

THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Defibrillation for Ventricular Fibrillation

A Shocking Update



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ABSTRACT

Cardiac arrest is defined as the termination of cardiac activity associated with loss of consciousness, of spontaneous breathing, and of circulation. Sudden cardiac arrest and sudden cardiac death (SCD) are terms often used interchangeably. Most patients with out-of-hospital cardiac arrest have shown coronary artery disease or symptoms during the hour before the event. Cardiac arrest is potentially reversible by cardiopulmonary resuscitation, defibrillation, cardioversion, cardiac pacing, or treatments targeted at the underlying disease (e.g., acute coronary occlusion). We restrict SCD hereafter to cardiac arrest due to ventricular fibrillation, including rhythms shockable by an automatic external defibrillator (AED), implantable cardioverter-defibrillator (ICD), or wearable cardioverter-defibrillator (WCD). We summarize the state of the art related to defibrillation in treating SCD, including a brief history of the evolution of defibrillation, technical characteristics of modern AEDs, strategies to improve AED access and increase survival, ancillary treatments, and use of ICDs or WCDs. (J Am Coll Cardiol 2017;70:1496-509) © 2017 by the American College of Cardiology Foundation.

Cardiac arrest is the cessation of cardiac activity associated with unresponsiveness, no normal breathing, and no signs of circulation (1). In the United States, 356,000 patients are treated annually by emergency medical services (EMS) providers for out-of-hospital cardiac arrest (OHCA); and 209,000 patients are treated for in-hospital cardiac arrest (2). In Europe, 249,000 patients are treated for OHCA annually (3,4). Of these 814,000 patients, approximately 163,000 have an initial recorded rhythm indicating ventricular fibrillation (VF), which hereafter includes pulseless ventricular tachycardia (VT) and rhythms interpreted as shockable by an automated external defibrillator (AED).

The incidence of VF has decreased over time in multiple communities (5-7). The overall incidence of OHCA appears to be static (5,8,9). The causes of this shift from first recorded rhythms that are shockable to those that are not shockable are unclear. Primary and secondary prevention with fish oil consumption (10), beta-blockers (9,11), and statins (12) appears to have a role.

Patients with OHCA who have another initial rhythm (e.g., pulseless electrical activity or asystole) may convert to VF during attempted resuscitation, but patients with pulseless electrical activity or asystole have a worse prognosis than those with VF as a first rhythm (2). Moreover, patients who develop VF



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during attempted resuscitation have a worse prognosis than those with VF as a first rhythm (13).

The terms sudden cardiac arrest and sudden cardiac death (SCD) are often used interchangeably. Conventionally, cardiac arrest is described as “sudden,” but most patients with OHCA had known coronary artery disease or symptoms during the hour before the event (14). If corrective measures are not taken rapidly, the arrest is fatal. Cardiac arrest is potentially reversible by cardiopulmonary resuscitation (CPR), defibrillation, cardioversion, pacing, or treatment of the underlying disease (e.g., acute coronary occlusion). Ordinarily this excludes those with traumatic injury. We restrict SCD hereafter to cardiac arrest due to VF, including rhythms shockable by an AED, implantable cardioverter-defibrillator (ICD), or a wearable cardioverter-defibrillator (WCD).

We sought to summarize the state of the art related to treatment of patients with SCD including use of AEDs; strategies to improve access to AEDs; ancillary treatments that augment the response to defibrillation; and use of ICDs or WCDs. Emphasis is placed on treatments demonstrated to significantly improve survival in adequately powered randomized trials.

DISPARITIES IN OUTCOMES AFTER CARDIAC ARREST

There are significant variations among layperson readiness to respond to OHCA (15), how patients with OHCA are cared for, and whether patients survive (16). Assessments of the association between patient race or socioeconomic status and outcome after OHCA are difficult because self-reported race is typically missing in a large proportion of cases included in cardiac arrest registries (17), and because race and socioeconomic status are collinear in health data sets (18). In a pooled analysis of 15 observational studies that included 22,826 patients, black patients were significantly less likely to have a witnessed arrest or shockable rhythm, receive bystander CPR, or survive to discharge, than white patients (19). Among nonelderly adult patients treated for in-hospital or out-of-hospital cardiac arrest at 2 hospitals in Pittsburgh, Pennsylvania (n = 155), after adjustment for patient and treatment characteristics not including patient race, unemployment before arrest was independently associated with a worse neurological outcome (20). Among patients treated for OHCA in Seattle or King County, Washington (n = 1,390), after adjustment for patient and treatment characteristics including patient sex, race, and occupation before arrest, education was not independently associated with survival to discharge (21). Among a large cohort

of patients with OHCA treated in multiple communities in the United States (n = 22,816), bystander treatments and survival after OHCA were significantly lower in neighborhoods with a higher percentage of black residents than in those with a lower percentage (22). Despite these disparities in the process and outcome of care after OHCA, survival in multiple communities is improving over time (23,24).

IMPROVEMENTS IN DEFIBRILLATION

Defibrillation was first demonstrated in 1899 (25). Application of defibrillation to convert VF into a perfusing rhythm occurred concurrently in multiple locations (26,27). The first successful use of an alternating-current internal defibrillator in a human was reported in 1947 (28). The first successful use of an alternating-current external defibrillator on a human was reported in 1956 (29). These defibrillators used energy from a landline (i.e., electricity from a wall socket). The first use of a portable direct-current external defibrillator (estimated weight: 3.2 kg) was reported in 1967 (30). The first portable defibrillator in the United States was commercially available in 1968 (estimated weight: 15.4 kg; LifePak 33, Physio-Control, Inc., Redmond, Washington).

Innovations to defibrillation of patients with VF since the 1960s are summarized in Table 1. These innovations continue to occur over time, especially those related to ease-of-use and portability. Improvements in the ability to store and deliver energy, as well as lower-energy waveforms used to do so that were initially developed for ICDs, have enabled marked reductions in the size and weight of AEDs (31). The smallest commercially available external defibrillator weighs 0.49 kg and can fit into a large pocket (available in Europe but not in the United States) (32). The characteristics of AEDs currently available for use in the United States are summarized in Table 1. There is a large heterogeneity in their performance characteristics. There are no published trials that demonstrate a significant difference in survival when AEDs with different characteristics are used.

GENERAL AED CHARACTERISTICS

Automatic refers to the ability of these devices to independently analyze the patient’s rhythm after the device is correctly applied to the patient’s chest and turned on. To do so, most contemporary AEDs

ABBREVIATIONS AND ACRONYMS

- AED** = automated external defibrillator
- CPR** = cardiopulmonary resuscitation
- ECG** = electrocardiography
- EMS** = emergency medical services
- ICD** = implantable cardioverter-defibrillator
- LVEF** = left ventricular ejection fraction
- OHCA** = out-of-hospital cardiac arrest
- PSAP** = public safety answering point
- SCD** = sudden cardiac death
- VF** = ventricular fibrillation
- VT** = ventricular tachycardia
- WCD** = wearable cardioverter-defibrillator

TABLE 1 Characteristics of AEDs Approved for Use in the United States

Manufacturer, Location	Cardiac Science, Waukesha, WI		Defibtech, Guilford, CT		Phillips, Bothell, WA		Physio-Control Inc., Redmond, WA				Zoll Medical Inc., Chelmsford, MA
	Cardiac Science G3	Cardiac Science G5	Lifeline VIEW	Lifeline AED	Philips FRx	Philips Onsite	Physio-Control LIFEPAK CR Plus	Physio-Control LIFEPAK Express	Heartsine 350P	Heartsine 450P	Zoll AED Plus
Photo											
Text prompts	No	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes
Voice prompts during event	Yes, keep pace with user	Yes	Yes	Yes	Yes, keep pace with user	Yes, keep pace with user	Yes	Yes	Yes	Yes	Yes
Feedback during event	No	Metronome or optional rate, depth, and recoil available separately	No	No	No	No	No	No	No	Rate only, and lack of compressions	Integrated rate and depth
Post-event debriefing software	No	Yes	Yes	Yes	Yes						
Infant/child cable and pads available	Yes	Yes	Yes	Yes							
Infant/child adapter key	No	No	No	No							
Estimated pad life	2 yrs	4 yrs	4 yrs	5 yrs							
Estimated battery life	4 yrs	2 yrs	2 yrs	4 yrs	4 yrs	5 yrs					
Battery self-test interval*	Daily	Daily	Daily	Daily	Daily	Daily	Weekly	Weekly	Weekly	Weekly	Monthly
Escalating energy	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes
Estimated time to charge	10 s	10 s	4 s	4 s	8 s	8 s	9 s	9 s	8 s	8 s	10 s
Weight, lbs	6.6	5.7	3	4.2	3.5	3.3	4.5	4.5	2.4	2.4	6.7
Size, cubic inches	434	361	160	271	152	172	217	217	114	114	574
Warranty	7 yrs	8 yrs	8 yrs	8 yrs	7 yrs						
Flight-certified	In process	In process	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes

All devices cleared for use in United States use biphasic waveform. Note that no device or feature shown in the table has been demonstrated to significantly improve survival or neurological function compared to another device or feature. Available features may change over time. For updated information, consult each manufacturer's website. *Not all devices perform a self-test of full capacitor discharge. Some only provide partial capacitor discharge.
AED = automated external defibrillator.

provide spoken prompts to the user; some also provide visual prompts on a display.

External refers to the application of electrode pads to the bare chest of a patient in presumed cardiac arrest, in contrast to ICDs, which have electrodes surgically implanted inside the body of a patient before the onset of arrest.

Defibrillation refers to passing an electrical current across myocardium to depolarize the muscle, in order to convert a dysrhythmia back into normal sinus rhythm. The battery contained in an AED is capable of storing a large amount of energy; however, it is stored at energy levels that are too low to defibrillate. The capacitor stores energy at a high enough level to

be able to deliver sufficient current for defibrillation. The capacitor consists of a pair of conductors (i.e., metal plates) that are separated by an insulator. Conductors gain and lose electrons easily, which allows current to flow. Insulators are intended to not lose electrons and so allow little current to flow.

Switching circuitry releases the energy stored in the battery to the capacitor and then applies it to the patient's chest in the appropriate time sequence to create a specific waveform. When a user opens or turns on an AED, its prompts guide the user to connect the electrodes to the patient. Then users are guided to avoid touching the patient so as to reduce false interpretation of rhythm by the AED. The device

evaluates the electrical output from the heart through the electrodes, then a software algorithm native to the AED determines if the patient is in a shockable rhythm. If the device determines that a shock is required, its battery charges its internal capacitor in order to be able to deliver shock through the chest. Once the AED is charged, prompts instruct the user to check that no one is touching the patient. Most available AEDs require a user to initiate shock delivery to reduce the possibility of injury to someone who is inadvertently touching the patient at the time of shock. After a shock is delivered, most available AEDs prompt the user to restart CPR.

The amount of energy delivered by a defibrillator is expressed in joules (J). This energy is a function of voltage, current, and time. Current is what actually defibrillates the heart and is expressed in ohms. This is the voltage-to-impedance ratio. The latter is the resistance to electrical flow, which can arise in the electrical circuit or in the patient due to the quality of contact between the pads and the skin, as well as diaphoresis, temperature, or body mass. Although AEDs are commonly described in terms of the energy they deliver, they differ widely in their peak and average currents, as well as in the duration of their waveforms (33).

The exponential decay of the voltage of a capacitor during its discharge determines the basic waveform for defibrillation. Waveforms differ according to the steepness of this decay (i.e., different capacitances), the duration (fixed-duration waveforms), or tilt (fixed-tilt waveforms). During defibrillation, electric current flows from the cathode (negative electrode) to the anode (positive electrode). With a monophasic waveform, the current passes from the cathode to the anode once. With a biphasic waveform, the current passes from one electrode to another and then back after polarity reversal.

Each shock moves in an opposite polarity between the pads. In small randomized trials in pigs (34,35), humans with atrial fibrillation, or survivors of VF (36), there were no significant differences in defibrillation threshold according to electrode polarity. In a moderately sized randomized trial in humans with out-of-hospital VF, there were no significant differences among the type of rhythm observed after defibrillation, the proportion of patients who had spontaneous circulation restored, or survival to discharge among patients who had the apex electrode positively charged ($n = 114$) compared to those who had the apex electrode negatively charged ($n = 91$).

The first commercially available AEDs used a monophasic waveform, which gave a high-energy shock of up to 360 J. This energy level required

large capacitors and inductors, was sometimes associated with cardiac injury after shock, and in some, cases second- and third-degree burns around the shock pad sites. Biphasic waveforms were initially developed for use in implantable defibrillators. These were adapted for use in AEDs because they require smaller batteries, capacitors, and insulators, as they usually successfully defibrillate VF at lower energy levels than monophasic waveforms. Contemporary AEDs use biphasic waveforms that give 2 sequential lower-energy shocks totaling 120 to 200 J. There is no American Association for Medical Instrumentation standard for biphasic waveforms. Therefore, each manufacturer has developed its own waveform, protected its design with patents, and promoted its characteristics in the marketplace.

DEFIBRILLATION WAVEFORM

All automated external or internal defibrillators approved for clinical use in the United States by the Food and Drug Administration (FDA) or that have the European Conformité Européenne (CE) mark, use biphasic waveforms. These waveforms differ in shape, peak current at their programmed energy setting, and whether and how their energy output is adjusted in response to patient impedance. In patients with atrial tachyarrhythmias, biphasic waveforms have greater shock efficacy and less post-shock injury than monophasic waveforms (37-39). In patients with VF, a truncated (40,41) or rectilinear biphasic waveform (42,43) has greater shock efficacy than monophasic waveforms. Although some external defibrillators previously used monophasic waveforms, these have fallen into disuse because of the greater energy output (and hence size of the battery, capacitor, and insulator) required to successfully convert VF. There is no published trial that demonstrates that one biphasic waveform achieves significantly greater survival versus another in patients with OHCA (44).

In a moderately sized case series of patients with out-of-hospital VF in France, a pulsed biphasic waveform at 130 J was associated with a similar shock efficacy as that reported historically in similar patients treated with an AED with a biphasic truncated exponential waveform at 150 or 200 J (45). This AED uses waveforms of short duration (14 ms) in recognition of the fact that long-duration waveforms can activate cells that have recovered their excitability and thereby reinduce VF (46). This AED is commercially available only outside of the United States. Other waveforms that use more than 2 electrodes or waveform phases are under investigation and may

offer some size, weight, or clinical advantage (47-49). To date, these have not been approved for clinical use in the United States.

FIXED VERSUS ESCALATING ENERGY

Different external defibrillators are programmed by their manufacturers to provide different energy doses for the first shock. Some are programmed to then provide the same energy dose; others are programmed to provide an escalating energy dose. Observational studies in humans with SCD suggest that an external biphasic shock of 200 J or less terminates VF in 85% to 98% of cases (50). In one trial that evaluated different AEDs made by the same manufacturer, sequential shocks with escalating energy increased termination of VF versus sequential shocks with fixed energy (51). In another trial that evaluated external defibrillators made by the same manufacturer, sequential shocks with escalating energy decreased termination of VF versus sequential shocks with fixed energy (52). There is no published trial that demonstrates that one initial or subsequent energy dose achieves greater survival versus another in patients with OHCA. Nor is there published evidence of significant differences in adverse events between initial or subsequent energy doses.

IMPEDANCE COMPENSATION

Commercially available AEDs differ in how they compensate for differences in chest wall impedance. In an animal model of VF, compensation by maintaining current with fixed shock duration was associated with greater conversion out of VF than compensation by prolonging shock duration (53). In similar animal models, current was associated with greater shock success than was energy (54,55). In a bench study of AEDs from multiple manufacturers, mean current was greater than expected at low impedance and less than expected at high impedance (56). Although use of current rather than energy to guide defibrillation is promising, there is no published evidence of significant differences in shock efficacy or adverse events with one method of impedance compensation versus another.

DEFIBRILLATION GUIDED BY WAVEFORM ANALYSIS

The characteristics of VF change over time. Coarse VF is observed earlier after the onset of arrest, then fine VF is observed later. The former is easier to convert to a perfusing rhythm than the latter. The presence or absence of some of these characteristics may predict

conversion out of VF after a subsequent defibrillation shock (57,58). Defibrillation guided by waveform analysis consists of incorporating software into a defibrillator that assesses the characteristics of VF then prompts the user to defibrillate at a time likely to be associated with successful conversion out of VF. Although manual CPR is traditionally paused during rhythm analysis, longer pauses are associated with lower survival (59,60). Some available AEDs filter out compression artifacts on the electrocardiographic (ECG) monitor so that the heart rhythm can be analyzed manually (by an EMS provider) or automatically (by an AED), without interruption of CPR. To date, defibrillation guided by automated waveform analysis has not significantly increased the likelihood of survival after OHCA versus standard care (61).

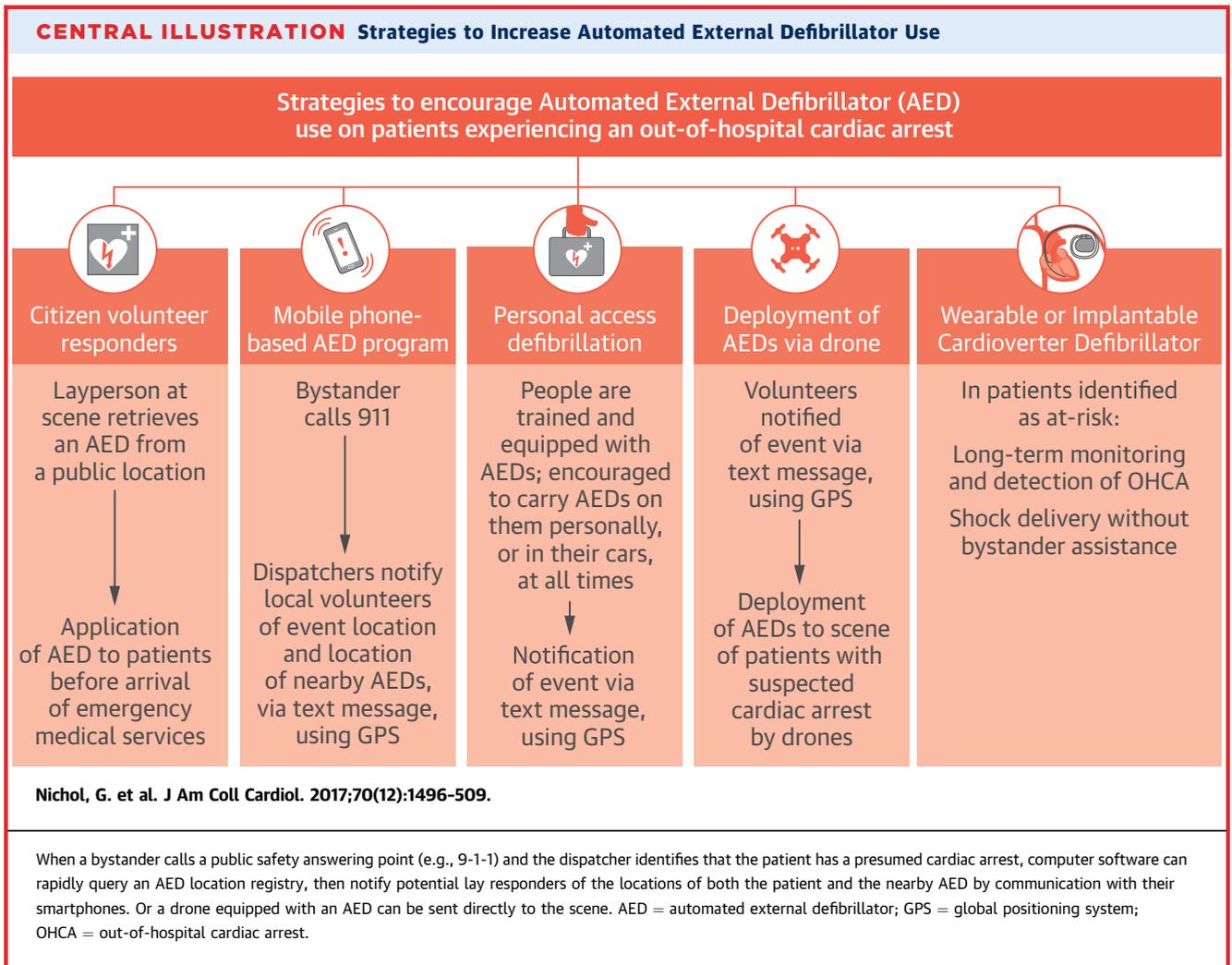
CHALLENGE OF TIME TO DEFIBRILLATION

The likelihood that a patient with OHCA will have a first rhythm that is shockable is highly correlated with the time of first rhythm analysis (62). Survival to discharge is strongly associated with whether the first rhythm is shockable (63,64). Thus, considerable efforts have been invested in reducing the time to defibrillation by increasing use of AEDs before the arrival of EMS providers on scene (**Central Illustration**).

LAY RESCUER PROGRAMS TO REDUCE TIME TO DEFIBRILLATION IN PUBLIC

Simple AEDs used by trained personnel at locations in which large numbers of people congregate reduce the time to defibrillation and improve survival (65). In a large community-based trial, patients with OHCA in locations where laypersons were trained and equipped to retrieve a stationary AED and use it before the arrival of EMS providers on scene had significantly greater survival to discharge versus those where laypersons were trained to perform CPR alone (66). Lay responder defibrillation is good value for the money (67). Since then, >2.5 million AEDs have been sold in the United States for use by laypersons before the arrival of EMS providers on scene (68). Despite this, a minority of patients with OHCA have had an AED applied by a layperson (2).

Most American states have passed laws or regulations that govern lay rescuer AED programs (69). Evidence-based guidelines recommend that implementation of a lay rescuer AED program includes an emergency response plan, training of potential bystanders, and periodic device maintenance. In Europe,



lay rescuer use of AEDs is permitted in some (e.g., Belgium, England, France) but not all countries.

In the Progetto Vita program in Piacenza, Italy, a cadre of dedicated laypersons implemented a community-based AED program. Citizen volunteer responders are encouraged to respond to patients they encounter with suspected OHCA before the arrival of EMS providers on scene. The lay response involves retrieval of an AED from a public location and application of it to the victim before the arrival of EMS, without intervening CPR. This program is entirely supported by community donations and maintained by a high degree of engagement by volunteers and resuscitated patients. Of 95 patients treated by Progetto Vita alone, 68% had a shockable rhythm, and 41% survived to discharge (70). Of 3,271 patients treated by EMS providers alone, 12% had a shockable rhythm and 6% survived to discharge. This suggests that lay rescuer AED programs can be maintained with community engagement. Although

some have criticized this emphasis of use of an AED over use of CPR (71), the concept of laypersons applying an AED to someone with witnessed OHCA is consistent with evidence-based recommendations that EMS providers apply a defibrillator as soon as feasible to an individual with witnessed OHCA (72).

HOME DEFIBRILLATION TO REDUCE TIME TO DEFIBRILLATION

A challenge to application of early defibrillation is that the majority of arrests do not occur in public locations. In patients known to be at high risk of VF (e.g., reduced left ventricular ejection fraction [LVEF] or demonstrated propensity to VF) the prophylactic use of an ICD is effective (73,74) and good value for the money (75), but lack of understanding of the risk and benefit of ICDs and cost constraints limit their use to a small proportion of the population at large (76).

Home defibrillation was proposed to address OHCA that occurs in private residences: training and equipping family members of those at low but increased risk of cardiac arrest (e.g., those with LVEF of 35%, those who have experienced previous anterior myocardial infarction, or those who are not candidates for an ICD) (77). In a large trial, home defibrillation did not significantly improve survival to discharge versus usual care. Of 450 deaths observed in this trial, 38% were caused by tachyarrhythmia. Of these, only 36% were witnessed at home. Only 8% of patients with a tachyarrhythmia had a witnessed arrest at home and underwent resuscitation. Possible reasons for the lack of difference in survival include rates of mortality lower than expected and SCD. However, 29% of those who had an AED applied for VF survived to discharge (compared with 20% after VF treated by EMS) (78). We attribute the lack of significant benefit of home defibrillation in part to arrests not being witnessed, to events occurring outside the home, and to the size and weight of the AEDs used, which made it impractical for participants to carry the AED at all times.

MOBILE PHONE-BASED SYSTEMS TO REDUCE TIME TO DEFIBRILLATION

Another challenge to the successful deployment of AEDs is that laypersons often do not know where the AEDs are located or are unable to retrieve them and return to the scene of OHCA before the arrival of EMS providers on scene. A variety of technologies have been tested to increase the use of AEDs by laypersons before the arrival of EMS providers on scene. These differ in the method of activation, number of individuals activated, and distance from which they are activated. In the Netherlands, a mobile phone-based system was initiated in approximately 2008 (79). This system requires volunteers to indicate their willingness to respond to OHCA by registration. When a public safety answering point (PSAP [i.e., a dispatch center]) identifies the fact that an emergency call is related to an individual with suspected cardiac arrest, volunteers are notified of the event location. Initially, this notification occurred by Short Message Service (SMS), commonly called text messaging. Over a 42-month observation period, volunteers alerted by SMS delivered the first shock in 13% of all SCDs (80). Subsequently, the technology switched to using the global positioning system (GPS) native to the mobile phone to locate potential responders and then notifying them of a nearby patient with suspected cardiac arrest.

In Sweden, physicians worked with software developers to develop and implement a similar mobile phone application that alerts volunteers to perform CPR or apply an AED (81). This system significantly increased the delivery of bystander CPR from 48% to 62% (82). This application is now maintained by an international technology company and is available for use in other countries.

In the United States and Canada, Atrus Inc. (Delray Beach, Florida) provides software that links AED location information to subscribing PSAPs so that dispatchers can be aware of AED locations close to calls related to OHCA (83). Its software also automatically notifies, by text and/or phone, any registered volunteers affiliated with AEDs that are nearby the event and asks them to respond to the scene. Two-way communication with the PSAP allows dispatchers to know who is responding. No special mobile phone application is required for this notification to occur.

A widely-used approach to improving the community response to OHCA in the United States is the PulsePoint program (PulsePoint Foundation, Pleasanton, California), which consists of a mobile phone application that allows users to view and receive alerts on calls being responded to by fire departments or EMS, as well as a mobile phone application that allows users to identify and report the locations of AEDs (84). These applications are integrated into PSAPs in participating communities to notify volunteers who are nearby a patient with OHCA based on GPS information native to the volunteer's mobile phone.

RESIDENTIAL RESPONSE

About 75% of OHCA occur in residential settings (85). As a consequence of this, efforts to improve the community response to OHCA by notifying volunteers of events in public locations may have limited impact on overall survival. Outside the United States, most mobile phone-based AED programs have required volunteers who intend to use this application to register with the program. In exchange, the program leaders allow volunteers to respond to suspected cardiac arrest events that occur in private homes.

MOBILE AEDs

Conventionally, mobile phone-based AED programs alert volunteers to retrieve an AED and take it to a suspected cardiac arrest event. Personal access

defibrillation consists of training and equipping laypersons with an AED and then encouraging them to carry the AED at all times. If notified, they would use it on a person in suspected cardiac arrest before the arrival of EMS providers on scene. In Singapore, a pilot program has trained taxi drivers to recognize and respond to OHCA and then apply AEDs before the arrival of EMS providers on scene. One hundred taxis have been equipped with AEDs (86). To date, this program has not reported any outcomes.

In rural Denmark, a similar pilot project trained home health providers to recognize and respond to OHCA and equipped their cars with AEDs (87). When a dispatcher identifies a suspected cardiac arrest event, providers in the 2 participating cars closest to the scene are notified of nearby events. Of 80 OHCA, 10 (13%) had home health providers arrive and begin CPR before the arrival of EMS providers on scene. One patient received a shock from an AED.

Recently, PulsePoint launched a pilot program in suburban Portland, Oregon, to register firefighters, equip them with AEDs, and then notify them to respond to suspected cardiac arrest events in residential settings when they are off duty (88). As of February 22, 2017, more than 200 off-duty firefighters had AEDs and are available to respond.

There are some barriers to success of these mobile phone-based approaches to improving the community response to OHCA. For example, only approximately 10% of notified volunteers arrive at the scene of the emergency (89). Volunteers may not hear the notification or may be unavailable to respond. The GPS attempts to accurately identify the location of the responders, but sometimes they are too far away from the event location to arrive before EMS providers. Recent improvements in methods of geolocation may increase the accuracy of identifying the locations of suspected cardiac arrest events and responders (90).

The window of opportunity for mobile phone-enabled volunteers may be brief in a high-functioning EMS system (91,92). OHCA events with longer EMS response intervals provide the opportunities for mobile phone-equipped responders to have an impact. A 1-min reduction in time to defibrillation is associated with a 10% increase in survival after VF (93). In Progetto Vita, lay rescuers were on scene 3 min before EMS providers, and AED deployment was not delayed by CPR maneuvers. In addition, the 75% of patients with OHCA who are not in a shockable rhythm may benefit from having a responder who is not fatigued from doing prolonged CPR and is ready to act.

Deployment of AEDs by drones to the scene of patients with suspected cardiac arrest has been

proposed as a novel method of reducing time to defibrillation (94). As of June 30, 2017, pilot studies of drone defibrillation are underway in Europe (95). To date, there is no method available to do so in the United States.

STRATEGIES TO CONVERT PROLONGED VF

A subset of patients who present with VF do not respond to early defibrillation. For example, approximately 10% of patients with OHCA may have refractory (or recurrent) VF, defined as VF still present after 5 shocks (96). Rapid sequential shocks may reduce the defibrillation threshold (97). Double sequential external defibrillation consists of nearly simultaneous application of defibrillation shocks using 2 defibrillators. This has long been used by electrophysiologists in patients with refractory VF induced during elective procedures (98). Case reports and case series suggest that double defibrillation may be associated with conversion of patients out of VF in the out-of-hospital setting (99-101). In the absence of concurrent control data, it is difficult to assess whether use of double defibrillation causes conversion to a perfusing rhythm. Importantly, nearly simultaneous application of defibrillation may damage the defibrillators used, with subsequent device failure in a future patient. To date, no trial has evaluated the effectiveness of double defibrillation.

IMPACT OF CONCURRENT RESUSCITATION INTERVENTIONS

Efforts to successfully defibrillate patients with SCD may be influenced by other treatments. Existing treatments for OHCA combine CPR and early defibrillation by bystanders or first responders, with advanced cardiac life support by EMS providers that includes CPR, defibrillation, and intravenous drugs and post-resuscitation care in hospital. In addition to early application of an AED by a layperson, briefer times from the call for assistance to dispatch of EMS providers (102) and their arrival on scene (103,104) and better quality of CPR (60,105-107) are associated with improved outcomes.

Importantly, no hospital-based therapy other than induced hypothermia (IH) has been demonstrated in trials to improve outcomes in patients with OHCA due to VF (108,109). In a trial in which patients achieved their target temperature more slowly than those who showed IH-improved outcomes, the benefit of IH was less clear (110). Other components of hospital-based post-resuscitation care are associated with good outcomes after OHCA (111). A recent pilot study demonstrated the feasibility of random allocation of patients

with OHCA to transportation to the closest facility versus a center with special ability in provision of post-resuscitation care (112). Additionally, U.S. National Institutes of Health recently funded a large trial of coronary angiography versus standard care in patients who were resuscitated from OHCA (113). Our knowledge of the interplay between defibrillation for VF and other concurrent interventions will evolve over time.

VF IN YOUNG ATHLETES

Sudden cardiac deaths of young persons (e.g., <35 years of age) while participating in a sport are visible, devastating, and highly reported events (114). Experts disagree about how often SCDs occur (115,116). One strategy to reduce the burden of SCDs in young persons is to place AEDs in schools. A competing alternative is to screen athletes for increased risk of SCD.

Young athletes with underlying cardiovascular abnormalities may have increased risk for SCD (often on the athletic field) versus nonathletes or competitive athletes without cardiovascular disease (117). Conversely, the larger population of nonathletes may have a similar risk and higher absolute number of SCDs (118). Electrocardiographic screening for risk of SCD among competitive athletes can yield large numbers of false-negative test results, as well as false-positive test results that lead to expensive secondary testing (119). The incremental cost effectiveness of such screening is more than that associated with commonly used health interventions (120). Note that this large incremental cost effectiveness contrasts with the cost effectiveness of placement of AEDs in public locations for use by laypersons before the arrival of EMS providers on scene.

A retrospective study reported that ECG screening of athletes was associated with an 89% decrease in SCD over 26 years in Veneto, Italy (121). In the absence of a large trial that demonstrates the effectiveness of ECG screening of athletes for risk of SCD, there are differences in opinion as to whether such screening is recommended or used. In the United States, experts recommended that screening consist of a focused history and physical examination (122). The European Society of Cardiology recommends addition of a 12-lead ECG to such screening programs (123). In Italy, screening before participation in competitive sport has been mandatory since the 1970s (124).

In the Netherlands, such screening was mandatory but was discontinued in 1984 due to lack of accuracy of the screening tests (125). In the United Kingdom, experts recommended that a national population screening program not be implemented (126). In the

United States and England, charitable organizations offer screening events for young athletes that include a focused history and physical examination, 12-lead ECG, and selective echocardiography (127,128). Until there is better evidence of the effectiveness of screening of competitive athletes, it is reasonable for such screening to be supported by such local resources but not third-party payers.

HEMODYNAMICALLY GUIDED RESUSCITATION

Greater blood flow, including cerebral perfusion pressure and coronary pressure during and after resuscitation, is associated with better outcomes in animals and humans with cardiac arrest (129-132). Evidence-based guidelines emphasize use of better quality chest compressions, as well as antiarrhythmic and vasopressor agents, to achieve better blood flow and consequently greater likelihood of restoration of circulation (133). It is impractical to place invasive monitors during attempted resuscitation of OHCA in most settings. Multiple methods are being developed to measure blood flow during resuscitation quickly and noninvasively (134-136). To date, these methods are not widely available and have not been demonstrated to improve survival in trials.

IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS

Insertion of a cardioverter-defibrillator into a patient identified as having at least moderate risk of SCD is intended to lower their subsequent risk of death due to primary or secondary VF and, thereby, decrease the incidence of OHCA in the community. Those who survive out-of-hospital SCD or symptomatic sustained VT have declared themselves at high risk of recurrent life-threatening ventricular arrhythmias. The exception to this is when the cause of the arrhythmia is attributable to a reversible trigger.

The benefits of ICD can be offset by device-related complications. Novel implantable devices are being developed to reduce device-related complications. An entirely subcutaneous ICD (S-ICD) was approved by the FDA in 2012 and has now been inserted in over 30,000 patients worldwide (137,138). The absence of transvenous leads is intended to reduce lead-related complications (139). The available S-ICD can only deliver shock therapy and, therefore, is not applicable to patients who also need bradycardia pacing, antitachycardia pacing for known monomorphic VT, or cardiac resynchronization therapy. Other innovative therapies have also focused on reducing complications from transvenous pacing leads (140).

Despite the benefits of ICD therapy to individual patients, the overall impact on the broader population of patients who will experience SCD is unclear. A retrospective analysis of registry data from Amsterdam, the Netherlands, suggests that one-third of the reduction in the incidence of out-of-hospital VF is attributable to use of ICD (141). Most patients who have SCD *do not* have the antecedent features that would have identified them as candidates for primary prevention ICD therapy. Their LVEFs are, on average, above 45%, and most have underlying coronary artery disease, characteristics that have not changed much over the past 4 decades, despite an overall lower incidence of OHCA (142). The cause of the reduction in incidence of VF that has been observed in multiple communities is likely multifactorial, rather than attributable to ICDs alone.

WEARABLE CARDIOVERTER-DEFIBRILLATOR

The benefits of an ICD are attributed to ongoing risk of arrhythmia over time, but SCD may be triggered by a transient or correctable cause. These underlying diseases often take time to detect and are not easy to reverse. The concept of WCD consists of long-term monitoring, detection of SCD, and shock delivery without bystander assistance or an implanted device to bridge an assessment period or to let optimal medical therapy deliver its benefit (143).

To date, 1 WCD has been approved for use in the United States and Europe. The LifeVest WCD (Zoll Lifecor Corp., Pittsburgh, Pennsylvania) was approved by the FDA in 2001. The sensing and therapy delivery component consist of 1 anterior and 2 posterior self-gelling defibrillation electrodes, as well as 4 nonadhesive electrodes, held together by an elastic chest garment. Dry tantalum oxide electrodes provide long-term ECG monitoring through 2 nonstandard leads (anteroposterior and left-right bipolar signals), whereas the defibrillation electrodes contain a vibration plate and multiple gel capsules. The vibration plate is intended to give the patient a tactile warning of an impending shock once a shockable rhythm detection occurs. Then defibrillation gel is released to minimize skin-pad impedance and prevent skin injury during shock delivery. When the patient receives tactile, audible, and visual alerts, the therapeutic shock can be aborted by

simultaneously pushing 2 buttons. The WCD is able to deliver shocks of up to 150 J, biphasic, with a programmable response time of 25 to 180 s (see Table 1 in Klein et al. [144]). Prospective registries from the United States (145) and Germany (146) have demonstrated that use of WCD is associated with survival after SCD. Compliance with wearing the device is high, with some patients reportedly wearing the device for more than 20 h/day (147). Reported rates of inappropriate therapies range from 0.4% to 0.5%, with fast supraventricular tachycardia and artifacts as the most common underlying causes (145,146). Inappropriate detection also occurs, which requires patients to be able to use the “abort” function. To date, no published trial defines the effectiveness of WCD versus that of alternative treatment or watchful waiting, but a randomized trial is ongoing (148). According to American and European practice guidelines, WCD may be considered in adult patients who present a high arrhythmic risk for a limited period, such as for transient causes of reduced LVEF, as a bridge to heart transplantation or left ventricular assist devices (149), in the 40 days after myocardial infarction or in the 3 months after a coronary artery bypass graft (150). Also, WCD can be considered when a transient contraindication to ICD is present, such as endocarditis or device-related infection (149,151).

FUTURE DIRECTIONS

Sudden cardiac death continues to be an important public health problem. Rapid response to cardiac arrest with highly trained EMS and use of AEDs, along with the use of ICDs in patients with indications, have contributed to a reduction in SCD. The most promising interventions to further reduce the burden of SCD include mobile phone-based reminder systems, personal defibrillation, and possibly, wearable anti-arrhythmic devices. Recent improvements in outcomes after SCD in multiple communities suggest that ongoing efforts to reduce its burden are warranted.

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