Supplemental Digital Content 2

COMMUNITY RESPONSE

Beyond real-time dispatcher-assisted CPR instructions, prospective public awareness of sudden cardiac arrest (SCA) and citizen alerting and activation to perform basic CPR are becoming the pillars of the community response. While widely recognized as a critical first step, bystander CPR rates remain far below 50% in many of the cities, states and countries analyzed. Rates of favorable outcome following SCA also vary widely between these jurisdictions indicating the potential for improvement by emulating best practices in certain geographic area or communities. Survival rates can be improved through public education efforts focusing on bystander recognition of cardiac arrest, calling for help (e.g., 9-1-1 in the U.S., 9-9-9 in U.K. in 1-1-3 in Europe, 0-0-0 in Australia) when someone has collapsed and is not breathing normally (51). Early bystander initiation of chest compressions and AED use increase the likelihood of survival (52, 53). Efforts to: 1) promote mandatory training of CPR and AED use in middle school, high school, college and the workplace; 2) improvements in dispatch-assisted CPR protocols; and 3) smart phone applications, hold the greatest potential to transform the community response to SCA (54-57). Such efforts can help establish confidence in applying these skills and transform cultures of inaction into progressive cultures of action for current and future generations.

Two major advances provide new opportunities to significantly increase lay rescuer recognition of SCA and encourage immediate treatment: 1) streamlined dispatch-assisted CPR; and 2) "crowd sourcing" via use of smart phone applications that notify lay rescuers of the location of the arrest and the nearest AED (29, 58). In cities such as Anchorage Alaska, 'just-in-time' hands-only CPR training using the “No-No-Go” approach when 9-1-1 is called, has now increased the percentage of patients receiving CPR from 46% to 79% with concomitant outcome improvements (27). Similarly, in both Palm Beach and Broward Counties in Florida, this approach has decreased the delay between initiation of the 9-1-1 call and bystander initiation of chest compressions -- from nearly 6 minutes to 2 minutes. Instead of going through a traditional series of questions and/or open interrogatory, dispatchers simply ask if the patient is awake/arousable, and if the patient is breathing normally. If the answers are “no” and “no”, they “go” right to CPR instructions. First pioneered in Seattle, this ‘just-in-time’ CPR instruction has the potential to reduce the “no-flow” time markedly, but experience has also indicated that it requires a dedicated and on-going effort by local cardiac arrest champions, EMS dispatchers, and local medical authorities, especially in the case of children (27).

A complementary approach to dispatch-assisted CPR involves “citizen activation” with use of smart phone applications to both alert persons who may be nearby about a likely SCA and also to guide the actions to take. Ideally these systems should be available nationwide, using GPS-based approaches and using technology similar to the “Amber Alert” programs used in some jurisdictions for child abductions. This approach has significantly improved rates and quality of bystander CPR before EMS arrival (29). About 1% of the population in the Netherlands (about 200,000 of the 18 million citizens) use such an application are, in turn, are basic life support (BLS) “certified” and registered as citizen responders. They can be alerted by the dispatcher to respond to a call for help when a person has collapsed utilizing a single, nationwide smartphone app. This initiative has markedly increased lay rescuer CPR performance and significantly shortened the time elapsed from collapse to first shock (59). In turn, this nationwide program, has contributed to overall frequency of survival to hospital discharge exceeding 25%. Accordingly, similar applications are now available in many other countries as well. Some of the applications can not only notify volunteers in the vicinity of the arrest and explicitly direct them to the patient to start CPR, but they also can notify other citizens to retrieve the nearest available AED and, in turn, apply it (60). Taxi drivers, local police, and postal workers can also be targeted with this type of app system to facilitate additional rapid intervention before EMS arrival.

Moreover, bystanders should be instructed to continue their efforts even when first responders arrive. Just because those professional rescuers have arrived, they do have to get oriented, set-up equipment and begin positioning for their pit-crew approach. Therefore, bystanders should not interrupt the CPR until the professional rescuers have instructed them to do so. In turn, dispatchers should alert the bystanders about that transition period and encourage the bystanders ahead of time to continue their efforts, especially in children (12). Dispatcher audiotapes have revealed an all-too-frequent and unnecessary discontinuation of CPR just because sirens were being heard. Not only should bystanders continue efforts until told not to by the arriving rescuers, in some cases, the first responders, even ask the bystanders to continue and even coach their technique in real-time.

Based on the successes of these approaches, it has been recommended that community-wide programs should be constructed in which persons who complete a BLS course should be motivated to register as “citizen responders”, thus becoming part of the regional (or national) activation system. Owners of AEDs should be encouraged to place their AED in a highly-visible and/or highly-accessible cabinet including standardized locations in businesses, public locations and schools. Even those placed in homes or other multi-occupant residences, owners should register the AED into the system, so it becomes available in case of a cardiac arrest in a given neighborhood or complex, let alone business district or other public places. In addition, AEDs could even provide real-time guidance in the performance of CPR to help guide the rescuer and increase survival rates (61, 62). Most importantly, all persons frequenting or working in a public, school or workplace type of setting should always know the exact location of the nearest AEDs in those places, be it a restaurant, an attorney's suite of offices, a hotel, school, athletic facility, shopping mall or courthouse. Knowing how to use it is insufficient. Experience has shown that, due to ease of use and electronic vocal guidance, knowing where to access AED immediately is even more important.

Like all other elements of the optimal bundle of cardiac arrest care, the elements here (such as dispatcher instructions, alerting applications, public training and locating the closest AED) must each be provided properly and in concert (41). In turn, these elements of effective community response are essential to improved outcomes and insufficient in isolation.

PROFESSIONAL FIRST RESPONDER BASIC LIFE SUPPORT (BLS) ACTIONS

The initiation of high-quality CPR, as soon as feasible, by first responders (in general, firefighters, police, lifeguards and security officers) is the next critical component of the optimal bundle of cardiac arrest care (1, 31). The transition from lay rescuer to BLS first responder CPR should be seamless, or even overlapping. As previously mentioned, dispatchers should alert bystanders ahead of time to continue CPR even after rescuer arrival and continue efforts until instructed otherwise by the first responders to ensure a seamless transition that avoids any interruption of chest compressions. Again, professional rescuers may even encourage and coach the bystanders in their technique while they are preparing the scene and getting set to take over compressions.

The EMS-10 often utilized technologies and tools to provide high-quality resuscitation, including real-time feedback systems to help assure the proper chest compression rate, depth and full recoil, and also tools to ensure appropriate ventilation rate and adequate tidal volume (61). Numerous studies have shown that poor quality CPR is all too common and that CPR can be improved with feedback tools (30, 61, 63, 64). Chest compressions performed at a rate of 100-110 per minute, with a depth of ~5.0 cm (while allowing full recoil of the chest wall) with a compression: ventilation ratio of 30:2 when performing bag-valve-mask ventilation (or breaths given during recoil of the chest when intubated) have been found to improve the likelihood of survival with favorable neurological function (22, 38, 39). Because of fatigue issues, rescuers should preferably rotate seamlessly every 2 minutes without interruption (e.g., the second rescuer approaching from the other side of the patient). Interruptions in chest compressions >5 seconds to change, or to check for pulses, apply devices or to manage the airway, should be avoided and strategies implemented to facilitate seamless transitions and minimize interruptions. Also, BLS providers should consider providing two minutes of high-quality chest compressions prior to delivering the first shock, unless the SCA was witnessed and occurs right in front of EMS providers and/or high-quality CPR has been provided by the lay rescuers (65).

One intervention uniformly recommended was mechanical CPR (mCPR) to ensure consistent performance of rate and depth as a substitute for traditional manual CPR (66). It has been shown that, in ideal circumstances, manual and mCPR can be equally capable of generating effective forward flow at the scene of the arrest. In that respect, ideal circumstances would include real-time immediate electronic feedback to the rescuers and frequent, recurrent CPR training.

Multiple clinical trials have now shown that high quality manual CPR and currently available mCPR devices provide equivalent long-term clinical survival rates (67, 68). However, mCPR does provide the advantages of allowing cognitive offloading, consistent, safe, prolonged CPR, and effective CPR during transport (67-70). Also, in retrospect, even across highly-monitored systems at large, CPR may not be adequately performed in as many as 80% of cases. Potential limitations of mCPR include cost, operational failures (pauses longer than 5 sec), and the potential for failure to monitor and modify care once the device has been started (71). Placement of the mCPR device should be continuously monitored as the position of the device can shift over time during resuscitation. Sudden changes in $ETCO_2$ or persistently low $ETCO_2$ values were one tool used that was indicative of displacement of mCPR devices. Also, inefficiencies in application may interrupt CPR far too long and thought to associated with worse outcomes. To address that concern, several of the EMS-10 systems provided training courses that allowed these to be applied in a matter of seconds. Few studies have assessed mCPR as part of a bundle of care prior to the current report.

Whether or not mCPR is used, the CPR skills of professional rescuers should be assessed and reinforced regularly, if not monthly, to optimize care delivery. One well-documented caveat, however, is that errors in compression rate, depth, ventilation rate, and ventilation volume and frequency are quite common. CPR feedback tools, both in training or in real-time resuscitations, can be invaluable, not only for quality improvement and performance reviews, but also to help maintain good muscle memory and enhance the likelihood of consistent high-quality manual CPR performance when needed and resulting improvements in outcome (30, 61).

Multiple studies demonstrate the physiological importance of generating negative intrathoracic pressure during the chest recoil phase of CPR to enhance hemodynamics and the likelihood of survival (31). Developed to enhance negative intrathoracic pressure during the decompression phase of CPR, the impedance threshold device (ITD) with a -16 cm H_2O cracking pressure (ITD-16), combined with an active compression-decompression (ACD) device, has been documented to increase long-term neurologically intact survival after SCA by as much as 50% (36, 72). However, this assumes that the right rate and depth of compressions and that the right rate and depth of ventilation are provided -- and that EMS personnel are properly trained in this technique (26). For example, when an ITD-16 was compared with conventional manual CPR, in a large clinical trial, no advantage in outcome was demonstrated (31, 73). However, subsequent analyses of that same trial found that CPR quality was inadequate in the majority patients and that ventilation was not strictly controlled. Subsequent work demonstrated that there was a significant device-quality of CPR interaction (22, 38, 39).

When the active ITD-16 was used in combination with high-quality conventional CPR, defined as compression rates between 80-120 per minute and compression depth between 4-6 cm, survival likelihood with favorable neurological function were doubled when compared with the sham (inactivated) ITD-16 (22). In contrast, the ITD-16 was of no benefit when used with poor quality CPR and was even potentially detrimental in that situation (38, 39). In essence, these findings emphasize that a particular intervention is not simply effective or ineffective, but it is dependent on numerous other factors in the bundle of care to improve outcomes.

In addition, initial hemodynamic studies (2002) with the ITD in animals unmasked two common performance errors during CPR, namely excessive ventilation rates and incomplete chest wall recoil (31). Moreover, these errors were found to be harmful (31). The large NIH-funded Resuscitation Outcomes Consortium (ROC) ITD clinical survival study revealed two additional common performance errors, compressions performed at rates and depths outside the recommended AHA and ILCOR Guidelines in >50% of the subjects enrolled when quality metrics had been measured (22, 38). Taken together, these studies serve to reinforce how critical it is to deliver all aspects of high-quality CPR (optimal rate, depth, recoil) and appropriate ventilatory techniques to facilitate the life-saving effect of CPR and CPR adjuncts in particular (38, 39). CPR quality feedback tools and automated CPR devices are recommended to help assure high-quality CPR while also using an ITD or, better yet an ITD in combination with an ACD device.

Most clinicians have come to appreciate the potential detrimental effects of overzealous positive pressure ventilation on mean intrathoracic pressure and diminished cardiac output (9). However, like the delivery of CPR (optimal combinations of rate, depth, recoil), ventilation has many integral components (frequency, volume, rate of delivery) that can vary, particularly during cardiac arrest conditions. In such low flow states, a breath given more than once every 8 or 10 seconds could be considered unnecessary and likely harmful if it obstructs inflow into the thorax, especially in the presence of hypovolemia or expiratory airway obstruction. This has been best exemplified in recent studies of childhood OHCA where previously there has been a focus on “respiratory etiology", implying for rescuers, that should not spare delivery of more breaths. However, in a recent investigation of pediatric OHCA, rapid on-scene interventions accompanied by very infrequently-delivered large lung inflations, dramatically improved outcomes (12).

Physiologically, during CPR, an adequate lung inflation, at least large enough to make a chest wall rise, should be provided to ensure recruitment of all available lung zones. Large tidal volumes not only improve oxygenation, but they also to better ensure adequate transpulmonary blood flow and diminish pulmonary vascular resistance when lung zones become atelectatic and collapse during repeated chest compressions. The larger breath is also more efficient in terms of ventilation (less dead space) further diminishing the need for more frequent positive pressure breaths that can raise mean intrathoracic pressure and impede circulation (74).

Moreover, in the presence of robust gasping, and as long as they continue to be strong, the need for providing assisted breaths can often be avoided for several minutes as they simultaneously pull open dependent lung zones and enhance negative intrathoracic swings, thus improving pre-load (75). In all cases, if blood flow is enhanced significantly through CPR adjuncts, then respiratory rates, guided by $ETCO_2$ and other parameters, may need to be increased accordingly.

In terms of evolving CPR adjuncts that can enhance blood flow, the limitations of the traditional approach of performing CPR in the supine, flat position have now been better delineated (76). Conventional chest compressions, while clearly life-saving, not only increase extra-thoracic arterial pressures, but also those on the venous side as well. In turn, cerebral (CPP) and coronary perfusion pressures (CoPP) can be compromised to degree, thus inhibiting a more optimal blood flow through the brain, heart and other vital regions (31). It is also speculated that the brain is further compromised by the observation of increased intracranial pressure (ICP) swings following compressions akin to a persistent concussive effect.

In an attempt to better optimize brain and coronary blood flow, animal studies have shown that elevation the thorax and head, in combination with ACD+ITD CPR, significantly improves brain blood flow by enhancing CPP and lowering ICP. Similarly, improvements in enhancing CoPP are observed as well. Not only does this strategically implemented positioning help to drain venous blood from the brain and venous sinuses, but it may also help to reduce the concussive-like effect with each compression on the brain (44, 45, 76, 77) However, these studies also emphasized the need for at least five combined and interdependent components being simultaneously employed correctly including: 1) attachment of the ITD; 2) quality CPR performance to permit ITD effectiveness; 3) some form of manual or mechanical ACD to further enhance the ITD effect; 4) gradual, controlled and properly-sequenced elevation of the head and thorax (about 9 cm for the chest and 12 cm for the head); adequate lung inflation by positive pressure (visible chest wall rise), preferably delivered on upswings of chest wall recoil, but also provided controlled frequency of breaths to minimize mean intrathoracic pressures. If significant spontaneous gasps are occurring, they may be the preferable form of respiration.

Like of the other elements of the resuscitation bundle of care, all of these key components of the CPR bundle must be in place at the same time. as they are not only interdependent for effectiveness, but also synergistic as well (23, 40, 78).

In that respect, head-up/chest-up CPR has become an important work-in-progress approach. Based on robust animal data and preliminary clinical studies, this important adjunct likely enhances neuroprotection during resuscitation. However, EMS personnel must be properly trained in this technique and introduced it properly (22). Based on best available data, CPR needs to be initiated first in the flat (supine) position to help better 'prime the system' for about two minutes and the other CPR adjuncts (ITD and ACD) also need to be in place. Then the head and thorax should be elevated slowly and consistently over the next two minutes or so to a prescribed height during ongoing CPR (44, 79). From well-vetted animal models, the head and thorax should not be elevated during conventional manual CPR by itself as conventional chest compressions alone do not usually generate enough forward flow to 'pump blood uphill' (45, 77). As standard compressions generate pressure waves up both the arterial *and* venous sides of the extra-thoracic vasculature, there is a finite compromise to forward flow with heightened intracranial pressure (ICP). Therefore, as noted previously, elevation of the head and thorax has been assessed both pre-clinically and in patients as part of a bundle of care that includes automated CPR or ACD and an ITD. In that context alone, head-up is associated with a doubling of survival to hospital admission (22). Accordingly, investigators emphasize that there are some 'do's and don'ts of elevating the head and thorax during CPR. First, use of conventional manual CPR alone (without adjuncts), elevation of the head too much or too rapidly can lead to poorer outcomes. Not priming the system properly with the mechanical/ACD compressions and ITD adjuncts may also create an ineffective process (80). Conversely, based on robust preclinical data, elevation of the head and thorax in a controlled and sequential manner with those circulatory enhancing adjuncts such can result in nearly normal cerebral perfusion pressures over a prolonged period of time (80-82).

In many systems, first responders are also equipped with supraglottic airways (SGAs) in addition to bag valve mask ventilation. These devices can help protect the airway and may improve the quality of ventilation. The benefit of SGAs overall on long-term neurologically-intact survival remains controversial (32, 83). Depending upon the specific type, SGAs may indeed help to maintain a tighter seal during both the compression and decompression phase of CPR (84-86). There are significant differences between different types of supraglottic airway products. Some appear to be better than others in terms of ease of (proper) placement, effective sealing, risk of dislocation, and whether or not they compress the neck vasculature (84-86). Stating this without conflict of interest, and basing that on best available data, most of the IRC investigators and clinicians indicated and agreed that are now utilizing the i-Gel product, both in adults and children, or that they were intending to do so.

One consistent part of the "bundle" identified was that, for on-going optimization of performance, EMS systems should have a formal surveillance system for cardiac arrest in place. Data should not only include the various components of CPR performance and timing of resuscitation procedures, but also outcome. Various standardized data collection methodologies are readily available and the most commonly used in high-functioning systems is the CARES registry. Minimally, such databases should accurately document the location of the arrest, whether it was witnessed, whether bystander CPR was performed, what the first recorded cardiac rhythm was, and whether there were signs of life during resuscitation (e.g. gasping, pupillary reactivity or movement during CPR). These factors (location, initial rhythm, signs of life) are each highly predictive of the likelihood of survival (75, 87). This clinical information should be recorded and be available in real-time for

ALS and hospital personnel (75). These very basic clinical data should then be linked to hospital outcome information including long term survival with favorable neurological function.

ADVANCED LIFE SUPPORT (ALS) ACTIONS

ALS-BASICS: In the highly functioning systems, the primary role is to ensure that all elements of first responder care are being provided appropriately. As with the bystanders not discontinuing efforts before instructed to do so, BLS-providing first responders should also continue their functions while ALS personnel get oriented and plan further strategies. Optimally, ALS providers should be initiating the methods to better guide and ensure delivery of high-quality CPR as outlined above. This includes applying tools to effect continuous end tidal carbon dioxide ($ETCO_2$) monitoring and even cerebral oximetry measurement. Depending on the number of arriving ALS personnel, those ALS rescuers can also proceed to immediately obtaining either secure intraosseous (IO) or intravenous access, and eventually more than one secure site (88, 89).

ALS providers should place an advanced airway (e.g. endotracheal tube (ETT) or SGA to better manage the airway and deliver positive pressure ventilation as indicated (90, 91). ETT placement is achieved in high functioning systems through experienced personnel, most often in tiered-response systems where ALS have achieved a much higher frequency of experience (92). Also, this procedure should be performed only if done expeditiously and without interruption (or very limited interruption) of chest compressions. Again, technologies serve as a facilitating adjunct. For example, the use of video-laryngoscopy (VL) can help improve first-pass success rate for intubation (93). Attention should be given when securing either the SGA or ETT to avoid compressing the vessels within the neck with the strap or tie-down system used to stabilize the airway as this can impair venous blood return from the brain and increase intracranial pressure (85).

Given the current challenges associated with performing high-quality CPR, many of the EMS-10 systems have transitioned from manual traditional CPR or manual ACD CPR to an automated mechanical CPR (mCPR) device after 10-20 minutes of high-quality CPR, if not much earlier, especially if there are not enough personnel available to perform continuous high-quality CPR for at least 30 minutes. In some venues, this was actually a BLS function. Further, mCPR may be particularly helpful in the settings of a rural cardiac arrest with lengthy transports by EMS or in in-hospital cardiac arrest (IHCA) or any situation in which CPR is not practiced enough to maintain excellence. This could include a cardiac catheterization laboratory where manual CPR is neither safe nor practical or could even be fire service crew from busy territory, but where individual firefighters may not practice their skills for months at a time (67, 68).

ALS-DRUGS: When available, amiodarone or lidocaine is consistently administered intravenously or IO after 1-2 failed attempts at defibrillation. While optimal timing for antiarrhythmic drug administration remains unknown, evidence points to usual concern that the earlier the intervention, the better the results. When ventricular fibrillation (VF) does not respond to the first shock, providers may even want to prepare the drug immediately for more rapid infusion to avoid delays. Recent studies do indicate the effectiveness of amiodarone in “witnessed” cardiac arrests, again inferring a circumstance with earlier administration (94).

The first dose of amiodarone is 300 mg has often been followed by second dose (150 mg) in conventional protocols. Although the 2nd dose traditionally is administered after 5 shocks, many EMS-10 provide it much earlier (95). When used, the first dose of lidocaine has been 100 mg IV/IO and the second, if needed, 50 mg with same caveats about timing. It is important to appreciate that some studies have shown a definitive benefit of using amiodarone as the first line antiarrhythmic agent while others have shown only a clear trend with this approach (96). The likely explanations for these discrepancies have been outlined in the main text (10).

The use of epinephrine remains controversial but, if used, the frequency of administration in the EMS-10 has shown a reduction to no more than 0.5-1 mg every 5-10 minutes (97-99). There is some inferences that lower doses (or even epinephrine infusions) may yield better outcomes than higher doses, especially in achieving increased cerebral perfusion and improved neurological outcomes (99, 100). Nevertheless, these conclusions have been hampered by the multiple confounding variables and effect modifiers discussed in the core text. Laboratory experience and current clinical investigations involving much earlier use of adrenaline in children both indicate effectiveness of the drug and improvement in neurological outcomes (12, 101).

ADVANCED TECHNOLOGICAL RESUSCITATION CONSIDERATIONS

Extracorporeal membrane oxygenation (ECPR) has recently been shown to be effective for the treatment of cardiac arrest as a mechanism to maintain circulation (18, 102-104). For patients with refractory VF, defined in some of the EMS systems as the persistence of VF after administration of amiodarone and 10-15 minutes of high-quality CPR, ECPR protocols may increase survival with favorable neurological function. However, that again requires that properly-trained EMS personnel, assigned hospital personnel, and the correct equipment are all seamlessly available (18). Current best practices indicate that ECPR should be started within 60 minutes of the cardiac arrest to be most effective, if not earlier. It can be effectively initiated by adequately trained pre-hospital or hospital medical personnel with excellent experience already evolving (18, 102, 103). Patients who have ongoing signs of life such as gasping, eye or limb movement, or even speech should be transported to specialized resuscitation centers even if they are in refractory cardiac arrest, and should be strongly considered for ECPR (75).

If ECPR is not available on-scene or at the hospital, ALS personnel should continue CPR on scene for at least 30 minutes and much longer in some situations as it may take an hour or more in some circumstances to achieve a stable ROSC with the new interventions described in this report. ALS personnel also record signs of life and transmit those findings to hospital personnel given the importance of such signs as positive prognostic indicators (87). Advanced communication tools that help to streamline dataflow from ALS personnel to hospital ED and ICU personnel are now available to help improve information transfer and overall care.

In general, and especially in the absence of ECPR protocols, it was agreed that patients should be treated at the scene for at least 30 minutes by BLS and ALS providers (26). It is well documented that application of manual CPR during transport may adversely affect the quality of CPR and is unsafe for rescue personnel (105). Therefore, EMS systems would be encouraged to provide mCPR during transport of patients who need ongoing chest compressions unless there are no other options other than manual CPR. Early clinical evidence has shown that the combination of properly-applied and properly-timed device-assisted controlled sequential elevation (DACSE) of the head and thorax used in conjunction with the ITD and certain mCPR devices, proper ventilatory techniques (adequate lung inflation, controlled frequency and rapid recoil) can optimize the circumstance for ECPR. Early pilot studies indicate that the large majority of patients, even among those presenting with asystole, will generate relatively normal or supra-normal levels of $ETCO_2$ during CPR. Not does this indicate significant improvements in perfusion and circulation over standard techniques, but some of these patients may now awaken, still in a state of refractory VF, requiring sedation.

Continuous waveform capnography during resuscitation efforts may be the only 'vital sign' available (106). $ETCO_2$ waveforms after placement of an advanced airway has helped to confirm proper airway placement, potential airway dislodgement, quality of CPR, and to detect of return of spontaneous circulation (ROSC). After ROSC, $ETCO_2$ can be used to optimize ventilation and avoid hypo- and hyperventilation. $ETCO_2$ values generally, though not always, correlate with circulation and can even serve as an important guide to determine when to continue or discontinue CPR. For example, in patients with levels of $ETCO_2$ >10 mmHg and certainly >20 mmHg, there remains a reasonably high likelihood of obtaining ROSC. The general opinion of IRC participants believed that resuscitation efforts should be continued for at least 30 minutes, and probably longer with the new tools now being employed (107). In patients in which $ETCO_2$ >20 mmHg cannot be obtained, consideration should be given to overzealous ventilation (very common), displaced or obstructed airway, airway cuff leak, a tension pneumothorax, profound hypovolemia or, most often, poor quality CPR and the absence of CPR adjuncts such an ITD or ACD. Although still infrequently used due to logistical challenges, intra-arterial blood pressures have also been demonstrated to be of both clinical research value during CPR (108).

Normothermic patients with persistently low ETCO2 values of <10 mmHg receiving ventilation at a frequency of 6 breaths per minute or less and otherwise receiving optimal care (excellent quality CPR, good intravascular volume status) are likely to have a futile condition such as a massive pulmonary thromboembolic event or lengthy period of arrest prior to treatment and collapsed clotted and impassable intrapulmonary vasculature resulting in a large dead space condition and no circulation (106). More recently regional cerebral oximetry (rSO_2), by itself or together with $ETCO_2$, has been shown to be helpful in the futility decision-making process as well (89, 109). Those with an unwitnessed arrest, an initial rhythm of asystole, and persistently low $ETCO_2$ and rSO_2 values have a negligible likelihood of neurologically favorable survival (106). In turn, these are invaluable tools in EMS-10 systems.

Once ROSC is obtained, patients should be carefully monitored for the potential of lapsing into another arrest particularly after the effect of initial infusions of epinephrine or have likely worn off or if unrecognized overzealous ventilation compromises circulation. $ETCO_2$ levels may be elevated at first, but if <60-70 mmHg, attempts should not be made to rapidly decrease $ETCO_2$ to “normalize” levels by increasing the ventilation rate but adjusted a few minutes later, but only if that persists, particularly with head and thorax elevation are instituted to optimize cerebral circulation.

Patients transported with ongoing CPR to a Resuscitation Center should be treated with supplemental O_2 hopefully as needed to maintain O_2 saturation levels (measured transcutaneously) between 94-98% (110). The optimal mean arterial blood pressure (MAP) target is unknown but participants conceded that a MAP of 80 mmHg seems reasonable (111). Intravenous fluid and catecholamines may be considered and vasoconstrictors (e.g. norepinephrine/vasopressin) may be administered to reverse the systemic vasodilation which often evolves after longer periods of cardiac arrest. Advanced hemodynamic monitoring is commonly employed to treat this complex combination of both post-arrest cardiogenic dysfunction and the vasodilatory distributive shock. There was no set agreement on whether maintaining a MAP of >80 mmHg is beneficial if moderate or high doses of inotropes/vasopressors are required to achieve this goal.

Importantly, if the post-ROSC ECG shows a clear-cut pattern of segmental ST-segment Elevation Myocardial Infarction (STEMI), then the patient should be treated just like any STEMI patient (e.g. aspirin, O_2, etc.). Multiple studies have shown that STEMI patients who go directly to the cardiac catheterization laboratory, bypassing the hospitals that cannot provide STEMI patient care and even the emergency department (ED) of those that do, have better outcomes (112).

In addition to providing optimal ventilation and circulation, targeted temperature management (TTM) with induce hypothermia should be started as soon as practical post ROSC (113). Participants even recommended including rapid application of ice packs as a means to effectively cool the axilla and groin areas in the ambulance and ED. Use of cold intravenous fluids in the pre-hospital setting are generally avoided, with the concern that this might increase the risk of re-arrest in certain patients (114).

Once at the hospital, myocardial function should be assessed using echocardiography if use of cold fluids is still considered in the hospital setting. Core temperature should be monitored as soon as possible once the patient has reached the hospital to avoid overcooling (<32^{o}C). Core temperatures <30^{o}C can increase risk of arrhythmias and patients should be slowly rewarmed if core temperature drops below this level. Mild-to-moderate hypothermia (30-36^{o}C) does not appear to increase the risk of arrhythmias.

Recently, transthoracic and transesophageal echocardiography (TEE) have been used to assess cardiac function and the quality of CPR (115, 116). Studies have shown that CPR compressions are often not delivered in the optimal location including hand placement that may compress the aortic outflow track. Thus, TEE can help guide optimal hand and mCPR placement in the future. However, care must be taken not to interrupt chest compressions when using transthoracic and transesophageal echo.

For both first responders and ALS providers, cardiac arrest will probably remain a low frequency event. Reviewing and debriefing the resuscitation afterwards, preferably based on objective data on performance, helps to improve the quality of care (117). Regional or national competitions with CPR simulation scenarios can also motivate staff to achieve high-performance and help build a culture of excellence.

HOSPITAL-BASED RESUSCITATION CENTERS

Immediately after ROSC, patients are often extremely unstable and require high-level tertiary and quaternary care. All of the EMS-10 systems used dedicated cardiac arrests “resuscitation centers. One criterion for such centers was a sufficiently high post-ROSC cardiac arrest volume (minimally >25 cases annually and preferably >100). Other criteria include medical and nursing staff that have enough experience to care for these patients in a routine manner similarly to a trauma center concept (118). In summary, IRC participants stipulated that these centers need to be able to provide multidisciplinary care with qualified intensivists, cardiologists and cardiovascular surgeons who are ideally able to provide ECPR, immediate cardiac catheterization, rapid treatment with targeted temperature management (TTM) and other means to provide cardiopulmonary and neurological support as needed.

In general, many community hospitals cannot provide this level of support (119). Beyond the procedural issues, the EMS-10 all reported ED personnel in those centers who were able to help triage and treat the post-arrest patient, as well as those with ongoing CPR. When ECPR is available, protocols have helped to streamline care such that vascular access can be performed rapidly, safely, and consistently (103). In most systems, this has performed in the cardiac catheterization laboratory, in the emergency department, or occasionally (but with increasing frequency) in mobile pre-hospital units (102).

For optimal care, resuscitated patients not requiring ECPR are brought to a cardiac catheterization laboratory to assess the coronaries, revascularize as indicated, or provide additional hemodynamic support with adjuncts such as an intra-aortic balloon pump, left-ventricular assist device, and/or similar devices depending on the clinical need (120-122). In general, all patients, regardless of a clinical suspicion of a STEMI or non-STEMI, were generally studied with angiography rapidly, and ideally within two hours of the cardiac arrest onset, largely to prevent re-arrest and further neurological injury (112). Furthermore, a head CT scan (must be available 24/7) should be performed urgently, and an MRI (available at a minimum daily during daytime) at a later stage to assess for potential brain edema, injury, intracranial bleed and acute ischemic injury (123).

In addition to ECPR, the TTM are in these centers (33, 124-126). The stated goal was 32-33ºC for at least 24 hours, and perhaps up to 72 hours, followed by a gradual and controlled rewarming at a rate of no more than 0.25ºC per hour (33, 124). It was concluded that the one study that found that 33ºC and 36ºC target temperatures were equivalent, the patient population had shorter arrest intervals, an extremely high frequency of early bystander CPR, more STEMIs and more patients with signs of brainstem function, and was therefore likely less severely injured than the general cardiac arrest population (124). Several other papers have now reported increased mortality rates and worsening neurological outcomes following a change in target temperature from 33ºC to 36ºC (124). If there was a specific counter-indication for hypothermia such as active bleeding, a target of 35-36ºC is appropriate (33). It was noted that TTM can significantly alter the clearance and effects of some drugs, as well as some laboratory values (20). Many drugs (especially those metabolized by the liver) have slower metabolism at 32-33ºC, and therefore lower doses are required. This includes medications such as opiates, most sedatives, and unfractionated heparin. Drugs that require liver activation, such as clopidogrel, were, per protocols, avoided during TTM (20). For dosing of unfractionated heparin anti-10 levels were routinely followed (127, 128).

Recent evidence and experience have suggested that, once rewarmed, great caution should be used before determining if and when the patient will eventually awaken (21, 129). Neuroprognostic tools are described in the European Resuscitation Council Guidelines in 2018 and the AHA in 2019 (130, 131). With no improvement in several days (lingering sedation effects must be ruled out), measuring sensory-evoked potentials, and use of MRI, EEG, and automated pupillometry are common. In the vast majority of patients, it was recommended that neuro-prognostication should not start until at least 72 hours after the arrest and all potential confounders such as sedative effects, electrolyte and metabolic markers need to be excluded and resolved (132). In most patients, withdrawal of care should not be considered in the first 96 hours following arrest, and usually longer, unless there is clear and unquestionable evidence of devastating injury based on combinations of evidence from of the tools above.

For example, patients with a witnessed arrest and/or a first recorded rhythm of VF have a high likelihood of waking up eventually and fully recovering, although they may not awaken for over a week (21). Functional MRI may also be helpful when available. No decisions related to termination of care should be considered in those patients with positive prognostic indicators including witnessed arrest, VF as the first rhythm, presence of gasping during CPR, lack of brain edema or infarcts on head CT, or improvements in aspects of the neurologic exam for at least a week after rewarming. This is critical, otherwise withdrawal of life sustaining therapy will preclude recovery for patients who might otherwise survive with good neurological outcome.

Prior to discharge from these centers, it was agreed that is essential to try to determine the etiology of the arrest. In those circumstances in which sudden death occurred without any warning, an implantable cardioverter defibrillator (ICD) is often provided (133). If there is doubt on the initial rhythm of the OHCA when an AED has been used, efforts should be made to retrieve the data from the AED to determine the actual initial rhythm. Patients should be protected with an ICD prior to discharge when there is residual ischemia, a low left ventricular ejection fraction, when long-QT or other channelopathies are suspected, and when the cause is most likely secondary to a rhythm abnormality and cannot be fully reversed.

Post-ICU care is also essential for effective physical and psychological healing. It can take many months and often more than a year for patients to fully recover after cardiac arrest. Programs should be in place to provide consistent care for all patients that include screening and treatment for PTSD, depression and anxiety. This is a multidisciplinary process. Programs should be started inside the hospital with assessment from, at a minimum, psychiatry/neuropsychiatry and rehabilitation medicine. Additionally, the medical community should provide or facilitate rapid and long term emotional and psychological and spiritual support for the survivor but perhaps even more importantly for the survivor’s family and loved ones. Finally, all family members should be trained in CPR prior to patient discharge.

IN HOSPITAL CARDIAC ARREST CARE

Patients who experience an IHCA should be treated in a similar manner as those with OHCA described above. The goals of therapy for IHCA are the same as those for OHCA but also rapid assessment and treatment of acute coronary occlusion when suspected, and appropriate imaging to exclude other causes of the event and the use of the in-patient record and context to treat reversible causes. Progressive adjunct to increase the likelihood of survival after IHCA include surveillance strategies (134), predictive analytics (135). and deployment of specialty rapid response teams to help to reduce the frequency of IHCA (136). Novel technology can help monitor patients on the wards, enabling prompt recognition of an IHCA even though the patient is not on a monitor like in the CCU/ICU (137).

The surveillance management and predictive analytic technologies utilize data from the electronic medical record in unique ways, integrating data in ways that would be extremely difficult to do for the individual clinician and thereby predicting which patients might be at risk (138, 139). It has been estimated that in-hospital mortality rates could be reduced by nearly 50% by widespread application of such techniques today (140). It is anticipated that as these approaches become more refined and sophisticated, their benefits will continue to grow. Ultimately, these methods may be extended to EMS systems as well.

PEDIATRIC CONSIDERATIONS

Similar to adults, infants and children lapsing into cardiac arrest need immediate implementation of quality chest compressions, physiological sound ventilatory practices. Circulatory adjuncts as described above for adult can also be beneficial, depending upon the patient size, to optimize perfusion to the pediatric heart and brain (12, 31). Similarly, therapeutic hypothermia should be utilized when the child or infant remains comatose after cardiac arrest. There are no recent data to support withholding of therapeutic hypothermia for pediatric patients who remain comatose after cardiac arrest. A number of advances have been made, not the least of which is the recognition that pre-arrival planning and discussion are essential (12, 141). This mental readiness impacts the confidence of EMS professionals prior to arrival on scene and ultimately impacts their ability to initiate high performance CPR in the presence of family and onlookers (141).

A pre-arrival discussion for pediatric calls arms EMS providers with critical information such as equipment sizing, advanced preparation of correct epinephrine dosing and defibrillation dosages and also signals team members to not only stay on scene but to consistently perform their respective roles in the resuscitation (12, 141).

A recent study demonstrated that when: 1) the epinephrine dose was prepared enroute knowing the child's age, 2) optimal compression, rate and depth were immediately initiated and 3) an IO was immediately placed while 4) another highly-skilled ALS provider placed an ETT (or iGel[R] SGA if a difficult try), and 5) the epinephrine was infused and chased with some fluid bolus, the rates of neuro-intact survival for children rose dramatically. This total focus on rapid simultaneous interventions accompanied by proper ventilation methods helped to achieve neuro-intact survival for more than one-third of the children versus negligible rates of resuscitation and survival prior to the focus on rapid on-scene. The intent was to avoid the more traditional evacuation of the child to the transport vehicle to avoid the volatile scene dynamics, the insecurity of infrequent skill usage and a sense to get to more definitive care at the hospital.

In addition to the rapid pit crew approach to simultaneous rapid airway, IO and epinephrine interventions, crews were disciplined to provide a large enough breath with positive pressure ventilation to raise the chest wall and then only provide such a breath every 10 seconds. With the adequate lung inflation, dependent lung zones are better recruited and ventilation is more efficient (less dead space). But, importantly, inadequate inflation can lead to compromise to blood flow by collapsing dependent lung zones which will raise pulmonary vascular resistance. Therefore, there is better oxygenation, more efficient CO_2 removal and better blood flow through the lungs with the larger breath.

With oxygenation better addressed by better lung inflation and supplemental O_2, the need to ventilate in a cardiac state is very small. Lowering the frequency of breaths significantly avoids further compromise to blood flow by diminishing the high mean intrathoracic pressures that will result from more frequent positive pressure breaths. With EMS personnel being told the etiology is “respiratory” in children, it has created a traditional sense that giving more breaths is good when, in reality, that does not make physiological sense and can be very detrimental. Respiratory etiology or not, once cardiac arrest has set in, the physiology is clearly changed, especially from the respiring child who is still creating negative intrathoracic pressures swings with each spontaneous breath.

An immediate post-incident review with the medical director, including a review of the 9-1-1 audio recording, further strengthens the message of high performance for on-scene care, while simultaneously providing a case-by-case evaluation of bystander and telephone CPR.
A similar and routine post-incident review is beneficial after an adult cardiac arrest as well. For both pediatrics and adults, a quarterly report evaluating the three pillars outlined above (bystander – telecommunicator – EMS) will provide a clear view of where the disparities exist and highlight areas for improvement within a given community.