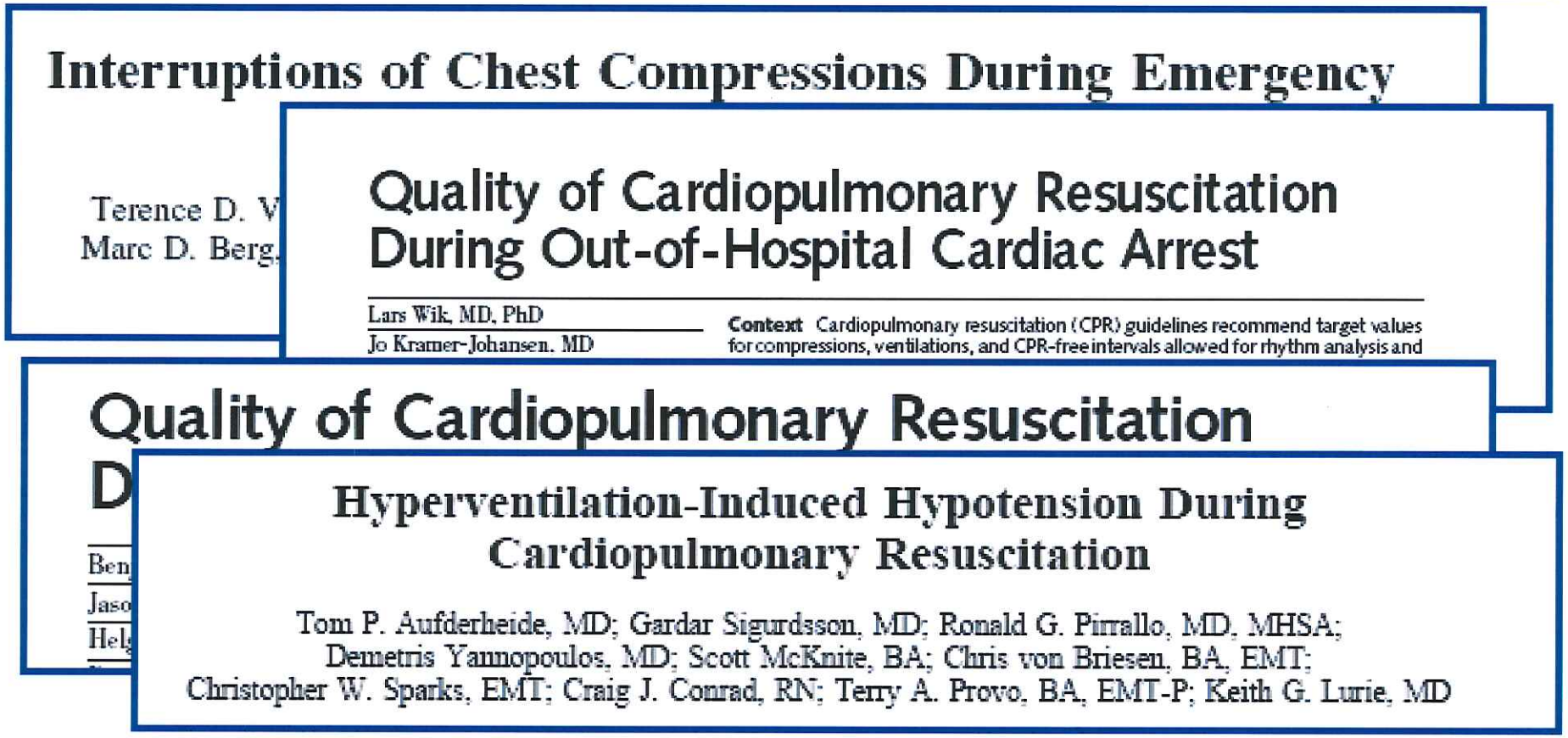
CPR renaissance: measuring CPR matters



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Interruptions of Chest Compressions During Emergency Medical Systems Resuscitation

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Background—Survival after nontraumatic out-of-hospital (OOH) cardiac arrest in Tucson, Arizona, has been flat at 6% (121/2177) for the decade 1992 to 2001. We hypothesized that interruptions of chest compressions occur commonly and for substantial periods during treatment of OOH cardiac arrest and could be contributing to the lack of improvement in resuscitation outcome.

Methods and Results—Sixty-one adult OOH cardiac arrest patients treated by automated external defibrillator (AED)–equipped Tucson Fire Department first responders from November 2001 through November 2002 were retrospectively reviewed. Reviews were performed according to the code arrest record and verified with the AED printout. Validation of the methodology for determining the performance of chest compressions was done post hoc. The median time from "9-1-1" call receipt to arrival at the patient's side was 6 minutes, 27 seconds (interquartile range [IQR, 25% to 75%], 5 minutes, 24 seconds, to 7 minutes, 34 seconds). An additional 54 seconds (IQR, 38 to 74 seconds) was noted between arrival and the first defibrillation attempt. Initial defibrillation shocks never restored a perfusing rhythm (0/21). Chest compressions were performed only 43% of the time during the resuscitation effort. Although attempting to follow the 2000 guidelines for cardiopulmonary resuscitation, chest compressions were delayed or interrupted repeatedly throughout the resuscitation effort. Survival to hospital discharge was 7%, not different from that of our historical control (4/61 versus 121/2177; $P=0.74$).

Conclusions—Frequent interruption of chest compressions results in no circulatory support during more than half of resuscitation efforts. Such interruptions could be a major contributing factor to the continued poor outcome seen with OOH cardiac arrest. (***Circulation.*** **2005;112:1259-1265.)**

Key Words: cardiopulmonary resuscitation ■ circulation ■ resuscitation ■ heart arrest

Hundreds of thousands of cardiac arrest victims continue to die each year despite our best efforts.[1] Resuscitation with neurologically normal long-term survival remains an elusive goal, even though updated cardiopulmonary resuscitation (CPR) guidelines are published nearly every 6 years.[2–6] Advances in resuscitation, such as use of automated external defibrillators (AEDs), can improve survival in specific circumstances[7–9] but have failed to improve overall survival rates in some communities.[10]

Recent studies have established that many professional providers struggle to accomplish the resuscitation tasks outlined in the guidelines.[11,12] For example, Wik et al[11] found that out-of-hospital (OOH) cardiac arrest victims treated by paramedics or nurse anesthetists received chest compressions only 52% of the time. In addition, 62% of the chest compressions given were less than the recommended depth (<38 mm).[11] Abella et al[12] found that in-hospital cardiac arrest response teams, comprising an ample number of highly trained medical personnel, had very similar difficulties in providing CPR according to the guideline's recommendations. In their prospective observational series of 67 patients with in-hospital cardiac arrest, these authors found that chest compressions were not being provided during 24% of the resuscitation time and that 37% of all chest compressions according to the guidelines were too shallow (<38 mm). Such experiences suggest that the actual performance of CPR, even by professional rescuers, may vary greatly from the intended ideal.

In our community, OOH cardiac arrest survival rates are tracked by the Tucson Fire Department (TFD). Despite continued efforts at quality improvement and incorporation of all revised resuscitation guidelines into the emergency medical systems (EMS) response protocols during the last 10 years, there has been no improvement in survival (Table 1).

This lack of improvement in OOH cardiac arrest survival motivated us to more carefully examine what actually occurs

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TABLE 1. Annual OOH Cardiac Arrest Survival Rates in Tucson, Arizona, 1992–2001

	Survival to Hospital Discharge Rate, %	
Year	All Initial Rhythms	VF Initial Rhythm
1992	7	14
1993	9	13
1994	4	7
1995	4	9
1996	4	8
1997	5	8
1998	7	9
1999	8	10
2000	5	8
2001	5	10

Overall survival to hospital discharge rate for the decade 1992–2001 was 6±2%. The survival to discharge rate of those with VF as the initial rhythm for the same period was 10±2%. Table includes all presenting rhythms of cardiac arrest. All EMS vehicles were equipped with AEDs by December 1997. Trauma arrests were not included.

during our guidelines-based TFD EMS resuscitations. Of note, all TFD personnel involved in EMS activities receive extensive retraining and skill refreshment on a regular basis (monthly). Quality improvement is performed through regular review of all resuscitation field records. We hypothesized that interruptions of chest compressions occur commonly and for substantial periods during treatment of OOH cardiac arrest. We therefore conducted a retrospective review of the TFD cardiac arrest resuscitation efforts during the 12-month period between November 2001 and November 2002 to determine the proportion of time spent doing chest compressions during each resuscitation attempt.

Methods

The TFD provides a 2-tiered, single EMS system for the City of Tucson (population 487 000; area 505 km^2). All TFD EMS first responders use a bag-mask device and work in at least pairs and sometimes a foursome, hence providing multirescuer CPR.

The database is part of a TFD quality improvement program for its treatment of OOH cardiac arrest. The TFD has statutory authority to collect and analyze cardiac arrest data as part of its public health quality assurance responsibilities. The local institutional review board has determined that consent to compile such data is unnecessary. If information is needed from the patient's hospital medical record, consent is obtained.

Case and Survival Definitions

All included subjects were at least 16 years old and had suffered a nontraumatic cardiac arrest. Whether or not a case was "witnessed" was determined by review of the dispatch and paramedic records. Performance of "bystander CPR" was visually determined by the EMS provider on arrival. Time from "collapse to 9-1-1 call" was not reliably available for all patients and therefore, was not reported. The "9-1-1 call to arrival at the patient's side" interval included the time needed to find the patient and begin assessment. "Arrival-to-diagnosis" interval included the time at the patient's side needed to make a rhythm diagnosis, and the "diagnosis-to-treatment" time interval encompassed the time from rhythm diagnosis to either defibrillation or chest compressions. "Total time on the scene" interval was from arrival at the patient until decision to transport the patient and did not include the time of transport to the hospital. "Survival to hospital admission" was defined as spontaneous circulation allowing admission to the intensive care unit. "Survival to hospital discharge" included discharge to home or another care facility.

Study Data

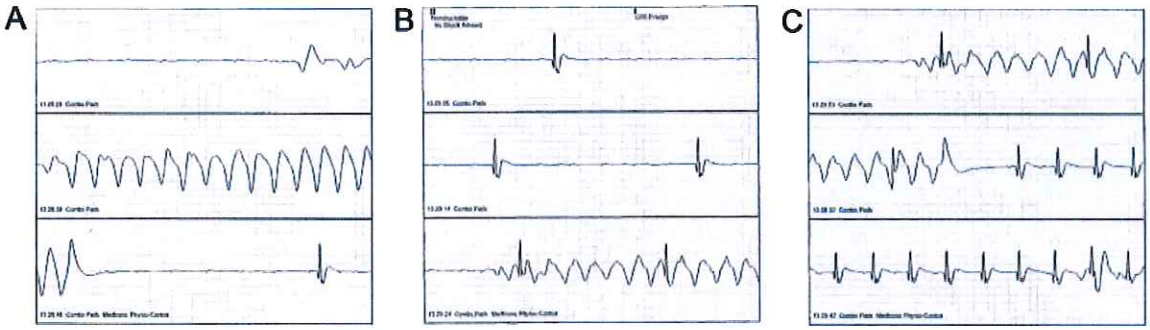
Cardiac arrest incidence and survival rates in Tucson, Arizona, were obtained from the TFD cardiac arrest database for a 10-year period (1992 to 2001) for historical comparison. The data reported in this study are from the 12-month period of November 2001 through November 2002. During this period, the TFD was using the 2000 guidelines algorithms for cardiac arrest resuscitation efforts. An ongoing, expanded Utstein-style[13] survey of prehospital cardiac arrest undertaken jointly by the TFD and the University of Arizona College of Medicine identified 61 cases of OOH cardiac arrest treated by TFD EMS first responders equipped with voice-recording AEDs during the designated 12-month study period. A total of 413 cardiac arrests occurred during this period, but most were not included in this analysis because the full AED data set (both voice and ECG) were unavailable. Most of these nonincluded cases were treated by paramedic first responders using either a manual defibrillator or a non–voice-recording AED. Resuscitation was not attempted in patients found with rigor mortis or other obvious evidence of irreversible death. Cases of cardiac arrest resulting from trauma, drowning, electrocution, known terminal illness, or sudden infant death syndrome were excluded. Details on the collection of data within the TFD cardiac arrest database have been previously reported.[14,15]

Quality Assurance

The TFD provides regular training about the EMS aspects of their professional responsibilities. Required, quarterly, all-day educational training sessions occur, during which resuscitation education and skill refreshment are included. A mandatory skills laboratory is required every 6 months as well. Quality assurance is performed through careful review of each and every resuscitation call and attempt. Indeed, the mandated purpose for the TFD resuscitation database was for quality improvement.

Data Collection and Call-to-Event Time Intervals

Collapse-to-event intervals were calculated through the use of monitor-defibrillator units (Lifepak 500 AED and Lifepak 12, Medtronic Emergency Response Systems) equipped with event documentation capacity. These units record the cardiac rhythm during each arrest. Within 24 hours of a cardiac arrest event, TFD personnel transmit by telephone line the recorded continuous waveform to 1 of 3 dedicated computers. The continuous ECG waveform begins when the device is powered on and ends when the device is powered off. The computer automatically synchronizes the time in the device and on the waveform with the atomic clock. Each event is reviewed in its entirety, and the waveform is examined with the Code Stat Suite Reviewer (Code Stat Suite version 4.1.1, Medtronic Emergency Response Systems). The Figure illustrates such AED ECG recordings. The cursor is placed at the beginning point of the first compression, and the time is documented in hours, minutes, and seconds. The cursor is then placed at the end point of the last compression before a delay for any reason, and the time is documented. This process continues throughout the resuscitation effort until transport begins, the prospectively identified termination point of the study, because previous experience with this system has shown that motion artifact markedly increases during transport and limits reliability. No assumptions or estimates are made in analyzing the recordings. The Lifepak 500 AEDs are also equipped with voice recording, which allows annotation of other interventions at the appropriate times (ie, intubation, etc). All annotations and time documentation become part of the event log. The event log was then reviewed by 2 of the authors, and the study time intervals were calculated.



An AED ECG record from a representative patient. A, The ECG record from the AED after a shock for prolonged VF resulting in asystole. Chest compressions were begun (15 delivered) followed by a pause of 2 ventilations. The ventilations are not well seen, but an isolated intrinsic QRS complex is noted. B, The slow intrinsic QRS complexes without assistance from chest compressions, followed by the resumption of chest compressions. C, The continued intrinsic QRS complexes during chest compressions, followed by a sustainable intrinsic and faster QRS rhythm. Abbreviations are as defined in text.

Statistical Methods

Descriptive statistics, such as proportions and percentiles, were used to highlight when chest compressions were and were not performed. Such data are reported as mean±SD. χ^2 or Fisher's exact test was used to compare such proportions with earlier reports from this database. The time interval data are reported as the median, with 25% to 75% interquartile range (IQR) because of the nonnormal distribution of these data. Other nonparametric testing was performed with a Mann-Whitney *U* test, and an unpaired, 2-tailed Student *t* test was performed on parametric data. A value of $P \leq 0.05$ was considered significant. All analyses were performed with either StatView 5.0 (SAS Institute) or InStat for Macintosh, version 3 (Graphpad Software) software.

Post Hoc Validation Study

A post hoc validation study was done in swine to confirm the accuracy of our methodology for determining the performance of chest compressions using the LifePak 12 AED continuous ECG record. All animal experiments were conducted with the approval of the University of Arizona Institutional Animal Care and Use Committee.

Four healthy, domestic swine (25±1 kg) were studied. Each was anesthetized and instrumented as previously reported from our laboratory.[16] The animal was shaved over the entire thorax, and an AED (Lifepak 12) was placed with the pads over the right anterior chest and the left lateral chest.

Experimental Measurements

Hemodynamics, including aortic systolic and diastolic pressures, right atrial systolic and diastolic pressures, and calculated coronary perfusion pressure (aortic diastolic pressure−simultaneous right atrial diastolic pressure), were measured throughout the CPR period. ECG monitoring was done both by standard limb leads and separately by the AED.

Experimental Protocol

After 7 minutes of untreated ventricular fibrillation (VF), each animal underwent attempted defibrillation, and then CPR (chest compressions and ventilations) was performed. According to the 2000 guidelines, chest compressions were periodically interrupted to reassess the animal and attempt further defibrillation, if indicated (eg, presence of VF). The time period during which chest compressions were performed was determined by 2 different techniques. The hemodynamic record was played back at real-time speed and reviewed by one investigator (R.W.H.). The cumulative time period during which chest compressions were actually performed was recorded with a stopwatch. A second investigator (L.L.C.) calculated the time during which chest compressions were performed using the AED continuous ECG waveform, as was done in the clinical portion of this study. The total time during which chest compressions were performed was calculated for each animal by the 2 different techniques. The total chest compression time was then compared between the 2 techniques with a simple regression analysis (Statview 5.0 statistical software, SAS Institute).

Results

The methodology of using the AED continuous-waveform data to determine when chest compressions were and were not performed was validated with the post hoc animal study. No difference in the proportion of time with and without chest compressions was found, whether such were calculated from the actual hemodynamic record during CPR or the AED ECG waveform data obtained during CPR. Assessing for chest compressions from the intra-aortic pressure waveform showed that the percentage of resuscitation effort with chest compressions for the 4 animals averaged 34.9±15.9%, whereas the AED ECG record revealed that chest compressions were performed 35.3±16.7% of the time. A comparison of the 2 techniques produced a correlation coefficient (r^2) of 0.997 ($P=0.0014$).

The demographics of the study population are shown in Table 2. No data are presented on time of collapse to 9-1-1 call. Such data are difficult to accurately collect and more so to verify.[17] The median time interval from 9-1-1 call to arrival at the patient's side was 6 minutes, 27 seconds (25% to 75% IQR, 5 minutes, 24 seconds, to 7 minutes, 34 seconds). Another 30 seconds (IQR, 13 to 57 seconds) was needed from arrival at the patient's side until a rhythm diagnosis was made. The time interval from making a diagnosis until rhythm-specific therapy was begun, ie, defibrillation for VF or chest compressions for non-VF, was 20 seconds (IQR, 12 to 25 seconds). The total time interval from 9-1-1 call to institution of definitive treatment (defibrillation or chest compressions) was 7 minutes, 33 seconds (IQR, 6 minutes, 28 seconds, to 8 minutes, 45 seconds).

The time interval from arrival at the patient in VF to delivering the first shock was 54 seconds (IQR, 38 to 74 seconds). The interval between the first and second shocks was 27 seconds (IQR, 25 to 63 seconds), with an additional 30 seconds (IQR, 22 to 70 seconds) between the second and third shocks. Overall, the time interval to deliver the 3 recommended shocks for refractory VF was 1 minute, 44

TABLE 2. Study Population Demographics

No.	61
Age, y (mean±SD)	63±18
Gender, n (%)	
Male	36 (59)
Female	25 (41)
Witnessed, n (%)	31 (51)
Not witnessed, n (%)	30 (49)
Bystander CPR,* n (%)	32 (52)
No bystander CPR, n (%)	29 (48)
Witnessed and bystander CPR, n/N (%)	18/31 (58)
Witnessed but no bystander CPR, n/N (%)	13/31 (42)
Initially detected rhythm, n (%)	
VF	20 (33)
Non-VF	41 (67)
Survival to hospital admission, n (%)	10 (16)
Survival to hospital discharge, n (%)	4 (7)

*Bystander CPR includes all who received CPR before arrival of EMS. Nineteen of these 32 (59%) had bystander CPR by medical personnel with a duty to respond (nursing home staff, registered nurses at dialysis units, physician at office, etc). Only 15 of the total 61 cases (25%) had bystander CPR by nonprofessionals without a "duty" to respond.

seconds (IQR, 1 minute, 34 seconds, to 1 minute, 54 seconds). Interestingly, it was uncommon that 3 shocks were needed to terminate VF (only 5 times in 21 cases of VF). The total time from 9-1-1 call to transport was 22 minutes, 43 seconds (IQR, 15 minutes, 50 seconds, to 27 minutes, 41 seconds).

Most notably, chest compressions were performed only 43±18% of the time during the resuscitation effort. Hence, no chest compressions were performed during the majority of the active resuscitation effort. Chest compressions were often not begun when EMS providers initially arrived at the patient in cardiac arrest and, once begun, were frequently interrupted for other resuscitation tasks. The time interval from arrival at the patient's side until the first chest compression recorded by the AED was a median of 78 seconds (IQR, 56 to 129 seconds). The longest continuous period of chest compressions was 122 seconds (IQR, 68 to 206 seconds), whereas the shortest continuous period was 11 seconds (IQR, 7 to 20 seconds). Similarly, the median time for the longest period without chest compressions was 172 seconds (IQR, 109 to 246 seconds). The shortest period of no chest compressions was 11 seconds (IQR, 8 to 18 seconds). The median time with continuous chest compressions was 55 seconds (IQR, 43 to 74 seconds), whereas the median time period when no compressions were performed was 57 seconds (IQR, 40 to 78 seconds).

The first 5 minutes of resuscitation effort for OOH cardiac arrest are crucial, because many of these individuals will have already been in cardiac arrest for 6 to 12 minutes before the arrival of professional EMS personnel. In reviewing our database specifically for what is actually done in the first 5 minutes on arrival at the patient's side, we found that chest compressions were being performed only 40±21% of the time during this crucial period. When we compared the first 5 minutes and the entire data set, no significant differences in the proportion of time with and without chest compressions, or in the average period of time when chest compressions were and were not performed, were found (Table 3).

Twenty-one patients (34%) had VF during the resuscitation requiring defibrillation. After the first shock, 17 of 21 were successfully defibrillated, but all converted to asystole (12/17) or pulseless electrical activity (5/17). Four patients remained in VF after the initial shock. Of note, no initial defibrillation shock resulted in a perfusing rhythm.

In 10 of the 61 patients, spontaneous circulation was restored and they were admitted alive. Eight of these 10 had an initial rhythm of VF. Nine of the 10 had a witnessed cardiac arrest, 8 received bystander CPR, and 8 were both witnessed and received bystander CPR. Those successfully resuscitated had significantly greater rates of each of these parameters compared with those who could not be resuscitated (Table 4). Four of 61 (7%) patients survived to hospital discharge.

Discussion

Weisfeldt and Becker[17] described 3 phases of VF cardiac arrest. In the first few minutes, the electrical phase, immediate defibrillation is crucial for optimal survival. After the first few minutes, the circulatory phase begins, wherein providing some circulation before defibrillation improves outcome.[18] This study shows that experienced, professional EMS responders perform chest compressions <50% of the time in their resuscitation efforts for OOH cardiac arrests. This is especially distressing, because almost all of these patients are in the circulatory phase of cardiac arrest on arrival of EMS providers. The current 2000 guidelines for CPR and emergency cardiovascular care emphasize the importance of rapid

TABLE 3. Comparison of First 5 Minutes vs the Entire Resuscitation Effort

	First 5 Minutes	Entire Effort	*P*
Time with CCs, %	40±21	43±18	NS
Time without CCs, %	60±21	57±18	NS
Longest period with CCs, seconds	65 (46, 84)	122 (68, 206)	0.0001
Average period with CCs, seconds	46 (30, 67)	55 (43, 74)	NS
Longest period without CCs, seconds	95 (70, 147)	172 (109, 246)	0.0001
Average period without CCs, seconds	56 (41, 87)	57 (40, 78)	NS

CC indicates chest compression. Time interval data are reported as median and (25%, 75% interquartile range).

TABLE 4. Outcome Data for OOH Cardiac Arrest

	Successfully Resuscitated	Not Resuscitated	*P*
n	10	51	
Age, y	66±19	62±18	0.51
Gender, %			
Male	30	65	0.08
Female	70	35	
Initial rhythm, %			
VF	80	33	0.02
Non-VF	20	67	
Witnessed, %	90	41	0.002
Bystander CPR, %	90	47	0.02
Witnessed and bystander CPR, %	80	24	0.002
9-1-1 call to arrival, seconds	333	391	0.11
Arrival to CCs, seconds	99	70	0.21
Total time at scene, seconds	549	1040	0.005
Time with CCs, %	34	49	0.09

CC indicates chest compression.

defibrillation because most survivors of OOH cardiac arrest are those with VF. The importance of rapid defibrillation for those with VF cannot be denied. However, statements such as "Give shocks as soon as a defibrillator is available"[19] have led to the relegation of all other efforts in favor of making a rhythm diagnosis (to detect VF), with immediate shock of all cases of VF, regardless of duration. In the current era of AED-equipped EMSs, this approach may result in significant periods during the initial resuscitation effort when no chest compressions are performed.[20,21] AEDs currently in use in many communities require substantial time to analyze, charge, shock, and then reanalyze, during which time the AED continually warns "Do not touch the patient." Newer versions of AEDs require considerably less time to perform these functions, during which chest compressions must be halted.

Other resuscitation tasks can also interrupt the performance of chest compressions. Reassessing the patient for pulses or rhythm changes, placement of intravenous lines, and intubation of the trachea can all interrupt chest compressions. Without careful attention, a substantial percentage of the resuscitation time can elapse without chest compressions (ie, without perfusion).

Recent data from Wik et al[18] show that with prolonged OOH cardiac arrest due to VF ("prolonged" defined as EMS arrival >5 minutes from emergency call), long-term survival rates were greater when chest compressions were provided before defibrillation. Such data highlight the importance of chest compressions for OOH VF cardiac arrest, unless defibrillation is available within 4 or 5 minutes of onset. The TFD data show that in a medium-size urban environment, it is uncommon for EMS personnel to reach OOH victims of cardiac arrest within this time period. Our average time interval from 9-1-1 call to arrival at the patient was >6½ minutes, and another 1 to 2 minutes were required from arrival at the patient's side to delivery of specific therapy. Even before including the interval from collapse to 9-1-1 call, the average duration of VF before EMS arrival is clearly within the time frame of the circulatory phase of VF cardiac arrest, when chest compressions and a period of hemodynamic support provided by professional EMS providers appear beneficial before attempts at defibrillation.[10,18]

Our initial defibrillation results illustrate what happens when prolonged VF is shocked before CPR is provided. None of the 21 initial shocks for VF resulted in a perfusing rhythm, similar to a recent report of the treatment of OOH cardiac arrest from the Netherlands, wherein only 4% (5/120) of initial shocks resulted in a return of spontaneous circulation without additional advanced cardiac life support therapy.[22] The majority of our Tucson OOH VF episodes were terminated with the initial shock (17/21), but always to a nonperfusing rhythm. Schneider et al[23] demonstrated similar results in the ORCA study, wherein they found that the first shock successfully terminated VF 77% (88/115) of the time. However, after prolonged VF, nearly all patients convert to a pulseless rhythm and fail to return to spontaneous circulation unless chest compressions are provided both before and after defibrillation.

The first few minutes of EMS therapy are probably the most important for successful resuscitation. Because almost all EMS resuscitation therapy will begin in the circulatory phase, simply because of the elapsed time from notification to arrival and treatment, providing circulation must be deemed the crucial early step. In the OOH scenario, chest compressions should occupy the majority of the first few minutes of EMS therapy. Unfortunately, comparing the first 5 minutes of treatment with the entire period of EMS-provided resuscitation effort revealed no differences in the percentage of time that chest compressions were performed (Table 3). In this crucial first 5 minutes of EMS resuscitation, chest compression–generated circulation was provided only 40% of the time! Animal studies have established that such interruptions of chest compressions are lethal in models of prolonged VF[24–26]; likewise, interruptions in either breathing or compressions can be harmful in asphyxial arrest.[27,28] It seems unreasonable to expect good outcomes after cardiac arrest when circulatory support is nonexistent for more than half of the resuscitation effort.

Wik et al[11] recently published similar data showing significant periods of no chest compressions during professional first-responder treatment of OOH cardiac arrest. These authors found that no chest compressions were performed during 48% of the time when the patient was without spontaneous circulation. We found a similar percentage (57%). Likewise, during the first 5 minutes of professional resuscitation, chest compressions were performed only 51% of the time in their series (vs 40% in ours). These results are strikingly similar and verify that in OOH resuscitation efforts by professional first responders, a significant amount of time elapses with no hemodynamic support in the absence of spontaneous circulation. Wik et al note that if their study is applicable to how CPR is delivered in other communities, then there is a great opportunity to improve current outcomes. Our study shows that similar challenges with interrupting

chest compressions during the performance of CPR exist among professional rescuers in the United States.

Stiell et al[29] recently reemphasized the importance of bystander CPR in improving resuscitation outcomes for OOH cardiac arrest. Our data also suggest that many patients who were successfully resuscitated in Tucson were those whose cardiac arrest was witnessed and who receive bystander CPR (Table 4). Bystander CPR did not result in a successful outcome in unwitnessed cardiac arrest (1/14 resuscitated, 0/14 survived). Unfortunately, more than one third of witnessed cardiac arrest victims in our study did not receive bystander CPR (11/31, 35%). We hypothesize that if bystander CPR were simpler and thereby easier to remember and perform, then more of these witnessed cardiac arrest victims would receive this important early step in the chain of survival.

A trend toward more time with chest compressions during the resuscitation effort in nonsurvivors is also noted in Table 4. This apparent contradiction can be explained by the observation that those resuscitated typically responded quickly (to early defibrillation in a bystander-witnessed arrest), whereas those still requiring resuscitation efforts after 10 minutes generally were in non-VF rhythms, and by that time, there was very little else to do but compress the chest; hence, minimal interruption of chest compressions occurred until transport or declaration of death.

On the basis of these data, we are now embarking on a joint project with the TFD, the City of Tucson, and the Sarver Heart Center at the University of Arizona to limit EMS chest compression interruptions and to increase the rate of bystander CPR in witnessed, adult cardiac arrest.

Limitations

This study is a selective, subgroup, retrospective analysis of the TFD quality assurance cardiac arrest database. The potential pitfalls of such analyses are well documented and acknowledged. The methodology of determining when chest compressions were and were not performed from the AED continuous waveform was validated in a post hoc animal experiment. Excellent correlation between the hemodynamic record and the AED record of chest compressions was found. Using our described methodology allowed such data to be collected without any additional equipment, as required in the 2 previous reports of Wik et al[11] and Abella et al.[12] Alternative approaches, such as direct observation of EMS-provided resuscitation care, introduces the potential for observed performance bias. Although EMS providers know that the AED records their resuscitation efforts, such devices have become so commonplace that the chance of enhanced performance while under observation is greatly decreased.

An alternative explanation for the flat survival rate during the last 10 years is that although AEDs and early defibrillation have improved outcome in sudden, witnessed VF arrest, the decreased incidence of initial VF in OOH cardiac arrest has made the impact of this improvement less noticeable. A number of studies have documented this decrease in VF as the initial rhythm detected in OOH cardiac arrest.[11,29–31] In the rising number of non-VF cardiac arrest cases, for whom the most effective treatment is perfusion of the myocardium and central nervous system, avoiding interruptions of chest compressions may be even more important.

Conclusion

Professional EMS providers give chest compressions less than half of the time during their resuscitation efforts. There are many causes for such interruptions, but certainly the lack of hemodynamic support during the majority of the resuscitation effort could be contributing to the poor long-term outcomes. More attention should be paid to eliminating such chest compression interruptions during treatment of cardiac arrest victims by EMS personnel. Prospective studies are needed to determine the impact on outcome of decreasing such interruptions.

Acknowledgments

We are grateful to the men and women of the TFD, without whom our community emergency response system would not and could not function.

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Quality of Cardiopulmonary Resuscitation During Out-of-Hospital Cardiac Arrest

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Context Cardiopulmonary resuscitation (CPR) guidelines recommend target values for compressions, ventilations, and CPR-free intervals allowed for rhythm analysis and defibrillation. There is little information on adherence to these guidelines during advanced cardiac life support in the field.

Objective To measure the quality of out-of-hospital CPR performed by ambulance personnel, as measured by adherence to CPR guidelines.

Design and Setting Case series of 176 adult patients with out-of-hospital cardiac arrest treated by paramedics and nurse anesthetists in Stockholm, Sweden, London, England, and Akershus, Norway, between March 2002 and October 2003. The defibrillators recorded chest compressions via a sternal pad fitted with an accelerometer and ventilations by changes in thoracic impedance between the defibrillator pads, in addition to standard event and electrocardiographic recordings.

Main Outcome Measure Adherence to international guidelines for CPR.

Results Chest compressions were not given 48% (95% CI, 45%-51%) of the time without spontaneous circulation; this percentage was 38% (95% CI, 36%-41%) when subtracting the time necessary for electrocardiographic analysis and defibrillation. Combining these data with a mean compression rate of 121/min (95% CI, 118-124/min) when compressions were given resulted in a mean compression rate of 64/min (95% CI, 61-67/min). Mean compression depth was 34 mm (95% CI, 33-35 mm), 28% (95% CI, 24%-32%) of the compressions had a depth of 38 mm to 51 mm (guidelines recommendation), and the compression part of the duty cycle was 42% (95% CI, 41%-42%). A mean of 11 (95% CI, 11-12) ventilations were given per minute. Sixty-one patients (35%) had return of spontaneous circulation, and 5 of 6 patients discharged alive from the hospital had normal neurological outcomes.

Conclusions In this study of CPR during out-of-hospital cardiac arrest, chest compressions were not delivered half of the time, and most compressions were too shallow. Electrocardiographic analysis and defibrillation accounted for only small parts of intervals without chest compressions.

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SINCE THE FIRST STANDARDS AND guidelines for cardiopulmonary resuscitation (CPR) were published 30 years ago[1] (with the latest update in 2000[2,3]) health care professionals in and out of the hospital have been trained accordingly around the world. The importance of CPR, defined as chest compressions and ventilation, for survival of cardiac arrest patients has been demonstrated,[4] and there are indications that the quality of CPR performance influences the outcome.[5-7]

When tested on mannequins, CPR quality performed by lay rescuers and health care professionals tends to deteriorate significantly within a few months after training,[8-10] but little is known about the quality of clinical performance on patients. Aufderheide et al[11] recently observed short periods with inappropriately high ventilation rates during advanced cardiac life support (ACLS), and van Alem et al[12] found long pauses in CPR when first responders used automated external defibrillators.

We therefore studied the performance of paramedics and nurse anesthetists during out-of-hospital ACLS by continuously monitoring all chest compressions and ventilations during resuscitation episodes using online defibrillators modified to collect such data.

See also pp 305 and 363, and Patient Page.

METHODS

Patient Inclusion and Recruitment

The study was approved by the regional ethics committees for Akershus, Norway, Stockholm, Sweden, and London, England. Informed consent for inclusion in the study was waived as decided by these committees in accordance with paragraph 26 in the Declaration of Helsinki.[13] The study was a case series involving patients older than

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18 years with out-of-hospital cardiac arrest of all rhythms. Noncardiac causes of cardiac arrest were included. Patients with cardiac arrest occurring between March 2002 and October 2003 were included in the study.

Equipment

Prototype defibrillators based on Heartstart 4000 (Philips Medical Systems, Andover, Mass) were deployed in 6 ambulances in each of the 3 regions. These ambulances were chosen based on historically high rates of cardiac arrest at their sites. The defibrillators were fitted with an extra chest pad to be mounted on the lower part of the sternum with double adhesive tape. This chest pad was fitted with an accelerometer (ADXL202e, Analog Devices, Norwood, Mass) and a pressure sensor (22PCCFBG6, Honeywell International Inc, Morristown, NJ). The heel of the rescuer's hand was placed on top of the chest pad and movement of the chest pad was considered equal to that of sternal movement during chest compressions. To avoid registering movements of the entire patient as chest compressions, only movements of the sternal chest pad with a parallel compression force greater than 2 kg were used in the automated analysis. A second accelerometer of the same kind was fitted within the defibrillator. Signals from this accelerometer were subtracted from signals from the chest pad accelerometer prior to depth calculation to compensate for possible vertical motion of the entire supporting surface. This technology has previously been reported to measure chest compression depth with an accuracy of ± 1.6 mm.[14]

Treatment Protocol

All ambulances were staffed by paramedics; in Stockholm, the second rescue vehicle at the scene also included a nurse anesthetist. Immediately prior to the study period, all involved personnel underwent a refresher course in ACLS according to international CPR guidelines[2,3] and in use of the modified defibrillator. In Akershus, a modification required that patients with ventricular fibrillation or pulseless ventricular tachycardia received 3 minutes of CPR before the first direct current shock and between unsuccessful series of 3 direct current shocks.[15] Resuscitation was otherwise attempted in accordance with the guidelines.[2,3] The defibrillators were used in manual mode in Akershus and in semiautomatic mode in the 2 other regions. The personnel were aware that we intended to study CPR performance and that the sternal pad recorded chest compressions. They were not informed that a primary focus was duration of time CPR was performed.

Data Collection and Processing

Data from each resuscitation episode were collected in 2 data cards; 1 standard card collected electrocardiographic signals, time, and events, and a second card fitted specially for this study recorded signals from the extra chest pad and thoracic impedance between the defibrillator pads as measured by applying a nearly constant sinusoidal current. After each CPR episode, all data were extracted and collected and the memory of the cards was cleared. One person at each site was responsible for this.

The raw data consisted of timeline and events, electrocardiographic signals, thoracic impedance, and values from the extra chest pad, all sampled at 500 Hz. For each episode, a copy of the ambulance record and other written documentation, including the Utstein format for out-of-hospital cardiac arrest,[16] were collected. All data were collected on a designated server at the facilities of Laerdal Medical Corp, Stavanger, Norway, and Laerdal personnel preprocessed the data by filtering and down-sampling to 50 Hz to facilitate display of the data for annotation and review. A custom-made computer program designed for the study (Sister Studio, Laerdal Medical) was used to view and annotate each cardiac arrest case. A second standard computer program (CodeRunner Web Express, Philips Medical, Andover, Mass) was used in parallel to provide further details about electrocardiography. For each episode, the initial rhythm and each subsequent change in rhythm were annotated. Pulseless electrical activity was defined as QRS complexes without blood flow, indicated either by a clinically detected pulse or blood flow–induced changes in thoracic impedance. Impedance changes coincident with cardiac contractions and arterial pressure pulses have been validated with echocardiography and blood pressure measurements in pigs.[17] In a pilot study, we found these changes to be in the range of 87 to 477 mΩ in 21 healthy volunteers, and an impedance amplitude of greater than 50 mΩ was used to indicate blood flow in the present study.

Spontaneous circulation was defined as QRS complexes with blood flow as indicated by the same factors. Time markers were set at the start of the first chest compression, 5 minutes thereafter, and at the end of the resuscitation episode, defined as discontinued monitoring or the end of treatment as judged from recordings and written information. The term *time* is used for time intervals in this article and *time point* for a specific point in time. The annotations were made by an experienced anesthesiologist with training and clinical practice in ACLS together with a research engineer with working knowledge of the Sister Studio program and the measurement systems.

Compressions were calculated by integrating the difference between the 2 accelerometers over a time window defined by the 2-kg threshold from the force transducer. Compression depth was characterized as appropriate for 38 to 51 mm (1.5-2 in),[2,3] too deep, or too shallow. Incomplete compression release was annotated if the chest pad pressure did not fall below 4 kg at any time during the compression-decompression cycle. Duty cycle was defined as the percentage of time with downward movement of the chest pad divided by the total cycle time. For each time period, the actual number of compressions per minute as well as the rate during compression periods (defined as

a period with <1.5 seconds between 2 compressions) were determined. No-flow time (NFT) was defined as total time minus the time with chest compressions or spontaneous circulation ($NFT = time_{total} - time_{compressions} - time_{spontaneous\ circulation}$), and the ratio between NFT and the total time without spontaneous circulation was defined as the no-flow ratio (NFR) [$NFR = NFT/(time_{total} - time_{spontaneous\ circulation})$]. The NFT and NFR represent the total time during the resuscitation episode without cerebral and myocardial circulation.

According to the guidelines,[2,3] chest compressions should not be given during rhythm analysis, defibrillator charging, shock delivery, and pulse checks. Adjusting the NFT by subtracting the time required for these procedures ($NFT_{adj} = NFT - time_{defibrillator}$) thus indicates time without blood flow due to performance of the rescuer team without interfering with rhythm analysis, defibrillation attempts, or pulse checks. $Time_{defibrillator}$ was determined for each episode. With the defibrillator in semiautomatic mode, actual recorded times from the defibrillator for automatic analysis, charging, and shock delivery were used. In manual mode, a maximum of 5 seconds was allowed for rhythm analysis. If an organized rhythm was present, palpation of pulse was allowed for a maximum of 10 seconds and included in $time_{defibrillator}$ [$NFR_{adj} = NFT_{adj}/(time_{total} - time_{spontaneous\ circulation})$].

The NFT_{adj} and NFR_{adj} represent the potential for reducing time without circulation without interfering with guidelines recommendations[2,3] and are less than the unadjusted values, which include NFT, as recommended in the guidelines.

Ventilations were automatically detected by changes in thoracic impedance, filtered and corrected for compression and blood flow–related signals. Ventilation measurement by impedance has been reported in many studies since 1944[18] and was recently validated for the use of defibrillator electrodes during cardiac arrest in pigs.[17] A recent study using the present defibrillator setup in volunteers showed strong correlation between impedance and spirometer waveforms.[19]

Table 1. Demographic and Annual Resuscitation Data for the 3 EMS Systems Investigated

	Akershus	London	Stockholm	Total
Demographic data				
Resuscitation episodes, No.	66	54	56	176
Male, No. %	42 (65)	40 (76)	47 (84)	129 (74)
Age, mean (SD), y (4 cases missing data)	68 (14)	65 (17)	70 (13)	68 (15)
Witnessed arrest, No. (%) (3 cases missing data)	54 (82)	35 (66)	37 (69)	126 (73)
Bystander CPR, No. (%)*	30 (51)	13 (25)	18 (35)	61 (37)
Response time, mean (95% CI), min*	9 (7-10)	6 (5-6)†	8 (7-9)	7 (7-8)
No. of shocks, median (95% CI)	2 (1-5)	1 (0-2)	2 (0-2)	1.5 (1-2)
Episodes with ≥1 shock, No. (%)	43 (65)	28 (52)	33 (59)	104 (59)
No. of shocks in episodes with ≥1 shock, median (95% CI)	5 (3-7)	6 (2-10)	4 (2-8)	5 (3-7)
Annual data				
Land area, km²	4587	1605	3472	...
Population, No.	493 000	7 200 000	1 680 000	...
Men, %	48	48	49	...
Older than 65 y, %	13	12	16	...
CPR attempts per million/y	373	590	292	...
Discharged from hospital, %‡	12	5	6	...

Abbreviations: CI, confidence interval; CPR, cardiopulmonary resuscitation; EMS, emergency medical service. Ellipses indicate data not applicable.
*Twelve cases with ambulance-witnessed cardiac arrests were excluded.
†Response time was significantly shorter in London ($P<.05$ by 1-way analysis of variance with Bonferroni correction for multiple comparisons).
‡The denominator for hospital discharge data is the total number of cardiac arrests with presumed cardiac origin for patients older than 18 years.

Outcome Measure

The primary outcome measure was adherence to international guidelines for CPR. Target values for compression rate were 100/min to 120/min; for depth, 38 to 52 mm; and for ventilation rate, 2 ventilations for every 15 compressions before intubation and 10/min to 12/min after intubation.

Statistical Analysis

All data from each resuscitation episode were collected and described using a spreadsheet program (Excel 2002, Microsoft Corp, Redmond, Wash) and a statistical analysis program (SPSS 12.0.1, SPSS Inc, Chicago, Ill). All statistical analyses were performed by J.K.-J. at the University of Oslo, Oslo, Norway. All numbers are given as mean (standard deviation) for the first 5 minutes after the start of recorded CPR and for the entire resuscitation episode. When variables had very skewed distributions, medians were used as the mid-point estimate and interquartile ranges as the variability measure. The results for the first 5 minutes of the resuscitation episode were analyzed vs the rest of the episode by a paired 2-sided t test, and 95% confidence intervals (CIs) are presented for these variables.

RESULTS

The annual statistics and demographic data from the 3 emergency medical service systems are shown in TABLE 1. The outcomes according to initial rhythm for patients in this study are shown in TABLE 2.

Of the total 243 episodes correctly included, 67 were excluded because of incompleteness of data. The main reasons for exclusion were failure to apply the additional chest pad (35/67) and technical problems with the 2 data cards or the defibrillator pads (26/67). In 13 episodes, signal quality made ventilation count impossible; thus, ventilation data are reported for 163 episodes.

Compression data are summarized in TABLE 3. For the first 5 minutes and for the entire resuscitation episode, the

mean (SD) fractions of the time without CPR (NFR) were 49% (21%) and 48% (18%), respectively, and when subtracting the time necessary for analysis and defibrillation, the $NFRs_{adj}$ were 42% (19%) and 38% (17%), respectively. There was no difference in the mean NFR in the first 5 minutes vs during the rest of the episode (49%; 95% CI, 46%-52% vs 50%; 95% CI, 47%-54%; $P=.58$), but there was a significant difference in NFR_{adj} (42%; 95% CI, 39%-45% vs 38%; 95% CI, 35%-41%; $P=.004$).

For the first 5 minutes and for the entire resuscitation episode, mean (SD) compressions were 60/min (25/min) and 64/min (23/min), respectively, significantly lower during the first 5 minutes than during the rest of the episode (60/min; 95% CI, 57-64/min vs 65/min; 95% CI, 61-69/min; $P=.02$). There were no significant differences with time for any other variables. For the first 5 minutes and for the entire resuscitation episode, mean (SD) chest compression rates were 120/min (20/min) and 121/min (18/min); mean (SD) compression depth was 35 mm (10 mm) and 34 mm (9 mm); the mean (SD) percentages of compressions with a depth between 38 and 51 mm were 27% (30%) and 28% (25%); and the mean (SD) percentages of inappropriately shallow compressions were 59% (37%) and 62% (33%). The compression parts of the duty cycle were 41% (5%) and 42% (4%). Incomplete release occurred after a median (interquartile range) of 0% (0%-1%) and 0% (0%-2%) of the compressions. During the first 5 minutes, there was no occurrence of incomplete release of compressions in 101 of 173 episodes (58%), and in only 16 episodes, more than 10% of the compressions had incomplete release. Mean (SD) ventilations were 8/min (4.6/min) and 11/min (4.7/min) for the first 5 minutes and for the entire episode, respectively (Table 3).

A total of 61 patients (35%) achieved return of spontaneous circulation, 34 (19%) were admitted to the hospital, and 6 (3%) were discharged from the hospital. Five of 6 patients who survived to hospital discharge had nearly normal neurological function (Table 2). Survival according to CPR quality indicators for patients with ventricular fibrillation as initial rhythm are presented in TABLE 4.

Table 2. Outcomes According to Initial Cardiac Rhythm for All Causes of Cardiac Arrest*

Initial Cardiac Rhythm	All (n = 243)	Usable (n = 176)	ROSC‡	Admitted Alive ‡	Discharged Alive (n = 176)†‡
VF	98 (40)	75 (43)	31 (41)	19 (25)	6 (8)
Asystole	91 (37)	64 (36)	15 (23)	8 (13)	0
PEA	54 (22)	37 (21)	15 (41)	7 (19)	0
Total	243 (100)	176 (100)	61 (35)	34 (19)	6 (3)

Abbreviations: PEA, pulseless electric activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.
*All data are expressed as No. (%).
†Five of 6 patients discharged alive had nearly normal neurological function (Cerebral Performance Category [CPC] 1: conscious, alert, normal cerebral function), and 1 was awake and oriented but reliant on others for activities of daily living (CPC 3: conscious, at least limited cognition, dependent on others for daily support).[16]
‡Denominators for percentages shown in these columns are the 75, 64, 37, and 176 patients with usable data for VF, asystole, PEA, and total, respectively.

Table 3. Performance of CPR During the First 5 Minutes and Entire Episode of CPR*

	First 5 Minutes of CPR	Entire Episode of CPR
No flow (n = 176)		
NFR, %	49 (21)	48 (18)
NFR_{adj}, %	42 (19)	38 (17)
Compression (n = 176)†		
Compressions/min	60 (25)	64 (23)
Compression rate, /min	120 (20)	121 (18)
Depth per episode, mm	35 (10)	34 (9)
38-51 mm with complete release	27 (30)	28 (25)
Too deep (>51 mm), median (IQR)	0 (0-3)	0 (0-5)
Too shallow (<38 mm)	59 (37)	62 (33)
Incomplete release, median (IQR), %	0 (0-1)	0 (0-2)
Duty cycle, %	41 (5)	42 (4)
Ventilation (n = 163)		
Ventilations/min	8 (4.6)	11 (4.7)

Abbreviations: CPR, cardiopulmonary resuscitation; IQR, interquartile range; NFR, no-flow ratio, the time without CPR as a percentage of the time without spontaneous circulation; NFR_{adj}, no-flow ratio, adjusted by subtracting time allowed for electrocardiographic analysis, possible defibrillation, and required pulse checks in the numerator.
*All data are expressed as mean (SD) unless otherwise noted.
†Compressions per minute refer to the actual number of compressions delivered per minute whereas compression rate refers to the mean rate of compressions, ie, the reciprocal of intervals between compressions in compression sequences.

Table 4. Quality of CPR Performance During the First 5 Minutes of CPR by Survival to Hospital Discharge for Patients With Ventricular Fibrillation as Initial Rhythm (n = 75)

	Discharged Alive, Mean (95% Confidence Interval)		
	No (n = 69)	Yes (n = 6)	*P* Value
NFR, %	49 (44-55)	40 (20-61)	.34
NFR_{adj}, %	40 (35-44)	32 (11-53)	.35
Depth of compressions, mm	38 (35-41)	38 (25-52)	.89
Ventilations/min	9 (7-10)	8 (5-12)	.94

Abbreviations: CPR, cardiopulmonary resuscitation; NFR, no-flow ratio, the time without CPR as a percentage of the time without spontaneous circulation; NFR_{adj}, no-flow ratio, adjusted by subtracting time allowed for electrocardiographic analysis, possible defibrillation, and required pulse checks in the numerator.

COMMENT

In this study of 176 adults with out-of-hospital cardiac arrest, chest compressions were given only half of the available time during these resuscitation events. Van Alem et al[12] reported that police and firefighters performed CPR a mean (SD) of only 45% (15%) of the duration during a median of 5 min-

utes of resuscitation before ambulance personnel took over. In that study, two thirds of the time without CPR could be explained by programmed interruptions from automated defibrillators. In our present study, CPR was performed by paramedics and nurse anesthetists, and only 15% to 20% of the time without CPR could be attributed to defibrillator use and required pulse checks. The periods without chest compressions and the relatively shallow compressions are not easily explained by focus on other tasks such as intubation or placement of an intravenous cannula. These interventions should occur during the initial minutes of ACLS, and there were only small differences in the results for the first 5 minutes and the rest of the episodes.

Only good-quality CPR improved the chance of survival in 3 studies of cardiac arrest patients.[5-7] Chest compressions appear to be the most important factor, both in human[6] and animal studies,[20,21] and even short 4- to 5-second interruptions in chest compressions decrease coronary perfusion pressure.[22] In addition to periods without chest compressions, more than half of chest compressions given in the present study were too shallow, indicating less-than-optimal circulatory effect of the CPR given. Arterial blood pressure increases with increasing compression force in humans,[23] and coronary blood flow increases with increasing compression depth from 38 mm to 64 mm in large pigs.[24] Most compressions in the present study were less than the recommended depth. This is in contrast with mannequin studies of professional rescuers, in which 30% to 50% of the compressions were too deep.[25,26]

In addition to compression depth, blood flow is dependent on compression rate, compression/decompression ratio, and low intrathoracic pressure in the decompression phase, avoiding "leaning" on the chest by the rescuer. In canine and swine models, highest blood flows are reported with chest compression rates of 90/min to 120/min,[27-29] leading to the guidelines recommendation of 100/min.[2,3] Mean compression rate tended to be too high in the present study, which might decrease cardiac output because of insufficient time for venous return to the heart during the decompression periods. "Leaning" on the chest wall during compressions was not a serious problem, although we cannot exclude that pressures lower than the 4 kg used to define leaning in the present study could have an unwanted effect. The compression/decompression ratio was satisfactory, with 41% to 42% compression time. The main problems were the long periods without any chest compressions and the shallow compression depth.

We did not find abnormally high ventilation rates, although we recorded the rate average over a minimum of 5 minutes. In contrast, Aufderheide et al[11] recently reported average ventilation rates of 30/min (3/min) with maximal rates during any 16-second period.[11] In animal models, ventilatory rates of 30/min vs 12/min decreased coronary perfusion pressure and also appears to decrease survival if sustained for 4 minutes.[11]

Training programs for CPR have been implemented worldwide during the last 4 decades following guidelines from the American Heart Association[2] and the European Resuscitation Council.[3] These programs specify criteria for correct performance of CPR, but neither the effects of such training programs on clinical CPR nor the effects of specific criteria or overall quality of ACLS on patient survival have been clinically documented. The present study was not powered to evaluate the effects of quality of CPR in a proper multivariate analysis with other factors known to influence survival, such as initial rhythm. A crude comparison between survivors and nonsurvivors with ventricular fibrillation as initial rhythm showed a tendency toward relatively less time without chest compressions among survivors, with no difference in compression depth or ventilation rate (Table 4).

All paramedics and nurse anesthetists in the present study had previous ACLS training with regular retraining, and all underwent a refresher course immediately prior to study initiation. Some of the deviations from the international 2000 guidelines[2,3] could be due to lack of knowledge retention, as most studies have reported deterioration in the performance of CPR within a few months after a course.[8,10,30] The failure to perform chest compressions half the available time has not been reported in such studies, but they are all in mannequins,[8,10,30] not in patients. It is possible that the highly complex physical and mental situation of treating a patient with cardiac arrest is too different from the training situation on mannequins, making the performance dramatically different and possibly less efficient. Based on this, the extrapolation from mannequin performance can be questioned, and as a recent international consensus document states, there is an urgent need to promote better CPR and improve the way CPR is taught.[31]

Whatever the reason, the resuscitation performance we measured was dramatically different from that recommended in the ACLS guidelines. It is tempting to question the focus on and the importance of details such as ventilation/compression ratios of 1:5 or 2:15 or biphasic vs monophasic defibrillators in our efforts to adjust evidence-based CPR guidelines, if the performance of vital skills is so far from the guidelines recommendations.

Whether some of these deficiencies can be improved by specific focus during training needs attention. Through better understanding of the mistakes made in a real-life cardiac arrest situation, training courses might be designed to focus on these aspects. Another approach would be to develop online tools that prompt the rescuer to improved performance. Audiotapes giving instructions on chest compression rate have been reported to improve the compression rate during cardiac arrest in patients.[16] In mannequin studies, audio feedback based on continuous online automated evaluation dramatically improved CPR performance within the first 3 minutes.[32,33] Ac-

cording to the international consensus, the ideal would be to have identically configured aids during both training and resuscitation attempts.[31]

If our study represents how CPR is delivered during resuscitation from out-of-hospital cardiac arrest in other communities, there is a great opportunity to improve CPR quality and, hopefully, patient survival by focusing on delivery of chest compressions of correct depth and rate, with minimal "hands-off" periods.

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Study concept and design: Wik, Kramer-Johansen, Myklebust, Steen.
Acquisition of data: Kramer-Johansen, Myklebust, Sørebø, Svensson, Fellows.
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Study supervision: Wik, Myklebust, Sørebø, Svensson, Fellows, Steen.
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Quality of Cardiopulmonary Resuscitation During In-Hospital Cardiac Arrest

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Context The survival benefit of well-performed cardiopulmonary resuscitation (CPR) is well-documented, but little objective data exist regarding actual CPR quality during cardiac arrest. Recent studies have challenged the notion that CPR is uniformly performed according to established international guidelines.

Objectives To measure multiple parameters of in-hospital CPR quality and to determine compliance with published American Heart Association and international guidelines.

Design and Setting A prospective observational study of 67 patients who experienced in-hospital cardiac arrest at the University of Chicago Hospitals, Chicago, Ill, between December 11, 2002, and April 5, 2004. Using a monitor/defibrillator with novel additional sensing capabilities, the parameters of CPR quality including chest compression rate, compression depth, ventilation rate, and the fraction of arrest time without chest compressions (no-flow fraction) were recorded.

Main Outcome Measure Adherence to American Heart Association and international CPR guidelines.

Results Analysis of the first 5 minutes of each resuscitation by 30-second segments revealed that chest compression rates were less than 90/min in 28.1% of segments. Compression depth was too shallow (defined as <38 mm) for 37.4% of compressions. Ventilation rates were high, with 60.9% of segments containing a rate of more than 20/min. Additionally, the mean (SD) no-flow fraction was 0.24 (0.18). A 10-second pause each minute of arrest would yield a no-flow fraction of 0.17. A total of 27 patients (40.3%) achieved return of spontaneous circulation and 7 (10.4%) were discharged from the hospital.

Conclusions In this study of in-hospital cardiac arrest, the quality of multiple parameters of CPR was inconsistent and often did not meet published guideline recommendations, even when performed by well-trained hospital staff. The importance of high-quality CPR suggests the need for rescuer feedback and monitoring of CPR quality during resuscitation efforts.

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SURVIVAL FROM CARDIAC ARREST remains low despite the introduction of cardiopulmonary resuscitation (CPR) more than 50 years ago.[1-3] The delivery of CPR, with correctly performed chest compressions and ventilations, exerts a significant survival benefit in both animal and human studies.[4-8] Conversely, interruptions in CPR or failure to provide compressions during cardiac arrest ("no-flow time") have been noted to have a negative impact on survival in animal studies.[7] Consensus guidelines clearly define how CPR is to be performed,[9] but the parameters of CPR in actual practice are not routinely measured, nor is the quality known.

There are multiple reasons for concern regarding the quality of CPR. Even though CPR training programs are ubiquitous, a number of studies demonstrate that these learned resuscitation skills deteriorate over time.[10,11] Furthermore, issues such as translation of skills from training environments to actual cardiac arrest settings, as well as rescuer fatigue during resuscitation,[12] may limit CPR quality. Recent investigations have revealed that patients may be hyperventilated during out-of-hospital arrest,[13] and that low chest compression rates are present during in-hospital arrest.[14,15]

Given the proven survival benefit of high-quality CPR and the lack of data on actual performance, we sought to determine whether well-trained hospital staff perform CPR compressions and ventilations according to guideline recommendations. The in-hospital environment was selected because it offers the added advantage of thorough pre-arrest documentation as well as resus-

See also pp 299 and 363 and Patient Page.

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Financial Disclosures: Mr Myklebust is an employee of Laerdal Medical Corporation, which developed the monitor/defibrillator. Dr Becker has received grant/research support from Philips Medical Systems, Laerdal Medical Corp, and Alsius Corp, and has served as a consultant for Abbott Laboratories and Philips Medical Systems.
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citation by ample numbers of highly trained personnel.

METHODS

Patient Enrollment

The study protocol and consent materials were approved by the institutional review board at the University of Chicago Hospitals, Chicago, Ill. Data collection was carefully structured to comply with all relevant Health Insurance Portability and Accountability Act of 1996 regulations. Consent was obtained from all members of the resuscitation teams via an oral consent process.

Resuscitation events were studied among inpatients at the University of Chicago Hospitals who experienced cardiac arrest, defined by the documented loss of a pulse and respirations as well as the delivery of chest compressions. Patients were excluded for analysis if they experienced arrest in the operating room or emergency department, were younger than 18 years, or if the CPR-sensing defibrillator was used without its chest compression–detecting mechanism.

Measuring Parameters of CPR Quality

During in-hospital cardiac arrests, an investigational monitor/defibrillator (IDE G020121) was used. This device is based on a commercially available monitor/defibrillator (Heartstart 4000SP, Laerdal Medical Corporation, Stavanger, Norway) with the additional investigational capabilities for capturing and recording rate and depth of chest compressions, rate and volume of ventilations, presence or absence of a pulse, as well as standard electrocardiogram and defibrillator shock event data. In addition, customized software for data analysis collected these parameters and calculated the no-flow time and no-flow fraction (NFF, fraction of cardiac arrest time without compressions being performed). These additional device features and analysis software were developed by engineers at Laerdal Medical Corporation.

Chest compression data were captured via a special chest compression pad outfitted with an accelerometer sensor (ADXL202e Analog Devices, Norwood, Mass) and a pressure sensor (22PCCFBG6, Honeywell, Morristown, NJ). The pad was placed on the mid-sternum of the patient under the hands of the rescuer performing compressions. This method has been previously validated in the laboratory setting, with compression depth data accurate to within 1.6 mm.[16,17] Components of the sensing and recording software have also been tested, validated, and published elsewhere.[18,19] Additional testing has demonstrated the use of impedance measurement for ventilation monitoring, in both swine[20] and healthy human volunteers (P. A. Steen, oral communication, 2003). This latter human study was performed as a validation pilot study to our current study and demonstrated a strong correlation between impedance and spirometry waveforms.

Ventilation and pulse data were obtained using impedance measurements captured from the defibrillation pads. All data collected by the device were stored on data cards for subsequent analysis using additional custom software that allowed for calculation of rates and other parameters. Per hospital regulation, all users of the device and CPR performers were originally certified in either basic life support (medical students and nurses), advanced cardiovascular life support (all physicians), or both. The study device was utilized by the hospital team that responds to all cardiac arrests. The study design was purely observational with no alteration in therapy or suggested change from standard resuscitation practice. Resuscitation teams were blinded to the results of defibrillator measurements during the arrest. The patients studied represented a convenience sample of all cardiac arrests during the study period, in that during some other cardiac arrests another defibrillator was used instead of the study device.

Data Analysis

To determine CPR parameters, chest compression rate, depth, ventilation rate, no-flow time, and NFF were calculated by Sister Studio software (Laerdal Medical Corporation). Correct chest compression depth was defined as between 38 and 51 mm (1.5-2.0 in). (Current CPR guidelines do not take adult patient characteristics into account in recommendations for CPR parameters; therefore, we did not perform adjustments for any of these variables.) Pauses in chest compressions of more than 1.5 seconds (for pulse checks and intubation) were excluded from rate calculations so as to not artifactually lower chest compression rate. Mean (SD) values were calculated for CPR parameters. No-flow time (time periods of cardiac arrest without compressions being performed) was mathematically defined as total time minus the time with chest compressions or spontaneous circulation, and NFF was defined as the no-flow time divided by cardiac arrest time (ie, total time minus time periods with spontaneous circulation). This measure of NFF represents the fraction of time during the resuscitation episode without cerebral or myocardial circulation.

All data were sent to the study investigator (H.M.) at Laerdal Medical Corporation, where data were processed by filtering and down sampling to 50 Hz to prepare files for annotation and review. Proprietary software designed for the study (Sister Studio) was used for processing each cardiac arrest file. Raw data from each patient were collected as 2 separate data files. One file contained impedance and chest compression data, while the second file contained elements collected by the recording defibrillator (electrocardiogram and shock times). These 2 data files were then conditioned, filtered, and merged into a single data set for each patient by the study sponsor. At this time the study sponsor did not analyze the data or perform interpretation of waveforms. The merged conditioned files were then sent back to the study site, where all data annotation,

analysis, and interpretation were conducted. This analysis involved a full annotation of the file to determine when a pulse was present vs when cardiac arrest was present; the software would then read compressions and ventilations, which were confirmed by a study investigator, before a final data file was prepared that contained the parameters of interest (compression rate, compression depth, ventilation rate, no-flow time). The study sponsor did not perform interpretation or access the data during this analysis phase. Secondary data analysis was performed using a spreadsheet application (Excel, Microsoft Corp, Redmond, Wash).

For our outcome measures of CPR quality, we analyzed the first 5 minutes of CPR, which was presumed to be both the best rescuer effort based on study of rescuer fatigue[12] and the most clinically important. Each 5-minute resuscitation episode was divided into 30-second segments, and both compression and ventilation rates were calculated. Segments in which either chest compression or ventilation signals were obscured by signal noise were excluded from analysis. Segments without compressions or ventilations were excluded from calculations of mean compression or ventilation rates, respectively. All files were manually evaluated by a physician investigator to ensure appropriate software marking of events such as compressions, ventilations, and rhythms. Similar analysis was also performed for entire cardiac arrest episodes to provide comparison with the initial 5-minute data. No-flow fraction was only calculated for the first 5-minute period.

Evaluation of Clinical Outcomes

Our study was not designed or powered to find CPR quality differences between survivors and nonsurvivors; however, we undertook this evaluation as a secondary analysis. Of the 67 arrest episodes, 60 had complete data sets for comparison of all parameters. Cardiopulmonary resuscitation parameters were compared between the cohort of patients that achieved return of spontaneous circulation (ROSC) vs those who died during resuscitation. This analysis was only conducted on data from the first 5 minutes of resuscitation efforts.

Statistical Analysis

All means (SDs) were calculated using a spreadsheet application (Excel). Differences in CPR parameters for outcome evaluation were assessed using a 2-tailed t test. Statistical evaluation of data was performed independent of the study sponsor in consultation with a biostatistician at our institution. $P<.05$ was considered statistically significant.

RESULTS

A total of 67 patients with cardiac arrest were treated using the study defibrillator with data collection from December 11, 2002, to April 5, 2004. Data analyzed from this cohort included 1073 segments (536.5 minutes) with chest compression and ventilation data. Patient demographic and cardiac arrest data are shown in TABLE 1. Mean (SD) patient age was 62.2 (17.4) years, and 34.3% of patients were women. Patient race included black (65.7%), white (23.9%), and other/unknown (10.5%) individuals. Cardiac arrest events took place in intensive care settings (52.2%), general wards (44.8%), or other locations (3.0%, radiology [n=1] and cardiac catheterization laboratory [n=1]). Frequencies of the presenting rhythm were 14.9% ventricular fibrillation/ventricular tachycardia, 59.7% pulseless electrical activity, 10.4% asystole, and 14.9% other (indeterminate). Return of spontaneous circulation was achieved in 40.3% of patients. Baseline characteristics and rate of ROSC are similar to data reported in other studies of in-hospital cardiac arrest.[21]

Cardiopulmonary resuscitation characteristics for the entire patient cohort are shown in TABLE 2. During the first 5 minutes of resuscitation, mean chest compression rate was less than 90/min 28.1% of the time and less than 80/min 12.8% of the time. Chest compression depth data revealed that chest compressions were too shallow (<38 mm depth) 37.4% of the time. Ventilation rates were calculated in a similar fashion to chest compression rates. In contrast with compressions, ventilation rates tended to be high; during 60.9% of segments, ventilations were performed at a rate of more than 20/min. Ventilation volumes did not appear to deviate greatly from physiological ranges and are not reported herein. Analysis of the time with cardiac arrest but without compressions (NFF) yielded a mean (SD) of 0.24 (0.18) with 40.3% of the segments having an NFF of more than 0.20.

Table 1. Demographic and Descriptive Clinical Data of Cardiac Arrest Cohort (N = 67)*

	Total Patient Cohort, No. (%)
Demographics	
Age, mean (SD) [range], y	62.2 (17.4) [21-94]
Race†	
Black	44 (65.7)
White	16 (23.9)
Other/unknown	7 (10.5)
Sex	
Men	44 (65.7)
Women	23 (34.3)
Descriptive clinical data	
Cardiac arrest location	
Intensive care setting	35 (52.2)
Hospital general ward setting	30 (44.8)
Other‡	2 (3.0)
Time of cardiac arrest	
Morning (6:00 AM-12:00 PM)	17 (25.4)
Afternoon (12:00 PM-6:00 PM)	14 (20.9)
Evening (6:00 PM-12:00 AM)	19 (28.4)
Night (12:00 AM-6:00 AM)	17 (25.4)
Initial rhythm	
Ventricular fibrillation/ventricular tachycardia	10 (14.9)
Pulseless electrical activity	40 (59.7)
Asystole	7 (10.4)
Perfusing rhythm	0
Other§	10 (14.9)
Return of spontaneous circulation	
Yes	27 (40.3)
No	40 (59.7)
Survival to hospital discharge	
Yes	7 (10.4)
No	60 (89.6)

*Percentages may not all total 100 due to rounding.
†Race was extracted from chart demographic data.
‡Includes radiology (n = 1) and cardiac catheterization laboratory (n = 1).
§Patients presenting with an indeterminate rhythm.

Although the intent of this investigation was only to objectively describe multiple parameters of CPR during cardiac arrest, we considered whether ROSC was associated with better CPR quality. We did not find any statistically significant differences in chest compression rate, depth, ventilation rate, or NFF between patients who achieved ROSC vs those who did not (TABLE 3). A trend toward lower NFF was observed for patients with ROSC compared with nonsurvivors. We did not expect to find clinical outcome differences given our small patient cohort and the nonrandomized nature of the study; therefore, we cannot draw any conclusions regarding the direct clinical impact of the quality of CPR on survival.

COMMENT

Our study represents, to our knowledge, the first multiparameter, quantitative recordings of actual CPR during in-hospital cardiac arrest. Using impedance measurement techniques, we found that quality of CPR was often deficient from guideline recommendations[9] in several specific parameters, including chest compression rate, compression depth, ventilation rate, and NFF. Specifically, chest compression rates were often less than the recommended 100/min, compression depth was often more shallow than the minimum 38 mm, ventilation rate was higher than the recommended 12 to 16/min, and NFF was longer than adherence to recommendations might allow (although not clearly specified in the guidelines, a 10-second pulse check every minute of CPR would yield an NFF of 0.17).

These data confirm other recent investigations[13-15] suggesting that CPR quality may be highly variable in actual practice. Just as we observed frequent overventilation, Aufderheide et al[13] recently showed that paramedics hyperventilate patients during out-of-hospital cardiac arrest, and parallel animal experiments confirmed that this degree of hyperventilation led to decreased survival. We recently documented low chest compression rates during in-hospital cardiac arrest in a multicenter study when recorded by observers equipped with a handheld device to record compression rate.[15] A smaller observer-based study found low chest compression rates during in-hospital arrest.[14]

Cardiopulmonary resuscitation performance in our study may have been affected by the knowledge that rescuers were being studied. This "Hawthorne effect"[22] would likely have led to improved CPR quality and would minimize our findings of significant deviations from recommended practice. In addition, due to institutional review board requirements, we did not link individuals performing CPR with CPR-quality data. However, resuscitation teams change each month (with resident rotations), with completely new rescuers. Therefore, it is unlikely that an individual rescuer performed CPR in more than approximately 4 to 5 cardiac arrests.

The paramount importance of CPR has been confirmed in both animal and human studies. In 2 clinical studies, survival from ventricular fibrillation arrest was improved if CPR was performed before defibrillation attempts.[23,24] In animal studies, coronary perfusion pressure, hemodynamic function, and survival were adversely affected by even short pauses

Table 2. CPR Parameters During Cardiac Arrest Episodes*

	First 5 Minutes of Cardiac Arrest Episode (N = 67)	Complete Cardiac Arrest Episode (N = 67)
Chest compression data		
Compression rate, /min		
Mean (SD)	102 (19)	105 (21)
<80	12.8	10.8
<90	28.1	23.7
>110	36.5	38.7
Compression depth, mm		
Mean (SD)	42 (13)	43 (14)
<38	37.4	36.3
Ventilation data		
Ventilation rate, /min		
Mean (SD)	21 (12)	20 (13)
<10	7.3	7.5
>20	60.9	58.9
Chest compression interruption		
NFF, mean (SD)	0.24 (0.18)	
30-s segments with NFF >0.20	40.3	

Abbreviations: CPR, cardiopulmonary resuscitation; NFF, no-flow fraction.
*Data are presented as percentages unless otherwise specified. Percentages refer to portion of time from respective episode (either 5 minutes or whole episode) that include the criteria as described. NFF is defined as the cumulative no-flow time for a given cardiac arrest divided by the total time without a pulse during that same episode.

Table 3. CPR Parameters and Resuscitation Outcomes*

	Return of Spontaneous Circulation, Mean (SD)		
	Yes (n = 27)	No (n = 33)	*P* Value
Compression rate, /min	98 (18)	107 (18)	.07
Compression depth, mm	42 (13)	41 (12)	.82
Ventilation rate, /min	20 (7)	22 (9)	.17
NFF, first 5 min	0.20 (0.14)	0.27 (0.21)	.16

Abbreviations: CPR, cardiopulmonary resuscitation; NFF, no-flow fraction.
*Data for the first 5 minutes are shown for the 60 patients with complete data in all parameters. None of the differences between patients who achieved return of spontaneous circulation (ROSC) and those who did not were statistically significant, although patients with ROSC had a trend toward fewer interruptions in chest compression as observed by the NFF.

in chest compressions.[25,26] Moreover, pauses in chest compression just before defibrillation worsened outcomes in a swine model.[27] Additionally, laboratory study has shown that physiological and survival outcomes are sensitive to CPR quality.[28,29] Mechanical devices that provide chest compressions at consistent rate and depth have shown promise toward improving survival.[30]

There are several limitations to our study. A primary limitation is that the precise contribution to survival of the specific parameters that were measured is unknown. Although an isolated compression rate of less than 100/min can be considered a failure to adhere to a published recommendation of the American Heart Association, we cannot determine whether this "deficiency" is directly linked to worsened survival. Support for objective CPR quality monitoring lies in the fact that this technology will allow future studies to carefully examine the effects of CPR parameters on survival.

Additional limitations are that filtered electrocardiogram and ventilation signals were occasionally overcome by artifact, which caused us to exclude some segments. Chest compression depth as studied was calibrated for presence of a backboard and therefore depth may be overestimated if a backboard was not used during the resuscitation. For this reason, we describe in our analysis only compressions that are too shallow. Although our study is limited by use of a single site for data collection, we believe these results are likely generalizable to other hospitals, just as our prior results demonstrated chest compression rate deficiencies when studied at 3 hospitals.[15] Performance difficulties during stressful and disorganized cardiac arrest settings, the lack of reliable internal timing to pace chest compressions, rescuer fatigue,[12] and infrequent recertification in CPR[31] may all contribute to the observed deficiencies. It is therefore likely that our findings are representative of a more general dilemma in resuscitation. Human factors in CPR performance are important and at this point underinvestigated areas of research.[32]

Our study has implications for the conduct and design of future clinical CPR studies. Cardiopulmonary resuscitation quality is currently an unmeasured but potentially important confounder in most published clinical studies involving cardiac arrest outcomes. The importance of this variable given the current ability to measure these parameters should be considered by researchers attempting to study methods for improving survival from cardiac arrest.

There are several potential practical solutions for helping to improve poor CPR quality. The first involves mechanical devices that can provide chest compressions reliably at a set rate and depth.[33] These devices may generate better hemodynamic characteristics than manual chest compressions.[34,35] Another solution is to improve monitoring and feedback to reduce human error during manual CPR, by using devices such as end-tidal CO_2 monitors[36] and "smart defibrillators," which can measure CPR characteristics and provide audio feedback to alert the rescuers to errors such as incorrect chest compression or ventilation rate.[18,19]

Author Contributions: Dr Becker had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Abella, Myklebust, Vanden Hoek, Becker.
Acquisition of data: Abella, Alvarado, Myklebust, Barry, O'Hearn, Becker.
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Do not let yourselves be discouraged or embittered by the smallness of the success you are likely to achieve in trying to make life better. You certainly would not be able, in a single generation, to create an earthly paradise. Who could expect that? But, if you make life ever so little better, you will have done splendidly, and your lives will have been worthwhile.
—Arnold Toynbee (1889-1975)

Dispatcher-assisted hands-only CPR

ORIGINAL ARTICLE

CPR with Chest Compression Alone or with Rescue Breathing

Thomas D. Rea, M.D., Carol Fahrenbruch, M.S.P.H., Linda Culley, B.A., Rachael T. Donohoe, Ph.D., Cindy Hambly, E.M.T., Jennifer Innes, B.A., Megan Bloomingdale, E.M.T., Cleo Subido, Steven Romines, M.S.P.H., and Mickey S. Eisenberg, M.D., Ph.D.

2010

Bystander contacted 9-1-1

standard CPR (n=960)	chest compression alone (n=981)
11.5%	14.4% (OR 2.9)

Survival to DC

ORIGINAL ARTICLE

CPR with Chest Compression Alone or with Rescue Breathing

Thomas D. Rea, M.D., Carol Fahrenbruch, M.S.P.H., Linda Culley, B.A., Rachael T. Donohoe, Ph.D., Cindy Hambly, E.M.T., Jennifer Innes, B.A., Megan Bloomingdale, E.M.T., Cleo Subido, Steven Romines, M.S.P.H., and Mickey S. Eisenberg, M.D., Ph.D.

ABSTRACT

BACKGROUND

The role of rescue breathing in cardiopulmonary resuscitation (CPR) performed by a layperson is uncertain. We hypothesized that the dispatcher instructions to bystanders to provide chest compression alone would result in improved survival as compared with instructions to provide chest compression plus rescue breathing.

METHODS

We conducted a multicenter, randomized trial of dispatcher instructions to bystanders for performing CPR. The patients were persons 18 years of age or older with out-of-hospital cardiac arrest for whom dispatchers initiated CPR instruction to bystanders. Patients were randomly assigned to receive chest compression alone or chest compression plus rescue breathing. The primary outcome was survival to hospital discharge. Secondary outcomes included a favorable neurologic outcome at discharge.

RESULTS

Of the 1941 patients who met the inclusion criteria, 981 were randomly assigned to receive chest compression alone and 960 to receive chest compression plus rescue breathing. We observed no significant difference between the two groups in the proportion of patients who survived to hospital discharge (12.5% with chest compression alone and 11.0% with chest compression plus rescue breathing, P=0.31) or in the proportion who survived with a favorable neurologic outcome in the two sites that assessed this secondary outcome (14.4% and 11.5%, respectively; P=0.13). Prespecified subgroup analyses showed a trend toward a higher proportion of patients surviving to hospital discharge with chest compression alone as compared with chest compression plus rescue breathing for patients with a cardiac cause of arrest (15.5% vs. 12.3%, P=0.09) and for those with shockable rhythms (31.9% vs. 25.7%, P=0.09).

CONCLUSIONS

Dispatcher instruction consisting of chest compression alone did not increase the survival rate overall, although there was a trend toward better outcomes in key clinical subgroups. The results support a strategy for CPR performed by laypersons that emphasizes chest compression and minimizes the role of rescue breathing. (Funded in part by the Laerdal Foundation for Acute Medicine and the Medic One Foundation; ClinicalTrials.gov number, NCT00219687.)

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Out-of-hospital cardiac arrest claims hundreds of thousands of lives each year worldwide.[1,2] Successful resuscitation is challenging but achievable, requiring an interdependent set of actions that consist of early arrest recognition, early cardiopulmonary resuscitation (CPR), early defibrillation, expert advanced life support, and timely postresuscitation care.[3]

Early initiation of CPR by a layperson can increase the patient's chances of surviving and having a favorable long-term neurologic recovery.[4,5] CPR performed by a layperson has traditionally consisted of chest compressions interspersed with rescue breathing, which allows some measure of both circulation and oxygenation.[6] Interest in CPR that focuses on chest compressions and minimizes or eliminates rescue breathing is increasing.[7] Chest compression alone may be more acceptable to some laypersons and has the potential physiological advantage of fewer compression interruptions, so that circulation is increased, as compared with traditional CPR, although at a possible cost to oxygenation.[8,9]

Studies in animal models that involve a primary cardiac cause of arrest and simulate challenges to laypersons performing CPR have shown increased circulation and improved survival with chest compression alone.[10,11] In contrast, results in animal models of arrest due to respiratory causes suggest that chest compression plus rescue breathing may be more beneficial.[12]

Cardiac arrest in humans is a heterogeneous condition. Although a primary cardiac cause is the most common mechanism of arrest, respiratory and mixed mechanisms are important contributing factors.[13-15] The pathophysiology of each arrest is dynamic, and the relative importance of oxygenation may depend on the time-dependent phase of the arrest.[16] In observational studies of bystander-initiated CPR, the two CPR approaches led to similar survival rates, although interpretation of these findings is limited by potential confounding.[14,15,17] In the only randomized trial comparing these two types of bystander CPR, there was no significant difference in survival between the two groups, although the observed survival difference between patients randomly assigned to chest compression alone and those randomly assigned to compression plus rescue breathing (14.6% vs. 10.4%) is clinically relevant.[18] This trial was conducted in a community with a very quick response by emergency medical services (EMS), and the study's main analysis was restricted to patients with a primary cardiac cause of arrest — characteristics that potentially favor the physiological effects of chest compression alone.

Figure 1 (facing page). Enrollment, CPR Status, and Eligibility.

ALS denotes advanced life support, CPR cardiopulmonary resuscitation, DNR do not resuscitate, and EMS emergency medical services.

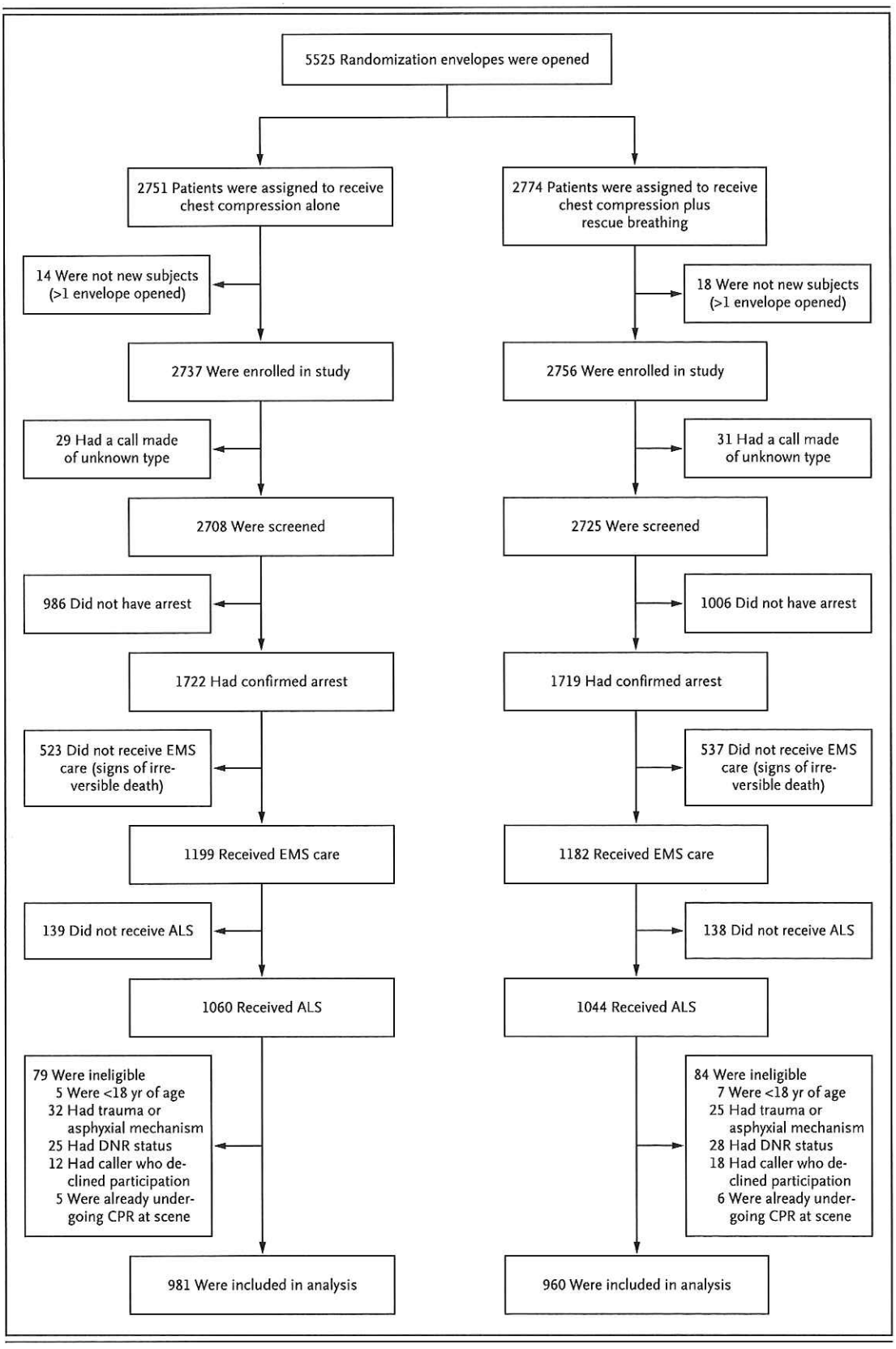
To help determine the best approach to bystander CPR, we undertook a randomized trial of dispatcher-assisted CPR to compare outcomes when instructions consisted of chest compression alone with outcomes when instructions consisted of chest compression plus rescue breathing. We hypothesized that instruction consisting of chest compression alone would result in higher survival rates than instruction consisting of chest compression plus rescue breathing.

METHODS

STUDY DESIGN, POPULATION, AND SETTING

The Dispatcher-Assisted Resuscitation Trial (DART) was a randomized trial of dispatcher-assisted CPR instruction. The study was approved by the appropriate review boards, and patients were enrolled without consent being obtained, although survivors were later informed that they had been enrolled in a clinical investigation of CPR.

The study considered consecutive calls by bystanders to the 911 system for patients in cardiac arrest. Patients were initially eligible if the dispatcher determined that they were unconscious and not breathing normally and that bystander CPR was not under way. If the caller was willing to undertake CPR with the dispatcher's assistance, a randomization envelope containing CPR instructions was opened. Dispatchers attempted to exclude patients with arrest due to trauma, drowning, or asphyxiation (from choking, strangulation, or suffocation), as well as patients who were under 18 years of age; and those who had do-not-resuscitate status or were already receiving CPR. Final eligibility required postrandomization exclusion and was restricted to patients who received basic and advanced arrest care from EMS


5525 Randomization envelopes were opened
2751 Patients were assigned to receive chest compression alone
2774 Patients were assigned to receive chest compression plus rescue breathing
14 Were not new subjects (>1 envelope opened)
18 Were not new subjects (>1 envelope opened)
2737 Were enrolled in study
2756 Were enrolled in study
29 Had a call made of unknown type
31 Had a call made of unknown type
2708 Were screened
2725 Were screened
986 Did not have arrest
1006 Did not have arrest
1722 Had confirmed arrest
1719 Had confirmed arrest
523 Did not receive EMS care (signs of irreversible death)
537 Did not receive EMS care (signs of irreversible death)
1199 Received EMS care
1182 Received EMS care
139 Did not receive ALS
138 Did not receive ALS
1060 Received ALS
1044 Received ALS
79 Were ineligible
5 Were <18 yr of age
32 Had trauma or asphyxial mechanism
25 Had DNR status
12 Had caller who declined participation
5 Were already undergoing CPR at scene
84 Were ineligible
7 Were <18 yr of age
25 Had trauma or asphyxial mechanism
28 Had DNR status
18 Had caller who declined participation
6 Were already undergoing CPR at scene
981 Were included in analysis
960 Were included in analysis

personnel. Thus, we excluded persons who were unconscious and not breathing normally but who were deemed not to be in arrest and persons who had had a confirmed arrest but were found to have signs of irreversible death, in which case EMS personnel did not attempt resuscitation.[19]

King County EMS (in Washington State), Thurston County EMS (in Washington State), and London Ambulance Service (in England) participated in the trial. At all three sites, callers use a common emergency number to speak with civilian employee dispatchers. King and Thurston Counties are served by a two-tiered EMS system in which personnel follow the core resuscitation strategy detailed by the American Heart Association guidelines. London is served by a single-tier EMS system in which personnel follow the United Kingdom Resuscitation Council Guidelines. Because of differences in enrollment rates and time required for review processes, enrollment took place from June 1, 2004, through April 15, 2009, in King County; from June 1, 2005, through April 15, 2009, in Thurston County; and from January 1, 2005, through March 15, 2008, in London.

INTERVENTION

On determining patients' initial eligibility, dispatchers enrolled and randomly assigned each patient to one of the two CPR strategies by opening an opaque, sequentially numbered envelope to determine which instructions to give the bystander. Randomization was stratified by dispatch center and blocked in sets of 10. The bystander was then instructed to perform either chest compressions alone, providing 50 consecutive compressions (one cycle), or chest compressions plus rescue breathing, with 2 initial rescue breaths followed by 15 chest compressions and subsequent cycles continuing the pattern in a ratio of 2 to 15 (see Fig. 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). With the dispatcher still on the telephone, the bystander then performed one cycle of CPR during which the dispatcher asked the bystander to count the chest compressions out loud. After the first cycle, the dispatcher could inquire about signs of life and, if warranted, encourage the bystander to continue CPR.

OUTCOMES

The primary outcome was survival to hospital discharge. Secondary outcomes were a return of spontaneous circulation at the end of EMS care and a favorable neurologic status at the time of hospital discharge, defined as a Cerebral Performance Category (CPC) of 1 or 2. (There are five CPC categories; category 1 represents good cerebral performance, 2 moderate cerebral disability, 3 severe cerebral disability, 4 coma or vegetative state, and 5 death.[20,21])

DATA COLLECTION AND DEFINITIONS

Dispatch, EMS, and hospital information was reviewed with the use of a uniform data-abstraction form.[21] The review of EMS and hospital information was done without knowledge of patients' randomization status. Step-by-step progress in the provision of instructions and the initiation of chest compressions by the bystander was determined by a review of the dispatch audiotape.

STATISTICAL ANALYSIS

The trial was designed to detect an absolute difference of 3.5 percentage points in the survival rates between the two study groups, with the use of a two-sided alpha level of 0.05 and a power of 80%. To compare the distribution of characteristics and outcomes for the two types of CPR instruction, we used the chi-square statistic for categorical variables and the independent-samples t-test or the nonparametric Mann–Whitney U test for continuous variables. Primary comparisons were performed according to randomization status. We also performed an efficacy analysis restricted to cases in which bystander CPR progressed to chest compression as a consequence of dispatcher instructions. Because one site was unable to assess neurologic status at discharge, we present the overall results as well as results restricted to the two sites that were able to ascertain neurologic status.

We conducted four prespecified subgroup analyses designed to examine the physiological mechanisms of the intervention as well as to provide a context for interpreting the results in relation to other investigations. The subgroup analyses stratified outcomes according to the underlying cause of arrest, presenting arrest rhythm, witness status, and EMS response interval among witnessed arrests (≤6 minutes vs. >6 minutes). No other subgroup analyses were performed. We used the Breslow–Day test for homogeneity to determine whether the intervention differed according to subgroup status. Statistical analyses were completed with the use of SPSS software, version 18.0 (SPSS).

Table 1. Characteristics of the Patients According to Dispatcher's CPR Instructions.*

Characteristic	Chest Compression Alone (N=981)	Chest Compression plus Rescue Breathing (N=960)	P Value
Site — no. of patients (%)			0.26
King County	588 (59.9)	552 (57.5)	
London	328 (33.4)	327 (34.1)	
Thurston County	65 (6.6)	81 (8.4)	
Age — yr	63.4±16.5	63.9±16.3	0.46
Male sex — no. of patients (%)	659 (67.2)	613 (63.9)	0.12
Cause of arrest — no. of patients (%)			0.63
Cardiac	700 (71.4)	709 (73.9)	
Respiratory	75 (7.6)	59 (6.1)	
Overdose	74 (7.5)	59 (6.1)	
Neurologic	18 (1.8)	15 (1.6)	
Other	114 (11.6)	118 (12.3)	
Arrest witnessed — no. of patients (%)	418 (42.6)	437 (45.5)	0.23
Location — no. of patients (%)			0.34
Residential location	845 (86.1)	837 (87.2)	
Public location	94 (9.6)	86 (9.0)	
Nursing home	41 (4.2)	34 (3.5)	
Time to initial EMS response — min	6.5±2.8	6.7±3.1	0.18
Time to advanced support — min	9.8±6.0	10.0±6.2	0.46
Shockable rhythm — no. of patients (%)	319 (32.5)	304 (31.7)	0.69

* Plus–minus values are means ±SD. CPR denotes cardiopulmonary resuscitation, and EMS emergency medical services.

The study was conducted according to the protocol. The funding organizations did not have a role in the study design, conduct of the study, or interpretation of the results.

RESULTS

PATIENTS, ARRESTS, AND PROGRESSION OF CPR INSTRUCTIONS

During the course of the trial, 5525 randomization envelopes were opened for patients presumed to be in cardiac arrest. Of these patients, 1941 (35%) met the inclusion criteria (Fig. 1). The two most common reasons for exclusion were that EMS personnel found the patient to be alive without arrest or to have signs of irreversible death (in which case resuscitation by EMS was not attempted). The distribution of exclusions in the two groups was similar according to randomization status.

Among the 1941 eligible patients, approximately 70% had arrests with a cardiac cause, less than half the arrests were witnessed, and nearly a third had a shockable rhythm. The average EMS response time from dispatch to arrival at the scene was 6.5 minutes. Patients, circumstance, EMS response, and presenting rhythm characteristics were similar in the two groups (Table 1). Patients randomly assigned to instructions for the bystander to perform chest compression alone were more likely to undergo bystander-performed chest compression (80.5% vs. 72.7%, P<0.001) (Table 2).

SURVIVAL TO DISCHARGE

Survival to hospital discharge could not be ascertained for seven subjects (0.4%), three randomly assigned to chest compression alone and four to chest compression plus rescue breathing. We ob-

Table 2. Progression of Bystander-Initiated CPR According to Dispatcher's Instructions.*

Furthest Step Taken in DART Instruction Protocol†	Chest Compression Alone (N=981)	Chest Compression plus Rescue Breathing (N=960)	Total (N=1941)
		number of patients (percent)	
Envelope opened, only preinstructions provided	143 (14.6)	127 (13.2)	270 (13.9)
Rescue-breathing instruction provided, but no rescue breathing performed	1 (0.1)	46 (4.8)	47 (2.4)
Rescue-breathing instruction provided, only rescue breathing performed	0	49 (5.1)	49 (2.5)
Compression instruction provided, but no compressions performed	30 (3.1)	24 (2.5)	54 (2.8)
Compression instruction provided, compressions performed	790 (80.5)	698 (72.7)	1488 (76.7)
Missing data	17 (1.7)	16 (1.7)	33 (1.7)

* Overall crossover between the assigned instructions occurred in 42 of 1941 cases (2.2%). Crossover from chest compression plus rescue breathing to chest compression alone was more common than was crossover from chest compression alone to chest compression plus rescue breathing (3.5% [34 of 960] vs. 0.8% [8 of 981]). CPR denotes cardiopulmonary resuscitation, and DART Dispatcher-Assisted Resuscitation Trial.

† Each category is exclusive. Classification was determined by audio review of the emergency call. If instruction was given but the reviewer was unable to determine whether the maneuver was actually performed, the level of progression was classified as instruction given but maneuver not performed.

served no significant difference in the proportion of patients surviving to hospital discharge according to randomization status (12.5% for instructions to perform chest compression alone and 11.0% for instructions to perform chest compression plus rescue breathing, P=0.31) or the proportion surviving to discharge with a favorable neurologic status (14.4% for chest compression alone and 11.5% for chest compression plus rescue breathing, P=0.13) (Table 3).

SUBGROUP ANALYSES

The Breslow–Day test showed some evidence that the effect of the two sets of CPR instructions on outcomes differed according to the underlying cause of arrest (P=0.007 for return of pulse, P=0.10 for survival to discharge, and P=0.06 for survival with a favorable neurologic status) and presenting arrest rhythm (P=0.14, P=0.09, and P=0.20, respectively). (Tests for heterogeneity showed no evidence that the outcome differed according to whether the arrest was witnessed [P>0.20].) For example, among patients whose arrest had a cardiac cause, there was a trend toward an increased proportion of patients surviving to hospital discharge (15.5%, vs. 12.3% for patients with other causes of arrest; P=0.09) and an increased proportion surviving with a favorable neurologic status at discharge (18.9% vs. 13.5%, P=0.03) with chest compression alone (Table 4). The survival rate among patients with a noncardiac cause of arrest was 5.0% with instructions to perform chest compression alone, as compared with 7.2% with instructions to perform chest compression plus rescue breathing (P=0.29).

In efficacy analyses restricted to patients for whom the intervention progressed to chest compression, the magnitude of outcome differences potentially favoring chest compression alone was typically larger than that observed in the effectiveness analyses (Tables 1 and 2 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial, CPR instructions consisting of chest compression alone did not increase survival to hospital discharge overall, as compared with instructions consisting of chest compression plus rescue breathing. However, the results suggest that chest compression alone may increase survival among certain subgroups of patients — those with a cardiac cause of arrest and those with ventricular fibrillation.

The current trial was designed to acknowledge the heterogeneity of the arrest condition and the potential for disparate intervention effects across the arrest population, providing in turn the tru-

est translation of the intervention effects to community-based care.[22-24] We found no significant difference between the two types of CPR instruction with respect to the proportion of patients who survived to hospital discharge. We did, however, observe a consistent trend toward clinically meaningful survival differences in favor of chest compression alone over chest compression plus rescue breathing among patients whose arrest was due to a cardiac cause (15.5% vs. 12.3%) and among those with a shockable arrest rhythm (31.9% vs. 25.7%). These findings in specific clinical groups are consistent with the results of investigations that have focused on the same subgroups of patients or have used corresponding animal models.[10,11,18] One possible explanation is that the beneficial physiological effects of continuous chest compressions outweigh the beneficial physiological effects of chest compressions interspersed with rescue breathing.[25] Alternatively, rescue breathing attempted by bystanders may have no physiological effects, so the comparison is essentially between two strategies: continuous chest compressions and interrupted chest compressions.

We did not observe significant differences in outcome among the patients with noncardiac causes of arrest or nonshockable rhythms, although the proportion of patients who survived was greater in the group randomly assigned to chest compressions plus rescue breathing. Because these two (nonexclusive) subgroups accounted for 14.0% (32 of 227) and 21.1% (48 of 227) of survivors, respectively, they cannot be dismissed as clinically unimportant. One interpretation of these results is that the type of bystander CPR does not make a difference in these subgroups. Alternatively, one may speculate that the potential difference is consistent with the physiological understanding of rescue breathing and that the study was underpowered to rigorously evaluate the type of CPR in these subgroups.

Taken together, the potential differential effects of CPR with and without rescue breathing may support a more targeted application of type-specific CPR. On the basis of data from the current study, such a tailored approach, if correctly applied according to the cause of arrest, would theoretically result in 156 survivors with a favorable neurologic outcome per 1000 patients, as compared with 144 per 1000 if chest compression alone were used for all patients or 115 per

Table 3. Outcomes.*

Outcome	All Sites				Two Sites Assessing Neurologic Status			
	Chest Compression Alone (N=981)	Chest Compression plus Rescue Breathing (N=960)	Absolute Difference (95% CI)†	P Value	Chest Compression Alone (N=653)	Chest Compression plus Rescue Breathing (N=633)	Absolute Difference (95% CI)†	P Value
	no. of patients/total no. (%)		*percentage points*		*no. of patients/total no. (%)*		*percentage points*	
Pulse present at end of EMS care	335/962 (34.8)	296/942 (31.4)	3.4 (−0.8 to 7.6)	0.12	279/653 (42.7)	234/633 (37.0)	5.8 (0.4 to 11.1)	0.04
Survival to hospital discharge	122/978 (12.5)	105/956 (11.0)	1.5 (−1.4 to 4.4)	0.31	110/653 (16.8)	93/633 (14.7)	2.1 (−1.8 to 6.1)	0.29
CPC 1 or 2 at hospital discharge‡	—	—	—	—	94/653 (14.4)	73/633 (11.5)	2.9 (−0.8 to 6.5)	0.13

* CI denotes confidence interval, and EMS emergency medical services.
† The absolute difference in outcome between the two groups was derived by subtracting the value for the group assigned to chest compressions plus rescue breathing from the value for the group assigned to chest compressions alone.
‡ In the Cerebral Performance Category (CPC) classification, category 1 represents good cerebral performance, 2 moderate cerebral disability, 3 severe cerebral disability, 4 coma or vegetative state, and 5 death.

Table 4. Outcomes in Subgroups of Patients.*

Outcome	All Three Sites				Two Sites Assessing Neurologic Status			
	Chest Compression Alone (N=981)	Chest Compression plus Rescue Breathing (N=960)	Absolute Difference† (95% CI)	P Value	Chest Compression Alone (N=653)	Chest Compression plus Rescue Breathing (N=633)	Absolute Difference† (95% CI)	P Value
	no. of patients/total no. (%)		*percentage points*		*no. of patients/total no. (%)*		*percentage points*	
Cause of arrest								
Cardiac								
Pulse present at end of EMS care	263/684 (38.5)	217/693 (31.3)	7.2 (2.1 to 12.1)	0.005	216/449 (48.1)	167/445 (37.5)	10.6 (4.1 to 16.9)	0.001
Survival to hospital discharge	108/697(15.5)	87/705 (12.3)	3.2 (–0.5 to 6.8)	0.09	97/449 (21.6)	77/445 (17.3)	4.3 (–0.9 to 9.5)	0.10
CPC 1 or 2 at hospital discharge‡	—	—	—	—	85/449 (18.9)	60/445 (13.5)	5.4 (0.6 to 10.3)	0.03
Noncardiac								
Pulse present at end of EMS care	72/278 (25.9)	79/249 (31.7)	–5.8 (–13.5 to 1.9)	0.14	63/204 (30.9)	67/188 (35.6)	–4.7 (–14.0 to 4.5)	0.32
Survival to hospital discharge	14/281 (5.0)	18/251 (7.2)	–2.2 (–6.6 to 1.9)	0.29	13/204 (6.4)	16/188 (8.5)	–2.1 (–7.7 to 3.2)	0.42
CPC 1 or 2 at hospital discharge‡	—	—	—	—	9/204 (4.4)	13/188 (6.9)	–2.5 (–7.5 to 2.2)	0.28
Arrest rhythm								
Shockable								
Pulse present at end of EMS care	185/315 (58.7)	151/300 (50.3)	8.4 (0.5 to 16.1)	0.04	160/243 (65.8)	119/218 (54.6)	11.2 (2.3 to 20.0)	0.01
Survival to hospital discharge	101/317 (31.9)	78/304 (25.7)	6.2 (–0.09 to 13.2)	0.09	92/243 (37.9)	69/218 (31.7)	6.2 (–2.5 to 14.7)	0.16
CPC 1 or 2 at hospital discharge‡	—	—	—	—	80/243 (32.9)	56/218 (25.7)	7.2 (–1.1 to 15.4)	0.09
Nonshockable								
Pulse present at end of EMS care	150/647 (23.2)	145/642 (22.6)	0.6 (–4.0 to 5.2)	0.80	119/410 (29.0)	115/415 (27.7)	1.3 (–4.8 to 7.5)	0.68
Survival to hospital discharge	21/661 (3.2)	27/652 (4.1)	–0.9 (–3.1 to 1.1)	0.35	18/410 (4.4)	24/415 (5.8)	–1.4 (–4.5 to 1.7)	0.36
CPC 1 or 2 at hospital discharge‡	—	—	—	—	14/410 (3.4)	17/415 (4.1)	–0.7 (–3.4 to 2.0)	0.61
Witness status								
Arrest witnessed								
Pulse present at end of EMS care	195/411 (47.4)	178/429 (41.5)	5.9 (–0.8 to 12.6)	0.08	166/303 (54.8)	142/308 (46.1)	8.7 (0.8 to 16.5)	0.03
Survival to hospital discharge	88/416 (21.2)	78/437 (17.8)	3.4 (–2.0 to 8.6)	0.23	79/303 (26.1)	69/308 (22.4)	3.7 (–3.1 to 10.4)	0.29
CPC 1 or 2 at hospital discharge‡	—	—	—	—	70/303 (23.1)	54/308 (17.5)	5.6 (–0.8 to 11.9)	0.09
Arrest not witnessed								
Pulse present at end of EMS care	138/546 (25.3)	118/512 (23.0)	2.3 (–2.9 to 7.4)	0.40	111/345 (32.2)	92/324 (28.4)	3.8 (–3.2 to 10.7)	0.29
Survival to hospital discharge	33/556 (5.9)	27/517 (5.2)	0.7 (–2.1 to 3.5)	0.61	30/345 (8.7)	24/324 (7.4)	1.3 (–2.9 to 5.5)	0.54
CPC 1 or 2 at hospital discharge‡	—	—	—	—	23/345 (6.7)	19/324 (5.9)	0.8 (–3.0 to 4.6)	0.67

EMS response time among witnessed arrests								
≤6 Min								
Pulse present at end of EMS care	119/203 (58.6)	103/223 (46.2)	12.4 (2.9 to 21.6)	0.01	112/178 (62.9)	89/182 (48.9)	14.0 (3.8 to 23.9)	0.007
Survival to hospital discharge	59/203 (29.1)	48/225 (21.3)	7.8 (−0.5 to 15.9)	0.07	56/178 (31.5)	44/182 (24.2)	7.3 (−2.0 to 16.4)	0.12
CPC 1 or 2 at hospital discharge‡	—	—	—	—	49/178 (27.5)	37/182 (20.3)	7.2 (−1.6 to 15.9)	0.11
>6 Min								
Pulse present at end of EMS care	76/208 (36.5)	75/206 (36.4)	0.1 (−9.1 to 9.3)	0.98	54/125 (43.2)	53/126 (42.1)	1.1 (−11.0 to 13.2)	0.86
Survival to hospital discharge	29/213 (13.6)	30/212 (14.2)	−0.6 (−7.2 to 6.1)	0.87	23/125 (18.4)	25/126 (19.8)	−1.4 (−11.2 to 8.3)	0.77
CPC 1 or 2 at hospital discharge‡	—	—	—	—	21/125 (16.8)	17/126 (13.5)	3.3 (−5.7 to 12.3)	0.47

* CI denotes confidence interval, CPC Cerebral Performance Category, and EMS emergency medical services.
† The absolute difference in outcome between the two groups was derived by subtracting the value for the group assigned to chest compressions plus rescue breathing from the value for the group assigned to chest compressions alone.
‡ In the Cerebral Performance Category classification, category 1 represents good cerebral performance; 2, moderate cerebral disability; 3, severe cerebral disability; 4, coma or vegetative state; and 5, death.

1000 if chest compression plus rescue breathing were used for all patients. Future investigation may consider whether straightforward, operational etiologic surrogates can facilitate type-specific CPR aimed at the underlying cause of arrest.

We also did not observe outcome differences overall when we evaluated neurologic status at discharge. This finding provides assurance that improved resuscitation with chest compression alone is not achieved at the cost of neurologic impairment. Indeed, there was some suggestion that the brain may derive specific benefit, given the increase in the magnitude of both the relative and absolute differences favoring chest compression alone over chest compression plus rescue breathing, as evident from the two contrasting outcomes — survival (16.8% and 14.7%, respectively) and survival with favorable neurologic status (14.4% and 11.5%) (Table 3). Because CPR has a host of effects, a brain-specific advantage related to chest compression alone may be plausible.[26]

It is also useful to contrast the effectiveness and efficacy results in this study. The trial was an effectiveness study, since about one fourth of the patients did not progress to chest compressions. Conversely, three fourths did progress to chest compressions (the group constituting efficacy results) — a finding that underscores the important contribution a well-trained, assertive emergency dispatch program can make to increase bystander CPR. The magnitude of outcome differences potentially favoring chest compression alone was typically larger in the efficacy analysis as compared with the effectiveness analysis (Tables 1 and 2 in the Supplementary Appendix). One interpretation is that the efficacy associations better reflect the intervention's true physiological effects, suggesting that the potential benefit of chest compression alone is not due simply to a greater proportion of bystanders implementing chest compressions but may be due instead to the specific physiological effects of chest compression alone.

The current trial has limitations. The intervention randomized bystander CPR either to chest compressions alone or to chest compressions interspersed with rescue breathing in a ratio of 2 breaths to 15 compressions. This 2:15 ratio was the guideline specified during the first portion of the trial. One might expect that the results — and specifically the differences observed — would be attenuated if the ratio had been 2:30.

Such an inference is uncertain given the incomplete understanding of the mechanisms underlying the benefit of CPR and the fixed logistic considerations of incorporating rescue breathing.[27] We were able to assess progress through the study protocol, although we were not able to objectively and quantitatively measure the core components of the resuscitation maneuver (e.g., chest compression depth).

This investigation involved dispatcher-instructed CPR. The results do not apply to health professionals, who have a duty to respond and are more practiced and proficient in CPR, often engaging at a later stage of arrest physiology. Also, the results do not necessarily apply to bystanders who have been previously trained, are able to identify a cardiac arrest, and can provide CPR without dispatcher assistance. Nonetheless, CPR performed by lay responders trained in compression plus rescue breathing often falls short of the guideline standards during an actual cardiac arrest.[28]

The optimal outcome measure incorporates both heart and brain resuscitation. Our study determined the neurologic status of survivors at two of the three trial sites. We do not know whether the distribution of neurologic status differed at the third site, although those who survived from the third site represent only about 10% of all the survivors.

Although nearly 2000 eligible patients were enrolled, the study may still be criticized for having insufficient power to detect clinically important differences. For example, the study would need approximately 4200 subjects to have 80% power to demonstrate a significant difference in survival with a favorable neurologic outcome between the group treated with chest compression alone and the group treated with chest compression plus rescue breathing (14.4% and 11.5%, respectively).

We used a 95% confidence interval to designate statistical significance, although multiple comparisons were performed. Thus, caution should be exercised when interpreting the results, since one might expect about 5% of comparisons to be statistically significant simply by chance.[29] It is important to note that the subgroup analyses were all prespecified. Moreover, the pattern of results across subgroups is consistent with the scientific understanding of type-specific CPR mechanistic effects, so collectively these results may strengthen the interpretation.

The study's limitations should be balanced against its strengths. Cardiac arrest is a major public health challenge for which high-level evidence to guide care is lacking. Our trial was conducted in three different emergency medical systems, the intervention was randomized and was validated through audio review, the outcomes are clinically meaningful, and the design allowed for capture of a comprehensive study population so that translation of the results to the community can be reasonably gauged.

In conclusion, this randomized trial showed that dispatcher CPR instruction consisting of chest compression alone did not increase survival when compared with chest compression plus rescue breathing overall. However, there was a consistent trend toward meaningful outcome differences in favor of chest compression alone in key clinical subgroups (i.e., patients with a cardiac cause of arrest and patients with shockable rhythms). The results, viewed within the context of other investigations, strengthen a layperson CPR strategy that emphasizes chest compression and minimizes the role of rescue breathing.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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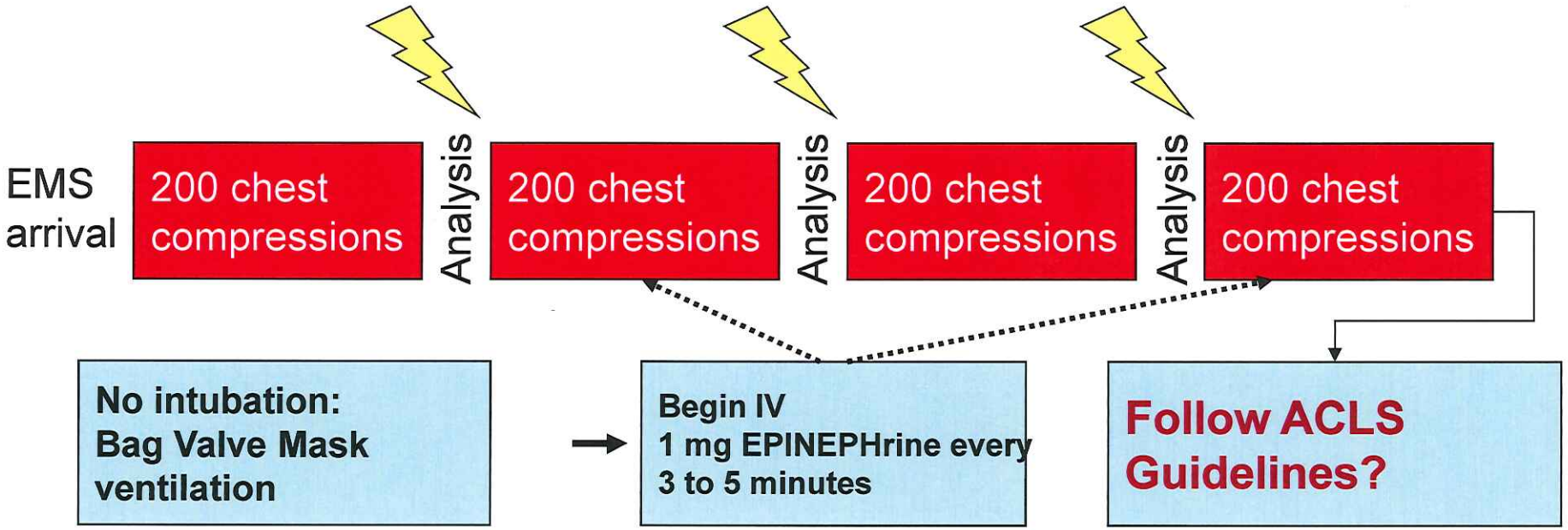
"Tucson" version (2003) Cardiocerebral Resuscitation (Intubation delayed; Bag Valve Mask ventilation)



•If adequate bystander chest compressions are provided, EMS providers perform immediate rhythm analysis and shock if indicated

Special Report

Cardiocerebral Resuscitation
The New Cardiopulmonary Resuscitation

Gordon A. Ewy, MD

"Why is it that every time I press on his chest he opens his eyes, and every time I stop to breathe for him he goes back to sleep?"[1]

This article reviews research that shows that cardiopulmonary resuscitation (CPR) as it has been practiced and as it is presently taught and advocated is far from optimal. *The International Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care,* hereafter referred to as "Guidelines 2000," were evidence based.[2] During their formulation, the greatest weight of evidence was given to placebo-controlled randomized trials in humans. Unfortunately, it is extremely difficult not only to obtain informed consent but also to obtain funding for studies of the magnitude necessary to answer critically important CPR questions. It is unfortunate that controlled CPR research in animals was given the lowest priority in the evidence-based scheme.[2] In our opinion, controlled animal experiments provide data that may be nearly impossible to obtain in human trials in which the circumstance, age, disease states, interventions, and response times to arrest are variable and often unknown. On the other hand, the use of swine for CPR research is not the perfect experimental solution, because they are easier to resuscitate in that they have no underlying heart disease (unless experimentally produced), they are younger, and they have more compliant chests than older adults with cardiac arrest.

Since the formulation of "Guidelines 2000," old and new research in animals and new research in humans have rendered them outdated. Although they will be revised, it is unknown when and what changes will be made. Nevertheless, in 2003, the CPR research information from both animal and humans was so compelling that we could not in good conscience wait for yet another set of new guidelines. Accordingly, our CPR research group, in cooperation with the Tucson Fire Department, initiated a new comprehensive resuscitation program in November 2003 in Tucson, Ariz, with emphasis on these new research findings.[3] We were encouraged in this effort by our colleagues in Europe,[4] and, as noted below, recent studies in humans have reinforced our conclusions.

Three Phases of Cardiac Arrest Due to Ventricular Fibrillation

One of the many important concepts to come forward since "Guidelines 2000" were published is the 3-phase, time-dependent concept of cardiac arrest due to ventricular fibrillation articulated by Weisfelt and Becker.[5] The first phase is the electrical phase, which lasts ≈5 minutes. During this phase, the most important intervention is prompt defibrillation. This is why the benefit of the automatic external defibrillator (AED) has been shown in a wide variety of settings, including airplanes, airports, casinos, and in the community.[6–10] The second phase of cardiac arrest due to ventricular fibrillation is the hemodynamic phase, which lasts for a variable period of time, but possibly from minute 5 to minute 15 of the arrest. During this time, generation of adequate cerebral and coronary perfusion pressure is critical to neurologically normal survival; however, if an AED is the first intervention applied during this phase, the subject is much less likely to survive for reasons that will be presented below. The third phase is the metabolic phase, for which innovative new concepts are needed, the most promising of which is the application of hypothermia. An appreciation of these 3 phases helps one put into context some of the recent findings in resuscitation research.

Physiology of Resuscitation From Cardiac Arrest

The opening quote above is from a woman who had been given 9-1-1 dispatch telephone instructions in cardiopulmonary resuscitation.[1] It is more than a decade old, but when I listened to this recording, I could not help but marvel at the importance of the observation made by this distraught woman trying to resuscitate her husband while awaiting the arrival of the paramedics. She correctly observed what our and others' research had found: that during cardiac arrest, maintenance of cerebral perfusion is critical to neurological function. During the hemodynamic phase, the most important determinant of cerebral perfusion is the arterial pressure generated during external chest compressions.[11–15] This perfusion pressure is lost when one stops chest compressions for rescue breathing.[11–15] The same can be said for maintaining viability of the fibrillating heart. The fibrillating ventricle can be maintained for long periods of time if there is adequate coronary or

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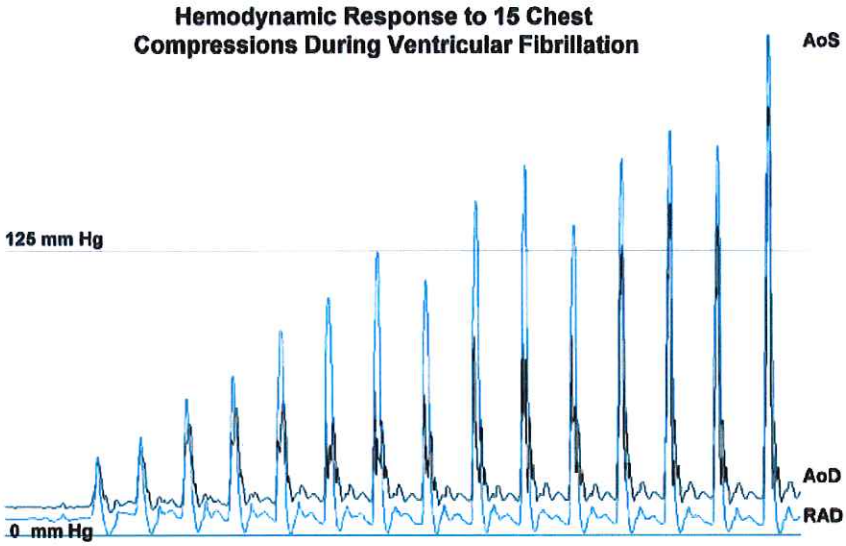

Figure 1. Simultaneous recording of aortic and right atrial pressures during first 15 external chest compressions in swine in cardiac arrest due to ventricular fibrillation. AoS indicates aortic "systolic" pressure during chest compression; AoD, aortic "diastolic" pressure during release phase; and RAD, right atrial pressure during "diastolic" or release phase of chest compression.

myocardial perfusion pressure produced and the coronary arteries are open. If early defibrillation is not available, a major determinant of survival from ventricular fibrillation cardiac arrest is the production of adequate coronary perfusion pressure.[11–15] The coronary perfusion pressure is the difference between the aortic "diastolic" pressure and the right atrial "diastolic" pressure. The word diastolic is in quotes because CPR "systole" is the chest compression phase, and CPR "diastolic" is the release phase of external chest compression (Figure 1). As shown in Figure 1, once chest compressions are begun, it takes time to develop cerebral and coronary perfusion pressures. When chest compression is interrupted for rescue breathing, the cerebral perfusion pressure drops abruptly, and the cardiac perfusion pressure drops significantly. During single-rescuer scenarios, it takes time for the cerebral and coronary perfusion pressures to increase with chest compressions, only to fall each time they are interrupted for ventilation.[16]

These perfusion pressures are important. It has been shown that during prolonged cardiac arrest, survival in animals (Figure 2) and return of spontaneous circulation in humans are related to the coronary perfusion pressures generated during chest compression.[15,17] There are several other major determinants of the perfusion pressure during closed-chest compression in cardiac arrest, including vascular resistance, vascular volume, and intrathoracic pressure. The importance of the vascular resistance during chest compression explains why vasopressors may improve perfusion pressures and vasodilators decrease perfusion pressures.[18–21] The effective intravascular volume is also critical, because an adequate perfusion pressure cannot be obtained and patients cannot be resuscitated if the vascular volume is low. Causes of low vascular volume include excessive blood loss and vascular fluid extravasation. Marked dilation of the venous system may also result in an effective low blood volume. The intrathoracic pressure is yet another determinant of perfusion pressure. A low or negative intrathoracic pressure during the "diastolic" or release phase of chest compression helps to augment venous return into the chest.[22] A high intrathoracic pressure during the relaxation or "diastolic" phase of chest compression inhibits venous return. Thus excessive ventilation, as will be detailed below, will decrease venous return to the thorax and decrease survival.[23]

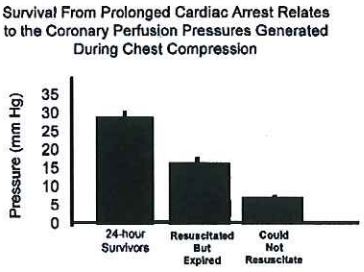

Figure 2. Survival from prolonged cardiac arrest in canines relates to coronary perfusion pressure generated during external chest compressions. See text.

However, there is a distinct window of time in which the perfusion pressure must be restored. Excellent perfusion pressures supplied too late (after the hemodynamic phase and during the metabolic phase) will not resuscitate the subject because irreversible tissue and organ damage has occurred.[14] An appreciation of the physiology of closed-chest resuscitation from cardiac arrest facilitates understanding of the research findings to be presented below.

Lack of Bystander-Initiated CPR

The first problem contributing to the dismal survival rates of out-of-hospital cardiac arrest is the lack of bystander- or citizen-initiated basic CPR. Although the majority of out-of-hospital cardiac arrests are witnessed, only 1 in 5 receive bystander- or citizen-initiated CPR.[24–26] A survey by our CPR Research Group indicated that only 15% of lay individuals would definitely do mouth-to-mouth resuscitation on a stranger.[27] Anonymous surveys have shown that lay individ-

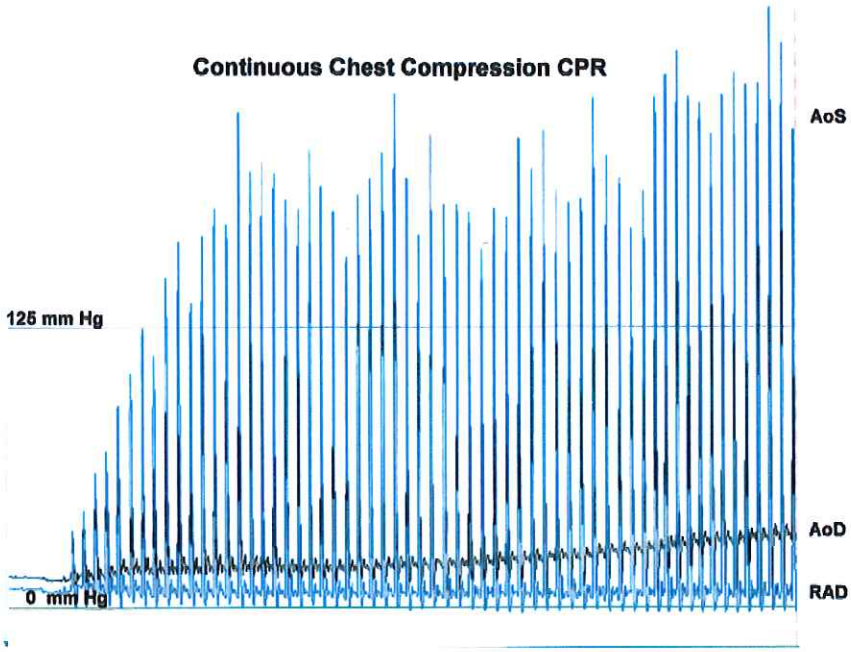

Figure 3. Simultaneous recording of aortic and right atrial pressures during continuous external chest compressions in swine in cardiac arrest due to ventricular fibrillation. AoS indicates aortic "systolic" pressure during chest compression; AoD, aortic "diastolic" pressure during release phase; and RAD, right atrial pressure during "diastolic" or release phase of chest compression.

uals are not the only ones reluctant to provide mouth-to-mouth resuscitation on strangers—so are certified CPR instructors and physicians.[28–31] Yet, in the absence of early defibrillation, bystander- or citizen-initiated chest compression is essential for improved survival for patients with out-of-hospital cardiac arrest.[32] A meta-analysis published in 1991 of 17 studies showed that individuals receiving bystander CPR were 4.5 times more likely to survive.[33] Since then, other studies confirmed the importance of bystander-initiated CPR for out-of-hospital sudden cardiac arrest victims.[24] In another study, those who received bystander-initiated CPR were 3 times more likely to survive to leave the hospital.[25] And a recent report from a 20-community study of adult out-of-hospital cardiac arrest found that citizen-initiated CPR was strongly associated with increased survival and better quality of life.[26] Yet, early bystander CPR is not being done, principally because of the bystander's reluctance to perform mouth-to-mouth rescue breathing. This information, along with our research findings, led us to ask whether chest-compression–only CPR, eg, without mouth-to-mouth rescue breathing, was better for out-of-hospital cardiac arrest than doing nothing until the paramedics arrived.

We compared 24-hour survival with 3 different approaches to bystander CPR using a swine model of prehospital single-rescuer CPR. The 3 interventions were chest-compression–only CPR, "ideal" standard CPR, and no bystander CPR.[1] The ideal standard CPR group was ventilated with hand-bag-valve ventilation via an endotracheal tube with 17% oxygen and 4% carbon dioxide, with 2 ventilations delivered within 4 seconds before each set of 15 chest compressions, to simulate "ideal" mouth-to-mouth rescue breathing. After one-half minute of untreated ventricular fibrillation, the swine were randomized. After 12 minutes of intervention (total duration of ventricular fibrillation 12.5 minutes), advanced cardiac life support was supplied, simulating the late arrival of paramedics. We found that all animals in both the chest-compression–only CPR (Figure 3) and the ideal standard CPR (Figure 4) groups were resuscitated successfully and were neurologically normal at 24 hours. In sharp contrast, only 2 of 8 animals in the group that had no chest compressions until 12.5 minutes (simulating no bystander CPR and the late arrival of emergency medical personnel) survived, and 1 of the 2 was comatose and unresponsive.[1] Our University of Arizona Sarver Heart Center CPR Research Group has published 6 studies with a total of 169 swine with variable durations of ventricular fibrillation arrest before initiation of basic life support (BLS), and various durations of "ideal" standard BLS and chest-compression–only BLS.[1,14,34–38] We found that chest-compression–only BLS and ideal standard BLS resulted in similar 24- or 48-hour normal or near-normal neurological survival and that both were dramatically better than simulated no-bystander–initiated BLS and late arrival of paramedics (Figure 5).[1,14,34–38] Others have confirmed these findings.[39]

These findings were enough for us to encourage bystander continuous-compression CPR without mouth-to-mouth rescue breathing for witnessed cardiac arrest in adults, eg, nonrespiratory cardiac arrests; however, "Guidelines 2000" did not make this recommendation. Although not previously willing to extend such a recommendation for everyone doing bystander-initiated CPR, American Heart Association guidelines have stated that, "If a person is unwilling to perform mouth-to-mouth ventilation, he or she should rapidly attempt resuscitation, omitting mouth-to-mouth ventilation."[40,41] Unfortunately in American Heart Association– and Red Cross–sponsored CPR courses, chest-compression–only CPR is rarely, if ever, mentioned.

After publication of "Guidelines 2000," a pivotal finding was reported from England.[42] Dr Karl Kern, a member of our CPR research group, was a coauthor of this study.[42] Videos of lay individuals doing CPR on manikins documented that it takes them an average of 16±1 seconds to deliver the "Guidelines 2000"–recommended 2 breaths.[42] Accordingly,

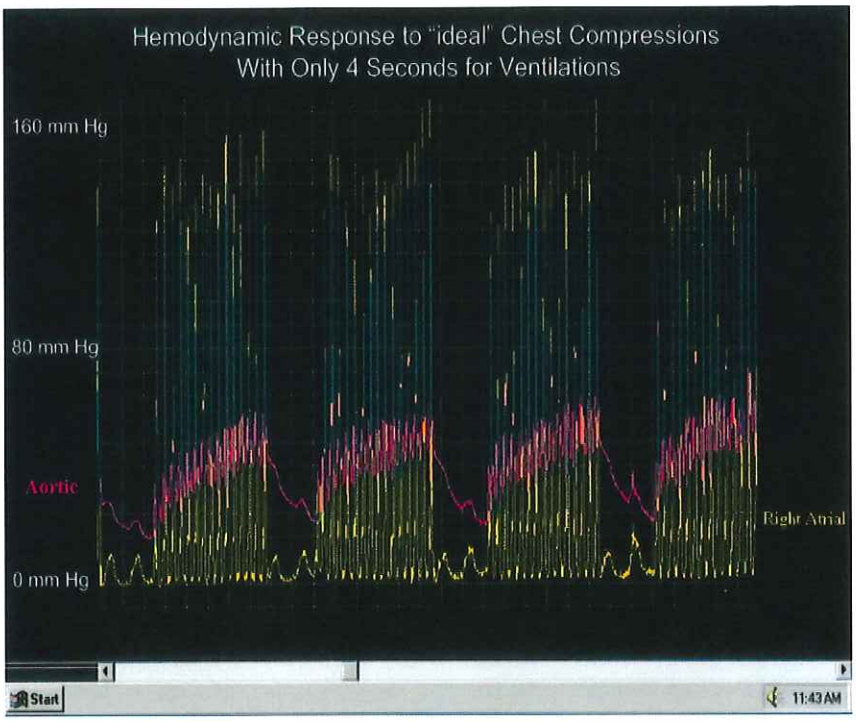

Figure 4. Simultaneous recording of aortic diastolic (red) and right atrial (yellow) pressures during CPR in which 2 ventilations are delivered within 4-second time period.

we conducted another experiment in swine in which continuous-chest–compression BLS was compared with standard BLS, in which we took 16 seconds to deliver the 2 breaths before each set of 15 compressions (Figure 6).[35] As recommended, each breath was delivered over an ≈2-second interval. After 3 minutes of untreated ventricular fibrillation, 12 minutes of BLS was initiated. Defibrillation was attempted at 15 minutes of cardiac arrest. Neurologically normal 24-hour survival was dramatically better with continuous-chest–compression CPR (CCC-CPR) versus BLS CPR the way it is actually done by lay individuals, that is, when 16 seconds is needed to deliver 2 rescue breaths before each set of 15 chest compressions. Continuous-chest–compression survival was 12 (80%) of 15 versus 2 (13%) of 15 for standard CPR.[35] In Figure 7, survival with CCC-CPR is shown as 73% rather than 80% because 73% is the average survival of the CCC-CPR groups in our 6 previously published studies involving 169 animal studies. The survival rate of 13% in our experimental model of out-of-hospital cardiac arrest was of intense interest because in Tucson, the average survival for individuals with out-of-hospital cardiac arrest due to ventricular fibrillation over the past decade was ≈13%.[22]

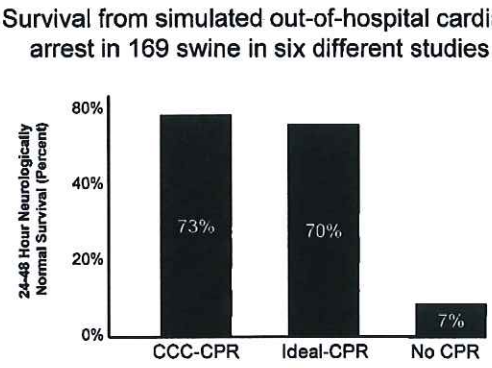

Figure 5. Survival from simulated out-of-hospital cardiac arrest due to ventricular fibrillation during single lay rescuer scenario. Results from 6 different studies are summarized (see text). Survival was the same with chest-compression-only CPR (CCC-CPR) and so-called ideal standard CPR, in which 2 breaths were delivered in 4 seconds (Ideal-CPR), and either was dramatically better than when no bystander CPR was initiated.

We wondered whether a younger population of highly motivated individuals, eg, our medical students, could deliver the recommend 2 breaths any faster. In a study using manikins, we found that it took medical students an average of 14±1 seconds to perform the 2 recommended breaths for rescue breathing.[43] We then recorded paramedics' performance and found that it took them an average of 10±1 seconds.[44] Thus, it takes a considerable amount of time for the 2 respirations that are to be given before each set of 15 chest compressions. This markedly limits the number of chest compressions being delivered.

Experimental and human data support the need for >80 compressions per minute to achieve optimal blood flow during CPR.[45–47] In addition, our studies have shown that compression rates of 100 to 120 per minute are better than 80 per minute and that the use of a metronome to ensure an appropriate chest compression rate improves perfusion in humans.[46,47] The guidelines for adult BLS were changed in the mid 1990s and recommended that a single rescuer deliver 2 ventilations before each set of 15 chest compressions. The revised recommended compression rate of 100 per minute was intended to increase the total number of delivered compressions to 64 per minute, with the assumption that the pause for the 2 ventilations takes 4 seconds[2]; however, as noted above, this appears to be physically impossible.

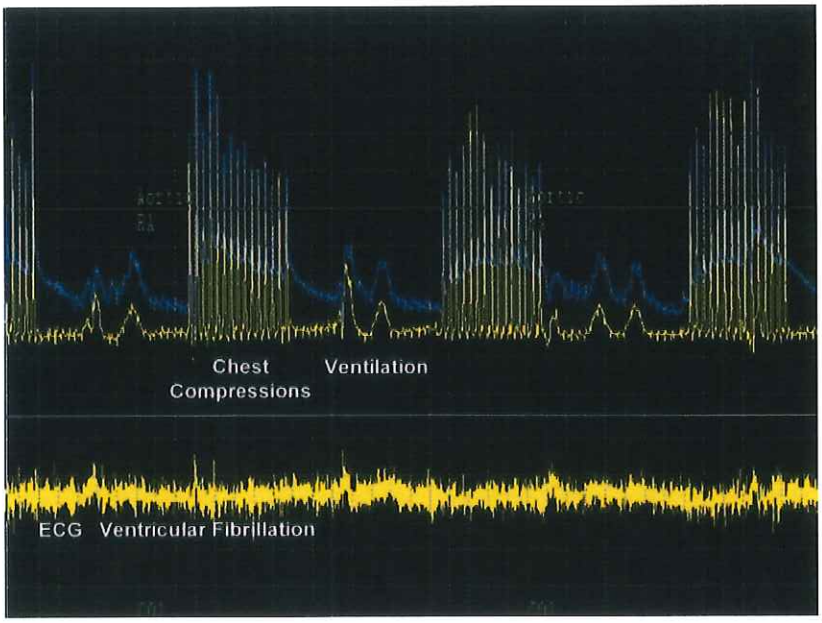

Figure 6. Simultaneous recording of aortic (blue) and right atrial (yellow) pressures during simulated single lay rescuer scenario in which each 2 ventilations are delivered within 16 seconds. ECG (bottom yellow) shows continuous ventricular fibrillation. Note that 15 chest compressions take less time than 2 ventilations (see text).

Another observation is that if a subject collapses with ventricular fibrillation, gasping lasts from 2 to 4 minutes. Gasping is both fortunate and unfortunate. It is fortunate because when chest compression is initiated promptly, the subject is likely to continue to gasp and provide self-ventilation. In fact, Kouwenhoven et al, in one of their early programs, indicated that ventilation was not necessary during chest compression as the subject gasped (W.B. Kouwenhoven, J.R. Jude, and G.B. Knickerbocker, demonstration of the technique of CPR for New York Society of Anesthesiologist 1960s; copy of demonstration provided on CD by J.R. Jude). However, gasping may be unfortunate, because most lay individuals interpret this as an indication that the individual is still breathing and do not initiate bystander CPR or call 9-1-1 as soon as they should. Our survey indicated that chest-compression–only CPR, or CCC-CPR, is more likely to be initiated by bystanders, and our research demonstrates that during the first 15 minutes of cardiac arrest due to ventricular fibrillation, CCC-CPR is dramatically better than standard CPR, because ventilation takes so long that the chest is being compressed less than half of the time.[27,35]

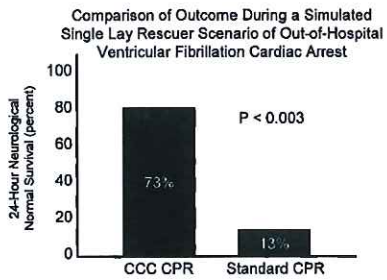

Figure 7. Comparison of 24-hour neurologically normal survival (percent) during simulated single lay rescuer scenario of out-of-hospital ventricular fibrillation cardiac arrest. CCC-CPR is continuous-chest-compression CPR without ventilation; Standard CPR is when each set of 15 chest compressions was interrupted for 16 seconds to deliver 2 ventilations.

On the basis of the above data, one aspect of our Sarver Heart Center/Tucson Fire Department Initiative for Excellence in CPR is our "Be A Lifesaver" program for the public.[22] This program encourages citizens to call 9-1-1 and then initiate continuous chest compression without mouth-to-mouth ventilation for out-of-hospital witnessed unexpected sudden collapse in adults until the paramedics/firefighters arrive. The purpose of this initiative is to dramatically increase the incidence of bystander- or citizen-initiated CPR.

The 3 steps of our Be A Lifesaver program are presented in the Table. Another major advantage of this program is that individuals can be taught CCC-CPR in a relatively short period of time. A demonstration can be seen by accessing the Sarver Heart Center World Wide Web site at www.arizona.heart.edu. Our Be A Lifesaver program also recognizes the importance of the use of AEDs early in witnessed unexpected sudden collapse in adults (Table).

It is of historical interest that physicians in the Netherlands were the first to recognize that if an adult develops ventricular fibrillation and suddenly collapses, his or her lungs, pulmonary veins, left heart, aorta, and all of the arteries are full of oxygenated blood.[48] They suggested that the mnemonic for cardiac arrest should not be ABC, for airway, breathing, and circulation, but CBA, for chest compression first, breathing, and then attention to airway if there was a problem with breathing.[48]

Our recommendations are for witnessed unexpected sudden collapse in an adult, a condition that is almost always due to cardiac arrest. In contrast, in patients with respiratory arrest, ventilation is critically important. Chest compressions plus mouth-to-mouth rescue breathing is markedly superior to either technique alone.[48] Nevertheless, studies of asphyxial cardiac arrest in swine have shown that chest compression is better, but only slightly better, than doing nothing.[49]

CCC-CPR Supported by Observations in Humans

Since our Tucson program was initiated, physicians from Tokyo, Japan, reported on their observational study of 7138

Be a Lifesaver With Continuous-Chest-Compression CPR

In witnessed sudden cardiac arrest in adults, mouth-to-mouth resuscitation is not necessary.* Follow these instructions to perform continuous-chest-compression CPR:

1. Direct someone to call 9-1-1 or make the call yourself.
2. Position the victim on his or her back on the floor. Place one of your hands on top of the other and place the heel of the bottom hand on the center of the victim's chest. Lock your elbows and begin forceful chest compressions at a rate of 100 per minute.
3. If an automated external defibrillator (AED) is available, attach it to the victim and follow the machine's instructions. If no AED is available, perform continuous chest compressions until paramedics arrive. Take turns if you have a partner.

*In cases involving children, suspected drowning, or suspected drug overdose, follow standard American Heart Association CPR procedures.

patients with out-of-hospital cardiac arrest.[50] They found that chest-compression–only CPR was the best independent predictor of their primary end point of neurologically normal hospital discharge, with an adjusted OR of 2.5 ($P=0.002$).[50]

Dispatch-Directed CCC-CPR

After "Guidelines 2000" were published, Hallstrom and associates[51] from Seattle, Wash, published a 6-year study involving 520 patients who were randomized to telephone dispatch–directed standard CPR or CPR with chest compression but without mouth-to-mouth resuscitation. They found that survival was 10.4% with standard CPR and 14.6% with chest-compression–only CPR.[51] Accordingly, as part of our overall program, the first change in the Tucson Fire Department Emergency Medical Service system was to have telephone dispatchers provide instructions for chest-compression–only CPR.

Present Guidelines for Paramedics Are Also Not Optimal

The Ontario Prehospital Advanced Life Support (OPALS) study tested the incremental effect on survival after out-of-hospital cardiac arrest of the addition of a program of advanced life support to a program of bystander BLS and encouraged use of AEDs.[26] They found that the addition of advanced life support intervention, as currently practiced, did not improve the rate of survival after out-of-hospital cardiac arrest in a previously optimized emergency medical service system of rapid defibrillation.[26] Does this mean we can do away with our expensive paramedic systems, or does this mean that the present approach and guidelines for the paramedics are also not optimal? We think the "Guidelines 2000" for the paramedics are also not optimal.

Chest Compressions Are Necessary Before Defibrillation During the Hemodynamic Phase of Cardiac Arrest

Cobb and associates[52] noted that as more of their paramedic/firefighter units were supplied with AEDs, the survival rate appeared to decline. Therefore, they changed their protocol so that the units performed 90 seconds of chest compression before applying the AED. They found that when this was done, survival improved.[52] This information was known at the time of the writing of "Guidelines 2000," but because this change in the Seattle protocols was made while another study was being done, this finding was not incorporated into the guidelines. Professor L. Wik, from Oslo, Norway, noted this controversy and studied this question.[53] In a randomized trial of 200 patients with out-of-hospital cardiac arrest, paramedics performed either 3 minutes of chest compression before defibrillation or defibrillated first.[53] They found that when the ambulance arrived in fewer than 5 minutes (during the electrical phase of cardiac arrest), there was no difference in outcome; however, when the ambulance arrived after 5 minutes (during the hemodynamic phase of cardiac arrest), there was a dramatic difference. In this group, the 1-year survival rate was 4% in the shock-first group and 20% in the chest-compression–first group.[53] A detailed analysis of the Seattle data revealed similar results.[53] In the group who were attended to within 4 minutes, there was no difference in survival to hospital discharge (31% for chest compression first and 32% for defibrillation first); however, in patients treated after 4 minutes, survival was greater (27%) in the group with 90 seconds of chest compression first than in the group who received AED shock first (17% survival).[54]

In Tucson, the average arrival time of paramedic/firefighters is ≈7 minutes, that is, in the hemodynamic phase of cardiac arrest. Accordingly, Tucson paramedic/firefighters have been instructed to give 200 chest compressions before defibrillation. We decided on 200 compressions at 100 compressions per minute because it was between the 90 seconds in the study by Cobb et al[52] and the 3 minutes used by Wik et al.[53] Two hundred chest compressions should take ≈2 minutes to perform and do not require the paramedics/firefighters to time the duration of the chest compressions, only to count them.

Limiting Interruptions of Chest Compressions by Paramedics/Firefighters

Associates from our CPR research group have documented that paramedics/firefighters are compressing the chest of the victim less than half of the time they are at the scene (Terry Valenzuela, MD, written communication, December 14, 2004). This lack of compressions appeared to be the result of the paramedics following guidelines and using AEDs. This was an astounding finding. Accordingly, the first change that was made in our paramedic program was to ensure that 1 paramedic/firefighter is compressing the chest continuously, with only short interruptions for defibrillation shock and rhythm analysis. Intubation is delayed until 3 series of 200 chest compressions, shock, 200 postshock chest compressions, and rhythm analysis are performed. Emphasis is placed on obtaining intravenous access. Intubation is delayed until after 3 series of compressions and defibrillations.

Support for delaying intubation and using a bag-valve-mask for ventilation is supported by the study of Gausche and associates.[54] Their controlled clinical trial of patients aged 12 years and younger or weighing an estimated 40 kg or less

showed no significant difference in survival between the bag-valve-mask group (30%) and the endotracheal intubation group (26%).[54] This important finding (that endotracheal intubation was not superior to bag-valve-mask ventilation even in the pediatric age group, a group in whom respiratory arrest is expected to be more common) supports the fact that endotracheal intubation, although commonly performed and commonly thought to be of the highest priority, is not critically important and is probably deleterious because it results in interruptions of chest compression.

Avoiding the Immediate Deployment of AEDs During the Hemodynamic Phase of Cardiac Arrest

Most AEDs available during and before 2003 took a significant amount of time to analyze the patient's rhythm, to recommend defibrillation shock, and then to analyze the postshock rhythm, such that minutes were added to the arrest time, which makes resuscitation less likely.[55,56] Accordingly, the immediate deployment of an AED by paramedics/firefighters arriving during the hemodynamic phase of cardiac arrest may decrease the chances of survival from out-of-hospital cardiac arrest.[56,57] These devices result in prolonged interruption of precordial compression during the hemodynamic phase of cardiac arrest and contribute to poor survival.[57] The Tucson paramedics/firefighters are instructed to use the "quick look" features of defibrillators if available.

Two Hundred Chest Compressions by Paramedics/Firefighters After Shock and Before Rhythm Analysis

As noted above, paramedics/firefighters are instructed to perform another 200 chest compressions after the shock before assessing the rhythm. This is based on the fact that after prolonged ventricular fibrillation, the shock frequently defibrillates, but to a nonperfusing rhythm. In fact, to produce pulseless electrical activity (PEA) in the experimental laboratory, one fibrillates the animal, does no chest compression for several minutes, then defibrillates, and the result is usually PEA, or the older term, "electrical mechanical dissociation" or "EMD."[58,59] If chest compression is applied and the heart is perfused after the defibrillating shock, the PEA is more likely to revert to a perfusing rhythm.[59]

If the paramedics/firefighters witness the arrest, they defibrillate first. Otherwise, they assume that the patient is in the hemodynamic phase of cardiac arrest and perform 200 chest compressions, deliver the shock, and immediately perform another 200 chest compressions before rhythm analysis. As noted above, this sequence is followed 3 times before an attempt to intubate. Before intubation, the patient is ventilated via bag-valve-mask.

Excessive Ventilation Avoided

Some time after advocating chest-compression-only CPR, we changed the designation to "continuous-chest-compression CPR." Our original thought was "ventilate all you want, just do not stop pressing on the chest." We now know that "ventilate all you want" is wrong as well. Excessive ventilation is a major problem in CPR, decreasing the chances of survival.[21]

After the recommended chest compression rate was increased from 60 compressions per minute to 80 to 100 compressions per minute, we had our CPR research nurse attend a number of cardiac arrests in the hospital to count the number of chest compressions per minute that physicians were providing. The nurse also counted the number of ventilations per minute.[60] The number of ventilations was consistently more than the recommended 12 to 15 per minute.[2] Some were ventilated at a faster rate than the chest was being compressed! The average number of ventilations was 37 per minute.[60] This number became of increased interest when Aufderheide and associates[23] recently reported the same average number of excessive number of ventilations by paramedics. They then studied the effect of ventilation rate on survival in a swine model of cardiac arrest and found that excessive ventilations decreased survival.[23] With simultaneous chest compressions and ventilations, there is a dramatic increase in intrathoracic pressure, decreasing venous return, and thus perfusion pressures. The study by Aufderheide and associates[23] indicates that 12 to 15 ventilations per minute are much better than the near 30 ventilations per minute that are often delivered.

There is a need for more research into the best way for ventilation to be delivered in the various phases of cardiac arrest, depending on whether rescue breathing was performed or not. The amount and type of ventilation studied by different groups are variable, and the results have been conflicting.[61,62] Is there a role for negative pressure during ventilation, as proposed and studied by Lurie and associates[22,61]? Wik and associates[53] found that optimal paramedic ventilation is 10 mL/kg at a frequency of 12 ventilations per minute. Is this what one should recommend? This is another area that needs more study.

Just as multicenter clinical trials are necessary to provide large enough numbers from a variety of locations to ensure their validity, we think there is a need for multicenter laboratory research using common protocols to give better direction and preliminary preclinical data to support the pursuit of expensive multicenter clinical trials. Standards and guidelines for CPR have been advocated for more than 40 years, and we still only have some of the answers.

The Metabolic Phase: Hypothermia

It has long been appreciated that survival from drowning is more likely with cold water rather than warm. Although improved neurological recovery was reported by Benson et al[63] in 1959 in a small number of comatose patients after resuscitation from cardiac arrest treated with hypothermia, it was not until the simultaneous reports from Austria and Australia of improved survival and neurological outcome that this concept was more generally accepted.[64,65]

After the publication of these studies, the International Liaison Committee on Resuscitation (ILCOR) issued a new statement on hypothermia.[66] It states, "Unconscious adults with spontaneous out-of-hospital cardiac arrest and an initial rhythm of ventricular fibrillation should be cooled to 32 to 34 degrees centigrade for 12 to 24 hours."[66] They added that, "Such cooling also may be beneficial for other rhythms or for in-hospital cardiac arrest."[66] More research is needed to define the best and safest methods for postresuscitation hypothermia.

Conclusions

This article reviewed the studies that led us to institute a new system of CPR for out-of-hospital witnessed arrest due to ventricular fibrillation in adults.[3] It is called cardiocerebral resuscitation (CCR), or continuous-chest–compression CPR (CCC-CPR) for witnessed unexpected sudden cardiac arrest in adults, to differentiate it from the presently taught CPR that may be better (but we do not think ideal) for patients with respiratory arrest. Sudden witnessed collapse in an adult is most often due to ventricular fibrillation, and the present CPR as articulated by "Guidelines 2000" results in excessive interruptions of chest compressions for other presently mandated tasks.[2] These excessive interruptions are lethal.

Some of the major unanswered questions are as follows: When is ventilation mandatory during prolonged cardiocerebral resuscitation? Ventilation is probably mandatory after ≈15 minutes of chest compression only in patients who are not gasping. This needs to be studied.

If one is willing to do mouth-to-mouth rescue breathing for witnessed cardiac arrest, what is the best compression-to-ventilation ratio? One of our studies suggests that it might be continuous chest compressions for the first 4 minutes, follow by 1 or 2 ventilations before each set of 100 compressions.[67]

If bystanders perform chest-compression–only CPR and the paramedics arrive within 8 to 15 minutes, what is the best sequence of ventilation for the paramedics/firefighters? Clearly, excessive ventilation is to be avoided, but are the recommended 12 to 15 ventilations per minute optimal? Should fewer ventilations and the use of the impedance valve mask be used? Continued research in cardiocerebral resuscitation is clearly needed, but we cannot wait for all the answers, nor until the next guidelines are published, to make some needed changes.

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Disclosure

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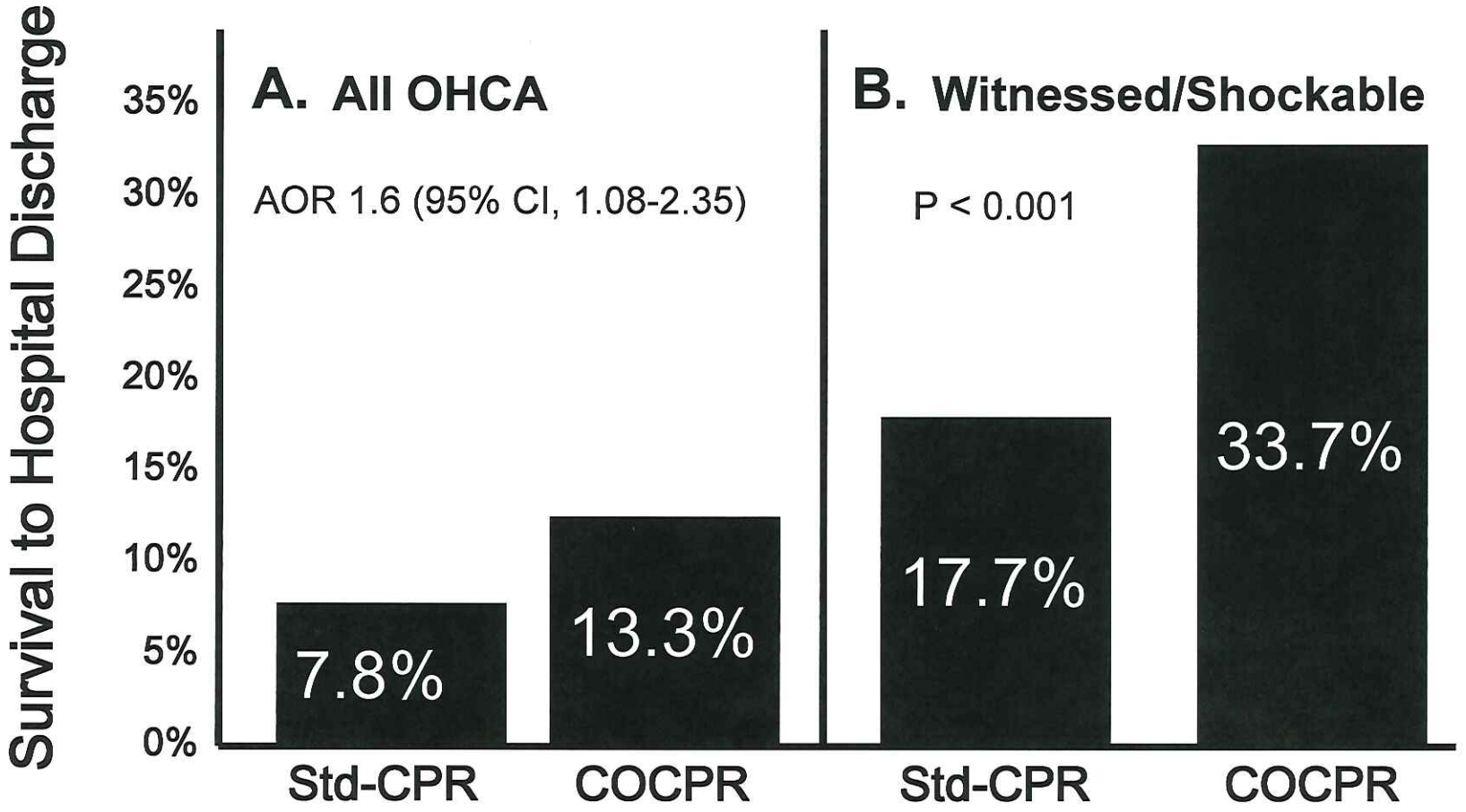
KEY WORDS: cardiopulmonary resuscitation ■ defibrillation ■ fibrillation ■ perfusion ■ cardiac arrest

Survival after Bystander CPR for OHCA in Arizona (2005 to 2010)
Compression Only CPR Advocated and Taught



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Chest Compression–Only CPR by Lay Rescuers and Survival From Out-of-Hospital Cardiac Arrest

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Context Chest compression–only bystander cardiopulmonary resuscitation (CPR) may be as effective as conventional CPR with rescue breathing for out-of-hospital cardiac arrest.

Objective To investigate the survival of patients with out-of-hospital cardiac arrest using compression-only CPR (COCPR) compared with conventional CPR.

Design, Setting, and Patients A 5-year prospective observational cohort study of survival in patients at least 18 years old with out-of-hospital cardiac arrest between January 1, 2005, and December 31, 2009, in Arizona. The relationship between layperson bystander CPR and survival to hospital discharge was evaluated using multivariable logistic regression.

Main Outcome Measure Survival to hospital discharge.

Results Among 5272 adults with out-of-hospital cardiac arrest of cardiac etiology not observed by responding emergency medical personnel, 779 were excluded because bystander CPR was provided by a health care professional or the arrest occurred in a medical facility. A total of 4415 met all inclusion criteria for analysis, including 2900 who received no bystander CPR, 666 who received conventional CPR, and 849 who received COCPR. Rates of survival to hospital discharge were 5.2% (95% confidence interval [CI], 4.4%-6.0%) for the no bystander CPR group, 7.8% (95% CI, 5.8%-9.8%) for conventional CPR, and 13.3% (95% CI, 11.0%-15.6%) for COCPR. The adjusted odds ratio (AOR) for survival for conventional CPR vs no CPR was 0.99 (95% CI, 0.69-1.43), for COCPR vs no CPR, 1.59 (95% CI, 1.18-2.13), and for COCPR vs conventional CPR, 1.60 (95% CI, 1.08-2.35). From 2005 to 2009, lay rescuer CPR increased from 28.2% (95% CI, 24.6%-31.8%) to 39.9% (95% CI, 36.8%-42.9%; $P<.001$); the proportion of CPR that was COCPR increased from 19.6% (95% CI, 13.6%-25.7%) to 75.9% (95% CI, 71.7%-80.1%; $P<.001$). Overall survival increased from 3.7% (95% CI, 2.2%-5.2%) to 9.8% (95% CI, 8.0%-11.6%; $P<.001$).

Conclusion Among patients with out-of-hospital cardiac arrest, layperson compression-only CPR was associated with increased survival compared with conventional CPR and no bystander CPR in this setting with public endorsement of chest compression–only CPR.

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OUT-OF-HOSPITAL CARDIAC arrest is a major public health problem, affecting approximately 300 000 individuals in the United States annually.[1] Although survival rates vary considerably, overall survival is generally less than 10% among those in whom resuscitation is attempted.[2] The provision of bystander cardiopulmonary resuscitation (CPR) significantly improves outcome[3] but is generally performed in less than 30% of cases.[2,4]

In 2005, because our evaluation of out-of-hospital cardiac arrest in Arizona revealed dismal outcomes, we established a statewide program aimed at improving survival. These efforts included changes in the approach to the care provided by both bystanders and emergency medical services (EMS) personnel[5] and were based on the increasing evidence in favor of minimizing interruptions in chest compressions during CPR.[6-10] This led to alterations in the resuscitative care provided by EMS personnel, termed *minimally interrupted cardiac resuscitation* (MICR).[11,12] Simul-

See also p 1493 and Patient Page.

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Box. Intervention: Chest Compression–Only Cardiopulmonary Resuscitation Campaign in Arizona

Web site (http://www.azshare.gov)

Brief online video training

In-person, free training in many settings and locations throughout the state (primarily sponsored by fire departments)

Free training kits sent to schools (n=1816) in Arizona with 6th through 12th grades (students were encouraged to teach family members)

Public service announcements made by the governor and local sports celebrities

Inserts mailed in utility bills

Tables set up at health and safety fairs by Boy Scouts, fire departments, schools, etc

Newspaper articles and editorials

Training video looped on public-access cable channels

Summer youth classes taught by youth corps volunteers

Local radio spots and interviews

Special features on local and national television

Frequent e-mail updates distributed to stakeholders

taneously, we launched a statewide, multifaceted effort to encourage bystanders to use compression-only CPR (COCPR) because this approach is easier to teach, learn, remember, and perform than conventional CPR.[13]

In this study, we evaluated whether intentional, widespread public endorsement of COCPR for adult sudden cardiac arrest would be associated with an increased likelihood that lay rescuers would perform CPR and an increased likelihood of survival to hospital discharge compared with no bystander CPR and conventional CPR.

METHODS

Arizona has 6.6 million residents and comprises 15 counties with demographics varying from urban to wilderness areas.[14] In 2005, 30 EMS agencies statewide participated in the state-sponsored quality improvement program for out-of-hospital cardiac arrest: the Save Hearts in Arizona Registry and Education (SHARE) program.[5,15] Participation increased each year of the study, and by 2009, 90 agencies (serving approximately 80% of the population) had joined SHARE. During the time period of this study, Arizona did not have a structured 911 dispatcher–assisted CPR program.

Because out-of-hospital cardiac arrest has been designated a major public health problem in Arizona and the goal of this program is quality improvement, the data collected were exempt from the Health Insurance Portability and Accountability Act (HIPAA). Permission to publish the deidentified data was obtained from the Arizona Department of Health Services human subjects review board and the University of Arizona institutional review board.

Data Collection and Definitions

This prospective, observational cohort analysis included patients who experienced out-of-hospital cardiac arrest in Arizona between January 1, 2005, and December 31, 2009. The study population comprised all adults (age ≥18 years) with an out-of-hospital cardiac arrest of presumed cardiac origin that was not witnessed by EMS personnel. The arrest was presumed to be of cardiac origin unless it was known to be caused by trauma, drowning, drug overdose, or asphyxia.[16,17] Patients with obvious evidence of death or those with do-not-resuscitate orders were excluded.

Data were collected prospectively and entered into an Utstein-style database.[16] Data elements included sex, age, location of arrest, whether arrest was bystander-witnessed, presumed etiology of arrest, EMS dispatch-to-scene-arrival ("response") interval, initial prehospital electrocardiographic (ECG) rhythm, whether bystander CPR was provided, type of bystander CPR (COCPR vs conventional), type of EMS protocol (MICR vs conventional BLS/ACLS [basic life support/advanced cardiac life support]), whether the patient received therapeutic hypothermia, survival to hospital discharge, and neurologic status.

Since a core question of this effort is related to the type of CPR provided, EMS personnel received special training and a documentation aid on how to code bystander CPR (available at http://www.azshare.gov). This training included instruction in documenting the person performing CPR as well as the type of CPR performed by bystanders. If the method of bystander resuscitation was not evident, EMS personnel were instructed to ask bystanders whether ventilations had been performed during CPR. For this analysis, because we were specifically interested in "true" layperson CPR, we excluded cases in which CPR was performed by bystanders with formal medical training (whether on or off duty). However, to assess the possibility of ascertainment bias, we compared the proportion of COCPR vs conventional CPR over time performed by lay bystanders and by bystanders with formal medical training. All cardiac arrests occurring in medical facilities were excluded.

Intervention

The SHARE program initiated a multifaceted, statewide public COCPR education campaign in 2005. The effort included multiple approaches to training and information dissemination (BOX). We estimate that at least 30 000 people have been directly trained in the COCPR technique and that more than 500 000 were exposed to at least 1 COCPR media forum.

In March 2008, the American Heart Association released an advisory statement supporting Hands-Only CPR,[13] which was widely publicized in Arizona as an additional aspect of the ongoing effort.

Main Outcome Measures

The primary outcome measure was survival to hospital discharge, determined by review of hospital records. Final outcomes were obtained through hospitals and the Office of Vital Statistics at the Arizona Department of Health Services. Cerebral Performance Cat-

egory (CPC) scores were assigned based on neurologic status at hospital discharge. The 5 CPC categories are good cerebral performance, moderate cerebral disability, severe cerebral disability, coma or vegetative state, and death.[16] Secondary measures were the frequency and type of bystander CPR provided. Predetermined subgroups for additional analyses were patients with a witnessed collapse and patients with a shockable rhythm on EMS arrival.

Statistical Analysis

Proportions were calculated for categorical data, whereas mean and standard deviation, or median and interquartile range (IQR), as appropriate, were calculated for continuous data. Statistical significance for categorical data was assessed using Fisher exact test or χ^2. Temporal trends for categorical data were assessed using a modified Wilcoxon signed rank test for trends across ordered groups (by year) if Fisher exact test or χ^2 were significant.

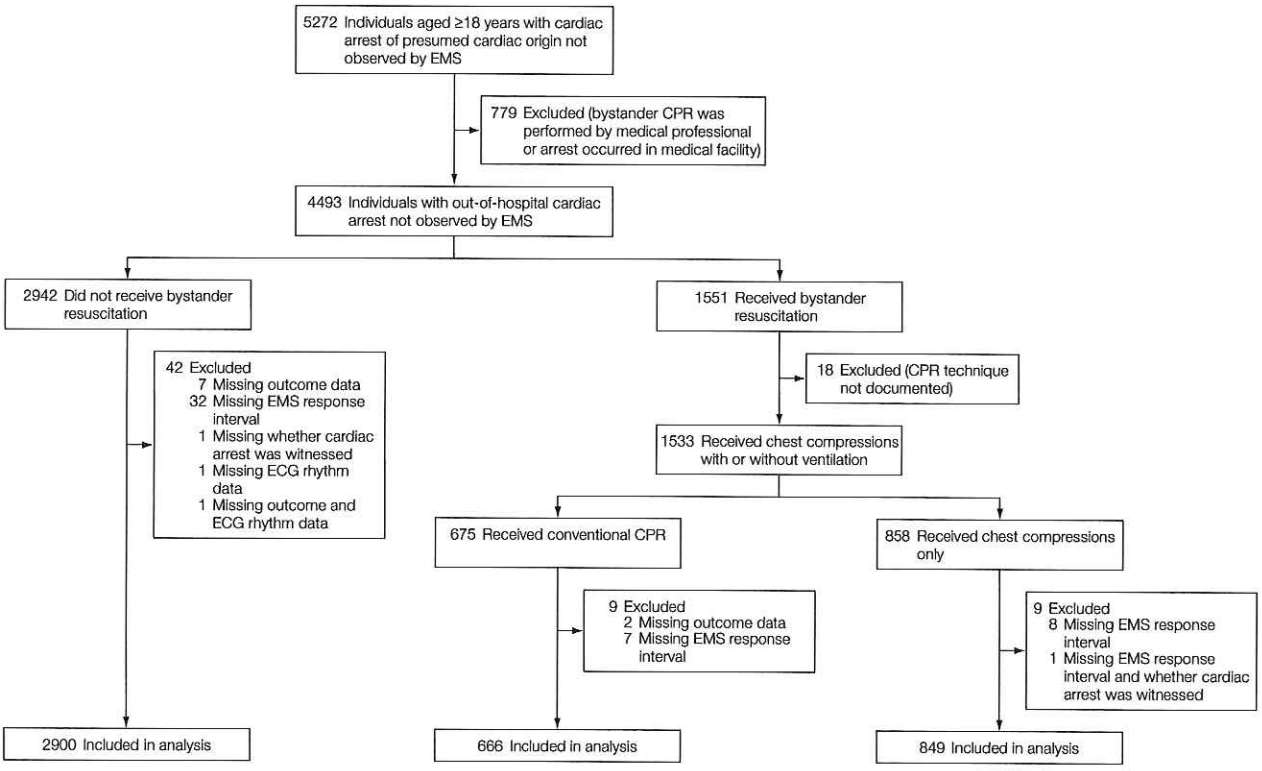
Multivariable logistic regression was used to model the association between CPR type (no CPR, conventional CPR, COCPR) with the probability of survival. The following covariates were considered for model inclusion: age, sex, witnessed arrest, shockable rhythm, bystander CPR provision and type, location of arrest, EMS response interval, EMS provision of MICR vs conventional BLS/ACLS, use of postarrest therapeutic hypothermia, and year. Continuous variables were assessed for linearity in the logit scale using quantiles, lowess smoothing, and fractional polynomials. Nonlinear covariates were categorized using cutpoints chosen to maximize model fit. Goodness of fit and the area under the receiver operator characteristic curve (ROC) were calculated to determine model fit and discrimination. The value of ρ was calculated for survival to hospital discharge among EMS systems and generalized estimating equations (GEEs) were used to determine the effect of clustering by EMS agency on survival.

Statistical significance was set a priori at $\alpha \leq .05$ (2-tailed). All statistical analyses were performed using Stata version 11.1 (StataCorp, College Station, Texas).

RESULTS

During the study period, 5272 adult out-of-hospital cardiac arrests of presumed cardiac etiology and not witnessed by EMS were reported. A total of 779 cases were excluded because bystander CPR was administered by a medical professional or the cardiac arrest occurred in a medical facility. A total of 78 cases were excluded because of missing data (1.7% of cases meeting inclusion criteria): 10 cases with missing outcome data, 2 cases missing data on whether cardiac arrest was witnessed by a bystander, 18 cases

Figure. Study Population Profile



EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; ECG, electrocardiographic.

without type of bystander CPR documented, 1 case with missing ECG rhythm data, and 47 cases with missing EMS response interval data. The final number of cases for analysis was 4415 (FIGURE).

TABLE 1 shows the demographic and clinical characteristics of the study population. The majority of arrests occurred in men (66.8%), and the mean (SD) age for all arrests was 65.3 (15.2) years (median age, 66 years). The cardiac arrest was witnessed in 45.1% of cases and a lay bystander performed CPR in 34.3%. Overall, 15.1% of patients received conventional bystander CPR and 19.2% received COCPR. Overall survival was 7.1%.

TABLE 2 shows the annual rates of bystander CPR and survival. The annual rate for lay rescuers providing any type of bystander CPR increased significantly over time, from 28.2% in 2005 to 39.9% in 2009 (χ^2 $P<.001$; test for trend, $P<.001$). Among patients who received bystander CPR, the proportion with COCPR increased significantly over time, from 19.6% in 2005 to 75.9% in 2009 (χ^2 $P<.001$; test for trend, $P<.001$). Overall survival also increased significantly over time: from 3.7% in 2005 to 9.8% in 2009 (χ^2 $P<.001$; test for trend, $P<.001$). Of 913 cases for which a medical professional provided bystander CPR, 71 received COCPR (7.8%; 95% confidence interval [CI], 6.0%-9.5%), whereas of 2019 cases for which a lay bystander provided CPR, 1086 received COCPR (53.8%; 95% CI, 51.6%-56.0%).

Multivariable logistic regression showed that COCPR was associated with improved odds of survival compared with no bystander CPR (odds ratio [OR], 1.59; 95% CI, 1.18-2.13) or conventional CPR (OR, 1.60; 95% CI, 1.08-2.35) after controlling for the following variables: witnessed arrest, shockable rhythm, EMS response interval, age, sex, location of arrest, provision of MICR by EMS personnel, and use of therapeutic hypothermia. TABLE 3 shows the crude and adjusted ORs for survival for all the variables in the final model. The goodness-of-fit test indicated adequate fit ($P=.98$) and the area under the ROC curve (0.854) indicated good model discrimination.

For out-of-hospital cardiac arrests that were witnessed by a lay bystander and had a shockable rhythm on EMS arrival (n=1017), survival was 17.6% in the no CPR group (reference group), 17.7% for conventional CPR (crude OR, 1.01; 95% CI, 0.68-1.52), and 33.7% for COCPR (crude OR, 2.39; 95% CI, 1.70-3.35). The adjusted ORs for survival (adjusted for all variables in the main

Table 1. Demographic Features, Clinical Characteristics, and Outcomes of Study Population According to Type of Bystander CPR

	All Out-of-Hospital Cardiac Arrest	Type of Lay Bystander CPR		
		None	Conventional	COCPR
Total, No. (%)	4415 (100)	2900 (65.7)	666 (15.1)	849 (19.2)
Age, mean (SD), y	65.3 (15.2)	66.2 (15.1)	63.8 (15.2)	63.1 (15.1)
Male sex, No. (%)	2951 (66.8)	1915 (66.0)	458 (68.8)	578 (68.1)
Witnessed arrest, No. (%)	1992 (45.1)	1177 (40.6)	388 (58.3)	427 (50.3)
Shockable rhythm (VF/VT) on arrival by EMS, No. (%)	1463 (33.1)	800 (27.6)	297 (44.6)	366 (43.1)
EMS resuscitation protocol used, No. (%)				
MICR	1726 (39.1)	1085 (37.4)	172 (25.8)	469 (55.2)
BLS/ACLS	2689 (60.9)	1815 (62.6)	494 (74.2)	380 (44.8)
Location of arrest, No. (%)				
Home/residential setting	3591 (81.3)	2517 (86.8)	474 (71.2)	600 (70.7)
Public setting	824 (18.7)	383 (13.2)	192 (28.8)	249 (29.3)
EMS response interval, median (IQR), min	5 (4-7)	5 (4-7)	5 (4-7)	5 (4-6)
Use of in-hospital therapeutic hypothermia, No. (%)	78 (1.8)	39 (1.3)	12 (1.8)	27 (3.2)
Year of arrest, No. (%)				
2005	596 (13.5)	428 (14.8)	135 (20.3)	33 (3.9)
2006	954 (21.6)	643 (22.2)	166 (24.9)	145 (17.1)
2007	845 (19.1)	571 (19.7)	144 (21.6)	130 (15.3)
2008	1009 (22.9)	650 (22.4)	124 (18.6)	235 (27.7)
2009	1011 (22.9)	608 (21.0)	97 (14.6)	306 (36.0)
Survival to hospital discharge, No. (%)	315 (7.1)	150 (5.2)	52 (7.8)	113 (13.3)
Neurologic outcome (CPC score), No. (%)				
1	138 (3.2)	60 (2.1)	25 (3.8)	53 (6.5)
2	44 (1.0)	26 (0.9)	9 (1.4)	8 (1.0)
3	24 (0.6)	9 (0.3)	2 (0.3)	13 (1.6)
4	11 (0.3)	7 (0.3)	1 (0.2)	3 (1.4)
5	4100 (95)	2750 (96.4)	614 (94.3)	736 (90.5)

Abbreviations: BLS/ACLS, basic life support/advanced cardiac life support; CI, confidence interval; COCPR, compression-only CPR; CPC, Cerebral Performance Category; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; IQR, interquartile range; MICR, minimally interrupted cardiac resuscitation (performed by EMS personnel); VF/VT, ventricular fibrillation/ventricular tachycardia.

Table 2. Annual Lay Bystander CPR Rates and Out-of-Hospital Cardiac Arrest Survival, 2005-2009[a]

	2005	2006	2007	2008	2009	Total
Cardiac arrest survival overall[b]	(n = 596)	(n = 954)	(n = 845)	(n = 1009)	(n = 1011)	(N = 4415)
No.	22	69	58	67	99	315
% (95% CI)	3.7 (2.2-5.2)	7.2 (5.6-8.9)	6.7 (5.2-8.6)	6.6 (5.1-8.2)	9.8 (8.0-11.6)	7.1 (6.4-7.9)
Survival from witnessed arrest with VF/VT[b]	(n = 130)	(n = 224)	(n = 224)	(n = 209)	(n = 230)	(n = 1017)
No.	14	50	42	47	70	224
% (95% CI)	10.8 (5.4-16.2)	22.3 (16.8-27.8)	18.8 (13.6-23.9)	22.5 (16.8-28.2)	30.4 (24.4-36.4)	21.9 (19.4-24.5)
Provision of any type of CPR by lay bystander[b]	(n = 596)	(n = 954)	(n = 845)	(n = 1009)	(n = 1011)	(n = 4415)
No.	168	311	274	359	403	1515
% (95% CI)	28.2 (24.6-31.8)	32.6 (29.6-35.6)	32.4 (29.3-35.6)	35.6 (32.6-38.5)	39.9 (36.8-42.9)	34.3 (32.9-35.7)
Type of CPR by lay bystander[b]	(n = 168)	(n = 311)	(n = 274)	(n = 359)	(n = 403)	(n = 1515)
Conventional						
No.	135	166	144	124	97	666
% (95% CI)	80.4 (74.3-86.4)	53.4 (47.8-59.0)	52.6 (46.6-58.5)	34.5 (29.6-39.5)	24.1 (19.9-28.3)	44.0 (41.5-46.6)
COCPR						
No.	33	145	130	235	306	849
% (95% CI)	19.6 (13.6-25.7)	46.6 (41.0-52.2)	47.5 (41.5-53.4)	65.5 (60.5-70.4)	75.9 (71.7-80.1)	56.0 (53.5-58.5)
Positive neurologic status (CPC score = 1 or 2)[c]	(n = 591)	(n = 939)	(n = 832)	(n = 994)	(n = 961)	(n = 4317)
No.	14	52	39	42	35	182
% (95% CI)	2.4 (1.1-3.6)	5.5 (4.1-7.0)	4.7 (3.2-6.1)	4.2 (3.0-5.5)	3.6 (2.5-4.8)	4.2 (3.6-4.8)

Abbreviations: CI, confidence interval; COCPR, compression-only CPR; CPC, Cerebral Performance Category; CPR, cardiopulmonary resuscitation; VF/VT, ventricular fibrillation/ventricular tachycardia.
[a] Percentages may not add to 100.0% because of rounding.
[b] Fisher exact test: $P \leq .001$; test for trend: $P < .001$.
[c] Fisher exact test: $P = .03$; test for trend: $P = .92$.

Table 3. Survival and Odds Ratios for Various Risk Factors

Characteristic	Survival		Odds Ratio (95% CI)	
	No./Total No.	% (95% CI)	Crude	Adjusted[a]
Bystander CPR				
None	150/2900	5.2 (4.4-6.0)	1 [Reference]	
Conventional	52/666	7.8 (5.8-9.8)	1.55 (1.12-2.15)	0.99 (0.69-1.43)
COCPR	113/849	13.3 (11.0-15.6)	2.81 (2.17-3.64)	1.59 (1.18-2.13)
Witnessed arrest				
No	48/2423	2.0 (1.4-2.5)	1 [Reference]	
Yes	267/1992	13.4 (11.9-14.9)	7.66 (5.60-10.48)	4.26 (3.04-5.98)
Shockable rhythm				
Nonshockable	62/3020	2.1 (1.6-2.6)	1 [Reference]	
VF/VT	257/1511	17.0 (15.4-19.2)	9.75 (7.32-12.97)	5.16 (3.78-7.05)
EMS protocol				
BLS/ACLS	129/2689	4.8 (4.0-5.6)	1 [Reference]	
MICR	186/1726	10.8 (9.3-12.2)	2.40 (1.90-3.03)	2.21 (1.70-2.88)
Age categories, y				
≥80	29/858	3.4 (2.2-4.6)	1 [Reference]	
60-79	139/2032	6.8 (5.7-7.9)	2.10 (1.40-3.16)	1.78 (1.15-2.75)
18-59	147/1525	9.6 (8.2-11.1)	3.05 (2.03-4.58)	2.27 (1.46-3.53)
EMS response interval, continuous per minute			0.85 (0.80-0.90)	0.87 (0.82-0.93)
Survival by location				
Residential	195/3591	5.4 (4.7-6.2)	1 [Reference]	
Public location	120/824	14.6 (12.2-17.0)	2.97 (2.33-3.78)	1.48 (1.11-1.96)
Provision of therapeutic hypothermia				
No	286/4337	6.6 (5.9-7.3)	1 [Reference]	
Yes	29/78	37.2 (26.4-48.0)	8.38 (5.22-13.47)	3.59 (2.09-6.19)
Survival by sex				
Male	219/2951	7.4 (6.5-8.4)	1 [Reference]	
Female	96/1464	6.6 (5.3-7.8)	0.88 (0.68-1.12)	1.42 (1.07-1.88)

Abbreviations: BLS/ACLS, basic life support/advanced cardiac life support; CI, confidence interval; COCPR, compression-only CPR; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; MICR, minimally interrupted cardiac resuscitation (performed by EMS personnel); VF/VT, ventricular fibrillation/ventricular tachycardia.
[a] Adjusted for all other variables in final model (goodness of fit, $P = .98$, area under receiver operator characteristics curve = 0.854, N = 4415).

logistic regression model, except for witnessed arrest and heart rhythm), using the no CPR group as the reference group, were 1.09 (95% CI, 0.70-1.69) for the conventional CPR group and 1.90 (95% CI, 1.31-2.75) for the COCPR group. Survival increased significantly over time for the subgroup of witnessed arrests with a shockable rhythm (Table 2), from 10.8% in 2005 to 30.4% in 2009 (Fisher exact test, $P<.001$; test for trend, $P<.001$).

The intraclass correlation value of ρ for survival among EMS agencies was 4×10^{-5} (95% CI, 0-0.00614), indicating no significant clustering. GEE logistic regression (random effects model) analyses converged on the same model as ordinary logistic regression and ORs (and 95% CIs) were identical, confirming there was no clustering effect by EMS agencies.

We were able to determine neurologic status for 4310 of 4515 cases of out-of-hospital cardiac arrest (217/315 survivors) of whom 4.2% (95% CI, 3.6%-4.8%) had a good neurologic status (CPC score of 1 or 2) (Table 1 and Table 2). Proportion of individuals with good neurologic status differed significantly based on the type of CPR provided: no CPR, 86 of 2852, or 3.0% (95% CI, 2.4%-3.6%); conventional CPR, 34 of 651, or 5.2% (95% CI, 3.5%-6.9%); COCPR, 62 of 814, or 7.6% (95% CI, 5.8%-9.4%) ($P<.001$). The unadjusted ORs for a good neurologic outcome for bystander resuscitation comparisons were as follows: conventional vs none, 1.77 (95% CI, 1.18-2.66); COCPR vs none, 2.65 (95% CI, 1.89-3.71); COCPR vs conventional, 1.50 (95% CI, 0.97-2.30).

For arrests of presumed noncardiac etiology, COCPR was performed in 60.0% (95% CI, 54.6%-65.4%) of all patients who received bystander CPR. For arrests of respiratory etiology, COCPR was administered in 9 of 150 patients (6%; 95% CI, 2.2%-9.8%). Survival for noncardiac etiologies was similar regardless of the type of CPR: no CPR, 24 of 803 patients (3.0%; 95% CI, 1.8%-4.2%); conventional CPR, 6 of 130 patients (4.6%; 95% CI, 0.1%-8.3%); and COCPR, 7 of 195 patients (3.6%; 95% CI, 0.1%-6.2%) ($P=.51$).

Of 297 pediatric cases of out-of-hospital cardiac arrest (age <18 years), 150 patients (50.5%) received bystander CPR (148 cases for which the type of resuscitation was identified). The proportions of children who received COCPR, stratified by age, were as follows: younger than 1 year, 7 of 77 patients (9.1%; 95% CI, 2.5%-15.7%); age 1 to 12 years, 3 of 50 patients (6.0%; 95% CI, 0%-12.8%); and older than 12 years, 9 of 21 patients (42.9%; 95% CI, 19.8%-65.9%).

COMMENT

Bystander CPR is a critical but incompletely understood link in the chain of survival for individuals who experience out-of-hospital cardiac arrest.[3,4,17-19] Although bystander CPR is associated with increased survival,[2,4] the rate of performing this intervention remains unacceptably low.[4,20,21] This has been cited as a potentially correctable reason for the poor survival rates in most communities.[2,22] Suggested causes for the low CPR rates include fear of causing harm, fear of contracting infectious disease, the complexity of the psychomotor task, panic, and reluctance to make mouth-to-mouth contact.[21,23-26] Because of these and other factors, increasing bystander CPR rates has been difficult in most settings.[4,22,27]

For more than a decade, preclinical reports have raised the possibility that it is not necessary to perform active ventilation during CPR soon after sudden collapse from out-of-hospital cardiac arrest. Animal studies have shown COCPR to be at least as effective as conventional CPR.[7-10]

This study is the first of which we are aware to report an intentional effort to encourage and endorse COCPR to the public. We identified 3 major findings: a significant increase in the rate of bystander CPR (from 28.2% to 39.9%), an increase in the likelihood of bystanders performing COCPR vs conventional CPR (from 19.6% to 75.9%), and a significant independent association between COCPR and survival when compared with conventional CPR (adjusted OR, 1.60; 95% CI, 1.08-2.35).

To our knowledge, this is the first report of a relationship between a public education effort and an increase in the rate of bystander CPR in a statewide jurisdiction. The nature of this study precludes determining the relative contributions of the various components of this statewide initiative. Encouraging a technique that is easier to perform and more acceptable to the public may have helped increase the CPR rate independent of the public education efforts. Ultimately, we suspect that only the combination of a local, state, and national public education campaign and the endorsement of COCPR made this effort successful. The Hands-Only CPR campaign now being led by the American Heart Association across the nation is timely and has the potential to increase the likelihood of success in other settings.

Our findings are consistent with other clinical studies suggesting that COCPR is associated with at least equivalent outcomes compared with conventional bystander CPR.[6,11,12,21,26,28-30] Two relevant clinical investigations have been conducted in Japan,[21,26] but these differ from our approach in that COCPR was never taught to the Japanese public. Cultural issues led to a significant number of Japanese bystanders performing chest compressions without rescue breathing despite the absence of specific COCPR training. In a comparison of outcomes between the conventional and "cardiac-only" CPR cohorts, Iwami et al[26] found no statistically significant difference in survival between the cardiac-only and the conventional CPR groups. However, in the similar SOS-KANTO study with 4068 witnessed cardiac arrests, a higher proportion survived with good neurologic outcome after cardiac-only CPR compared with conventional CPR (adjusted OR, 2.2; 95% CI, 1.2-4.2).[21]

The 3 studies that randomized dispatcher-assisted CPR telephone instructions to teach either conventional or compression-only techniques showed a statistically nonsignificant increase in survival to hospital discharge for COCPR (10.4% vs 14.6%, $P=.18$[6]; 12.3% vs 15.5%, $P=.09$[28]; and 14.8% vs

19.1%, $P=.16$[29]). In the largest of these studies, there was a statistically significant increase in neurologically intact survival (18.9% vs 13.5%, $P=.03$).[28] In our study, there also was a significant difference between good neurologic status (CPC score of 1 or 2) in the COCPR group (62/814; 7.6%; 95% CI, 5.8%-9.4%) compared with the conventional CPR group (34/651; 5.2%; 95% CI, 3.5%-6.9%) ($P<.001$).

However, all 3 of the randomized trials[6,28,29] evaluated dispatcher-assisted CPR and, thus, studied cases of out-of-hospital cardiac arrest in which bystanders did not immediately attempt resuscitation. Cases were excluded from randomization if bystander CPR had been initiated prior to the 911 call. Thus, these studies compared delayed COCPR vs delayed conventional CPR and excluded bystanders trained in CPR—those who would have likely been the most proficient resuscitators.

Minimizing interruptions in chest compressions during resuscitation attempts by EMS personnel also has been associated with significant increases in survival when compared with conventional BLS/ACLS protocols.[11,30] Thus, it is not surprising that minimizing interruptions during bystander care would also be associated with improved outcomes.

There are multiple reasons COCPR might have advantages over conventional CPR techniques. These include the rapid deterioration of forward blood flow that occurs during even brief disruptions of chest compressions,[8,31] the long ramp-up time to return to adequate blood flow after resuming chest compressions,[8,31] the reduction of cardiac venous return with the use of positive pressure ventilation,[32] the complexity of conventional CPR,[21,33] the significant time required to perform the breaths,[28,33,34] the critical importance of cerebral and coronary circulation during arrest,[8,31,35,36] the reduced time required for emergency medical dispatchers to instruct a bystander over the telephone how to perform COCPR,[6] and the reluctance to perform mouth-to-mouth ventilation on strangers.[25,26,28,37]

Although our statewide program consistently and carefully advocated for conventional CPR for suspected noncardiac etiology arrests and children, we realize that lay rescuers might perform COCPR on these individuals. To assess this, we examined the incidence and survival of presumed noncardiac etiology arrests by the type of bystander CPR and found a similar and low survival rate regardless of the type of CPR. Also, the total number of pediatric cases of out-of-hospital cardiac arrest was relatively small (297/5272, 5.6%), and importantly, in the group in which rescue breathing would provide the most benefit (children aged <12 years), the proportion who received COCPR was only 10 of 127 children (7.9%).

The limitations of our observational study include that the COCPR intervention was not tested in a randomized controlled trial. However, because the decision to perform conventional CPR, COCPR, or no CPR was at the discretion of the bystanders, it would be impossible to randomize this intervention. We believe a large statewide prospective, observational design was the best methodology to evaluate this important issue. It is possible the outcome differences we found were associated with unknown confounders rather than the type of bystander CPR. We attempted to minimize this by prospectively collecting data known to affect outcomes. In addition, our a priori hypotheses supported by the results were biologically plausible based on multiple animal studies.[8,9,31]

There is also a risk of ascertainment bias in documenting the type of bystander CPR. EMS personnel who classified the type of bystander CPR may have misclassified COCPR vs conventional CPR. We attempted to prospectively mitigate the potential for ascertainment bias by intentionally and specifically training EMS personnel on how to document the presence and type of bystander CPR. The finding that lay bystanders performed COCPR 53.8% of the time overall compared with medical professional bystanders (7.8%) argues against a systematic bias in the documentation of CPR type. It is unlikely EMS personnel would misclassify type of CPR by lay bystanders differently than that by health care professionals.

CONCLUSION

Implementation of a 5-year, multifaceted, statewide public education campaign that officially endorsed and encouraged chest compression–only CPR was associated with a significant increase in the rate of bystander CPR for adults who experienced out-of-hospital cardiac arrest. Furthermore, chest compression–only CPR was independently associated with an increased rate of survival compared with no bystander CPR or conventional CPR.

Author Contributions: Dr Bobrow had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Bobrow, Spaite, Berg, Sanders, Kern, Vadeboncoeur, Clark, Mullins, Humble, Ewy.
Acquisition of data: Bobrow, Clark, Gallagher, Ewy.
Analysis and interpretation of data: Bobrow, Spaite, Berg, Stolz, Sanders, Kern, Vadeboncoeur, Stapczynski, LoVecchio, Ewy.
Drafting of the manuscript: Bobrow, Stolz, Sanders, Kern, Vadeboncoeur, Clark, Ewy.
Critical revision of the manuscript for important intellectual content: Bobrow, Spaite, Berg, Stolz, Sanders, Kern, Vadeboncoeur, Gallagher, Stapczynski, LoVecchio, Mullins, Humble, Ewy.
Statistical analysis: Bobrow, Stolz, Vadeboncoeur.
Administrative, technical, or material support: Sanders, Vadeboncoeur, Clark, Ewy.
Study supervision: Bobrow, Berg, Stapczynski, Ewy.
Financial Disclosures: Drs Bobrow, Ewy, and Spaite reported that the University of Arizona has received support from the Medtronic Foundation involving community-based translation of resuscitation science. Dr Bobrow reported being a member of the American Heart Association Basic Life Support Committee and in the past having received a grant from the American Heart Association to study ultrabrief CPR video training. No other disclosures were reported.
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Gasping Should Not Distract from Recognizing Patient in Cardiac Arrest

- EMD recordings of 445 witnessed cardiac arrests
- Non-witnessed arrest: 16% gasping
- Witnessed arrest: 55% gasping ($p < 0.001$)

Clark et al. *Ann Emerg Med* 1992;21:1464

Incidence and significance of gasping or agonal respirations in cardiac arrest patients

Mickey S. Eisenberg

Purpose of review

This review examines the clinical significance of agonal respirations associated with cardiac arrest.

Recent findings

Observational data indicate that agonal respirations are frequent (55% of witnessed cardiac arrests and probably higher) and that they are associated with successful resuscitation. They also are found more commonly in ventricular fibrillation compared with other rhythms. Agonal respirations pose the greatest challenge to bystanders at the scene and to emergency dispatchers. Bystanders are often lulled into thinking the person is still breathing thus identification of cardiac arrest may be missed by the dispatcher. In a study from King County, Washington, cardiopulmonary resuscitation instructions were not provided by emergency dispatchers in 20% of cardiac arrest cases because the caller reported signs of life – typically abnormal breathing.

Summary

Agonal respirations occur frequently in cardiac arrest. Emergency dispatchers and the general public must be more aware of their presence and significance.

Keywords

agonal respiration, cardiac arrest, cardiopulmonary resuscitation, dispatcher, heart arrest

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Abbreviation

CPR cardiopulmonary resuscitation

1070-5295

Introduction

Agonal respirations are an important sign associated with cardiac arrest, yet they are difficult to define and difficult to study. They are commonly seen in sudden cardiac arrest yet they are often falsely perceived as a sign of life. They are strongly associated with successful resuscitation yet they pose the greatest challenge to lay rescuers and emergency dispatchers [1••]. This review will describe the complex, contradictory, and sometimes confusing issues circulating about agonal respirations.

Definition

The term agonal refers to something occurring at the time of death. Thus agonal respirations are those at the time of or shortly before death. Laypersons probably associate the term with 'death rattle', presumably caused by partially occluded airways from secretions or mucus. When laypersons are asked by emergency dispatchers to describe what they see or hear when reporting cardiac arrest, they use terms such as barely or occasionally breathing, problem or irregular breathing, heavy or labored breathing, sighing, noisy, gurgling, moaning, groaning, or snorting [2,3]. To clinicians, agonal respirations are characterized as being on a continuum from slow, shallow respirations seen in respiratory demise to ineffective, gasping respirations seen in sudden cardiac arrest. I will confine this discussion to agonal respirations associated with sudden cardiac arrest.

The physiology of agonal respirations

Agonal respirations are difficult to study in humans given the need for other therapeutic interventions during cardiac arrest. Animal experiments [4] suggest distinct patterns of abnormal respirations localized to specific levels in the brainstem. Depending upon the level of malfunction, breathing may become apneustic, gasping, or ataxic [5]. It is doubtful that there is a stereotypic pattern in all patients given the dynamic state of brain oxygenation in the period immediately before and shortly after cardiac arrest. Clearly, during cardiac arrest the brain and brain stem are deprived of forward blood flow and thus oxygen and glucose. The pattern and duration of agonal respiration may likely vary depending on whether the arrest is truly sudden (such as with ventricular fibrillation) or more gradual (such as with certain arrhythmias or during cardiogenic shock). It is unclear whether or to what extent agonal respirations result in air exchange. It is possible that some types of agonal breathing lead to minimal

respiratory function while other types may be totally ineffective.

The incidence and duration of agonal respirations

The emergency medical service system in King County, Washington studied agonal respirations [2]. The researchers listened to recordings of every cardiac arrest call to emergency dispatch centers. Of 445 calls reporting cardiac arrest, agonal respirations occurred in 196 (40%). For witnessed cardiac arrest agonal respirations occurred in 55% compared with 16% of unwitnessed arrests. The identification of agonal breathing came from the callers' descriptions (and actually hearing agonal sound in some recordings). There was, of course, no independent observer at the scene. Thus the true incidence of agonal respirations is likely higher than reported since a knowledgeable observer would likely have recognized additional cases of agonal respirations. The authors also had the opportunity to compare agonal respirations with the rhythm associated with cardiac arrest. Of the patients in ventricular fibrillation, 56% had agonal respirations compared with 34% of patients without ventricular fibrillation. The duration of agonal respirations was estimated by determining the number of times emergency personnel noted agonal activity when they arrived. Of the 196 cases with agonal respiration described by the caller, continued agonal activity was noted upon arrival of emergency medical service personnel in 60 cases. The median response time for these cardiac arrests was 4 min. Thus it may be estimated that agonal respirations last approximately 4 min in at least one-third of cases.

The significance of agonal respirations

The study from King County found a very strong association of agonal respirations with survival. Twenty-seven percent of patients with agonal respirations were discharged alive compared with 9% of patients without agonals. Among discharged patients, 68% had agonal respirations.

The conundrum of agonal respirations

The data indicate that agonal respirations are frequent (55% of witnessed cardiac arrests and probably higher) and that they are associated with survival. They are also found more commonly in ventricular fibrillation compared with other rhythms. Witnessed cases of ventricular fibrillation are the type of cardiac arrests with the very best survival likelihood. In some communities this survival is as high as 40% [6]. Yet, agonal respirations pose the greatest challenge to bystanders at the scene and to emergency dispatchers. Bystanders are often lulled into thinking the person is still breathing, thus identification of cardiac arrest may be missed by the dispatcher. In another study from King County, cardiopulmonary resuscitation (CPR) instructions were not provided by emergency dispatchers in 20% of cardiac arrest cases because the caller reported signs of life – typically abnormal breathing [7]. Similar findings were reported in Goteborg, Sweden [3]. Because of this finding, dispatchers are trained to specifically ask all callers 'Is the person conscious?' If the answer is no or there is uncertainty, the dispatcher asks, 'Is the person breathing normally?' Dispatchers in King County, Washington are specially trained in the incidence and significance of agonal respiration and they understand the significance of the word normally. If there is doubt, the dispatcher will ask the caller to move the phone by the patient or will probe with questions such as 'Does the chest rise?' Many communities do not have dispatchers asking the question 'Is the patient breathing normally?' for possible cardiac arrest cases. It is possible that in these communities many cases of cardiac arrest are missed. It is ironic since cardiac arrests with agonal respiration have the highest likelihood of survival and are the cases in which bystander CPR may be crucial to a good outcome.

What is to be done?

There is currently much controversy over when and whether CPR should precede defibrillation. Some investigators recommend a defined period (such as 2 or 3 min) of CPR prior to defibrillation [8,9]. Others have found no benefit with this strategy [10]. It may be that in some instances immediate defibrillation may be the best strategy and in other instances a period of CPR may be useful. For example, perhaps in witnessed cardiac arrests immediate defibrillation is the best option but for unwitnessed cardiac arrest CPR may be needed to fill the left ventricle and provide oxygenated blood for the coronary arteries. Determining whether the collapse is witnessed is sometimes problematic. The presence of agonal respirations as reported by the caller, however, may be a surrogate for witnessed collapse. Such a finding may suggest the order of resuscitation interventions.

Whether the presence of agonal respirations should prompt certain interventions remains to be seen. For the moment it seems prudent that all emergency dispatch agencies have special training in the recognition and significance of agonal respirations. It also seems prudent to emphasize agonal respirations during CPR training of the general public.

Conclusion

Agonal respirations occur frequently in cardiac arrest and they are highly correlated with ventricular fibrillation and survival. Emergency dispatchers and the general public must be more aware of their presence and significance.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 279).

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The priority is quality compressions

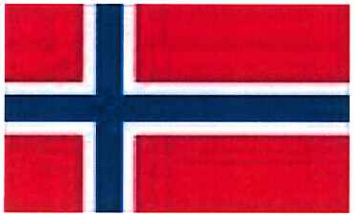
Intravenous Drug Administration During Out-of-Hospital Cardiac Arrest
A Randomized Trial

Theresa M. Olasveengen, MD
Kjetil Sunde, MD, PhD
Cathrine Brunborg, MSc
Jon Thowsen
Petter A. Steen, MD, PhD
Lars Wik, MD, PhD

Context Intravenous access and drug administration are included in advanced cardiac life support (ACLS) guidelines despite a lack of evidence for improved outcomes. Epinephrine was an independent predictor of poor outcome in a large epidemiological study, possibly due to toxicity of the drug or cardiopulmonary resuscitation (CPR) interruptions secondary to establishing an intravenous line and drug administration.

Objective To determine whether removing intravenous drug administration from an ACLS protocol would improve survival to hospital discharge after out-of-hospital cardiac arrest.

2009



Randomized trial of EPINEPHrine versus no EPINEPHrine For EMS treated cardiac arrest → NO BENEFIT IN SURVIVAL TO DISCHARGE FROM HOSPITAL!

Intravenous Drug Administration During Out-of-Hospital Cardiac Arrest

A Randomized Trial

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Context Intravenous access and drug administration are included in advanced cardiac life support (ACLS) guidelines despite a lack of evidence for improved outcomes. Epinephrine was an independent predictor of poor outcome in a large epidemiological study, possibly due to toxicity of the drug or cardiopulmonary resuscitation (CPR) interruptions secondary to establishing an intravenous line and drug administration.

Objective To determine whether removing intravenous drug administration from an ACLS protocol would improve survival to hospital discharge after out-of-hospital cardiac arrest.

Design, Setting, and Patients Prospective, randomized controlled trial of consecutive adult patients with out-of-hospital nontraumatic cardiac arrest treated within the emergency medical service system in Oslo, Norway, between May 1, 2003, and April 28, 2008.

Interventions Advanced cardiac life support with intravenous drug administration or ACLS without access to intravenous drug administration.

Main Outcome Measures The primary outcome was survival to hospital discharge. The secondary outcomes were 1-year survival, survival with favorable neurological outcome, hospital admission with return of spontaneous circulation, and quality of CPR (chest compression rate, pauses, and ventilation rate).

Results Of 1183 patients for whom resuscitation was attempted, 851 were included; 418 patients were in the ACLS with intravenous drug administration group and 433 were in the ACLS with no access to intravenous drug administration group. The rate of survival to hospital discharge was 10.5% for the intravenous drug administration group and 9.2% for the no intravenous drug administration group ($P=.61$), 32% vs 21%, respectively, ($P<.001$) for hospital admission with return of spontaneous circulation, 9.8% vs 8.1% ($P=.45$) for survival with favorable neurological outcome, and 10% vs 8% ($P=.53$) for survival at 1 year. The quality of CPR was comparable and within guideline recommendations for both groups. After adjustment for ventricular fibrillation, response interval, witnessed arrest, or arrest in a public location, there was no significant difference in survival to hospital discharge for the intravenous group vs the no intravenous group (adjusted odds ratio, 1.15; 95% confidence interval, 0.69-1.91).

Conclusion Compared with patients who received ACLS without intravenous drug administration following out-of-hospital cardiac arrest, patients with intravenous access and drug administration had higher rates of short-term survival with no statistically significant improvement in survival to hospital discharge, quality of CPR, or long-term survival.

Trial Registration clinicaltrials.gov Identifier: NCT00121524

JAMA. 2009;302(20):2222-2229 www.jama.com

INTRAVENOUS ACCESS AND DRUG ADministration are integral parts of cardiopulmonary resuscitation (CPR) guidelines.[1] Millions of patients have received epinephrine during advanced cardiac life support (ACLS) with little or no evidence of improved survival to hospital discharge.[1,2] The use of epinephrine is based on preclinical evidence of increased cerebral and coronary perfusion by redirected peripheral blood flow.[1,2] Beneficial short-term effects of epinephrine have been shown in animal studies,[3-5] but there is increasing concern for increased myocardial dysfunction[6,7] and disturbed cerebral microcirculation after cardiac arrest.[8] Epinephrine was an independent predictor of poor outcome in a large retrospective registry study,[9] but this observational, nonrandomized study cannot prove a causal relationship. Despite its near-universal use, epinephrine has, to our knowledge, not been tested in a randomized controlled study with a no-drug comparison group.

If a negative association between epinephrine and survival is causal, it may be due to the drug or to inadequate CPR quality associated with drug adminis-

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tration. Drug administration includes time-consuming factors like establishing intravenous access, preparation, and administration of drugs and saline, thereby potentially removing focus from good-quality CPR. There are recent reports of poor-quality CPR and protocol adherence among professional CPR providers,[10,11] and some consider intubation and intravenous access more important than giving good-quality chest compressions.[12] With inadequate CPR quality, effects of drugs administered peripherally also may be diminished or absent.[13] Because there are no randomized controlled studies showing improved survival to hospital discharge with any drugs routinely administered during CPR, we concluded such a study was warranted.

In this prospective, randomized controlled trial of intravenous drug administration during out-of-hospital cardiac arrest, we compared outcomes for patients receiving standard ACLS with intravenous drug administration (control) and patients receiving ACLS without intravenous drug administration (intervention).

METHODS

The city of Oslo has a single-tiered emergency medical service system administered by the Oslo University Hospital for a population of 540 000. On weekdays between 7:30 AM and 10:00 PM, an ambulance staffed by 2 paramedics and an anesthesiologist functions on the same level as the regular paramedic-staffed ambulances. Until January 2006, ACLS was performed according to the International Guidelines 2000,[14] with the modification that patients with ventricular fibrillation received 3 minutes of CPR before the first shock and between unsuccessful series of shocks.[15] The European Resuscitation Council Guidelines for Resuscitation 2005[16] were implemented in January 2006, incorporating this same modification of 3-minute periods of CPR. Defibrillators in manual mode are used and endotracheal intubation is standard for securing the airways. Two ambulances are routinely dispatched for suspected cardiac arrest. The physician-staffed ambulance is dispatched whenever available.

All hospitals in Oslo have goal-directed postresuscitation protocols including therapeutic hypothermia regardless of initial rhythm or arrest etiology.[17] A prehospital 12-lead electrocardiogram is routinely transmitted to the cardiologist on call after return of spontaneous circulation (ROSC). If coronary angiography is indicated for possible percutaneous coronary intervention, patients are transported directly from the scene to 1 of 2 university hospitals (Oslo University Hospital, Ullevaal and Rikshopitalet) with this capacity 24 hours per day.

Study Design and Recruitment

All patients older than 18 years with nontraumatic, out-of-hospital cardiac arrests between May 1, 2003, and April 28, 2008, were randomized by ambulance personnel on-site. Simple randomization occurred directly after ambulance personnel confirmed the cardiac arrest and then opened the sealed envelopes provided by the investigators. Patients were randomized to receive either ACLS with access to intravenous drug administration (intravenous group) or ACLS without access to intravenous drug administration (no intravenous group). In the no intravenous group, intravenous access was to be established 5 minutes after ROSC, and drugs could then be given if indicated.

Exclusion criteria were (1) cardiac arrest witnessed by ambulance crew because these patients almost always have an intravenous needle in place at the time of the cardiac arrest, (2) resuscitation initiated or interrupted by physicians outside of the ambulance team, or (3) cardiac arrest induced by asthma or anaphylactic shock (which were the last criteria added in October 2006). The study was approved by the regional ethics committee. Informed consent for inclusion was waived as decided by this committee, but was required from survivors with 1-year follow-up.

Equipment and Data Collection

Standard defibrillators (LIFEPAK 12 Physio-Control, Medtronic, Redmond, Washington) were used. Electrocardiograms with transthoracic impedance signals from these defibrillators were routinely transferred to a server at the National Competence Center for Emergency Medicine (Oslo, Norway) following cardiac arrest. Utstein cardiac arrest forms[18] routinely completed by paramedics were submitted to the study supervisor along with a copy of the ambulance run sheet. Automated, computer-based dispatch center time records supplemented ambulance run sheets with regard to response intervals. For admitted patients, additional hospital records were obtained.

All trial data were documented according to the Utstein style.[18] The primary end point was survival to hospital discharge. Secondary outcomes were 1-year survival, survival with favorable neurological outcome (using cerebral performance categories from 1 to 4),[18] hospital admission with ROSC, and quality of CPR (ie, chest compression rate, pauses, and ventilation rate). The study was monitored annually with interim analysis by an external researcher who did not reveal any results to the investigators.

Data Processing

Data from each case were viewed and annotated using CODE-STAT 7.0 (Physio-Control, Medtronic) for detection of ventilations and chest compressions by changes in transthoracic impedance. Written information from patient report forms and locally adapted Utstein style forms were compared with typical changes in CPR patterns as shown using CODE-STAT 7.0. Initial rhythm assessment registered on patient report forms were confirmed by these electrocardiographic recordings if possible. Time without spontaneous circulation, time without compressions during time without spontaneous circulation (hands-off time), preshock pauses, compression rate and actual number of compressions, and ventilations per minute were calcu-

lated for each episode. Hands-off ratio is defined as hands-off time divided by total time without ROSC. Electrocardiographic analysis was performed by 1 researcher (T.M.O.).

Statistical Analysis

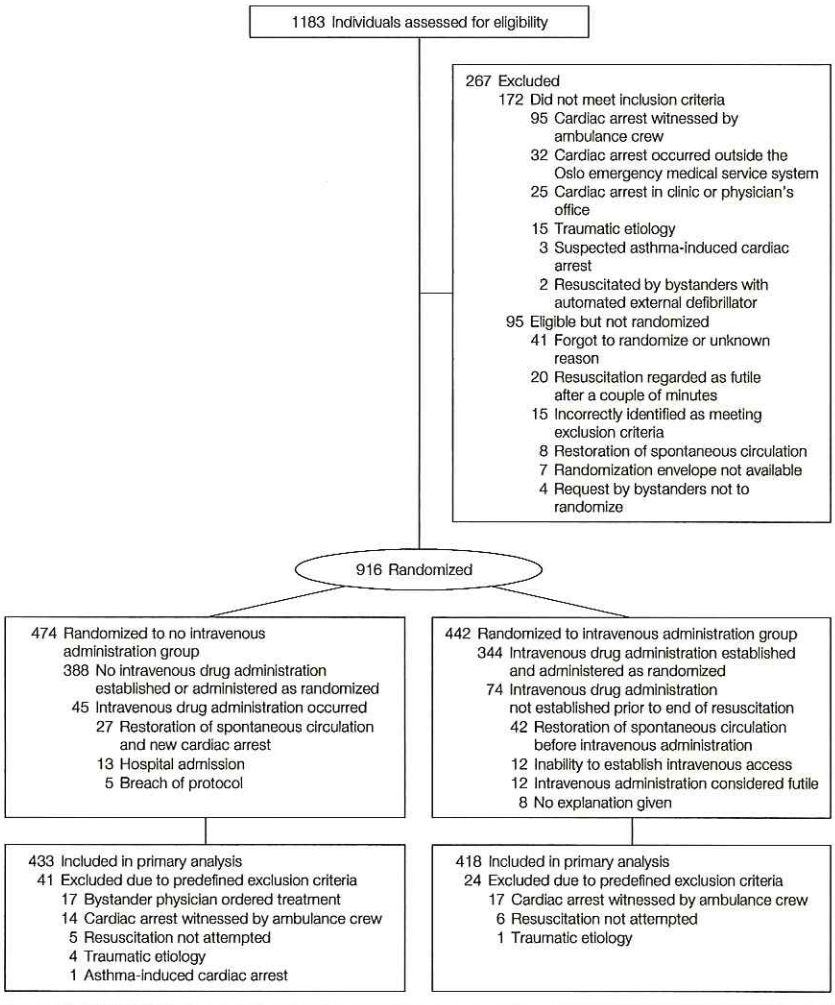
Initial power analysis was based on survival statistics for the Oslo emergency medical service system and assumed that the survival rate would be doubled among patients not receiving epinephrine, as described previously in an observational study.[9] With a projected survival rate of 7% in the intravenous group and 14% in the no intravenous group, 900 patients provided a power level of 91.4% with a type I error of 5%.[19]

Analysis was performed on an intention-to-treat basis regardless of which treatment was actually given. Patients who were initially randomized, but were later found to meet predefined exclusion criteria were not included in the intention-to-treat analysis. Demographic and clinical data are presented as means with 95% confidence intervals (CIs), medians with ranges, or proportions. Crude effects between the 2 trial groups and survival were quantified by odds ratios (ORs) with 95% CIs. The χ^2 test for contingency tables with different degrees of freedom was used to detect associations between categorical independent variables. For continuous variables, the *t* test was used for normally distributed data and the Mann-Whitney test was used for nonnormally distributed data.

Confounders were identified and quantified by using the Mantel-Haenszel test for both short-term and long-term survival, and subsequent manual backward-elimination procedures were performed. Correlations between potential confounders were investigated. Comparison of Kaplan-Meier survival curves was obtained using the Breslow and log-rank test statistics for short-term and long-term survival, respectively.[20,21]

Two-sided *P* values of less than .05 were considered significant. The statistical analyses were performed using the software packages SPSS version 15.0 and SamplePower version 2.0 (SPSS Inc, Chicago, Illinois) and Egret version 2.0.31 (Cytel Software Corporation, Cambridge, Massachusetts).

Figure 1. Randomization Profile



RESULTS

Resuscitation was attempted in 1183 patients who experienced cardiac arrest during the study period, and 851 of 946 eligible patients were successfully randomized with 418 patients in the intravenous group and 433 patients in the no intravenous access group. For reasons listed in FIGURE 1, 95 eligible patients were not randomized and further randomization and inclusion details are illustrated. Eligible, nonrandomized patients did not differ significantly from randomized patients with regard to demographic characteristics and outcomes.

Baseline demographic characteristics and CPR-quality parameters are listed in TABLE 1. Defibrillation was attempted in more patients in the intravenous group compared with the no intravenous group (47% vs 37%, respectively; OR, 1.16 [95% CI, 0.74-1.82]). More defibrillation shocks were delivered to those who received defibrillation in the intravenous group compared with the no intravenous group

(median, 3 [range, 1-22] vs 2 [range, 1-26], respectively; $P=.008$). Both groups had adequate and similar CPR quality with few chest compression pauses (median hands-off ratio, 0.15 for the intravenous group and 0.14 for the no intravenous group) and the compression and ventilation rates were within the guideline recommendations (Table 1).

In the intravenous group, 44 of 418 patients (10.5%) survived to hospital discharge vs 40 of 433 (9.2%) in the no intravenous group (OR, 1.16; 95% CI, 0.74-1.82; $P=.61$). Survival with favorable neurological outcome was 9.8% for the intravenous group and 8.1% for the no intravenous group (OR, 1.24; 95% CI, 0.77-1.98; $P=.45$). Short-term survival was significantly better in the intravenous group than in the no intravenous group with 40% vs 25%, respectively, achieving ROSC (OR, 1.99; 95% CI, 1.48-2.67; $P<.001$), 43% vs 29% admitted to the hospital (OR, 1.81; 95% CI, 1.36-2.40; $P<.001$), and 30% vs 20% admitted to the intensive care unit (ICU) (OR, 1.67; 95% CI, 1.22-2.29; $P=.002$) (TABLE 2). In-hospital treatments, including therapeutic hypothermia and percutaneous coronary intervention, were equally distributed between the 2 groups. There were no differences in cause of death among patients admitted to the ICU and most deaths were due to brain damage (Table 2).

Patients were divided into 2 predefined subgroups based on their initial rhythms (TABLE 3). In patients with an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia, there were no differences in short-term or long-term outcomes. In the subgroup with nonshockable rhythms (initial rhythm of asystole or pulseless electrical activity), the ROSC rate was 3-fold higher with intravenous treatment ($P<.001$), but there was no difference in long-term outcome because the survival rate among those admitted to the ICU tended to be almost 3 times higher in the no intravenous group ($P=.07$; Table 3).

A public cardiac arrest location, response interval, and initial ventricular fibrillation were identified as potential confounders and were included in the logistic regression analysis. Multivariate logistic regression analyses for short-term survival (admitted to the ICU) and long-term survival (discharged from the hospital) were performed. After adjustment for confounders, patients in the intravenous group had a nonsignificant 15% increased chance of surviving to hospital discharge (adjusted OR [AOR], 1.15; 95% CI, 0.69-1.91) compared with patients in the no intravenous group. Patients with ventricular fibrillation or pulseless ventricular tachycardia as the initial rhythm had a 10-fold improvement in long-term survival (AOR, 10.47; 95% CI, 5.47-20.03). Patients with bystander-witnessed cardiac arrests or cardiac arrests in public places had a 2-fold improvement in long-term survival (AOR, 2.13 [95% CI, 1.02-4.45] and AOR, 2.03 [95% CI, 1.19-3.44], respectively), whereas the odds of long-term survival decreased by

Table 1. Demographics and Quality of Cardiopulmonary Resuscitation (CPR)[a]

	No Intravenous (n = 433)	Intravenous (n = 418)	*P* Value[b]
Age, mean (SD), y	64 (17)	64 (18)	.85
Male sex, No. (%)	303 (70)	302 (72)	.51
Cardiac etiology, No. (%)	305 (70)	300 (72)	.72
Location of arrest, No. (%)			
Home	238 (55)	237 (57)	.72
Public	159 (37)	144 (34)	.50
Other	34 (8)	37 (9)	.70
Bystander witnessed, No. (%)	273 (63)	283 (68)	.18
Bystander basic life support, No. (%)	274 (63)	261 (62)	.86
Initial rhythm, No. (%)			
Ventricular fibrillation or pulseless ventricular tachycardia	142 (33)	144 (34)	.66
Asystole	228 (53)	192 (46)	.06
Pulseless electrical activity	63 (15)	82 (20)	.06
Physician-staffed ambulance present	160 (37)	157 (38)	.91
Response interval, mean (95% CI), min	10 (9-10)	10 (9-10)	.28
Intubation, No. (%)	363 (84)	368 (88)	.10
Intravenous drugs during resuscitation, No. (%)	42 (10)	343 (82)	<.001
Epinephrine	37 (9)	330 (79)	<.001
Atropine	20 (5)	194 (46)	<.001
Amiodarone	17 (4)	69 (17)	<.001
Defibrillation	160 (37)	194 (46)	.005
No. of shocks when defibrillated, median (range)	2 (1-22)	3 (1-26)	.008
Electrocardiogram available for analysis, No. (%)	329 (76)	314 (75)	.83
CPR duration, mean (95% CI), min	18 (17-19)	22 (20-23)	<.001
Hands-off ratio, median (range)[c]	0.14 (0.01-0.59)	0.15 (0.02-0.89)	.16
Compression rate, mean (95% CI)[d]	116 (115-117)	117 (116-119)	.12
Compressions, mean (95% CI), min^{-1}[e]	94 (93-96)	94 (92-96)	.90
Ventilations, mean (95% CI), min^{-1}[e]	11 (10-11)	11 (11-11)	.48
Preshock pause, median (range), s	11 (1-74)	12 (1-82)	.58

Abbreviation: CI, confidence interval.
[a] Data are missing for 80 patients in the group with advanced cardiac life support without intravenous access or administration (no intravenous) and 79 patients in the group with advanced cardiac life support and intravenous access and administration of drugs (intravenous).
[b] The differences between groups were analyzed using the χ^2 test with continuity correction for categorical data and the *t* test or Mann-Whitney test for continuous data as appropriate.
[c] Indicates the proportion of time without chest compressions during the resuscitation effort.
[d] Indicates the rate of compressions when delivered.
[e] Indicates the average number of compressions actually given per minute during the resuscitation effort.

17% for each minute of prolonged response interval (AOR, 0.83; 95% CI, 0.77-0.90). When adjusted for the same confounding factors, survival to ICU admission was higher for patients in the intravenous group (AOR, 1.78; 95% CI, 1.26-2.51).

The cumulative postcardiac arrest survival rate at 7 days was 14.6% (95% CI, 11.3%-17.9%) for patients in the intravenous group vs 12.8% (95% CI, 9.7%-15.9%) for patients in the no intravenous group, 11.3% (95% CI, 8.4%-14.2%) vs 8.8% (95% CI, 6.1%-11.5%), respectively, at 1 month, and 9.8% (95% CI, 6.9%-12.7%) vs 8.4% (95% CI, 5.9%-10.9%) at 1 year (FIGURE 2). Short-term survival was significantly higher for patients in the intravenous group compared with patients in the no intravenous group (Breslow $P=.004$), although there was no difference in long-term survival (log-rank $P=.23$)

COMMENT

Our results represent the first attempt, to our knowledge, to evaluate the effect of intravenous access and intravenous drug administration on outcome in patients with an out-of-hospital cardiac arrest. Short-term survival was higher in the intravenous group, but these nearly universally applied interventions were not associated with a statistically significant improvement in survival to hospital discharge.

Administration of intravenous drugs did not appear to interfere with the quality of CPR. Ambulance personnel delivered good-quality CPR with few pauses and with rates within guideline recommendations[1] in both groups. This is important because potential improvements in intravenous medication administration during ACLS will not need to overcome an intrinsic tendency to degrade CPR.

We did not confirm the previous observational finding that intravenous epinephrine was an independent predictor for poor outcome.[9] Our results are consistent with a multicenter study by Stiell et al[22] that found no difference in survival after implementing intravenous drug administration during out-of-hospital cardiac arrest (OR, 1.1; 95% CI, 0.8-1.5).

Without differences in the predefined primary outcome, patients in the intravenous group received more defibrillations, were resuscitated for a longer period, and more frequently had ROSC. With similar and adequate CPR quality, this is likely due to the pharmacological effects of the drugs used (epinephrine, atropine, and/or amiodarone). This finding is consistent with previous animal studies with epinephrine,[6,7] and clinical studies evaluating the effects of amiodarone,[23] atropine,[24] and even high-dose epinephrine,[25] all of which documented improved short-term effects without improving long-term outcomes. While epinephrine can produce more spontaneously beating hearts in animal models, it is also associated with increased postresuscitation myocardial dysfunction that might partly explain these clinical observations.[6,7] Negative postresuscitation effects of epinephrine also are reported to be more prominent after longer, more clinically relevant cardiac arrest periods (eg, 4-6 minutes) than short cardiac arrest periods (eg, 2 minutes).[7] Moreover, an experimental study has recently documented detrimental effects of epinephrine on cerebral microcirculation.[8]

The clinical implications of an increased ROSC rate in the intravenous group are difficult to interpret. Should improved short-term outcome be regarded as unfulfilled potential that

Table 2. In-Hospital Treatment and Outcome

	No Intravenous (n = 433)	Intravenous (n = 418)	*P* Value[a]
Any ROSC during resuscitation	107 (25)	165 (40)	<.001
Admitted to hospital	126 (29)	178 (43)	<.001
ROSC	89 (21)	133 (32)	<.001
Ongoing CPR	37 (9)	45 (11)	.33
Admitted to ICU[b]	88 (20)	125 (30)	.002
Awake at ICU admission	8 (9)	7 (6)	.48
Therapeutic hypothermia	62 (70)	90 (72)	.93
Angiography or PCI	43 (49)	50 (40)	.33
Time in ICU, median (range), d[c]	6 (1-31)	4 (1-44)	.05
Cause of death in ICU[d]			
Brain	29 (69)	52 (70)	>.99
Cardiac	8 (19)	12 (16)	.90
Multiorgan failure	5 (12)	10 (14)	>.99
Discharged alive	40 (9.2)	44 (10.5)	.61
Cerebral performance score at discharge			
1 (good cerebral performance)	30 (7.0)	37 (8.9)	.31
1-2 (good cerebral performance to moderate cerebral disability)	35 (8.1)	41 (9.8)	.45
2 (moderate cerebral disability)	5 (1.2)	4 (1.0)	>.99
3 (severe cerebral disability)	3 (1.0)	3 (1.0)	>.99
4 (coma or vegetative state)	2 (<1.0)	0	.50
Discharged from hospital if admitted to ICU	40 (45)	44 (35)	.17
Alive 1 y after cardiac arrest[e]	36 (8)	41 (10)	.53

Abbreviations: CPR, cardiopulmonary resuscitation; ICU, intensive care unit; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation.

[a] The differences between groups were analyzed using the χ^2 test with continuity correction for categorical data and the Mann-Whitney test for number of days in the ICU.

[b] Includes patients admitted to the ICU only.

[c] Data are missing for 3 patients in each group.

[d] Includes patients who died in the ICU only. Data are missing for 6, leaving 42 as the denominator in the group with advanced life support without intravenous accss or drug administration (no intravenous), and 7, leaving 74 as the denominator in the group with advanced cardiac life support and intravenous access and administration of drugs (intravenous).

[e] Two patients in the no intravenous group and 1 patient in the intravenous group were lost to 1-year follow-up.

Table 3. Outcome for Subgroups With and Without Ventricular Fibrillation or Pulseless Ventricular Tachycardia Rhythms

	With Rhythms, No. (%)			Without Rhythms		
	No Intravenous (n = 142)	Intravenous (n = 144)	*P* Value[a]	No Intravenous (n = 291)	Intravenous (n = 274)	*P* Value[a]
Any ROSC during resuscitation	75 (53)	85 (59)	.35	32 (11)	80 (29)	<.001
Admitted to hospital	79 (56)	94 (65)	.12	47 (16)	84 (31)	<.001
Admitted to ICU	60 (42)	74 (51)	.15	28 (10)	51 (19)	.003
Discharged alive	32 (23)	39 (27)	.45	8 (3)	5 (2)	.65
Discharged with CPC score of 1-2	29 (20)	37 (26)	.36	6 (2)	4 (2)	.82
Discharged if admitted to ICU	32 (53)	39 (53)	>.99	8 (29)	5 (10)	.07

Abbreviations: CPC, cerebral performance score; ICU, intensive care unit; ROSC, return of spontaneous circulation.
[a]The differences between the groups were analyzed using the χ^2 test with continuity correction.

might be addressed with better post-ROSC care, or unproductive resuscitation of patients whose vital organ injury makes them unlikely candidates for long-term survival? In the present study, most patients who died in the hospital after initial successful resuscitation in both groups had severe cerebral damage. If present pharmacological interventions only facilitate cardiac resuscitation in patients who will ultimately experience irreversible cerebral damage, this may cause an additional burden on already overburdened ICUs.

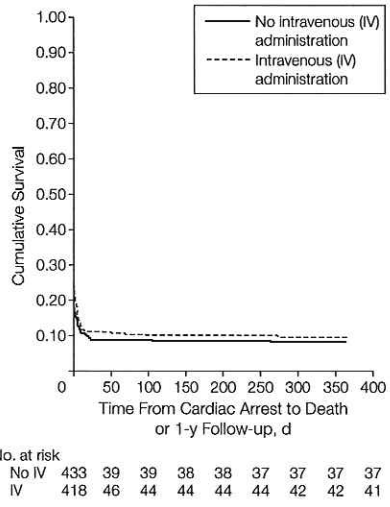
However, long-term survival cannot be achieved without first restoring circulation. Improved brain-directed postresuscitation treatment might at some point prevent irreversible cerebral damage and increase survival. At present, the only established brain-directed treatment is therapeutic hypothermia,[26,27] and the rate of which was high in both groups (71% and 72%). It is possible that for some patients in our study with early postresuscitation cardiac death, advanced options such as mechanical chest compression devices,[28] extracorporeal membrane oxygenation,[29] or left ventricular assist devices[30] could enable corrective treatment of underlying causes and theoretically improve survival.

The results of our study highlight the question of whether patients presenting with initial shockable rhythms and nonshockable rhythms should be treated differently. Initial shockable rhythm was a potential effect modifier in our statistical analysis, indicating that the degree of benefit or harm of intravenous drug administration during cardiac arrest may depend on the presenting rhythm. No differences in outcome were found for patients with shockable rhythms, while patients with nonshockable rhythms had higher rates of ROSC in the intravenous group, but an opposite tendency toward a lower rate of survival to hospital discharge among those admitted to the hospital. This suggests that late toxicity after intravenous drug administration contributes importantly to the poor outcomes of these patients.

Several studies have identified dissimilar etiologies in subgroups with shockable and nonshockable rhythms,[31-33] and it seems reasonable that differences in treatment strategies will emerge.[34] Retrospective subgroup analysis for cardiac arrest times (<5 minutes, 5-10 minutes, or >10 minutes) did not reveal any suggestive information either alone or combined with initial rhythm (data not presented but available from authors upon request). However, our study was not powered for formal subgroup analysis and no conclusions should be drawn.

The present data indicating good-quality CPR in both groups suggest that the lack of improved long-term outcome with ACLS with intravenous drug administration cannot be explained by poor-quality CPR.[13] This does not exclude the possibility that other drug regimens might improve outcome. Early administration, as recently advocated,[35,36] must be evaluated in systems with shorter ambulance response intervals or other intravenous drug regimens and priorities that are different from the present guidelines.

Figure 2. Cumulative Survival for Up to 1 Year After Cardiac Arrest



Our study has several limitations. First, ambulance personnel could not be blinded to the randomization. Closely related to this, only patients who were randomized to the no intravenous group could be monitored with regard to protocol compliance. If intravenous drugs were administered to a patient in the no intravenous group, violation of the study protocol could be documented. If intravenous drugs were not administered to a patient in the intravenous group, several valid reasons could exist, such as rapid ROSC. We have no reason to believe that personnel refrained from establishing intra-

venous access under the pretense that the procedure was unsuccessful. The ambulance personnel involved were strongly committed to testing the hypothesis presented, but we cannot totally rule out possible bias toward procedures such as intravenous access and administration of drugs, which have been important in Norwegian culture for decades.

Second, quality of CPR could only be assessed in 75% of cases. Still, this is, to our knowledge, the first clinical intervention study reporting CPR quality data, and no significant differences were found between these data and those unavailable for analysis. Also, we do not have reliable time points for drug administration. Paramedics in the Oslo emergency medical service system are highly trained and both the guidelines and training emphasize early intravenous access and drug administration and intubation with the shortest possible pauses in chest compressions.

Third, this is a single center study and the results may not be generalized to systems with different training, infrastructure, treatment protocols, or quality of CPR. Fourth, while time from cardiac arrest to the initiation of ACLS is important for patient survival, the estimated time of cardiac arrest is imprecise and one-third of the cardiac arrests were unwitnessed. This variable is therefore not included in the anlysis. Only the emergency medical service response interval was included.

Finally, a type II error cannot be ruled out. Although based on the best available evidence at the time,[9] the power analysis was, in retrospect, optimistic in assuming a doubling in survival for the patients in the no intravenous group. For the observed difference between the groups to be statistically significant, a sample size of 14 000 patients would be needed. Because this sample size has not been considered inappropriate in cardiovascular interventions, our results could be background for such a large study that could be positive for intravenous access and drug administration. At a minimum, our results indicate that clinical equipoise exists on the efficacy of intravenous drugs in the treatment of cardiac arrest and that more definitive trials could be ethically undertaken. Alternatively, the poor survival rates after cardiac arrest, which do not seem to be significantly improved by intravenous drug administration, indicate that research should be directed at new pharmacological interventions that hold promise of greater effect.

CONCLUSION

Despite improved short-term survival among patients randomized to receive intravenous access and drug administration, these nearly universal interventions were not associated with a statistically significant improvement in survival to hospital discharge. Larger trials examining resuscitation without intravenous access and drug administration, as well as of existing or new drugs, appear to be justified.

Author Contributions: Dr Olasveengen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Thowsen, Steen, Wik.
Acquisition of data: Olasveengen, Thowsen, Wik.
Analysis and interpretation of data: Olasveengen, Sunde, Brunborg, Steen.
Drafting of the manuscript: Olasveengen, Sunde, Steen.
Critical revision of the manuscript for important intellectual content: Brunborg, Thowsen, Wik.
Statistical analysis: Olasveengen, Brunborg.
Obtained funding: Steen.
Administrative, technical, or material support: Thowsen, Wik.
Study supervision: Sunde, Brunborg, Steen, Wik.
Financial Disclosures: Dr Olasveengen reported receiving speakers' fees from Medtronic (Oslo, Norway) and research support from Laerdal Medical Corporation (Stavanger, Norway). Dr Steen reported being a member of the board of directors for Laerdal Medical and the Norwegian Air Ambulance. Dr Wik reported being on a medical advisory board for Physio-Control, consulting for Laerdal, Zoll, and Jolife, and being a principle investigator for a multicenter mechanical chest compression device study sponsored by Zoll. Dr Sunde, Ms Brunborg, and Mr Thowsen did not report any financial disclosures.
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Additional Contributions: Martin Samdal assisted in data collection as required research exposure as a medical student at the University of Oslo and did not receive any financial compensation for his work. Andres Neset is enrolled in a combined MD/PhD program at the University of Oslo and assisted with data analysis and did not receive any financial compensation for his work. Morten Pytte, MD, PhD, provided useful feedback in preparing the manuscript and did not receive any financial compensation for his work. Knut Arvid Kirkebøen, MD (University of Oslo), provided useful feedback in preparing the manuscript and did not receive any financial compensation for his work. Norman Paradis, MD (vice president and chief medical officer at Zoll Circulation), provided useful feedback and advice in preparing the manuscript and did not receive any financial compensation for his work. We thank all of the physicians and paramedics working in the Oslo emergency medical service system.

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I have learned throughout my life as a composer chiefly through my mistakes and pursuits of false assumptions, not by my exposure to founts of wisdom and knowledge.

—Igor Stravinsky (1882-1971)

Notes