

BMJ Open Protocol of a Multicenter International Randomized Controlled Manikin Study on Different Protocols of Cardiopulmonary Resuscitation for laypeople (MANI-CPR)

Enrico Baldi,^{1,2,3} Enrico Contri,^{1,2,4} Roman Burkart,^{5,6} Paola Borrelli,⁷ Ottavia Eleonora Ferraro,⁷ Michela Tonani,^{1,8} Amedeo Cutuli,¹ Daniele Bertaia,² Pasquale Iozzo,⁹ Caroline Tinguely,¹⁰ Daniel Lopez,¹⁰ Susi Boldarin,¹¹ Claudio Deiuri,¹¹ Sandrine Dénéréaz,¹² Yves Dénéréaz,¹² Michael Terrapon,¹³ Christian Tami,^{14,15} Cinzia Cereda,^{14,15} Alberto Somaschini,^{1,3} Stefano Cornara,^{1,3} Andrea Cortegiani¹⁶

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For numbered affiliations see end of article.

Correspondence to

Dr Enrico Baldi;
enrico.baldi88@gmail.com

ABSTRACT

Introduction Out-of-hospital cardiac arrest is one of the leading causes of death in industrialised countries. Survival depends on prompt identification of cardiac arrest and on the quality and timing of cardiopulmonary resuscitation (CPR) and defibrillation. For laypeople, there has been a growing interest on hands-only CPR, meaning continuous chest compression without interruption to perform ventilations. It has been demonstrated that intentional interruptions in hands-only CPR can increase its quality. The aim of this randomised trial is to compare three CPR protocols performed with different intentional interruptions with hands-only CPR.

Methods and analysis This is a prospective randomised trial performed in eight training centres. Laypeople who passed a basic life support course will be randomised to one of the four CPR protocols in an 8 min simulated cardiac arrest scenario on a manikin: (1) 30 compressions and 2 s pause; (2) 50 compressions and 5 s pause; (3) 100 compressions and 10 s pause; (4) hands-only. The calculated sample size is 552 people. The primary outcome is the percentage of chest compression performed with correct depth evaluated by a computerised feedback system (Laerdal Q CPR).

Ethics and dissemination Due to the nature of the study, we obtained a waiver from the Ethics Committee (IRCCS Policlinico San Matteo, Pavia, Italy). All participants will sign an informed consent form before randomisation. The results of this study will be published in peer-reviewed journal. The data collected will also be made available in a public data repository.

Trial registration number NCT02632500.

BACKGROUND

Out-of-hospital cardiac arrest (OHCA) affects about 1 person in 1000 every year and is one of the principal causes of death in industrialised

Strengths and limitations of this study

- This is the first randomised controlled manikin study to verify whether the inclusion of different intentional interruptions during the cardiopulmonary resuscitation (CPR) could increase lay rescuers' CPR quality compared with the hands-only technique.
- The study is international, involving multiple training centres.
- The participant's performance lasts 8 min, which is the mean time to intervention of emergency medical services on a cardiac arrest scenario in Europe. The performance is evaluated by a reliable computerised feedback system.
- The main limitation of the study is that it is conducted on manikin, so there cannot be direct evidence of the benefit on patient's outcome.

countries^{1,2} with a mean survival rate at hospital discharge of about 7%.^{3,4} The chance of survival following OHCA depends on the Chain of Survival,⁵ as well as the steps taken in the first few minutes following the event (early recognition and call for help, early cardiopulmonary resuscitation (CPR), early defibrillation and postresuscitation care). With better implementation of the links of this chain, cardiac arrest survival can be improved.⁶ During the last years, there has been a growing interest on hands-only CPR, meaning continuous chest compressions until the arrival of emergency medical services (EMS) without interruptions to perform ventilation. The main reasons for this are that hands-only CPR seems to be more accepted by lay rescuers,⁷ it is easier to remember and to perform,⁸ and, above all, it

has been demonstrated that there are no significant differences in terms of efficacy compared with standard CPR at least in the first minutes after OHCA,^{9–16} which are the minutes in which it is more probably that a lay rescuer can intervene. For these reasons, the International Liaison Committee on Resuscitation (ILCOR) 2015 recommendations suggested this technique for untrained bystanders or for bystanders who are unwilling to give rescue breaths.¹⁷ ILCOR 2015 recommendations have also pointed out the need for high-quality CPR, namely a CPR with compressions of adequate rate (between 100 and 120/min), adequate depth (between 5 and 6cm), with complete chest recoil between compressions and with minimised interruptions between compressions. High-quality CPR can improve the survival after an OHCA,^{8,17} but it has been demonstrated that the quality of hands-only CPR decreases after 1 min.¹⁸ Since the mean time to intervention of EMS on a cardiac arrest scenario in Europe is about 8min,¹⁹ it is easy to understand that it is very difficult to perform a high-quality CPR until the arrival of EMS with the hands-only technique. It has also been shown that a 10s pause in the hands-only CPR protocol can increase its quality,²⁰ but there is limited evidence to support any CPR protocols for lay rescuers who are unwilling to give rescue breaths, except to perform chest compressions continuously until EMS arrival.

The aim of our study is to verify whether the inclusion of intentional interruptions of different frequency and duration during the CPR could increase lay rescuers' CPR quality during an 8 min scenario compared with the hands-only technique.

METHODS AND ANALYSIS

Trial centres

This randomised study will be performed in eight training centres, four in Italy and four in Switzerland. The full list of participating centres can be found at the trial registration website (NCT02632500). All the involved centres have experience in organising Basic Life Support/Automatic External Defibrillation (BLS/AED) courses for laypeople according to ILCOR 2015 guidelines, with the use of visual CPR feedback systems. The enrolment started in April 2016 and we expected to conclude the enrolment by August 2018.

Participants, study flow and recruitment

For the purpose of this study, laypeople within an age range of 18–80 follow a standard BLS/AED course according to ILCOR 2015, with a maximum certified instructor:participants ratio of 1:6, using Laerdal QCPR feedback system. Laerdal QCPR is a real-time visual feedback system able to measure CPR quality that can be connected wireless to a training manikin (Laerdal Resusci Anne QCPR). Other information about this system can be retrieved at the manufacturer's website.²¹ All the centres use the real-time feedback during their courses according to the recent evidence that this type of feedback improves the CPR performance of the laypeople.^{22–27} Figure 1 shows the study flow and

figure 2 shows the timeline as recommended by the Standard Protocol Items: Recommendations for Interventional Trials. The standard BLS/AED course used by all the participating centres is detailed in online supplementary file 1. Participants will perform 1 min training during the course with Laerdal QCPR to check and correct their CPR skill. At the end of each course, in order to test participants' performance, 1 min of compression-only CPR on the Resusci Anne QCPR manikin without visual feedback will be recorded. We chose the duration of 1 min in order to minimise the deterioration of chest compression quality due to fatigue according to the results from Nishiyama *et al*.¹⁸ This performance will be saved according to the required standard (surname, name, age, sex, height in cm, weight in kg, 1 min). People reaching $\geq 75\%$ in the parameters 'percentage of compressions with correct rate', 'percentage of compressions with correct depths', 'percentage of correctly released compressions' and 'percentage of compressions with correct hand position' at 1 min test will be asked to participate in the study. We decided to enrol only the people who reached that performance in order to eliminate any bias due to heterogeneity of the individual quality of CPR. Considering the aim of the study, which is to verify the superiority of a technique respect to another one, we prefer to select only people who reached a good-quality CPR because this approach reduces the possibility of differences in baseline and anthropometric characteristics among the four techniques. In particular, the value of 75% was chosen according to manufacturer's indications, which considers 'Advanced CPR Performer' those who reach that value. This was also confirmed by consensus among authors and was already used in a previous study performed in one of the centres participating in this protocol.²² People must sign an informed consent before participating and must fill in the International Physical Activity Questionnaire concerning the physical activities that people do as part of their everyday lives (online supplementary file 2).

Study groups and tests

The enrolled participants will be randomised to one of four study techniques (30 compressions and 2s of pause (30c2s), 50 compressions and 5s of pause (50c5s), 100 compressions and a 10s of pause (100c10s) or continuous chest compressions without any interruptions (hands-only). People will be asked to carry out an 8min performance according to the randomised technique on the Laerdal Resusci Anne QCPR manikin connected to the QCPR software without any type of feedback or help. At the end, the performance of each subject will be saved according to the previously described standard specifying the technique at which they were assigned. We chose single rescuer CPR for 8min considering the mean time of EMS intervention on an OHCA in Europe and the fact that about 70% of OHCA occurs at home, where it is more probable that the bystander is alone, as confirmed by the evidence present in literature.^{28,29} Before the test, the investigators will explain to the participant that if during the test he/she should not be able to continue according to the protocol scheme for

CONSORT 2010 Flow Diagram

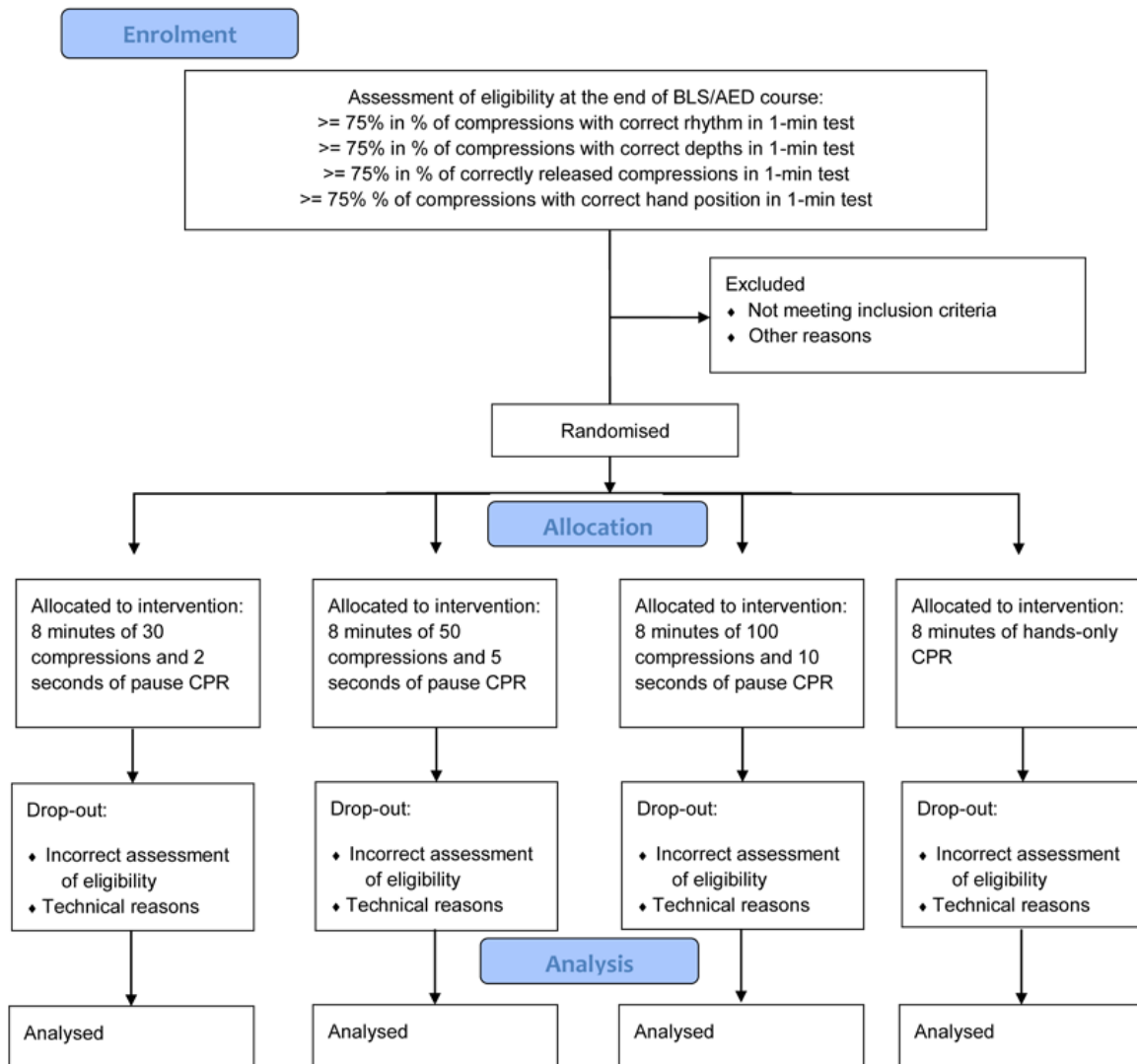


Figure 1 Flow chart of the study. BLS/AED, Basic Life Support/Automatic External Defibrillation; CPR, cardiopulmonary resuscitation.

fatigue, he/she could stop to rest, if needed. The registration, however, will continue until the end of the 8 min. Each participant should continue the test, according to his/her possibilities, up to the end of 8 min, as in a real scenario. In order to ensure the highest possible quality of data and consistency between the different participating centres, the 8 min test for each participant will be video-recorded.

Outcomes

The primary endpoint is the percentage of compressions with correct depth (at least 5 cm) among the groups. Secondary endpoints are the percentage of correctly

released compressions, the percentage of compressions with correct hand position, the compression rate, the number and the lengths of the interruptions taken to rest and flow fraction, namely the percentage of time where compressions were given. All the endpoints will be evaluated considering the whole 8 min performance carried out by each participant. All the variables will be registered by the Laerdal Q CPR software.

Sample size calculation and randomisation

We calculated the sample size to assess the superiority of each chest compression technique, differentiated for the

	STUDY PERIOD			
	Enrolment	Allocation	Post-allocation	Close-out
TIMEPOINT**	<u>1-minute test</u>	<u>0</u>	<u>8-minute test</u>	<u>Saving performance</u>
ENROLMENT:				
<u>Eligibility screen</u>	<u>X</u>			
<u>Informed consent</u>	<u>X</u>			
<u>Allocation</u>		<u>X</u>		
INTERVENTIONS:				
<u>30c2s protocol</u>			<u>X</u>	
<u>50c5s protocol</u>			<u>X</u>	
<u>100c10s protocol</u>			<u>X</u>	
<u>Hands-only CPR protocol</u>			<u>X</u>	
ASSESSMENTS:				
<u>Age, Sex, Height in cm, Weight in Kg, IPAQ score</u>	<u>X</u>			
<u>"percentage of compressions with correct rate", "percentage of compressions with correct depths", "percentage of correctly released compressions", "percentage of compressions with correct hand position", "number and the lengths of the interruptions taken to rest" and "flow fraction"</u>				<u>X</u>

Figure 2 Timeline of enrolment, interventions and assessments. CPR, cardiopulmonary resuscitation; IPAQ, International Physical Activity Questionnaire.

corresponding break in seconds, compared with ‘hands only’ technique and taking into account the results of unpublished pilot study from our group—the information for all the techniques in study is made from a pilot study where data come from 20 voluntaries (the percentage of compressions with correct depth, the primary outcome for this study, for each technique was found to be 66.5% for ‘hands only’, 84.7% for the 30c2s, 91.7% for the 50c5s and 81.7% for the 100c10s) — with a 90% power at a two-tailed significance level of 5%. We also assume a 20% increase in the sample size to take into account potential dropout. The calculated number of participants for each technique is 138 for a final sample of 552.^{30 31} A randomisation list for each centre, balanced for each technique, will be created out using a web resource.³¹

Blinding

During the BLS/AED courses, investigators are blinded to allocation group. The randomisation group for each

participant is specified in sealed opaque envelopes that must be opened after the 1 min test.

Data extraction and statistical analysis

Data will be extracted through a computer-based process. At the end of each participant’s performance, Laerdal QCPR creates a Microsoft Excel file (.xml) in a computer folder. All these files will be extracted and sent to the coordinating centre at the end of enrolment. The coordinating centre will exclude any file not compliant for technical reasons or for incorrect assessment for eligibility (dropout). These data will be incorporated in a single Microsoft Excel 2016 database and then will be analysed as follows.

The main descriptive statistics as mean and SD or median and IQR will be used to describe all the variables collected during the study. The X^2 test will be used to evaluate differences between categorical variables, whereas one-way analysis of variance or the Student’s t-test will be used to evaluate differences in continuous variables. If the

condition of normality will be not respected, an analogous non-parametric test (Mann-Whitney or Kruskal-Wallis test) will be used. To investigate the differences of each chest compression technique to ‘hands only’, a multiple test for proportion will be performed. At the end of data collection, a quality control of data will be made, and in-depth analysis will also be evaluated. We will perform a stratified analysis to control the possible confounders.

The P value of 0.05 will be considered significant in any case, except for multiple comparisons where the level of significance will be divided for the number of comparisons of interest. All the statistical analyses were performed using Stata V.14.

ETHICS AND DISSEMINATION

Research ethics approval

The study has been submitted to a regional ethics committee for medical research (IRCCS Policlinico San Matteo, Pavia, Italy) and was considered exempted from evaluation, in accordance with the Italian law, due to the nature of the study not involving real patients.

Consent or assent

At the end of the BLS/AED, after passing the 1 min test, participants were asked to sign an informed consent form to join the trial. The form explicitly contains also the request to record a video during the 8 min performance. All the documents are written in the language of the region in which each training centre operates.

Confidentiality

The original documents and files will be kept at the trial sites for 15 years. The lead investigator is responsible for data and file storage. All the files and videos of the 1 and 8 min performances are sent to the coordinating centre (Pavia nel Cuore, Pavia, Italy) for quality evaluation and statistical analysis. The lead investigator (EB) is responsible for data and files storage from all centres for 15 years.

PERSPECTIVE

In this protocol, we described our randomised trial comparing four CPR strategies performed by laypeople in a simulated 8 min cardiac arrest scenario in terms of CPR quality measured by a computerised feedback system. The strengths of this trial are the multicentre randomised design, the inclusion of participant with an objective and equal performance quality and the use of a reliable feedback system (Laerdal QCPR) for both training and data registration.^{26 27 30} The main limitation of our study is that it was performed on manikin, so there cannot be direct evidence of benefit on patient’s outcome. Another limitation is that our study design is able to detect superiority of three different CPR protocols compared with hands-only CPR. The eventual superiority of one CPR protocol over

the others, excluding hands-only, would be analysed in post hoc analyses or future trials.

Steering committee

Enrico Baldi, Enrico Contri, Roman Burkart, Andrea Cortegiani.

Author affiliations

¹Pavia nel Cuore ONLUS, Pavia, Italy

²Robbio nel Cuore ONLUS, Robbio, Italy

³School of Cardiovascular Disease c/o Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy

⁴Department of Anesthesia and Intensive Care, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

⁵Swiss Resuscitation Council, Bern, Switzerland

⁶Fondazione Ticino Cuore, Breganzona, Switzerland

⁷Unit of Biostatistics and Clinical Epidemiology, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy

⁸Emergency Medicine Department, Ospedale Maggiore di Lodi, Lodi, Italy

⁹General Intensive Care Unit, Policlinico Paolo Giaccone, University of Palermo, Palermo, Italy

¹⁰Emergency Training Center, Cugy, Switzerland

¹¹Centro Studi e Formazione Gymnasium, Pordenone, Italy

¹²École Supérieure d’Ambulancier et Soins d’Urgence Romande (ES-ASUR), Lausanne, Switzerland

¹³FormaMed Sàrl, Cortaillod, Switzerland

¹⁴Federazione Cantonale Ticinese Servizi Autoambulanze, Lugano, Switzerland

¹⁵Accademia di Medicina d’Urgenza Ticinese (AMUT), Breganzona, Switzerland

¹⁶Section of Anesthesia Analgesia, Intensive Care and Emergency, Department of Biopathology and Medical Biotechnologies (DIBIMED), Policlinico Paolo Giaccone, University of Palermo, Palermo, Italy

Contributors RB, AS and SC were involved in drafting the study protocol. PB and OEF were involved in statistical planning and drafting of the study protocol. MT, AC, DB, PI, CT, DL, SB, CD, SD, YD, MT, CT and CC were involved in the involvement and management of participating centres. AC was involved in drafting and revising the study protocol. EC developed the idea for this trial and was involved in drafting and revising the study protocol. EB conceived and developed the idea for this trial, was involved in drafting and revising the study protocol and was the principal investigator of this trial. All authors are involved in data acquisition and approved the final version of the manuscript.

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Disclaimer Laerdal Italia had no role in the study design and will have no role in the data collection, analysis or dissemination of study results.

Competing interests None declared.

Patient consent Obtained.

Ethics approval IRCCS Policlinico San Matteo, Pavia, Italy

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