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Progressing from initial non-shockable rhythms to a shockable rhythm is associated with improved outcome after out-of-hospital cardiac arrest☆

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ABSTRACT

Background: Cardiac arrest patients with initial non-shockable rhythm progressing to shockable rhythm have been reported to have inferior outcome to those remaining non-shockable. We wanted to confirm this observation in our prospectively collected database, and assess whether differences in cardiopulmonary resuscitation (CPR) quality could help to explain any such difference in outcome.
Materials and methods: All out-of-hospital cardiac arrest (OHCA) cases in the Oslo EMS between May 2003 and April 2008 were retrospectively studied, and cases with initial asystole or pulseless electrical activity (PEA) were selected. Pre-hospital and hospital records, Utstein forms, and continuous ECGs were reviewed. Quality of CPR and outcome were compared for patients who progressed to a shockable rhythm and patients who remained in non-shockable rhythms.
Results: Of 753 cases with initial non-shockable rhythms 517 (69%) had asystole and 236 (31%) PEA. Ninety-eight (13%) patients progressed to a shockable rhythm, while 653 (87%) remained non-shockable during the entire resuscitation effort (two unknown). Hands-off ratio was higher in the shockable than the non-shockable group, 0.21 ± 0.12 vs. 0.16 ± 0.10 ($p = 0.000$) with no significant difference in compression and ventilation rates. Overall survival to hospital discharge was 3%; 7% in the shockable and 2% in the non-shockable group ($p = 0.014$). Based on a multivariate logistic analysis young age, initial PEA, and progressing to a shockable rhythm were associated with better outcome.
Conclusion: Progressing from initial non-shockable rhythms to a shockable rhythm was associated with improved outcome after OHCA. This occurred despite more pauses in chest compressions in the shockable group, probably related to defibrillation attempts.

Introduction

The relative frequency of asystole and pulseless electrical activity (PEA) as the first recorded rhythm in out-of-hospital cardiac arrest (OHCA) has increased gradually over the last decades. In recent population-based studies 60–80% of the patients now present with these initial non-shockable rhythms.[1–4] This is partly due to reduced absolute incidence of ventricular fibrillation (VF) as the first recorded rhythm,[1,3] and a relative or absolute increase in cardiac arrest of non-cardiac origin.[1,2]

Survival rates for patients initially presenting with asystole or PEA is much lower than for patients presenting with initial shockable rhythms and usually reported in the range 2–3%.[4,5] The current treatment strategies for OHCA are largely based on research from patients with cardiac aetiologies and initial shockable rhythms, and a better understanding of patients presenting with asystole or PEA is necessary to further improve survival rates in this group.

A small proportion of patients with initial non-shockable rhythms progress to shockable rhythms during the resuscitation efforts.[6,7] In the recent ASPIRE trial, comparing manual and mechanical cardiopulmonary resuscitation (CPR), this occurred in 22% of the patients, and Hallstrom et al. reported that survival was superior if the patients stayed in a non-shockable rhythm; 5% vs. 1% for those converting.[7] They presented one possible explanation for their findings as less than optimal attention to good quality CPR in the converting group due to the treatment protocols themselves.[7]

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We wanted to confirm the earlier finding[7] that patients progressing from non-shockable to shockable rhythms during the resuscitation efforts actually have inferior outcome from our prospectively collected database, and assess whether differences in CPR quality could help to explain any such difference in outcome.

Material and methods

Description of EMS and in-hospital treatment

The city of Oslo has a one-tiered centralised community run EMS system for a population of 540,000. On weekdays between 7:30 and 22:00, a physician-manned ambulance staffed by two paramedics and an anaesthesiologist functions on the same level as the regular paramedic staffed ambulances. The Norwegian version of the 2005 ERC guidelines[8] were implemented January 2006, prior to this a modified version of the 2000 ERC guidelines was followed. In both versions the modification consisted of three instead of 1 min (2000) or 2 min (2005) of CPR before and in between defibrillation. Stacked shocks were used prior to 2006. All paramedics are trained to use the defibrillators in manual mode. Endotracheal intubation was the standard method for securing the airways, followed by uninterrupted chest compressions with 10–12 interposed ventilations per minute.

Nurses and paramedics staff the dispatch centre. Due to an ongoing randomized study of the effect of intravenous access and drugs (the IV study) in the Oslo Emergency Medical Service (EMS), some of our included patients are also included in this study registered at www.clinicaltrials.gov (NCT00121524). Less than half of the patients will therefore be expected to have received intravenous drugs during resuscitation.

All hospitals in Oslo have standardised goal directed post-resuscitation protocols including therapeutic hypothermia. The post-resuscitation protocols are applied to all patients regardless of initial rhythm or aetiology if active treatment is desired.[9]

Study design and recruitment

All patients older than 18 years suffering from non-traumatic out-of-hospital cardiac arrests of all causes from May 2003 to 28 April 2008 were retrospectively studied. Locally adapted Utstein style forms[10] (with information on type of bystander CPR upon arrival of first ambulance), dispatcher recordings, and ambulance and hospital records are routinely collected and reviewed at The National Competence Centre for Emergency Medicine (Ulleval University Hospital, Oslo, Norway).

Data collection

Utstein forms are routinely filled out by ambulance personnel after every cardiac arrest and submitted to the study supervisor along with a copy of the ambulance run sheet. Automated, computer-based time records from the dispatch centre supplement ambulance run sheets with regards to response times. For all admitted patients, additional hospital records were obtained from the respective receiving hospitals. Information from Utstein forms, ambulance run sheets, dispatch and hospital records are linked together with continuous ECG tracings as described below.

Based on these records the patients with initial non-schockable rhythms (PEA or asystole) were divided into two groups; the shockable group (patients progressing to a shockable rhythm during the resuscitation effort) or the non-shockable group (patients remaining in a non-shockable rhythm).

Equipment and data processing

Standard LIFEPAK 12 defibrillators (Physio-Control, a Division of Medtronic, Redmond, WA, USA) were used, which routinely measure transthoracic impedance by applying a near constant sinusoidal current across the standard defibrillation pads. After a CPR effort the ECGs with transthoracic impedance signals were normally transferred to a local server at The National Competence Centre for Emergency Medicine (Ulleval University Hospital, Oslo, Norway), and data from each case were viewed and annotated using a CODE-STAT™ 7.0 (Physio-Control, Redmond, WA, USA) for detection of chest compressions and ventilations from transthoracic impedance changes. Annotations were made while reviewing available clinical information from the Utstein forms and ambulance records. Total time without spontaneous circulation (CPR time), time without chest compressions divided by CPR time (hands-off ratio), compression rate and the actual number of compressions and ventilations per minute were calculated for each episode.

All available continuous ECGs were also reviewed to assess whether the shocks delivered were appropriate, and only patients receiving shocks for a shockable rhythms (ventricular fibrillation, VF and pulseless ventricular tachycardia, VT) were included in the shockable group. Patients receiving shocks for non-shockable rhythms (asystole or PEA), were included in the non-shockable group. In cases where ECGs were not available for analysis, the information from pre-hospital and hospital records were used to classifying patients according to initial and pre-shock rhythms.

Statistical analysis

Statistical calculations were performed using a spreadsheet program (Excel 2002, Microsoft Corp., Redmond, WA, USA) and a statistical software package (SPSS 14.0, SPSS Inc., Chicago, IL, USA). Values are given as means with standard deviations (S.D.), except for response times given as medians with 25th and 75th percentiles. Differences between the two groups were analysed using Student's *t*-tests for continuous data and chi-squared with continuity correction for categorical data. *p*-values less than 0.05 were considered significant. Prognostic factors found to be significant in preliminary univariate and bivariate analyses were included in a multivariate logistic regression analysis together with progression to shockable rhythm (dependent variable: discharged from hospital alive). The results from the multivariate logistic regression analysis were reported as adjusted odds ratios with 95% confidence intervals (95% CI) and *p*-values.

Results

Between 1 May 2003 and 28 April 2008 the Oslo EMS responded to 1133 cardiac arrests where resuscitation was attempted. There were 753 cases with initial non-shockable rhythms; 517 (69%) with asystole and 236 (31%) with PEA. Ninety-eight (13%) patients progressed to a shockable rhythm, while 653 (87%) remained in a non-shockable rhythm during the entire resuscitation effort (two unknown). Sixteen patients in the non-shockable group received shocks for non-shockable rhythms (none of whom survived) (Figure 1).

There was a non-significant trend towards a slightly shorter response time ($p = 0.061$) and more bystander and ambulance witnessed arrests in the shockable group. Endotracheal intubation was performed more often in the shockable than the non-shockable group (92% vs. 82%, respectively, $p = 0.018$) No other significant demographic differences were found between the two groups (Table 1).

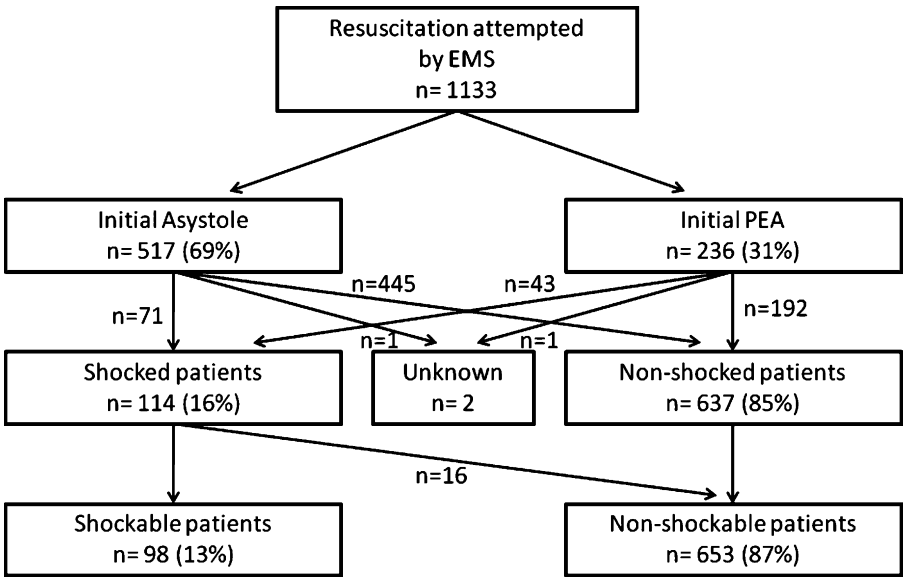

Figure 1. Eligibility. EMS = emergency medical services, PEA = pulseless electrical activity; shocked patients = patients actually receiving shocks; shockable patients = patients receiving shocks for ventricular fibrillation or pulseless ventricular tachycardia.

The hands-off ratio was higher in the shockable than the non-shockable group (0.21 ± 0.12 vs. 0.16 ± 0.10, respectively, $p = 0.000$), and resuscitation was carried out significantly longer in the shockable group (25 ± 11 min vs. 18 ± 9 min, respectively, $p = 0.000$). There were no significant differences in compression and ventilation rates (Table 2).

In the shockable group 41% achieved return of spontaneous circulation (ROSC) and 26% were admitted to an intensive care unit (ICU) compared to 20% and 15% in the non-shockable group ($p = 0.000$ and 0.013, respectively). Overall survival to hospital discharge for patients initially presenting with non-shockable rhythms was 3%; 7 patients (7%) in the shockable group and 14 patients (2%) in the non-shockable group, respectively ($p = 0.013$). In both groups the majority of survivors had favourable outcome (CPC 1 and 2); 2% in the non-shockable group and 5% in the shockable group ($p = 0.128$), respectively (Table 3).

Table 1
Demographic characteristics.

	Non-shockable	Shockable	*p*-Value
Patients included	653 (87)	98 (13)	
Age (years)	64 ± 18	63 ± 18	0.674
Males (%)	419 (64)	63 (64)	1.000
Cardiac aetiology (%)	386 (59)	55 (56)	0.640
Location of arrest			
Home	420 (64)	61 (62)	0.775
Public	156 (24)	30 (31)	0.189
Other	75 (12)	7 (7)	0.266
Bystander witnessed	315 (48)	56 (57)	0.125
Ambulance witnessed	72 (11)	16 (16)	0.176
Bystander BLS	331 (51)	48 (49)	0.836
Initial rhythm			
Asystole	453 (69)	63 (64)	0.370
PEA	200 (31)	35 (36)	0.370
Response time (min)	8 (5, 11)	7 (3, 11)	0.061

All variables given as numbers (percentages in parenthesis) except age (mean ± S.D.) and response time (minutes, median with 25th and 75th percentile). Differences between groups were analysed using Student's *t*-tests for continuous data and chi-squared for categorical data. BLS = basic life support. PEA = pulseless electrical activity. Response time = time from call for ambulance to arrival at patient's side.

Table 2
Quality of CPR.

	Non-shockable	Shockable	*p*-Value
ECG available for analysis	448 (67)	75 (77)	0.141
CPR time (min)	18 ± 9	25 ± 11	0.000
Pre-shock pause (s)	N/A	15 (3, 22)	N/A
Hands-off ratio	0.16 ± 0.10	0.21 ± 0.12	0.000
Compression rate	116 ± 10	118 ± 9	0.119
Compressions min^{-1}	95 ± 13	90 ± 15	0.005
Ventilations min^{-1}	11 ± 4	11 ± 3	0.088

All values given as means with standard deviation except pre-shock pause given as median with 25th and 75th percentiles. Rates are in min^{-1}. Differences between groups were analysed using Student's *t*-tests for continuous data and chi-squared for categorical data.

This same trend can be found in subgroup analysis of patients presenting with asystole and PEA. In patients presenting with PEA; 9% survived with favourable neurological outcome if they progressed to a shockable rhythm compared to 5% if they remained in a non-shockable rhythm ($p = 0.657$). In patients presenting with asystole 6% survived to hospital discharge in the shockable group compared to 1% in the non-shockable group ($p = 0.006$), but only 3% and 1% were discharged with favourable neurological outcome in the respective groups ($p = 0.222$) (Figure 2).

Table 3
Outcome—admitted to hospital, admitted to ICU and discharged from hospital.

	Non-shockable	Shockable	*p*-Value
Any ROSC during resuscitation	132 (20)	40 (41)	0.000
Admitted to hospital	175 (27)	43 (44)	0.001
With ROSC	109 (17)	25 (26)	0.047
With ongoing CPR	66 (10)	18 (18)	0.025
Admitted to ICU	98 (15)	25 (26)	0.013
Discharged alive	14 (2)	7 (7)	0.014
CPC 1–2	13 (2)	5 (5)	0.128
CPC 3–4	1	2	
Discharged if admitted ICU	14%	28%	0.192

All variables given as numbers (percentages in parentheses). Differences between groups were analysed using chi-squared. ROSC = return of spontaneous circulation. ICU = intensive care unit. CPC = cerebral performance category.

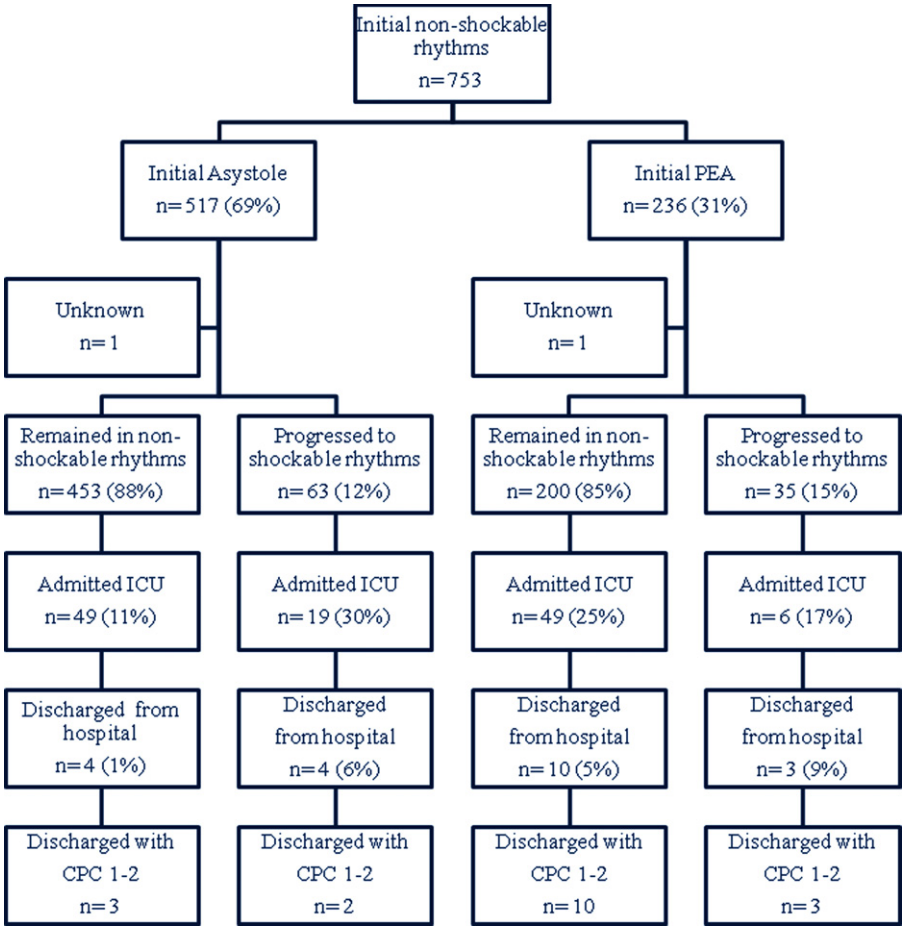

Figure 2. Outcome for asystole and PEA subgroups. PEA = pulseless electrical activity. ICU = intensive care unit. CPC = cerebral performance score.

The following prognostic factors were found to be significant in preliminary univariate and bivariate analyses and included in multivariate analysis: progression to a shockable rhythm ($p = 0.014$), response time ($p = 0.009$), age ($p = 0.000$), initial PEA ($p = 0.005$) and initial asystole ($p = 0.005$). Initial asystole was not included in the regression analysis, as it is represented by not being initial PEA. The logistic analysis confirmed the association between progressing to a shockable rhythm and a positive outcome. A positive association was also found for young age and initial PEA (Table 4).

Altogether, 74% and 75% of patients were included in the above-mentioned IV study for the shockable and non-shockable groups, respectively, and there was an even distribution of the two randomisation groups in the 751 patients investigated.

Discussion

In contrast to the previous study reporting worse outcome if patients with non-shockable rhythms progressed to shockable rhythms,[7] we found the opposite in our EMS with a threefold higher survival rate for these patients compared to patients remaining in non-shockable rhythms. Although not statistically significant, it was also a clear trend to more survivors with favourable outcome (5% vs. 2%) in the shockable group. Our findings support Herlitz et al.'s observation from the Swedish registry where defibrillation was identified as one of the factors associated with positive outcome in patients with initial non-shockable rhythms.[11]

We confirmed the hypothesis that patients who progressed to shockable rhythms had increased pauses in chest compressions compared to patients in persistent non-shockable rhythms, but they still had a higher survival rate. It is pertinent to point out that both groups had reasonably good CPR quality. The increased pauses in chest compressions were probably related to defibrillation attempts,[12] so the statistically significant difference in chest compression pauses might be of limited clinical importance.

Patients who progressed to shockable rhythms also had longer resuscitation episodes. As an initial shockable rhythm is a well-known positive predictive feature among advanced life support (ALS) providers, it seems reasonable that their efforts would be prolonged also when a shockable rhythm occurs during a resuscitation attempt as suggested in the guidelines.[13] Also, all patients where a resuscitation effort is thought to be futile within a few minutes as ALS providers gain more information about the patient, are expected to be found in the non-shockable group. In addi-

Table 4
Multivariate logistic regression analysis of prognostic factors for survival.

Prognostic factors	Adjusted odds ratio	95% CI	*p*-Value
Initial PEA	4.88	1.82, 13.12	0.002
Shock administered	3.02	1.07, 8.57	0.038
Age (per additional year)	0.94	0.92, 0.96	0.000
Response time (per additional min)	0.92	0.82, 1.02	0.116

Prognostic factors that were found to be significant in preliminary univariate and bivariate analyses were included in this multivariate logistic regression analysis to detect independent factors potentially affecting survival in the shockable vs. non-shockable group. 95% CI = confidence interval. PEA = pulseless electrical activity.

tion to explaining differences in resuscitation length, the latter factor might also explain the difference in proportion of patients being intubated. Intubation has not previously been associated with improved survival in cardiac arrest studies,[14,15] but it could be speculated that patients with prolonged resuscitation efforts could benefit from intubation as this has been shown to reduce pauses in chest compressions.[16]

An approach to increase survival after non-VF/VT cardiac arrest was put forward by Hallstrom et al., suggesting chest compression quality could be improved by limiting the use of defibrillators for these patients.[7] Good quality chest compressions with minimal pauses is believed to be important for outcome,[17–19] and rhythm checks and shock administrations cause detrimental pauses leaving vital organs without any perfusion for periods of time.[20,21] Hallstrom et al. reported that only one in 738 included patients benefited from the use of a defibrillator, and this patient survived but was discharged to a nursing home.[7] If patients with initial asystole or PEA progressing to shockable rhythms could consistently be shown to have such dismal survival rates, it might be reasonable to explore a treatment strategy that limited the use of defibrillators to only assessing the initial rhythm. However, patients progressing to VF/VT will almost always need defibrillation to have any chance of achieving return of spontaneous circulation. Depriving these patients of a potentially curative treatment is impossible to justify when a reasonable survival statistic can be demonstrated for this patient group.

Several authors have attempted to characterise the underlying causes of non-VF/VT cardiac arrests.[22–24] Increasing research efforts to improve our knowledge and help to identify the underlying mechanisms of cardiac arrest has been advocated, and is hoped to provide specific, corrective therapy, treating the underlying cause of arrest.[25] This might hold the key to further improved survival in patients with cardiac arrest due to non-cardiac causes, often presenting with initial asystole or PEA. Studies to deliver therapies that may be effective in certain subgroups have not been successful when delivered to undifferentiated patients (e.g. fibrinolytics in TROICA[26] and Vancouver[27]). Survival is generally dismal for patients with non-VF cardiac arrest, and an improvement in a subgroup of non-VF patients will often not yield significant differences overall.

The study is limited by being retrospective and observational, and there might be important unknown confounders between our two study groups. ECGs were not available for confirmation of patient classification according to rhythm in 19% of shocked cases, but we had ECG rhythm confirmation in five of the seven survivors in this group. Compared to the Hallstrom study,[9] a larger and more random proportion of patients in our study most likely did not receive any IV drugs. Similarly, the Hallstrom's study was based on data from another randomized controlled study assessing the effect of a mechanical chest compression devise on outcome after cardiac arrest (ASPIRE study).[10] Both these factors might be important confounders in the respective studies. There are also several differences in demographic characteristics between the two studies. Hallstrom reported a higher proportion of patients with cardiac aetiology (~80% vs. 64%) and about a minute shorter response times, while we report a higher proportion of patients with witnessed arrests (33% vs. 49%) occurring in public (14% vs. 35%) with bystander initiated BLS (26% vs. 49%). All these factors are known to positively influence outcome after cardiac arrest, but it is uncertain how the combination of these demographic differences might affect the differences in outcome found in the two studies. Finally, caution should be stated in generalising these results into other EMS, as the patients were treated following Norwegian Guidelines, with 3 min of CPR loops instead of 2 min.[8]

Conclusions

Progressing from initial non-shockable asystole or PEA to a shockable rhythm was associated with improved outcome after out-of-hospital cardiac arrest. This occurred despite more pauses in chest compressions in the shockable group, probably related to defibrillation attempts. Previously suggested protocols limiting the use of defibrillators in this group in an attempt to improve quality of CPR is hard to justify.

Conflict of interest

Olasveengen has received honoraria from Medtronic (Oslo, Norway) and research support from Laerdal Medical Corporation (Stavanger, Norway). Steen is a member of the board of directors for Laerdal Medical and The Norwegian Air Ambulance. Wik is on a Medical Advisory Board for Physio-Control, has in the past consulted for Zoll, Laerdal and Jolife, and is the principle investigator for a multi-centre mechanical chest compression device study sponsored by Zoll. Samdal and Sunde have no conflicts to declare.

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