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Clinical paper

Minimizing pre- and post-shock pauses during the use of an automatic external defibrillator by two different voice prompt protocols. A randomized controlled trial of a bundle of measures☆

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ABSTRACT

Background: Previous large retrospective analyses have found an association between duration of peri-shock pauses in cardiopulmonary resuscitation (CPR) and survival. In a randomized trial, we tested whether shortening these pauses improves survival after out-of-hospital cardiac arrest (OHCA).
Methods: Patients with OHCA between May 2006 and January 2014 with shockable initial rhythm, treated by first responders, were randomized to two automated external defibrillator (AED) treatment protocols. In the control protocol AEDs performed post-shock analysis and prompted rescuers to a pulse check (Guidelines 2000). In the experimental protocol a 15 s period of CPR during and after charging of the AED was added to the voice prompts and CPR was resumed immediately after defibrillation (modification of the Guidelines 2005). Survival was assessed at hospital admission and discharge.
Results: Of 1174 OHCA patients, 456 met the inclusion criteria: 227 were randomly assigned to the experimental protocol and 229 to the control protocol. The experimental group experienced shorter pre-shock pauses (6 [5–11] s vs. 20 [18–23] s; $P < 0.001$), and shorter post-shock pauses (7 [6–9] s vs. 27 [16–34] s; $P < 0.001$). Similar proportions of patients survived to hospital admission (experimental: 62% vs. control: 65%; RR [95%CI] 0.96 [0.83–1.10], $P = 0.51$), and hospital discharge (experimental: 42% vs. control: 38%; RR [95%CI] 1.09 [0.87–1.37], $P = 0.46$).
Conclusion: In patients with OHCA and shockable initial rhythms, treatment with AEDs with the experimental protocol shortened pre-shock and post-shock CPR pauses, and increased overall CPR time, but did not improve survival to hospital admission or discharge.
Clinical trial registration: http://www.isrctn.com unique identifier: ISRCTN72257677.

Introduction

According to the Guidelines 2000 for emergency cardiac care, automated external defibrillators (AEDs) should prompt for pauses in cardiopulmonary resuscitation (CPR) for rhythm analysis, shock delivery and pulse checks similar to procedures for manual defibrillators.[1,2] These pauses however limit the delivery of chest compressions to less than 50% of the time spent in the resuscitation attempt.[3–6] To decrease hands-off time, Guidelines 2005[7,8] eliminated post-shock pauses for rhythm analysis and pulse checks. After these changes, two observational studies showed improved survival.[9,10] It is however unclear to which of the multiple changes in all phases of the resuscitation process the improvements in survival can be attributed.

AEDs require time to analyze the heart rhythm, to charge and to advise to shock. This results in prolonged pre-shock pauses that are not eliminated in the current guidelines. Several retrospective analyses have found that short pre-shock pauses are even more strongly associated with improved neurological outcome from out-of-hospital cardiac arrest (OHCA than post-shock pauses.[11,12] One randomized trial has studied pre- and post-shock pauses, and found no improvement in return of spontaneous circulation (ROSC) or survival to hospital admission or discharge, despite improvements to the chest compression fraction (CCF) and significant shortening of pre- and post-shock pauses.[13]

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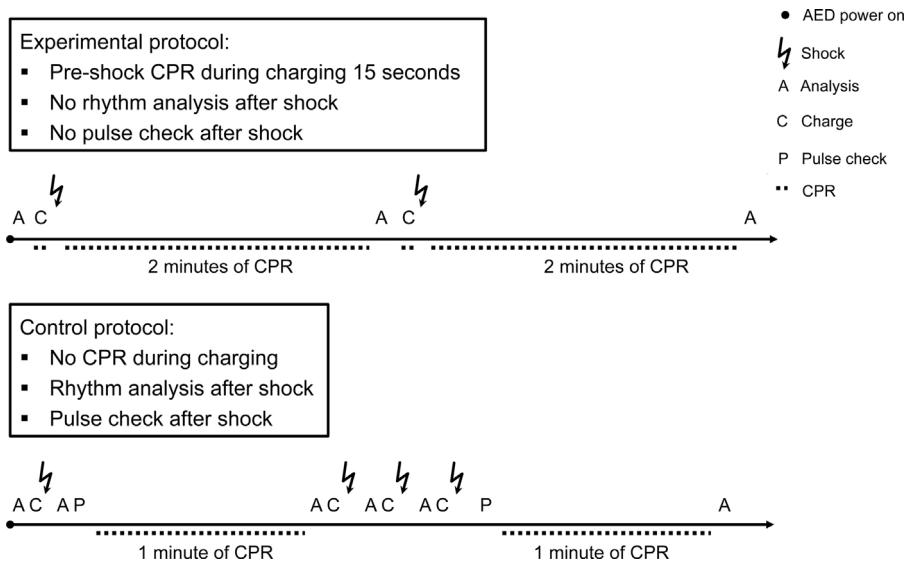

Fig. 1. Schematic example of the control (Guidelines 2000) and experimental protocol (Guidelines 2005). The dashed line reflects the periods in which CPR is given. A, indicates interruption of CPR for rhythm analysis; C, AED charging; and P, interruption of CPR for pulse check. In both protocols, the compression:ventilation ratio is modified to 30:2.

This study aims to evaluate a modification of the AED voice prompts to shorten both pre- and post-shock pause duration. The objective of this randomized controlled trial is to test whether modification of the AED voice prompts to shorten pre- and post-shock pauses, allows for more CPR and improved CCF, and results in improved survival of patients with OHCA with shockable initial rhythm.

Method

Study setting

The study was performed within the framework of the AmsteRdam REsuscitation STudies (ARREST). ARREST is an ongoing, prospective registry of all OHCAs in the Dutch province North-Holland. In the ARREST study data are collected according to the Utstein recommendations.[14] Details of the design of the data collection in the ARREST study are described elsewhere.[15]

In the Netherlands, AEDs are mostly deployed by first-responders, who carry the AED with them. They are dispatched simultaneously with two ambulances by the EMS dispatch center in case of a suspected OHCA. A dispatched first responder can be a police officer, firefighter or a lay-rescuer alerted by a text message.

Study population and randomization

For this study we included patients with OHCA, treated by the firefighters of Amsterdam and Amstelveen, the police of Kennemerland and Texel, general practitioners (GP) on home visit and the AEDs placed at Schiphol Airport, who all used the LIFEPAK 500 and LIFEPAK 1000 AED (Physio-Control Inc., Redmond, USA).

Treatment allocation was random per patient. After every AED use, dedicated study personnel downloaded the AED recordings and changed the settings of the AED for its next use to either the experimental protocol or the control protocol, guided by a randomization envelope. The settings were unknown to the next rescuer until the AED was connected to the patient, as the voice prompts clearly differed between experimental and control voice prompt design.

Patients were excluded from analysis if they had a non-shockable initial rhythm, were aged <8 years or had a cardiac arrest with a non-cardiac cause.

Study design

In this randomized control trial we compared two voice prompt protocols. The experimental protocol was according to the Guidelines 2005[7,8] but modified, by introducing a 15-s period of CPR during charging before delivering a shock. The control protocol followed the Guidelines 2000,[2] where no CPR was given during analysis of the heart rhythm or during charging before the shock. After each shock, CPR was withheld while the AED repeated rhythm analysis, and prompted for a pulse check or, if needed, a second (200J) or third (360J) shock. If no pulse was detected, CPR was resumed for 1 min (Fig. 1). In both protocols, the compression:ventilation ratio was 30:2 (Table 1). The recommended compression depth was 38–52 mm in both groups until 2010, when the Guidelines recommended a compression depth of more than 50 mm, but not exceeding 60 mm. The randomization of the study ended at the moment of AED disconnection from the patient and connection to the EMS defibrillator.

Endpoints

The primary endpoint of the study was admission alive to the hospital after ROSC. The secondary endpoints of the study were number of shocks delivered; success of the first AED shock; pre- and post-shock pause; CCF (defined as percentage of the total

Table 1
Settings of the AEDs in the two randomization groups.

	Experimental protocol	Control protocol
Pre-shock CPR time, s	15	0
Post shock rhythm analysis	OFF	ON
Pulse check duration, s	0	10
Time interval shock – CPR prompt, s	7	32
CPR time, shockable rhythm, s	120	60
Shock sequence	1 single shock	Max. 3 stacked shocks
Compressions:ventilation ratio	30:2	30:2

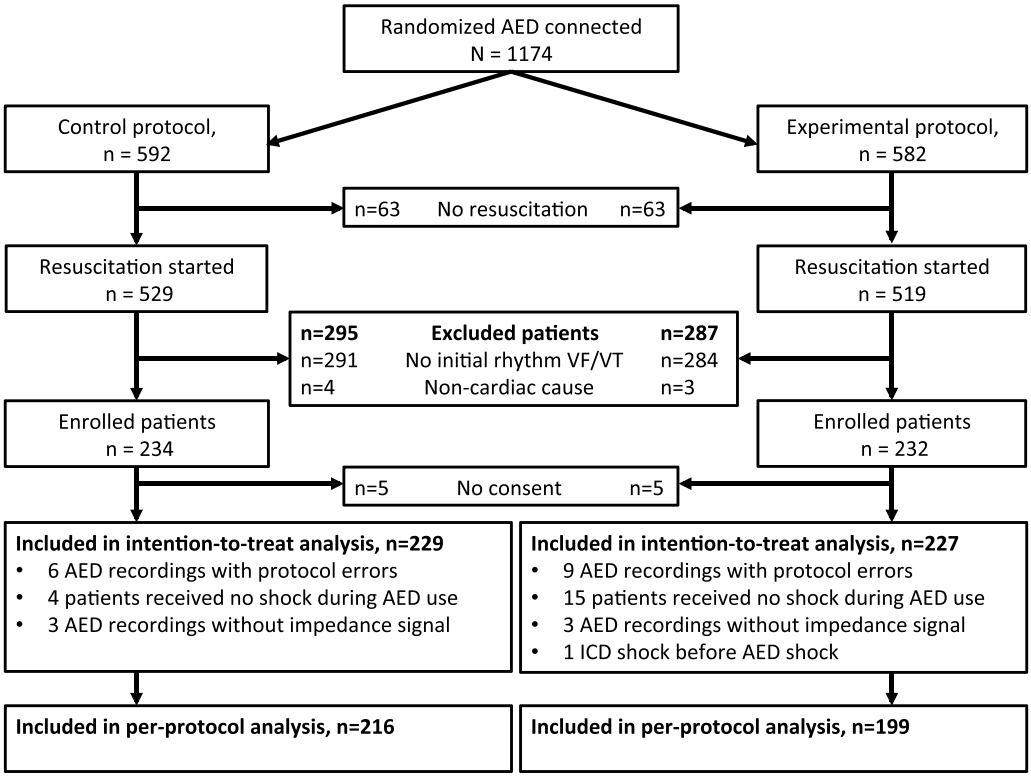

Fig. 2. Flowchart of patient inclusion.

connection time in with chest compressions were delivered); chest compression rate, time from connection AED to first shock; rate of recurrence of VF; survival to emergency room; discharge alive from the hospital; and Cerebral Performance Category (CPC) at discharge from the hospital. CPC category 1 represents good cerebral performance; category 2, moderate cerebral disability; category 3, severe cerebral disability; category 4, coma or vegetative state; and category 5, death. Survival with favorable neurologic outcome was defined as CPC score ≤ 2.[14]

Data collection and definitions

All first responders contacted the study center if they had used an AED. Study personnel visited the resuscitation site and downloaded the ECGs from all AEDs, which were stored and reviewed with CODE-STAT with Advanced CPR Analytics (Physio-Control Inc., Redmond, USA).

The clock times of the AED recordings were synchronized with the dispatch system clock. First recorded rhythm, time of first recorded rhythm and time of shocks were derived from these recordings. Chest compressions were identified from the impedance signal. The interval between the last chest compression and shock (pre-shock pause) and between shock and first post shock compression (post-shock pause) were derived from this impedance signal. Time stamped dispatch data were obtained from the dispatch center. A successful shock was defined as VF termination for at least 5 s after the shock regardless of the subsequent rhythm.

Power calculation

We assumed that 46%[16] of the patients with initial rhythm VF/VT would be admitted to the hospital with ROSC. We hypothesized that the probability to be admitted to the hospital would increase from 46 to 60%. For this hypothesis (alpha = 0.05, power = 0.80) the collection of data from 2×196 patients with VF/VT as initial rhythm was required.

Ethical approval

The Medical Ethics Review Board of the Academic Medical Center, Amsterdam approved the study and considered the study exempt for informed consent prior to treatment. Written informed consent was obtained from all surviving patients.

Statistical analyses

Survival differences were presented as percentage and as relative risk with 95% confidence interval. The Chi-square statistic was used for dichotomous data. For continuous variables, we used the Student's *t*-test in case of normally distributed data; for non-normally distributed data, we used the Mann–Whitney *U* test. AED recordings without impedance signal and AED recordings of resuscitation efforts where rescuers failed to give a shock after a shock advice were excluded in the secondary outcomes analysis.

In addition to these analyses a per-protocol analysis was done. All data were analyzed using the statistical software package of SPSS (SPSS for Mac, version 20.0, IBM SPSS Inc.). A *P*-value of <0.05 was considered to be statistically significant.

Results

During the study period (May 2006 – January 2014) a randomized AED was connected to a total of 1174 patients; 592 patients were randomized to the control protocol and 582 patients to the experimental protocol. Of the 592 resuscitation attempts that were started in the control protocol, 291 were excluded because of a non-shockable initial rhythm and four for having a non-cardiac cause. In the experimental protocol, 284 resuscitation attempts were excluded because of a non-shockable initial rhythm and three

Table 2
Baseline and operational patient characteristics.

	Experimental (*N* = 227)	Control (*N* = 229)	*P*-value	Missing *N* (%)
Age, y[a]	65 (13.1)	64 (13.4)	0.37	0 (0)
Male, *n* (%)	181 (80)	180 (79)	0.77	0 (0)
OHCA at public location, *n* (%)	93 (41)	89 (39)	0.65	0 (0)
Witnessed OHCA, *n* (%)	199 (88)	205 (90)	0.53	0 (0)
CPR before AED connection, *n* (%)	140 (62)	138 (61)	0.94	4 (0.9)
Time from 112-call to connection AED, min[b]	7.1 (5.0–9.2)	6.8 (4.7–8.8)	0.55	3 (0.7)
Duration of AED connection, min[b]	3.2 (2.1–5.4)	3.4 (2.2–5.6)	0.45	0 (0)
PCI, *n* (%)	60 (27)	60 (26)	0.87	6 (1.3)
Therapeutic hypothermia, *n* (%)	96 (43)	105 (47)	0.48	7 (1.5)

AED, automated external defibrillator, OHCA, out-of-hospital cardiac arrest.
[a] Mean (SD).
[b] Median (25–75th percentile).
All *P*-values were calculated with the Chi-square except variable 'mean age' calculated with Student's *t*-test and variable 'time from 112-call to connection AED' and 'duration AED connection' with Mann–Whitney *U* test.

because of a non-cardiac cause. For analyses of the primary outcome 229 cases were included in the control protocol and 227 cases in the experimental protocol (Fig. 2). The baseline characteristic variables did not differ between the two groups (Table 2); repeating this analysis per protocol showed comparable results (Supplemental Table 1).

Survival

Survival to hospital admission did not differ significantly between the control and experimental group (experimental: 62% vs. control: 65%; RR [95%CI] 0.96 [0.83–1.10], $P = 0.51$). Repeating the analysis per protocol showed comparable results (Supplemental Table 2).

The overall survival to discharge did not differ significantly (experimental: 42% vs. control: 38%; RR [95%CI] 1.09 [0.87–1.37], $P = 0.46$), nor did the percentage of patients who survived to discharge with favorable neurologic outcome (experimental: 40% vs. control: 36%; RR [95%CI] 1.12 [0.88–1.42], $P = 0.36$).

Secondary outcomes

The CCF was significantly higher in the experimental group compared to the control group (experimental: 58% [47–65] vs. control: 42% [31–52]; $P < 0.001$). The experimental group had significantly shorter pre-shock pauses in chest compressions (experimental: 6 [5–11] s vs. control: 20 [18–23] s; $P < 0.001$), shorter post-shock pauses (experimental: 7 [6–9] s vs. control: 27 [16–34] s; $P < 0.001$), and received fewer shocks (experimental: 1.5 [0.8] vs. control: 1.8 [1.2] shocks; $P = 0.01$ [Table 3]). Chest compression rates did not significantly differ between the two groups. The time from connection of the AED to first shock was significantly shorter in the control group than the experimental group (experimental: 34 [31–38] s vs. control: 21 [19–24] s; $P < 0.001$), due to the introduction of 15 s of CPR before in shock in the experimental protocol. The per-protocol analysis showed comparable results for the secondary outcomes (Supplemental Table 3).

Recurrent VF

In the experimental protocol the first AED shock was successful in 89%, and in the control protocol the first shock was successful in 87% ($P = 0.42$). In the group with a successful first shock, VF recurred during either AED use or use of the ambulance defibrillator in 72% of the experimental protocol and in 68% of the control protocol ($P = 0.26$). Repeating this in the per-protocol analysis gave comparable results (Supplemental Table 4).

Discussion

This randomized trial compared outcomes in patients with OHCA, treated according to two AED voice prompt protocols. The experimental protocol minimized pre-shock pauses by introducing a period of pre-shock CPR but also shortened post-shock pauses by omitting rhythm checks and pulse checks according to the Guidelines 2005.[7,8] The control protocol followed the Guidelines 2000.[2] The experimental protocol significantly shortened pre- and post-shock pauses and significantly improved the CCF, but did not result in increased survival to hospital admission or discharge.

Our study confirms, in a different study setting, the results from one other randomized controlled trial[13] and is in contrast with the findings from several observational studies that

Table 3
Secondary outcomes.

	Experimental (*N* = 209)[c]	Control (*N* = 222)[d]	*P*-value
Number of shocks delivered[a]	1.5 (0.8)	1.8 (1.2)	0.01
Successful first shock of the AED, *n* (%)	187 (89)	193 (87)	0.42
Pre-shock pause[b]	6 (5–11)	20 (18–23)	<0.001
Post-shock pause[b]	7 (6–9)	27 (16–34)	<0.001
Chest compression rate, /min[b]	119 (109–127)	117 (105–127)	0.13
CCF, %[b]	58 (47–65)	42 (31–52)	<0.001
Time from connection AED to first shock, s[b]	34 (31–38)	21 (19–24)	<0.001

AED, automated external defibrillator; CCF, chest compression fraction; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest.
[a] Mean (SD).
[b] Median (25–75th percentile).
[c] 18 patients could not be analyzed because no impedance signal was visible or no shock was given.
[d] 7 patients could not be analyzed because no impedance signal was visible or no shock was given.
P-values for proportions were calculated with the Chi-square test and Mann–Whitney *U* test for continuous variable.

suggest a strong relationship between shorter pre- and post-shock pauses, higher CCF and survival.[9–12] In accordance with our study, an observational study of Olasveengen et al. found only a weak, and not significant trend toward improved survival to hospital discharge from the reduction of post-shock pauses.[17] A recent study of Brouwer et al. also found such an association between shorter pre-shock pause and survival but their new finding was the observation that longer pauses that were not associated with a shock were equally associated with lower survival.[18]

Why do observational studies consistently show an association between short pre- and post-shock pauses and better survival, whereas randomized trials fail to confirm this association? There are several possible explanations. Randomized trials have the potential capability to demonstrate causality, which is not possible with observational studies, no matter how well controlled for (known) potential confounders they may be. This suggests that the observed relationship indeed is not causal, but an indicator for another phenomenon that is the true causal factor. Success or failure of resuscitation is multifactorial and it is not easy to specifically attribute each factor to success or failure of a resuscitation attempt.

An alternative explanation could be that the "new" guidelines (2005 onward) contain a bundle of measures that may indeed improve survival (such as the short pre-shock pauses and increased CCF), but also contain elements that have a (unintended) negative effect on survival. Several elements have changed in the guidelines in 2005 that may fit with this second explanation. For instance, after a single defibrillation shock approximately 10% of cases are still in VF. The advised duration of CPR before the next rhythm check was prolonged from 1 to 2 min, leaving such patients in VF twice as long.

Recurrence of VF is observed in 60–70% of cases and repeated recurrence also occurs frequently.[19] Berdowski et al.[20] showed that immediate resumption of chest compressions as advised in the 2005 guidelines led to an earlier recurrence of VF after the first shock, and that longer time spent in recurrent VF was associated with a decrease in survival. However, a study by Conover et al. did not find a relationship between chest compression resumption and VF recurrence after analyzing all shocks.[21] While there are important differences in methods of analysis, their study also confirmed that 74% of their patients had recurrence of VF (median two recurrences) and almost 50% of these had a recurrence within 30 s after successful defibrillation. The consequence of doubling the time interval between two rhythm analyses after the introduction of the Guidelines 2005 could be that patients are longer in VF.

A study by Hoogendijk et al.[22] supports this notion. This study showed that VF increases cardiac oxygen consumption and hampers restoration of the myocardial energy state and ventricular contractile function during simulated resuscitations following 7 min of cardiac arrest. Early detection and defibrillation of recurrent VF during CPR may improve survival of OHCA, by reducing the energy consumption by the ischemic myocardium. Algorithms that allow detection of VF without interruption of chest compressions may enhance the viability of this concept.

Although the CCF improved significantly in the experimental group, in both groups the median CCF was <60%. This overall low CCF can be explained by the time dependent character of CCF in OHCA patients with a shockable rhythm.[23] The CCF in our study represents the early part of the resuscitation and only in AED recordings from patients with a shockable initial rhythm. AED connection times were median 3 min because EMS usually arrives within minutes after AED connection. Also, it is possible that the changes in Guidelines such as reducing pre-and post-shock pauses have their benefit mainly in resuscitations with longer response times or lower overall survival rates.

An unexpected finding was the larger number of cases in the experimental group (15 vs. 4 in the control group, $P = 0.009$) where no shock was delivered while this was prompted by the AED voice. A possible explanation for this difference could be that the voice prompt in the experimental protocol orders to resume CPR for 15 s before the shock. Some rescuers may be confused by this prompt, and may have thought this prompt started a new 2-min cycle of CPR, thus ignoring the voice prompt to shock 15 s later.

Limitations

In this study we modified the voice prompts of the AED aiming to reduce pre- and post-shock pauses. Modification of the AED protocol results in only a short period of increased CPR time and shorter pre- and post-shock pauses during CPR before the manual defibrillator of the ambulance is connected. Possibly, this resuscitation time interval with AED employment before EMS arrival is too short to have a significant impact on outcome. Another explanation could be that the guidelines 2005 contain a bundle of measures that may improve survival, but also contain elements that have a (unintended) negative effect on survival. The single shock protocol and the 2 min CPR before rhythm check as introduced in the Guidelines 2005 potentially have an independent influence on outcome. Because in our study all these measures were part of the bundle of measures in the experimental protocol, we cannot determine the relative contribution of each factor to the outcome.

Conclusion

An AED protocol with a period of CPR immediately before shock delivery and shortened post-shock pauses improved overall CCF, but did not improve survival to hospital admission or discharge of patients with OHCA with a shockable initial rhythm. Pre- and post-shock pauses may not be causally related to survival.

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Conflict of interest statement

Dr. Koster reports financial and non-financial support from Physio-Control during the conduct of the study; grants from Physio-Control, grants from Zoll Medical, grants from Cardiac Science, grants from Philips Medical, grants from Defibtech, outside the submitted work; and Unpaid Medical Advisor for Physio-Control and HeartSine. The remaining authors declare no conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.resuscitation.2016.06.009.

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