Circulation: Cardiovascular Quality and Outcomes

ORIGINAL ARTICLE

Compression-Only or Standard Cardiopulmonary Resuscitation for Trained Laypersons in Out-of-Hospital Cardiac Arrest: A Nationwide Randomized Trial in Sweden

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BACKGROUND: The ongoing TANGO2 (Telephone Assisted CPR. AN evaluation of efficacy amonGst cOmpression only and standard CPR) trial is designed to evaluate whether compression-only cardiopulmonary resuscitation (CPR) by trained laypersons is noninferior to standard CPR in adult out-of-hospital cardiac arrest. This pilot study assesses feasibility, safety, and intermediate clinical outcomes as part of the larger TANGO2 survival trial.

METHODS: Emergency medical dispatch calls of suspected out-of-hospital cardiac arrest were screened for inclusion at 18 dispatch centers in Sweden between January 1, 2017, and March 12, 2020. Inclusion criteria were witnessed event, bystander on the scene with previous CPR training, age above 18 years of age, and no signs of trauma, pregnancy, or intoxication. Cases were randomized 1:1 at the dispatch center to either instructions to perform compression-only CPR (intervention) or instructions to perform standard CPR (control). Feasibility included evaluation of inclusion, randomization, and adherence to protocol. Safety measures were time to emergency medical service dispatch CPR instructions, and to start of CPR, intermediate clinical outcome was defined as 1-day survival.

RESULTS: Of 11 838 calls of suspected out-of-hospital cardiac arrest screened for inclusion, 2168 were randomized and 1250 (57.7%) were out-of-hospital cardiac arrests treated by the emergency medical service. Of these, 640 were assigned to intervention and 610 to control. Crossover from intervention to control occurred in 16.3% and from control to intervention in 18.5%. The median time from emergency call to ambulance dispatch was 1 minute and 36 s (interquartile range, 1.1–2.2) in the intervention group and 1 minute and 30 s (interquartile range, 1.1–2.2) in the control group. Survival to 1 day was 28.6% versus 28.4% (P=0.984) for intervention and control, respectively.

CONCLUSIONS: In this national randomized pilot trial, compression-only CPR versus standard CPR by trained laypersons was feasible. No differences in safety measures or short-term survival were found between the 2 strategies. Efforts to reduce crossover are important and may strengthen the ongoing main trial that will assess differences in long-term survival.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02401633.

Key Words: cardiopulmonary resuscitation ■ heart arrest ■ mouth breathing ■ out-of-hospital cardiac arrest ■ resuscitation

See Editorial by Rea et al

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WHAT IS KNOWN

- Early cardiopulmonary resuscitation (CPR) increases survival in out-of-hospital cardiac arrest.
- Guidelines state that trained laypersons should perform standard CPR with 30 chest compressions followed by 2 rescue breaths (30:2).
- Chest compressions only CPR, omitting mouth-to-mouth breathing, has emerged as an alternative for laypersons not trained in CPR or unable or unwilling to perform rescue breaths as compression-only CPR is easier to perform and disseminate on a large scale.
- TANGO2 (Telephone Assisted CPR. AN evaluation of efficacy amonGst cOmpression only and standard CPR) trial is a randomized clinical trial designed to test whether CPR performed by trained laypersons with compression-only CPR is noninferior to standard CPR in witnessed, adult out-of-hospital cardiac arrest of presumed cardiac origin.

WHAT THE STUDY ADDS

- The present study presents data from the TANGO2 pilot designed to assess feasibility, safety, and intermediate clinical outcomes.
- Compression-only CPR versus standard CPR by trained laypersons was feasible and safe.
- No difference in the proportion of patients admitted alive to hospital was found. The clinical outcomes should be interpreted with caution because (1) this trial was not designed to detect such differences in clinical outcomes and (2) survival to hospital admission is a short-term clinical outcome and long-term survival was not assessed.
- Efforts to reduce crossover are important and may strengthen the ongoing main trial.

Nonstandard Abbreviations and Acronyms

CO-CPR	compression-only cardiopulmonary resuscitation
CPR	cardiopulmonary resuscitation
EMS	emergency medical service
IQR	interquartile range
OHCA	out-of-hospital cardiac arrest
S-CPR	standard cardiopulmonary resuscitation

Early cardiopulmonary resuscitation (CPR) is associated with increased survival after out-of-hospital cardiac arrest (OHCA).[1,2] Today, basic life support is thought with standard CPR (S-CPR) composed of 30 chest compressions followed by 2 rescue breaths (30:2).[3]

The importance of high-quality chest compressions with short interruptions is well established,[4–6] and even short interruptions can be associated with adverse hemodynamic effects.[7] There has also been concern that mouth-to-mouth ventilation could act as a barrier to or delay CPR-start.[8] Chest compression-only CPR (CO-CPR), omitting mouth-to-mouth breathing, has emerged as an alternative for laypersons not trained in CPR or unable or unwilling to perform rescue breaths.[3,9] CO-CPR is easier to teach and perform, and dissemination of this method has been associated with higher rates of CPR initiation and overall survival.[10,11] However, omitting ventilation leads to faster desaturation[12] and could potentially aggravate cerebral hypoxia.

Observational studies comparing CO-CPR to S-CPR performed by lay rescuers have shown neutral or conflicting results.[13,14] Three previous randomized trials of dispatcher instructions to untrained responders, comparing CO-CPR with instructions to perform compression and rescue breaths (15:2), showed neutral results, but a meta-analysis of those trials indicated better survival with compression only.[15–18] Based on these trials, the European Resuscitation Council recommends compression only for dispatcher-assisted CPR in adult OHCA to laypersons without previous CPR training.[19]

However, there is no clear evidence about the optimal form of dispatcher CPR instructions for lay bystanders with previous CPR training or the effect of compression-only versus standard resuscitation before the arrival of medical-trained personnel. Finally, no randomized trial has compared the impact on survival between CO-CPR to the present form of S-CPR with 30:2.

The TANGO2 (Telephone Assisted CPR. AN evaluation of efficacy amonGst cOmpression only and standard CPR) trial is a nationwide, randomized clinical trial designed to test whether CPR performed by trained laypersons with chest compression only is noninferior to S-CPR in witnessed, adult OHCA of presumed cardiac origin (https://www.clinicaltrials.gov; NCT02401633 and NCT03981107). This study presents data from the TANGO2 pilot that is designed to assess feasibility, safety, and intermediate clinical outcomes as part of the main trial.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Trial Overview

The TANGO2 study is an academic investigator-initiated, randomized, 1:1, open-label, multicenter study that tests the hypothesis that in witnessed, adult OHCA, CO-CPR by laypersons previously trained in CPR is noninferior to S-CPR in the outcome of 30-day survival. The study is performed with an adaptive seamless design approach with a pilot phase evaluating safety, feasibility, and intermediate clinical outcomes (reported here).

All patients from this study will also be included in the main TANGO2 trial. The primary outcome of the TANGO2 trial (30-day survival) is not revealed to investigators. The study started on January 1, 2017. For a full description of the trial protocol, please see Supplemental Method S1.

Ethics

The study was approved by the regional Ethical Review Board in Stockholm (Dnr 2014/97-31/2, Dnr 2015/1833-32, and Dnr 2019-0489). Patients who survived were informed about their participation in the trial, their right to review all data gathered about them, and their unconditional right to withdraw from further participation and follow-up.

Settings and Emergency Medical Services

Sweden had a population of 10.1 million people (December 31, 2017), covering an area of 450 000 km^2. There is 1 national emergency number (112) administered by a government-owned emergency coordinating agency (SOS Alarm AB). SOS Alarm AB is organized in 15 dispatch centers, all operating nationwide. In medical emergencies, SOS Alarm AB is responsible for the medical interview, giving medical advice if needed, triage, and coordinating emergency medical service (EMS) dispatch in 18 of 21 regions in Sweden. In the remaining 3 regions, medical emergencies are redirected to regional emergency medical dispatch centers, Sjukvårdens Larmcentral, for medical interviews, medical advice as needed, triage, and dispatch.

Dispatchers follow a criteria-based protocol for triage of medical emergencies.[20] A cardiac arrest should be suspected when a patient is described as unconscious and not breathing normally. Since 2011, instructions for dispatcher-assisted CPR have been composed of compression-only for adult victims of OHCA in accordance with the European Resuscitation Council guidelines.[21] For asphyxia-related cardiac arrest and OHCA in children, instructions include chest compressions and rescue breaths (30:2/15:2).

Suspected cardiac arrest triggers a response of 2 ambulances staffed with registered nurses with additional training in emergency medicine and anesthesiology. Ambulances perform advanced life support in accordance with the European Resuscitation Council guidelines.[21] In some areas, first responders such as firefighters or the police, are dispatched in parallel to the EMS.[22] First responders are trained in basic life support and are equipped with automated external defibrillators. The yearly incidence of EMS-treated OHCA is 56/100 000.[23]

Lay Responder CPR in Sweden

Teaching of basic life support has been mandatory in the compulsory schooling since 2011. Dissemination of CPR knowledge to the public is otherwise voluntary and taught by instructors certified by the Swedish CPR Council. All CPR education in Sweden follows European Resuscitation Council guidelines, and CPR is taught with 30 compressions alternated with 2 rescue breaths. There is no hands-only CPR education or any campaigns promoting compression-only. Between 1984 and 2018, there were over 5 million attendees at basic CPR courses (not individuals),[24] and the rate of CPR before EMS arrival was 71% in 2016.[25]

Study Population, Inclusion Criteria, and Randomization

All calls of suspected OHCA identified at the dispatch centers were eligible for screening for inclusion. When an emergency call is characterized as suspected OHCA, the inclusion criteria automatically appear as checkboxes on the desktop of the dispatcher as yes or no questions. Study inclusion criteria were given as follows:

1. Is the event witnessed (seen or heard)? Yes/No
2. Is there anyone on sight who has performed a CPR course (at any time)? Yes/No
3. Is the victim over 18 years old? Yes/No
4. Is the collapse likely caused by a medical condition (not in association with trauma, drowning, asphyxia, intoxication, or pregnancy)? Yes/No

If all inclusion criteria were present, the call could undergo randomization by a Web link, which generated a 1:1 allocation using a computerized random constructor (Microsoft Int32). After randomization, assignment to intervention (CO-CPR) or control—S-CPR—appeared as a pop-up on the desktop of the operator, together with instructions to provide to the caller (Figures S1 through S7).

In the intervention group, dispatchers were instructed to deliver the following phrases to the caller:

1. An ambulance is dispatched and is on its way to you.
2. Perform CPR with chest compressions only.
3. Push hard on the chest at a pace of 100 per minute without interruptions for rescue breathing.

In the control group, dispatchers were instructed to deliver the following phrases to the caller:

1. An ambulance is dispatched and is on its way to you.
2. Perform CPR with chest compressions and rescue breathing.
3. Push hard on the chest 30 times and give 2 rescue breaths. The pace of the compressions should be 100 per minute.

The intervention period continued until the arrival of EMS or dispatched first responders.

In addition, dispatchers were instructed to stay in connection with the callers until the arrival of EMS or first responders, to instruct callers to put the phone on loudspeaker, and to ask callers to count aloud while performing chest compressions, as all this is part of standard care procedures. Dispatchers were encouraged to suggest switching the CPR provider every 2 minutes if multiple rescuers were on the scene. An educational program was designed to inform all dispatch operators of the study procedure together with dispatcher-assisted CPR training (Supplemental Method S2).

Study Objectives

The objectives of the pilot study were to assess feasibility, safety, and an intermediate clinical outcome.

Feasibility measures were defined as follows:

1. Evaluation of inclusion, randomization, adherence to protocol by dispatchers including crossover, validation of data collection, and rate of inclusion.

Safety measures were defined as follows:

1. Time intervals for screening for inclusion and randomization, time to EMS dispatch, time to CPR instructions, time to start of CPR, correct inclusion, and proportion of patients correctly identified as cardiac arrests.

Intermediate clinical outcome was defined as survival to 1 day.

Data Collection

For all randomized calls, event times were collected from the dispatch center (time of incoming call, dispatch of EMS, screening for inclusion, randomization, and arrival of EMS).

All randomized calls were matched with the Swedish registry for CPR. The register follows a standardized format of reporting data and measures during resuscitation in OHCA.[26] All EMS organizations in Sweden participate in reporting to the register. The register has been described in detail elsewhere.[27,28] If there was no matching report in the register, ambulance records were reviewed; if EMS had performed CPR or the patient had been defibrillated by an automated external defibrillator, the case was classified as EMS-treated. Patients who had not been treated with CPR by EMS, that is, not cardiac arrest (other condition), certain signs of death at EMS arrival, or previous decision that CPR should not be initiated (ie, in terminal illness or palliative care) were excluded. Please see the consort flowchart in Figure S8.

Patient and resuscitation characteristics were obtained for all EMS-treated OHCAs. The clinical outcome of 1-day survival was defined as if the patient was alive on the first day after the cardiac arrest and data were obtained through the Swedish population register.

Audio logs of included calls were reviewed using a standardized template for evaluation of dispatcher-assisted CPR (Cardiac Arrest Registry to Enhance Survival).[29] The study inclusion criteria and type of CPR instructions were added as auxiliary variables. Please see Supplemental Method S3. Evaluators were blinded to the randomized assignment during call evaluation, and the assessment of interrater variability was performed.

All data were entered into a study-specific database. During all steps of data collection, blinding of the randomized assignment was concealed from investigators.

Statistical Analysis

All randomized EMS-treated OHCAs were included in the analysis. For descriptive statistics, time and age were treated as continuous variables and summarized as medians with interquartile ranges (IQRs). Categorical variables are presented as frequencies and proportions. To test for differences between groups, X^2 tests with continuity correction were used for categorical variables and the Wilcoxon rank-sum test was used for continuous variables. The α level was set at 0.05.

For intermediate clinical outcomes, results were analyzed on both a modified intention-to-treat basis and in a prespecified per-protocol population. We defined the modified intention-to-treat population as all randomized EMS-treated OHCA patients and the per-protocol population as the subset of the intention-to-treat population where the caller received assigned instructions by the dispatch operator. This pilot trial used superiority/inferiority testing as part of the safety analysis and for the assessment of intermediate clinical outcomes. The upcoming main survival trial will also use noninferiority testing, which was not used in the present study; for details about the main trial power calculation, please see Supplemental Method S1 for the full trial protocol.

RESULTS

Feasibility Measures

Inclusion and Randomization (Flowchart)

During the study period, a total of 11 838 calls were screened for inclusion (at least 1 of the inclusion questions were answered), whereof 2168 calls fulfilled all inclusion criteria and were randomized, 1107 (51.1%) to CO-CPR, and 1061 (48.9%) to S-CPR. After the exclusion of calls that were not EMS-treated OHCA, a total of 1250 (57.7%) remained, 640 in the CO-CPR group, and 610 in the S-CPR group (Figure).

Due to the outbreak of the coronavirus disease (COVID-19), the International Liaison Committee on Resuscitation and the Swedish Resuscitation Council issued temporary guidelines for layperson CPR in OHCA, recommending only looking for signs of life and performing chest compressions only.[30,31] Therefore, this present study was put on hold on date: March 12, 2020. This study includes patients from January 1, 2017, to March 12, 2020 (eg, pre-COVID-19).

Patient Characteristics

The median age was 73 and 74 years in the CO-CPR and S-CPR groups, respectively. The proportion of females was similar in both groups (35.8% versus 34.0%). The majority of OHCA occurred at home in both groups (72.9% versus 69.5%). The median time from the start of the emergency call to EMS arrival was 12.0 (IQR, 7.7–17.4) versus 11.6 min (IQR, 7.7–17.5) for CO-CPR and S-CPR, respectively. Any CPR before EMS arrival was initiated in 565 cases (90.4%) in the CO-CPR group and 536 (88.7%) in the S-CPR group. The number of patients found with ventricular tachycardia/ventricular fibrillation at first-rhythm analysis was 174 (27.9%) in the CO-CPR group and 180 (29.9%) in the S-CPR group (Table 1).

Evaluation of Audio Instructions to Caller and Adherence to Protocols

There were 1063 audio files available for review (85.0%). CPR was ongoing at the time of call pickup in 7.8% of the CO-CPR group and 11.3% of the S-CPR group. In the CO-CPR group, a total of 358 (65.4%) participants received CO-CPR instructions, and crossover (instructions on compressions and rescue breaths) was found in 88 (16.3%) calls. In the S-CPR group, 338 (64.5%) participants received instructions to provide compressions and rescue breaths, and crossover to instructions of chest compressions only was found in 97 (18.5%) calls (Table 2).

Some calls were not classified to any of the 2 instructions. This could be due to barriers hindering CPR instructions such as if the caller was not at the sight, hung up or left the phone, or inability to move the patient to a flat surface. This occurred in 93 (17.2%) calls in the

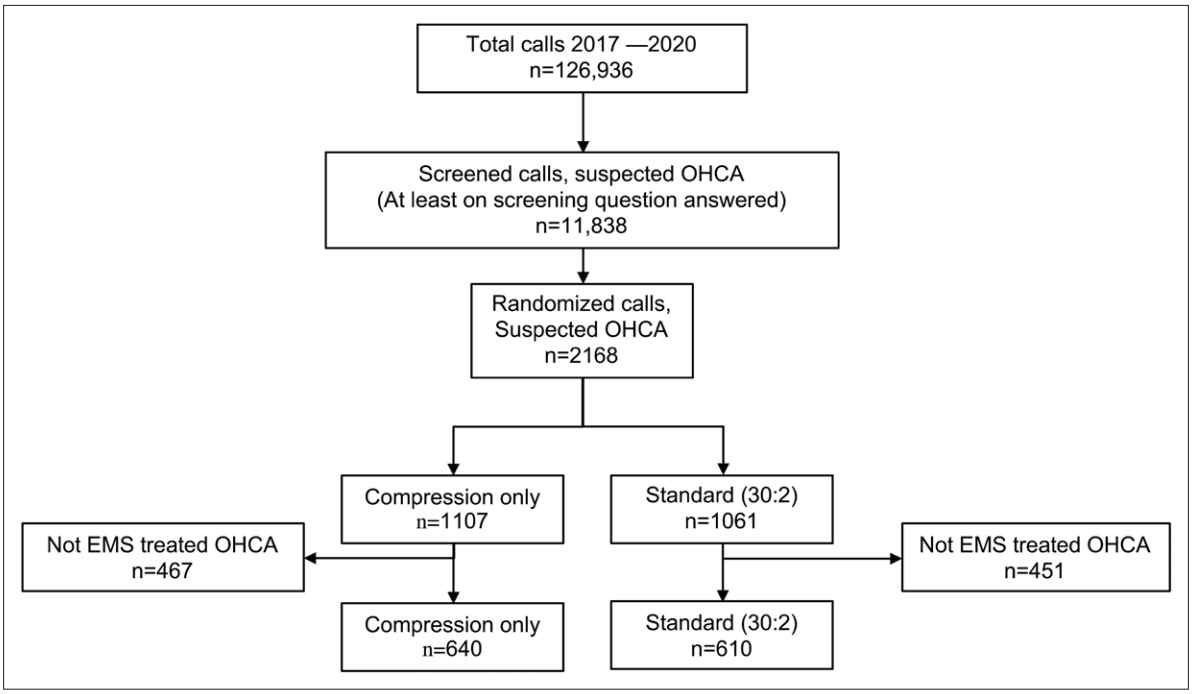

Figure. Flowchart inclusion and randomization.
EMS indicates emergency medical service; and OHCA, out-of-hospital cardiac arrest.

intervention group and 89 (17.0%) calls in the control group. Please see Table S1.

Safety Measurements

Time Delays

The median time from call to cardiac arrest recognition was 1.5 minutes (IQR, 0.8–2.7) for CO-CPR and 1.7 minutes (IQR, 0.9–3.0) for S-CPR (*P*=0.071). The corresponding time to EMS dispatch was 1.6 min (IQR, 1.1–2.2) and 1.5 min (IQR, 1.1–2.2) and from call to first chest compression instructions 3.4 min (IQR, 2.3–4.8) and 3.5 min (IQR, 2.2–4.8) for CO-CPR and S-CPR. respectively (*P*=0.665). The median time from call to randomization was 4.5 min (IQR, 2.8–7.1) in the CO-CPR group and 4.6 min (IQR, 3.0–7.2) in the S-CPR group (Table 3).

Correct Inclusion

Of the 2168 randomized patients, 1250 (57.7%) received CPR by the EMS. Of those, 60 cardiac arrests were later judged by the EMS to be due to asphyxia, trauma, or intoxication (4.8%).

Intermediate Clinical Outcomes

The numbers of patients at 1-day survival were 179 (28.6% [95% CI, 25.2–32.3]) in the CO-CPR group and 168 (28.4% [95% CI, 24.9–32.1]) in the S-CPR group (*P*=0.984). When analyzed on a per-protocol basis, the number of patients at 1-day survival was 103 (29.5% [95% CI, 25.0%–34.5%]) in the CO-CPR group versus 95 (28.9% [95% CI, 24.2%–34.0%]) in the S-CPR group (*P*=0.922; Table 4).

DISCUSSION

The TANGO2 study has been designed to compare survival after compressions-only CPR versus S-CPR in witnessed, adult OHCA, of presumed cardiac cause, in a noninferiority design.

Our main finding in this pilot phase of the study is that randomization to a strategy of CO-CPR versus S-CPR was feasible and appears to be safe. We found no differences between the 2 intervention strategies in time to dispatch of ambulance to CPR instructions to callers or in the proportion of patients admitted alive to the hospital. However, the clinical outcomes must be interpreted with caution because (1) this trial was not designed to detect such differences in clinical outcomes and (2) 1-day survival is a short-term clinical outcome and long-term survival was not assessed.

Feasibility Measures

The number of screened calls during the study period was lower than expected. Active recording of screening for inclusion was not mandatory. Therefore, dispatchers might not have formally screened calls that did not fulfill the inclusion criteria. However, the low number of screened calls indicates selection bias. For example, calls with difficulties in communication between the caller and emergency dispatcher may not have been screened for inclusion even if eligible. Conversely, it is possible that calls that included callers with high CPR competency and ongoing CPR at the time of call pickup might also

Table 1. Baseline Characteristics

	Compression only	Standard (30:2)	SMD	Missing (% of row)
n	640	610		
Age, y; median, IQR	73 (64–82)	74 (64–82)	0.035	2.6
Female sex, n (%)	228 (35.8)	206 (34.0)	0.039	0.6
Location, n (%)			0.079	0.7
At home	463 (72.9)	421 (69.5)		
Other	50 (7.9)	57 (9.4)		
Public	122 (19.2)	128 (21.1)		
Witnessed event, n (%)	508 (81.2)	482 (80.7)	0.011	2.2
Crew witnessed, n (%)	4 (0.7)	2 (0.4)	0.048	14.5
Cause as judged by EMS, n (%)			0.093	8.7
Medical	488 (82.6)	463 (84.2)		
Asphyxia	22 (3.7)	18 (3.3)		
Trauma	4 (0.7)	5 (0.9)		
Intoxication	4 (0.7)	7 (1.3)		
Unknown	73 (12.4)	57 (10.4)		
Layperson CPR before EMS, n (%)	565 (90.4)	536 (88.7)	0.054	1.7
First responder CPR before EMS, n (%)	190 (31.0)	162 (27.6)	0.076	3.9
Layperson AED use, n (%)	39 (7.3)	48 (9.2)	0.071	15.7
AED defibrillation before EMS, n (%)	23 (7.6)	26 (9.0)	0.051	52.5
Any ROSC, n (%)	259 (42.5)	247 (42.3)	0.005	4.6
Year, n (%)			0.098	0.0
2017	221 (34.5)	211 (34.6)		
2018	140 (21.9)	149 (24.4)		
2019	195 (30.5)	187 (30.7)		
2020	84 (13.1)	63 (10.3)		
EMS dispatch, min; median, IQR	1.6 (1.1–2.2)	1.5 (1.1–2.2)	0.055	15.0
ALS dispatch, min; median, IQR	2.2 (1.5–3.4)	2.1 (1.3–3.8)	0.075	94.6
Fire dispatch, min; median, IQR	2.6 (1.7–4.1)	2.6 (1.7–4.4)	0.038	28.0
Police dispatch, min; median, IQR	3.4 (2.4–4.9)	4.0 (2.4–6.4)	0.082	73.8
SMS volunteer dispatch, min; median, IQR	3.0 (2.1–4.4)	3.6 (2.3–5.5)	0.058	77.8
Screening question 1, min; median, IQR	3.9 (2.5–6.2)	4.0 (2.5–6.8)	0.058	9.2
Screening question 2–min; median, IQR	3.6 (2.2–5.8)	3.7 (2.3–6.2)	0.076	8.8
Screening question 3, min; median, IQR	4.0 (2.5–6.3)	4.1 (2.6–6.8)	0.067	9.0
Screening question 4, min; median, IQR	4.2 (2.7–6.6)	4.4 (2.9–7.1)	0.061	9.8
Randomization, min; median, IQR	4.5 (2.8–7.1)	4.6 (3.0–7.3)	0.045	0.4
EMS arrival–min; median, IQR	12.0 (7.7–17.4)	11.6 (7.7–17.5)	0.044	15.4
ALS arrival, min; median, IQR	15.3 (11.7–25.8)	13.8 (11.6–21.2)	0.163	95.3
First rhythm VT/VF, n (%)	174 (27.9)	180 (29.9)	0.043	2.0
Admitted alive, n (%)	179 (28.6)	168 (28.4)	0.005	2.6

AED indicates automated external defibrillator; ALS, advanced life support; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; IQR, interquartile range; ROSC, return of spontaneous circulation; SMD, standardized mean difference; SMS, short message service; VF, ventricular fibrillation; and VT, ventricular tachycardia.

not have been screened because the dispatcher did not see any need for CPR instructions.

Time delays to CPR instructions and start to CPR were long but comparable to previously reported results and to OHCAs not randomized during the study period. The time delays to CPR start are somewhat surprising given the inclusion criteria of callers with previous CPR training. We can only speculate about the reasons; these could include inefficient call handling, language barriers during call taking, and over examination of the condition of the patient. As stated above, the overall rate of CPR started before the emergency call was around 10%. This could indicate that many lay bystanders in this study needed confirmation and assistance from the dispatch operator to start CPR, even if they had undergone CPR training at some point in time. These results highlight the key role of the dispatch operator in OHCA.

We chose to include only bystander-witnessed events and those where there is a bystander on sight with CPR training. These inclusion criteria might have decreased

Table 2. Call Evaluation and Type of Instructions (Audit of Audio Logs)

Randomization allocation	Compression only (n=640)	Standard (n=610)	*P*
Not audited/missing audio file, n (%)	101 (15.7)	86 (14.1)	
Calls audited, n	539	524	
Type of instruction			<0.001
Compression+rescue breathing, n (%)*	88 (16.3)	338 (64.5)	
Compressions only, n (%)*	358 (65.4)	97 (18.5)	
Not applicable (caller not on sight, et cetera)*	59 (10.9)	59 (11.3)	
Unknown, undefined instruction*	34 (6.3)	30 (5.7)	

*Percentages correspond to the total number of available audio logs.

the inclusion rate more than expected. We thought it was important to be able to answer whether the effect of CO-CPR is time-dependent. In unwitnessed OHCA, the time of collapse is unknown. Therefore, we chose to include only witnessed OHCA, given that it is possible to approximate the time from collapse to the start of treatment. Finally, survival in unwitnessed OHCA is low. When comparing 2 different forms of CPR, including nonwitnessed OHCA might dilute the differences between groups, which could be problematic.

Crossover occurred in a little less than one-fifth of all calls, somewhat more so from S-CPR to CO-CPR. We can only speculate about the causes of crossover. One possibility might be that the call taker deviated from randomized allocation and provided instructions that they believed to be more suitable based on the perceived competence of the caller. A crossover from S-CPR to CO-CPR instructions might have occurred as a result of less experienced bystanders being more comfortable of performing CO-CPR and in the case of barriers during the emergency call. Inversely, it is possible that callers with good basic life support knowledge might have had a tendency to crossover to CO-CPR from S-CPR because they were trained and able to provide rescue breaths. In other words, crossover could have occurred for different reasons depending on the assigned randomization.

Our finding is in contrast to the previous trial by Rea et al,[16] where the rate of crossover was very low (0.8%–2.2%). In the study by Svensson et al[15], the crossover was not reported.

Safety Measures and Intermediate Clinical Outcomes

A complete safety analysis is not possible in a study with a relatively limited sample size. However, some major safety aspects can be addressed.

First, the time delays to cardiac arrest recognition and EMS dispatch are within American Heart Association-acceptable standards for telephone-assisted CPR.[32] Time delays to CPR instructions were long but comparable to previously reported results and to OHCAs not randomized during the study period.[33,34] In summary, we found no indication of time delays to EMS dispatch or CPR instructions caused by the trial itself.

Second, we found no significant differences in 1-day survival. These findings must be interpreted with extreme caution given that (1) this trial was not designed to detect such differences in clinical outcomes and (2) 1-day survival is a short-term clinical outcome and long-term survival was not assessed.

The objective of this trial was to exclude cardiac arrest caused by hypoxia before randomization. Determining the cause of a cardiac arrest is difficult, even for medically trained personnel.[35] However, the proportion of randomized patients later judged by the EMS to be caused by asphyxia, intoxication, or trauma was <5%.

Strengths and Limitations

This study has several limitations. First, this is an open-label trial because it is not possible to blind treatment to either dispatchers or CPR providers. However, EMS personnel were not aware if the patient was included in the trial. Also, blinding was preserved during all steps of data collection until the final analysis. Second, the low screening rate could indicate some sort of selection bias as discussed above, which could impact generalizability. Due to the nature of the situation, precise evaluation of the type of CPR actually provided or CPR quality is lacking, which is a major limitation. Finally, in some calls, CPR was ongoing at the time of call pickup. We do not know the type of CPR performed before an emergency call, and this has the potential to dilute the effect of the intervention.

Table 3. Call Evaluation and Time Measurements (Audit of Audio Logs)

Randomization allocation	Compression only (n=539)	Standard (n=524)	*P*	SMD	Missing
Time to CA recognition, min; median, IQR	1.5 (0.8–2.7)	1.7 (0.9–3.0)	0.071	0.094	26.5
Time to first chest compression, min; median, IQR	3.3 (2.1–4.7)	3.2 (1.9–4.9)	0.665	0.023	25.7
Time to start of CPR instruction, min; median, IQR	3.4 (2.3–4.8)	3.5 (2.2–4.8)	0.827	0.003	40.3

CA indicates cardiac arrest; CPR, cardiopulmonary resuscitation; IQR, interquartile range; and SMD, standardized mean difference.

Table 4. Clinical Outcome

Randomization allocation	Compression only	Standard (30:2)	*P*	Missing (%)
Modified intention to treat*				
n	640	610		
Admitted alive, n (%)	179 (28.6 [95% CI, 25.2–32.3])	168 (28.4 [95% CI, 24.9–32.1])	0.967	2.6
Per protocol†				
Instructions provided	Only compressions	Compressions+rescue breathing		
n	358	338		
Admitted alive, n (%)	103 (29.5 [95% CI, 25.0–34.5])	95 (28.9 [95% CI, 24.2%–34.0%])	0.922	

EMS indicates emergency medical service; and OHCA, out-of-hospital cardiac arrest.
*All randomized EMS-treated OHCAs.
†All randomized EMS-treated OHCAs where instructions were received in accordance with randomized assignment.

The study also has some important strengths, such as the prospective design and nationwide coverage.

Implications for the Main Trial

An independent data monitoring and safety committee reviewed all data and recommended the study to continue without modifications in May 2022. The temporary COVID-19 guidelines were removed on April 1, 2022, and the main trial was relaunched in September 2022.

To optimize screening (which may influence the validity and generalizability of the ongoing larger main trial), a mandatory screening log for all calls of suspected OHCA has been implemented. As our results also revealed an important limitation in terms of crossover, a renewed educational campaign has been initiated. In parallel to this, a project has just started, which has the purpose of timely audit and feedback of all cardiac arrest calls at each dispatch center to optimize the call handling process in accordance with the American Heart Association goals for dispatcher-assisted CPR.[36]

We believe that these efforts have the potential to improve performance in dispatcher-assisted CPR, decrease time delays to CPR instructions, and also to reduce crossover within the study.

Conclusions

In this national randomized pilot study, CO-CPR versus S-CPR by trained laypersons was feasible. No differences in time to ambulance dispatch, to CPR instructions to callers, or in the proportion of patients admitted alive to the hospital were seen between the 2 strategies; however, this pilot phase was not designed to detect clinically meaningful differences, and long-term survival was not assessed. Efforts to reduce crossover are important and may strengthen the ongoing main trial that will assess differences in long-term survival.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Supplemental Methods S1–S3
Figures S1–S8
Table S1

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