors (12). Finally, singular interventions instituted for the purposes of making improvements will not alter outcomes without coordinating and including all of the other interdependent components.

CONCLUSIONS

Several EMS agencies independently demonstrated significantly improved OHCA outcomes within their respective jurisdictions after each had introduced a very similar portfolio of interdependent clinical, procedural, and technological interventions. A proposed "bundle" of conventional and innovative care techniques for OHCA assimilated from these agencies can be used to reproduce the likelihood of favorable neurologic function for other communities (23, 40). As EMS-10 survival frequencies were, on average, nearly 30% higher than the national average of prudent EMS systems measuring and reporting outcomes, these findings further create a compelling argument that methodical, conscientious quality-improvement approaches to SCA management, such as the assimilated bundled care strategies compiled here, are reproducible and that they can further improve cardiac arrest outcomes, even within other high-performing EMS systems.

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Dr. Lurie who is a coinventor of multiple CPR devices and founder of Advanced CPR Solutions LLC, that develops novel resuscitation technologies. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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