Original Investigation

Mechanical Chest Compressions and Simultaneous Defibrillation vs Conventional Cardiopulmonary Resuscitation in Out-of-Hospital Cardiac Arrest
The LINC Randomized Trial

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IMPORTANCE A strategy using mechanical chest compressions might improve the poor outcome in out-of-hospital cardiac arrest, but such a strategy has not been tested in large clinical trials.

OBJECTIVE To determine whether administering mechanical chest compressions with defibrillation during ongoing compressions (mechanical CPR), compared with manual cardiopulmonary resuscitation (manual CPR), according to guidelines, would improve 4-hour survival.

DESIGN, SETTING, AND PARTICIPANTS Multicenter randomized clinical trial of 2589 patients with out-of-hospital cardiac arrest conducted between January 2008 and February 2013 in 4 Swedish, 1 British, and 1 Dutch ambulance services and their referring hospitals. Duration of follow-up was 6 months.

INTERVENTIONS Patients were randomized to receive either mechanical chest compressions (LUCAS Chest Compression System, Physio-Control/Jolife AB) combined with defibrillation during ongoing compressions (n = 1300) or to manual CPR according to guidelines (n = 1289).

MAIN OUTCOMES AND MEASURES Four-hour survival, with secondary end points of survival up to 6 months with good neurological outcome using the Cerebral Performance Category (CPC) score. A CPC score of 1 or 2 was classified as a good outcome.

RESULTS Four-hour survival was achieved in 307 patients (23.6%) with mechanical CPR and 305 (23.7%) with manual CPR (risk difference, −0.05%; 95% CI, −3.3% to 3.2%; $P > .99$). Survival with a CPC score of 1 or 2 occurred in 98 (7.5%) vs 82 (6.4%) (risk difference, 1.18%; 95% CI, −0.78% to 3.1%) at intensive care unit discharge, in 108 (8.3%) vs 100 (7.8%) (risk difference, 0.55%; 95% CI, −1.5% to 2.6%) at hospital discharge, in 105 (8.1%) vs 94 (7.3%) (risk difference, 0.78%; 95% CI, −1.3% to 2.8%) at 1 month, and in 110 (8.5%) vs 98 (7.6%) (risk difference, 0.86%; 95% CI, −1.2% to 3.0%) at 6 months with mechanical CPR and manual CPR, respectively. Among patients surviving at 6 months, 99% in the mechanical CPR group and 94% in the manual CPR group had CPC scores of 1 or 2.

CONCLUSIONS AND RELEVANCE Among adults with out-of-hospital cardiac arrest, there was no significant difference in 4-hour survival between patients treated with the mechanical CPR algorithm or those treated with guideline-adherent manual CPR. The vast majority of survivors in both groups had good neurological outcomes by 6 months. In clinical practice, mechanical CPR using the presented algorithm did not result in improved effectiveness compared with manual CPR.

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Many factors affect the chances of survival after cardiac arrest, including early recognition of arrest, effective cardiopulmonary resuscitation (CPR) and defibrillation, and postresuscitation care. One important link is the delivery of high-quality chest compressions to achieve restoration of spontaneous circulation (ROSC).[1-4]

The effectiveness of manual chest compressions depends on the endurance and skills of rescuers, and manual compressions provide only approximately 30% of normal cardiac output.[5,6] Manual CPR is also limited by prolonged hands-off time, and its quality is particularly poor when it is administered during patient transport.[7,8] Mechanical chest compression devices have therefore been developed to improve CPR.

CPC *Cerebral Performance Category*
CPR *cardiopulmonary resuscitation*
ECG *electrocardiogram*
EMS *emergency medical services*
ROSC *restoration of spontaneous circulation*

Experimental studies with the mechanical chest compression device used in this study have shown improved organ perfusion pressures, enhanced cerebral blood flow, and higher end-tidal CO_2 compared with manual CPR, with the latter also supported by clinical data.[9-11] This device sustains adequate circulation during percutaneous coronary intervention and has been used in cases of hypothermia/drowning.[12,13]

Two randomized pilot studies (N = 328 and N = 149) of out-of-hospital cardiac arrest compared manual and mechanical chest compressions using this device and did not find any outcome differences.[14,15] To date, there has been no evidence from large randomized trials about the effectiveness and safety of this mechanical device compared with manual CPR.

The LINC (LUCAS in Cardiac Arrest) study was designed to evaluate the effectiveness and safety of an algorithm using mechanical chest compressions combined with defibrillation during ongoing compressions (mechanical CPR) compared with manual CPR according to guidelines.[16,17] The rationale for this design of the algorithm with mechanical chest compressions was based on studies suggesting the importance of compressions before defibrillation and a minimal hands-off interval.[4,18,19] The primary objective was to assess whether treatment with mechanical CPR would result in superior 4-hour survival in patients with out-of-hospital cardiac arrest compared with treatment with manual CPR.

The LINC study was initiated by Uppsala University and sponsored by Physio-Control/Jolife AB. The study was approved by the regional ethical review board in Uppsala, Sweden, the research ethics committee in the United Kingdom, and the United Human Subjects Research Committees in the Netherlands. It was conducted in accordance with regulatory requirements, Good Clinical Practices, and the ethical principles of the Declaration of Helsinki. All survivors with sufficient mental capacity were given information about the study. If further participation was agreed on, written consent was obtained. If survivors did not have sufficient mental capacity, information was presented to family, who provided written consent if they decided to further participate. Consent was waived for included nonsurvivors by the ethical committees.

Methods

Study Design and Algorithms

This multicenter randomized clinical trial enrolled patients from January 2008 to August 2012 in 6 advanced life support emergency medical systems (EMS): Gävle, Malmö, Västerås, and Uppsala in Sweden, Utrecht in the Netherlands, and Dorset in the United Kingdom. Its protocol has been described in detail.[17] For inclusion, patients had to be adults with unexpected out-of-hospital cardiac arrest for whom an attempt of resuscitation was considered appropriate. Exclusion criteria were traumatic cardiac arrest (including hanging), age younger than 18 years, known pregnancy, and a body size too large or small to fit the chest compression device. Patients undergoing defibrillation before the device arrived on scene and patients with crew-witnessed cardiac arrest who achieved ROSC after immediate defibrillation were not eligible for the study.

The LUCAS Chest Compression System (Physio-Control/Jolife AB) is a mechanical CPR device with an integrated suction cup designed to deliver compressions according to resuscitation guidelines. The device and a randomization envelope were placed on all ambulances and brought to all patients with dispatch codes of sudden cardiac arrest or unconsciousness and when called for by local guidelines.[17] Enrollment was performed on scene immediately when the EMS recognized a cardiac arrest. Manual CPR was started and patients who met the eligibility criteria were immediately randomized in 1:1 balance using sealed opaque envelopes at the patient's side.

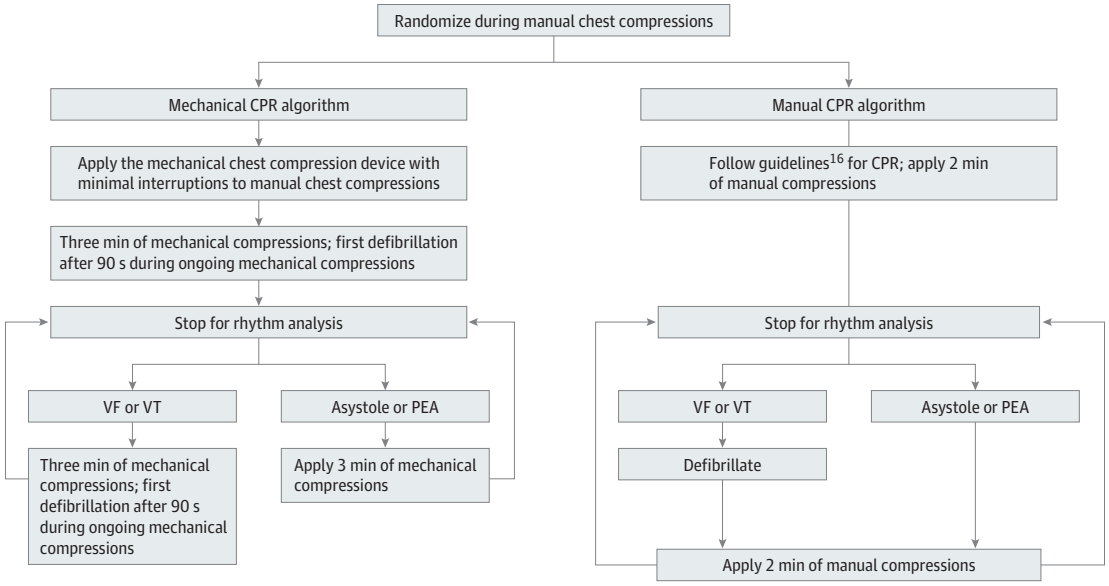
Patients randomized to the mechanical CPR algorithm (**Figure 1**) were immediately treated with manual chest compressions until the device was deployed. Mechanical compressions were initiated and continued for 3 minutes; first defibrillation shock was delivered during ongoing compressions, without pausing to check the heart rhythm, 90 seconds into the first 3-minute cycle. Heart rhythm was checked after each 3-minute cycle; if a shockable rhythm was observed, a new 3-minute cycle was started and a countershock was delivered after 90 seconds of compressions without pausing. If no shockable rhythm was observed, a 3-minute cycle without interruption started. Patients randomized to receive manual CPR were treated in accordance with the 2005 European Resuscitation Council guidelines.[16] In both groups, ventilation and drugs were given according to guidelines.[16]

To ensure adherence to the study design, all EMS personnel were trained in both study algorithms before starting the study and were retrained every 6 months during the entire study period. For randomly chosen EMS personnel, skill level and adherence to the algorithms were evaluated using manikins by 2 supervisors visiting the sites once a year. Feedback of their skills was given by the supervisors.

Outcome Variables

The primary outcome was 4-hour survival after successful ROSC. Secondary outcomes included ROSC defined as spontaneous palpable pulse, arrival to the emergency depart-

Figure 1. Description of Study Intervention Algorithms



Ventilation and medication were given according to guidelines[16] in both groups. VF indicates ventricular fibrillation; VT, ventricular tachycardia; and PEA, pulseless electrical activity.

ment with a spontaneous palpable pulse, and survival with good neurological outcome to intensive care unit discharge, to hospital discharge, and at 1 and 6 months. Cerebral Performance Category (CPC) scores were used in survivors to define neurological outcome, with CPC scores of 1 or 2 indicating good outcome and CPC scores of 3 or 4 indicating poor outcome (**Box**).[20] This was done by the on-site responsible nurse or physician who had access to the study documentation. Follow-up after hospital discharge was performed by telephone or visits to the clinic at 1 and 6 months after the cardiac arrest. To monitor the clinical safety of the device, adverse device events and serious adverse events were recorded by the EMS and hospital personnel for each individual patient. An interim analysis of the primary end point of 4-hour survival was performed during spring 2011 by an independent safety committee within the Scandinavian Society of Anaesthesiology and Intensive Care Medicine. The committee recommended continuing the study.

Postresuscitation Care

Patients with ROSC were treated with mild hypothermia to 32°C to 34°C (89°F-93°F) for 24 hours, regardless of initial electocardiogram (ECG) rhythm, if no contraindications were present. Acute coronary angiography was considered during the first 48 hours and, if indicated, including ST-segment elevation on a 12-lead ECG, a percutaneous coronary intervention was performed.

Statistical Analysis

Monitoring, database management, and all statistical analyses were coordinated independently by Uppsala Clinical Research Center, Uppsala, Sweden. All predefined analyses were performed in accordance with the protocol on the intention-to-treat population, comprising all randomized patients except surviving patients who refused participation in the trial. All outcomes were analyzed using Wald 95% confidence intervals for the difference in proportions and a 2-sided Fisher exact test. Missing values were imputed as the worst outcome, as predefined, so that for the CPC end points patients lost to follow-up were analyzed as not being alive with CPC scores of 1 or 2. Statistical significance for the primary variable was defined as $P < .048$ in accordance with the interim analysis plan. It was assumed that in the manual CPR group, the proportion of 4-hour survival would be 25% and with mechanical CPR at least 31%. To detect the anticipated difference of at least 6% with a power of 90% in the final analysis, the study required a total of 2500 patients; ie,1250 patients in each treatment group in the intention-to-treat population. Further details of the group-sequential design and sample size calculation are described elsewhere.[17] All statistical analyses were performed using SAS version 9.3, SAS Institute.

Box. Cerebral Performance Category (CPC) Scale

CPC 1: Full recovery or mild disability

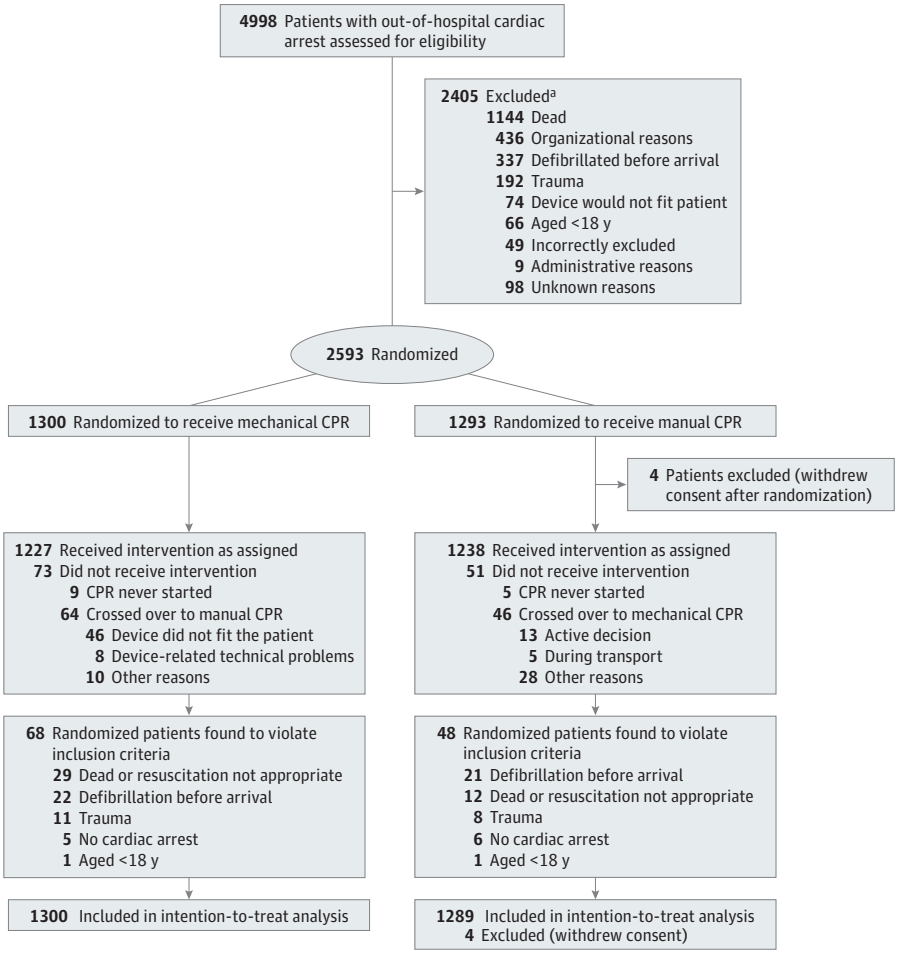
CPC 2: Moderate disability but independent in activities of daily living

CPC 3: Severe disability; dependent in activities of daily living

CPC 4: Persistent vegetative state

CPC 5: Dead

Figure 2. Participant Flow



CPR indicates cardiopulmonary resuscitation.
[a] An unknown number of patients were excluded who had crew-witnessed ventricular fibrillation/ventricular tachycardia and return of spontaneous circulation at first defibrillation.

Results

Study Population and Background Variables

During the study, 4998 cases of cardiac arrest were screened, of which 2593 were included in randomization. Four patients were excluded because of withdrawn informed consent, resulting in 2589 included patients in the intention-to-treat population, with 1300 patients in the mechanical CPR group and 1289 patients in the manual CPR group. After randomization, 116 patients were found either to meet exclusion criteria or not to meet inclusion criteria; for this intention-to-treat analysis, however, all patients were analyzed in the group they were randomized to regardless of this or eventual crossover or other protocol deviations (**Figure 2**).

Cardiac arrest background variables and events are described in **Table 1**. The notable differences between groups were the number of defibrillations delivered by the EMS crew and time to first defibrillation, which was delivered 1.5 minutes later in the mechanical CPR group, a possible result of the difference between the 2 treatment algorithms.

Primary and Secondary Outcomes

For the primary outcome, there was no significant difference in 4-hour survival between the mechanical CPR group and the manual CPR group (307/1300 [23.6%] vs 305/1289 [23.7%]; risk difference, −0.05%; 95% CI, -3.3% to 3.2%; $P<.99$). Similarly, there was no significant difference between groups in any of the secondary outcomes (**Table 2**).

Among the surviving patients in the mechanical CPR vs manual CPR groups, 62% vs 54% had CPC scores of 1 or 2 at intensive care unit discharge, 92% vs 86% had such scores at hospital discharge, 94% vs 88% at 1 month, and 99% vs 94% at 6 months after cardiac arrest. The CPC scores of surviving patients are shown in Table 2.

Postresuscitation Care

Among patients admitted to the hospital after ROSC, 198 (63%) were treated with hypothermia in the mechanical CPR group vs 214 (66%) in the manual CPR group (risk difference, -3.4%; 95% CI, -10.8% to 4.0%). Median duration of the treatment was 24.0 and 24.5 hours, respectively. Coronary angiography was performed in 118 patients (37%) in the mechanical CPR group

Table 1. Cardiac Arrest Background Variables and Events[a]

	Mechanical CPR (n = 1300)	Manual CPR (n = 1289)	Total (n = 2589)
Age, mean (range), y	69.0 (16-100)	69.1 (15-99)	69.1 (15-100)
Male	869 (67)	857 (66)	1726 (67)
Suspected cause of cardiac arrest[b]			
Heart disease	840 (65)	811 (63)	1651 (64)
Pulmonary disease	64 (5)	69 (5)	133 (5)
Respiratory arrest	59 (5)	47 (4)	106 (4)
Intoxication	35 (3)	41 (3)	76 (3)
Drowning	6 (0)	4 (0)	10 (0)
Other	172 (13)	181 (14)	353 (14)
Witnessed cardiac arrest[c]	861 (66)	840 (65)	1701 (66)
Crew-witnessed cardiac arrest	96 (7)	87 (7)	183 (7)
Bystander CPR[c]	745 (57)	709 (55)	1454 (56)
Initial rhythms			
Ventricular fibrillation or pulseless ventricular tachycardia	374 (29)	383 (30)	757 (29)
Pulseless electrical activity	255 (20)	254 (20)	509 (20)
Asystole	610 (47)	594 (46)	1204 (47)
Sinus rhythm	12 (1)	13 (1)	25 (1)
Other pulse-giving rhythms	29 (2)	29 (2)	58 (2)
Missing	20 (2)	16 (1)	36 (1)
No. of defibrillations on scene[c]			
0	308 (24)	697 (54)	1005 (39)
1	499 (38)	167 (13)	666 (26)
2	152 (12)	96 (7)	248 (10)
3	114 (9)	82 (6)	196 (8)
4-20	209 (16)	233 (18)	442 (17)
Mechanical CPR device brought to the patient from start, No. (%)[d]	1024 (79)	1016 (79)	2040 (79)
Time from cardiac arrest to emergency response			
To emergency call			
No. (%) with data	1204 (93)	1210 (94)	2414 (93)
Median time (IQR), min	2 (0-5)	2 (0-5)	2 (0-5)
To ambulance arrival			
No. (%) with data	1204 (93)	1212 (94)	2416 (93)
Median (IQR), min	10 (7-14)	9 (6-14)	10 (7-14)
To start of manual CPR by crew			
No. (%) with data	1184 (91)	1206 (94)	2390 (92)
Median (IQR), min	11.5 (7-16)	11 (7-15)	11 (7-16)
To start of mechanical CPR device			
No. (%) with data	1125 (87)	37 (3)	1162 (45)
Median (IQR), min	15 (10-20)	18 (10-27)	15 (10-20)
To first defibrillation			
No. (%) with data	937 (72)	565 (44)	1502 (58)
Median (IQR), min	17 (12-22)	15.5 (11-23.5)	16 (12-22)
To intubation			
No. (%) with data	852 (66)	828 (64)	1680 (65)
Median (IQR), min	20 (15-25)	18 (14-23)	19 (14-24)
To start of transportation			
No. (%) with data	839 (65)	811 (63)	1650 (64)
Median (IQR), min	38 (30-47)	35 (28-44)	37 (29-45)
To arrival at hospital			
No. (%) with data	841 (65)	809 (63)	1650 (64)
Median (IQR), min	47 (37-58)	44 (35-54)	45 (36-56)

(continued)

Table 1. Cardiac Arrest Background Variables and Events[a] (continued)

	Mechanical CPR (n = 1300)	Manual CPR (n = 1289)	Total (n = 2589)
Time to ROSC from start of manual CPR by crew			
No. (%) with data	460 (35)	446 (35)	906 (35)
Median (IQR), min	17 (11-25)	14 (9-21)	16 (9-23)
Medical history, No. (%) with data	814 (63)	775 (60)	1589 (61)
Coronary heart disease	304 (37)	295 (38)	599 (38)
Diabetes	111 (14)	122 (16)	233 (15)
COPD/asthma	106 (13)	97 (13)	203 (13)
Stroke	68 (8)	55 (7)	123 (8)
Cancer	68 (8)	54 (7)	122 (8)
None of above diagnoses	215 (26)	195 (25)	410 (26)
Not known	138 (17)	140 (18)	278 (17)

Abbreviations: COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; IQR, interquartile range; ROSC, restoration of spontaneous circulation.

[a] Data are presented as No. (%) of participants unless otherwise indicated. Percentages may not sum to group totals because of rounding.

[b] 10% in mechanical CPR group and 11% in manual CPR had missing data.

[c] 1% in both mechanical and manual CPR groups had missing data.

[d] 2% in mechanical CPR group and 1% in manual CPR group had missing data.

Table 2. Primary and Secondary Outcomes

Outcomes	No. (%) of Participants		*P* Value	Treatment Difference, % (95% CI)
	Mechanical CPR (n = 1300)	Manual CPR (n = 1289)		
4-Hour survival[a]	307 (23.6)	305 (23.7)	>.99	−0.05 (−3.3 to 3.2)
ROSC[b]	460 (35.4)	446 (34.6)	.68	0.78 (−2.9 to 4.5)
Arrival at emergency department with palpable pulse	366 (28.2)	357 (27.7)	.83	0.46 (−3.0 to 3.9)
Survival to discharge from ICU with CPC 1-2[c]	98 (7.5)	82 (6.4)	.25	1.18 (−0.8 to 3.1)
Survival to hospital discharge with CPC 1-2[c]	108 (8.3)	100 (7.8)	.61	0.55 (−1.5 to 2.6)
1-Month survival with CPC 1-2[d]	105 (8.1)	94 (7.3)	.46	0.78 (−1.3 to 2.8)
6-Month survival with CPC 1-2[d]	110 (8.5)	98 (7.6)	.43	0.86 (−1.2 to 3.0)
Survival to discharge from ICU[e]	158 (12.2)	153 (11.9)	.86	0.28 (−2.2 to 2.8)
With CPC 1	54(4.2)	34(2.6)	.04	1.52 (0.1 to 2.9)
With CPC 2	44 (3.4)	48 (3.7)		
With CPC 3	34 (2.6)	40 (3.1)		
With CPC 4	26 (2.0)	29 (2.2)		
Survival to discharge from hospital[e]	117 (9.0)	118 (9.2)	.89	−0.15 (−2.4 to 2.1)
With CPC 1	89 (6.8)	67 (5.2)	.08	1.65 (−0.2 to 3.5)
With CPC 2	19 (1.5)	33 (2.6)		
With CPC 3	9 (0.7)	15 (1.2)		
With CPC 4	0	1 (0.1)		
1-Month survival[f]	112 (8.6)	109 (8.5)	.89	0.16 (−2.0 to 2.3)
With CPC 1	92 (7.1)	74 (5.7)	.17	1.34 (−0.6 to 3.2)
With CPC 2	13 (1.0)	20 (1.6)		
With CPC 3	7 (0.5)	13 (1.0)		
With CPC 4	0	1 (0.1)		
6-Month survival[g]	111 (8.5)	104 8.1)	.67	0.47 (−1.7 to 2.6)
With CPC 1	103 (7.9)	88 (6.8)	.29	1.10 (−0.9 to 3.1)
With CPC 2	7 (0.5)	10 (0.8)		
With CPC 3	1 (0.1)	6 (0.5)		
With CPC 4	0	0		

Abbreviations: CPC, Cerebral Performance Category score; CPR, cardiopulmonary resuscitation; ICU, intensive care unit; ROSC, restoration of spontaneous circulation.

[a] One patient in mechanical CPR group and 3 in manual CPR group with unknown 4-hour survival were imputed as nonsurvivors.

[b] Two patients in mechanical CPR group and 1 in manual CPR group with unknown ROSC were imputed as having no ROSC.

[c] 10 patients in mechanical CPR group and 8 in manual CPR group with unknown outcome were imputed as having a bad outcome.

[d] 14 patients in mechanical CPR group and 15 in manual CPR group with unknown outcome were imputed as having a bad outcome.

[e] 10 patients in mechanical CPR group and 6 in manual CPR group with unknown outcome were imputed as nonsurvivors.

[f] 14 patients in mechanical CPR group and 14 in manual CPR group with unknown outcome were imputed as nonsurvivors.

[g] 14 patients in mechanical CPR group and 15 in manual CPR group with unknown outcome were imputed as nonsurvivors.

and in 130 (40%) in the manual CPR group (risk difference, -2.8%; 95% CI, -10.3% to 4.8%); 75 mechanical CPR patients (24%) and 87 manual CPR patients (27%) (risk difference, -3.1%; 95% CI, -9.9% to 3.6%) were treated with percutaneous coronary intervention, respectively.

Adverse Events

Twenty-three device-related adverse events were reported among 1282 uses of mechanical CPR. Of these, 8 cases involved a device malfunction in which the use of the mechanical device was discontinued. In the remaining 15 cases, me-

chanical CPR could be continued; in 7 of these cases, the device had to be repositioned and in 8 cases, minor technical issues were reported.

There were 7 reported serious adverse events in the mechanical CPR group and 3 in the manual CPR group. In the mechanical CPR group the following were reported: 1 case of possible airway bleeding; 1 case of suspected rupture of the spleen seen on computed tomography that was not confirmed when an autopsy was done; 1 case of pneumothorax; 1 case of a fractured thoracic vertebra in which bystander CPR was provided in the patient's bed followed by mechanical CPR; 1 flail chest (noted before deploying mechanical chest compressions); 1 migration of the device due to mucus on the chest, leading to subsequent removal of the device; and 1 case of preexisting stomach distension preventing the device from being properly applied. In the manual CPR group, 1 case of flail chest and abdominal aortic aneurysm, 1 case of flail chest, and 1 case of pneumothorax were reported.

Discussion

In this large, randomized, multicenter trial, an algorithm combining mechanical chest compressions and defibrillation during ongoing compressions provided no survival advantage over manual CPR administered according to guidelines. No difference in survival or neurological outcome was seen for up to 6 months after the cardiac arrest as, by then, the vast majority of survivors had CPC scores of 1 or 2, and most patients with initial CPC scores of 3 or 4 had either improved or died. The numbers of serious adverse events and device-related adverse events were low.

We chose 4-hour survival as the primary end point to study the effect of the 2 prehospital interventions because it would minimize any influence of expected variations in postresuscitation care. However, postresuscitation care was similar between the groups, supporting the validity of the observed similarity in secondary end points at time points up to 6 months. The current sample size has a 95% confidence interval for the 4-hour survival ranging from −3.3% to +3.2%. Translated another way, while the point estimate for treatment effect was near 0.0, our study could not rule out the possibility of a 3.2% benefit or a similarly sized harm from mechanical CPR relative to standard CPR. Similar considerations will affect the interpretation of the secondary outcomes of survival (ie, survival with good neurological outcome up to 6 months), which may be an even more relevant measurement of treatment outcome.

Rather than simply replacing manual compressions with mechanical ones, the mechanical CPR algorithm bundled several other changes to the resuscitation algorithm. Most notably, a first countershock was to be delivered to each patient in this group regardless of the presenting rhythm during ongoing compressions. This provided a continuous period of mechanical compressions leading up to the shock, eliminating the usual preshock pause to assess rhythm, and thereby potentially improving outcomes for patients presenting in ventricular fibrillation. As a consequence, many patients with nonshockable initial rhythms received an unnecessary shock. Inappropriate shocks have previously been shown to be relatively common during manual defibrillator use, and there is little or no evidence that they are harmful.[21] The consensus of the steering committee designing the study was that this initial shock without analysis in the mechanical CPR group had more potential for benefit than harm. Also of note, the mechanical CPR algorithm used 3-minute CPR periods rather than conventional 2-minute periods. With mechanical devices, compressions can be delivered for 3 minutes without concern about rescuer fatigue, and the approach might improve outcomes by increasing chest compression fraction.[22]

If the mechanical CPR group received consistently good chest compressions with few pauses, we can only speculate about why our hypothesis was not supported. Perhaps manual chest compressions were also consistently good or the delay of defibrillation in the mechanical CPR group caused by the specific algorithm was detrimental. By specifying initial defibrillation without any prior ECG rhythm analysis in that group, the aim was to minimize any delays to mechanical compressions and to the first defibrillation. However, the first defibrillation occurred 1.5 minutes later in the mechanical CPR group than in the manual CPR group (Table 1). By protocol, the first countershock was to be delivered 90 seconds after starting mechanical compressions; if it had been delivered at the start of mechanical compressions instead, time to defibrillation could have been similar in the 2 groups. This adjustment to the protocol might improve survival in the mechanical CPR group by several percent.[23] However, it is also possible that the additional compressions before defibrillation were beneficial.

Except for the difference in the number of defibrillations provided, which reflects the 2 different algorithms, background and demographic variables did not differ between the groups. This, together with the dropout of only 4 patients not willing to provide informed consent, supports the robustness of our results.

To better evaluate the mechanical CPR algorithm, our design excluded patients treated with defibrillation before arrival of the EMS crew (n = 337) and patients with crew-witnessed cardiac arrest achieving ROSC after the first defibrillation (numbers unknown). Because these excluded patients have relatively high survivability, the survival rate across all treated cardiac arrests in the participating communities is probably higher than the survival rate observed in our study.

Good clinical outcomes with a medical device depend in part on the usability and reliability of the device. This study documented a low rate of device malfunctions (<1%). Before randomization, 1.5% of the patients were deemed to be too large or too small to fit and were excluded. After randomization, 3.5% of the patients randomized to mechanical CPR did not fit the device; 2.3% were too big and 1.2% too small. This suggests the device can be expected to fit about 95% of cardiac arrest patients.

There were some limitations. The adherence to the 2 different algorithms was not evaluated on scene but is reflected

in the number of defibrillations delivered. Even if monitoring on scene would have been performed, available technology allowed recordings only of compression rate and pauses and not of correct depth or optimal positioning of hand or suction cup on the chest. In approximately 10% of the patients, impedance data (Code-Stat, Physio-Control Inc) was recorded and showed a chest compression fraction of 0.78 in the manual CPR group vs 0.84 in the mechanical CPR group. The mechanical CPR algorithm called for a first shock to all patients, without any prior cardiac rhythm analysis. At least 1 defibrillation was delivered to 75% of the patients in the mechanical CPR group vs 45% in the manual CPR group (Table 1). With 1% of patients receiving an unknown number of defibrillation shocks, we believe that responders did not fully adhere to the mechanical CPR algorithm in 24% of the cases. Of those, 93% were nonshockable rhythms; therefore, we suspect that some of the responders looked at the ECG before the shock. But we do not know if the responders registered the first rhythm as being the rhythm seen after the first defibrillation or before the first defibrillation in the mechanical CPR group. However, the distribution of the initial rhythms is similar in the 2 groups and similar to that in other large randomized trials within this patient population.[24-26]

We cannot tell to what degree the unique components of the 2 different algorithms or to what degree the mechanical and manual chest compressions alone have influenced the results. The question of whether this mechanical CPR device should replace manual chest compressions while maintaining other components of the guideline-directed resuscitation algorithm has to be investigated separately. However, we studied mechanical CPR implemented in an algorithm expected to work in most EMS organizations without unreasonable requests for resources.

Conclusions

In patients with out-of-hospital cardiac arrest, mechanical chest compressions in combination with defibrillation during ongoing compressions provided no improved 4-hour survival vs manual CPR according to guidelines. There was a good neurological outcome in the vast majority of survivors in both groups, and neurological outcomes improved over time. Thus, in clinical practice, CPR with this mechanical device using the presented algorithm can be delivered without major complications but did not result in improved outcomes compared with manual chest compressions.

ARTICLE INFORMATION

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REFERENCES

1. Steen S, Liao Q, Pierre L, Paskevicius A, Sjöberg T. The critical importance of minimal delay between chest compressions and subsequent defibrillation: a haemodynamic explanation. *Resuscitation*. 2003;58(3):249-258.

2. Sato Y, Weil MH, Sun S, et al. Adverse effects of interrupting precordial compression during cardiopulmonary resuscitation. *Crit Care Med*. 1997;25(5):733-736.

3. Paradis NA, Martin GB, Rivers EP, et al. Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation. *JAMA*. 1990;263(8):1106-1113.

4. Eftestøl T, Sunde K, Steen PA. Effects of interrupting precordial compressions on the calculated probability of defibrillation success

during out-of-hospital cardiac arrest. *Circulation*. 2002;105(19):2270-2273.

5. Rubertsson S, Grenvik A, Zemgulis V, Wiklund L. Systemic perfusion pressure and blood flow before and after administration of epinephrine during experimental cardiopulmonary resuscitation. *Crit Care Med*. 1995;23(12):1984-1996.

6. Weil MH, Bisera J, Trevino RP, Rackow EC. Cardiac output and end-tidal carbon dioxide. *Crit Care Med*. 1985;13(11):907-909.

7. Wik L, Kramer-Johansen J, Myklebust H, et al. Quality of cardiopulmonary resuscitation during out-of-hospital cardiac arrest. *JAMA*. 2005;293(3):299-304.

8. Olasveengen TM, Wik L, Steen PA. Quality of cardiopulmonary resuscitation before and during transport in out-of-hospital cardiac arrest. *Resuscitation*. 2008;76(2):185-190.

9. Steen S, Liao Q, Pierre L, Paskevicius A, Sjöberg T. Evaluation of LUCAS, a new device for automatic mechanical compression and active decompression resuscitation. *Resuscitation*. 2002;55(3):285-299.

10. Rubertsson S, Karlsten R. Increased cortical cerebral blood flow with LUCAS; a new device for mechanical chest compressions compared to standard external compressions during experimental cardiopulmonary resuscitation. *Resuscitation*. 2005;65(3):357-363.

11. Axelsson C, Karlsson T, Axelsson AB, Herlitz J. Mechanical active compression-decompression cardiopulmonary resuscitation (ACD-CPR) vs manual CPR according to pressure of end tidal carbon dioxide ($P(ET)CO_2$) during CPR in out-of-hospital cardiac arrest (OHCA). *Resuscitation*. 2009;80(10):1099-1103.

12. Wagner H, Terkelsen CJ, Friberg H, et al. Cardiac arrest in the catheterisation laboratory: a 5-year experience of using mechanical chest compressions to facilitate PCI during prolonged resuscitation efforts. *Resuscitation*. 2010;81(4):383-387.

13. Wik L, Kiil S. Use of an automatic mechanical chest compression device (LUCAS) as a bridge to establishing cardiopulmonary bypass for a patient with hypothermic cardiac arrest. *Resuscitation*. 2005;66(3):391-394.

14. Axelsson C, Nestin J, Svensson L, Axelsson AB, Herlitz J. Clinical consequences of the introduction of mechanical chest compression in the EMS system for treatment of out-of-hospital cardiac arrest—a pilot study. *Resuscitation*. 2006;71(1):47-55.

15. Smekal D, Johansson J, Huzevka T, Rubertsson S. A pilot study of mechanical chest compressions with the LUCAS device in cardiopulmonary resuscitation. *Resuscitation*. 2011;82(6):702-706.

16. Nolan JP, Deakin CD, Soar J, Böttiger BW, Smith G; European Resuscitation Council. European Resuscitation Council guidelines for resuscitation 2005, section 4: adult advanced life support. *Resuscitation*. 2005;67(suppl 1):S39-S86.

17. Rubertsson S, Silfverstolpe J, Rehn L, et al. The study protocol for the LINC (LUCAS in Cardiac Arrest) study: a study comparing conventional adult out-of-hospital cardiopulmonary resuscitation with a concept with mechanical chest compressions and simultaneous defibrillation. *Scand J Trauma Resusc Emerg Med*. 2013;21:5.

18. Cobb LA, Fahrenbruch CE, Walsh TR, et al. Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA*. 1999;281(13):1182-1188.

19. Wik L, Hansen TB, Fylling F, et al. Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. *JAMA*. 2003;289(11):1389-1395.

20. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet*. 1975;1(7905):480-484.

21. Kramer-Johansen J, Edelson DP, Abella BS, Becker LB, Wik L, Steen PA. Pauses in chest compression and inappropriate shocks: a comparison of manual and semi-automatic defibrillation attempts. *Resuscitation*. 2007;73(2):212-220.

22. Christenson J, Andrusiek D, Everson-Stewart S, et al; Resuscitation Outcomes Consortium Investigators. Chest compression fraction determines survival in patients with out-of-hospital ventricular fibrillation. *Circulation*. 2009;120(13):1241-1247.

23. Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP. Estimating effectiveness of cardiac arrest interventions: a logistic regression survival model. *Circulation*. 1997;96(10):3308-3313.

24. Aufderheide TP, Frascone RJ, Wayne MA, et al. Standard cardiopulmonary resuscitation vs active compression-decompression cardiopulmonary resuscitation with augmentation of negative intrathoracic pressure for out-of-hospital cardiac arrest: a randomised trial. *Lancet*. 2011;377(9762):301-311.

25. Jacobs IG, Finn JC, Jelinek GA, Oxer HF, Thompson PL. Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial. *Resuscitation*. 2011;82(9):1138-1143.

26. Olasveengen TM, Sunde K, Brunborg C, Thowsen J, Steen PA, Wik L. Intravenous drug administration during out-of-hospital cardiac arrest: a randomized trial. *JAMA*. 2009;302(20):2222-2229.