A Multicenter International Randomized Controlled Manikin Study on Different Protocols of Cardiopulmonary Resuscitation for Laypeople

The MANI-CPR Trial

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Background: Compression-only cardiopulmonary resuscitation (CPR) is a suggested technique for laypeople facing out-of-hospital cardiac arrest (OHCA). However, it is difficult performing high-quality CPR until emergency medical services arrival with this technique. We aimed to verify whether incorporating intentional interruptions of different frequency and duration increases laypeople's CPR quality during an 8-minute scenario compared with compression-only CPR.
Methods: We performed a multicenter randomized manikin study selecting participants from 2154 consecutive laypeople who followed a basic life support/automatic external defibrillation course. People who achieved high-quality CPR in 1-minute test on a computerized manikin were asked to participate. Five hundred seventy-six were enrolled, and 59 were later excluded for technical reasons or incorrect test recording. Participants were randomized in an 8-minute OHCA scenario using 3 CPR protocols (30 compressions and 2-second pause, 30c2s; 50 compressions and 5-second pause, 50c5s; 100 compressions and 10-second pause, 100c10s) or compression-only technique. The main outcome was the percentage of chest compressions with adequate depth.
Results: Five hundred seventeen participants were evaluated. There was a statistically significant difference regarding the percentage of compressions with correct depth among the groups (30c2s, 96%; 50c5s, 96%; 100c10s, 92%; compression only, 79%; $P = 0.006$). Post hoc comparison showed a significant difference for 30c2s ($P = 0.023$) and for 50c5s ($P = 0.003$) versus compression only. Regarding secondary outcome, there were a higher chest compression fraction in the compression-only group and a higher rate of pauses longer than 10 seconds in the 100c10s.
Conclusions: In a simulated OHCA, 30c2s and 50c5s protocols were characterized by a higher rate of chest compressions with correct depth than compression only. This could have practical consequences in laypeople CPR training and recommendations.
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Key Words: Compression-only CPR, high-quality CPR, laypeople, training.

Out-of-hospital cardiac arrest (OHCA) affects approximately 1 in 1000 people every year and is one of the main causes of death in industrialized countries,[1–4] with a mean survival rate at hospital discharge of approximately 7%.[5,6] During the last several years, there has been a growing interest in compression-only cardiopulmonary resuscitation (CO-CPR) performed by laypeople

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until the arrival of emergency medical services (EMS). Factors supporting this technique are that it is more accepted by laypeople and it is easier to remember and perform, and seems to be similar in terms of efficacy compared with standard CPR, with interruption for ventilation with 30:2 ratio, at least in the first minutes after OHCA.[7–11] For these reasons, the International Liaison Committee on Resuscitation (ILCOR) 2015 recommendations suggest this technique for untrained bystanders or for bystanders who are unwilling to give rescue breaths.[12]

High-quality CPR can improve survival after an OHCA,[13] and its execution is encouraged by ILCOR recommendations[12] both for laypeople and healthcare providers. However, it has been shown that the quality of CO-CPR decreases rapidly after only 1 minute.[14] Because the mean time to intervention of EMS on a cardiac arrest scenario is approximately 8 minutes in many countries all over the world,[15–18] it is evident that it is very difficult to perform high-quality CPR with the compression-only technique for as long as it is needed. It has also been shown that a 10-second pause in the CO-CPR can increase its quality.[19] Thus, it remains unclear which is the best CPR protocol for lay rescuers who are unwilling to give rescue breaths; the only current recommendation being to perform chest compressions continuously, without any interruption, until EMS arrival. Our hypothesis was that the inclusion of intentional interruptions of different frequency and duration during the CPR could increase laypeople's CPR quality compared with the compression-only technique, so we designed this study to verify it during an 8-minute scenario.

METHODS

Study Centers and Oversight

We performed a randomized manikin study in 8 training centers (4 in Italy and 4 in Switzerland) between April 16, 2016, and April 26, 2019. All the enrolling centers had experience in organizing basic life support/automatic external defibrillation (BLS/AED) courses for laypeople according to ILCOR 2015 recommendations, with the help of visual CPR feedback systems. The trial was prospectively registered in clinicaltrials.gov (NCT02632500) on December 16, 2015. The protocol and statistical analysis plan were published[20] and are available in Supplemental Digital Content 1 (see PDF, Supplemental Digital Content 1, http://links.lww.com/SIH/A560, which contains the protocol and statistical analysis plan).

The Foundation Istituto di Ricovero e Cura a Carattere Scientifico Policlinico San Matteo, Pavia, Italy, ethics committee considered it exempted from evaluation in accordance to the Italian law, as the study did not involve human patients.

Participants, Study Flow, and Recruitment

Laypeople within an age range of 18 to 80 years followed a standard BLS/AED course according to ILCOR 2015 recommendations,[12] with a ratio of 1:6 certified instructor to participants at most, using Laerdal QCPR feedback system. This is a real-time visual feedback system, which measures CPR quality that can be connected wirelessly to a training manikin (Laerdal Resusci Anne QCPR).[21–23] Other information about the system can be retrieved at the manufacturer's website.[24] An outline of the standard BLS/AED course used by all the enrolling centers is available in Supplemental Digital Content 2 (see PDF, Supplemental Digital Content 2, http://links.lww.com/SIH/A561, which contains the outline of standard BLS/AED course).

During the course, participants performed a 1-minute training with Laerdal QCPR to check and correct their CPR skills. At the end of each course, to test participants' performance, 1-minute of CO-CPR on the Resusci Anne QCPR manikin, without visual feedback, was recorded.[14] People reaching a result of 75% or greater ("Advanced CPR performer" according to the manufacturer)[24] in the parameters "percentage of compressions with correct rate," "percentage of compressions with correct depth," "percentage of correctly released compressions," and "percentage of compressions with correct hand position" during this preliminary test, were invited to join the study voluntarily. Subjects who accepted to participate signed the written informed consent. They were subsequently asked to complete, by themselves, the International Physical Activity Questionnaire (IPAQ)[25] concerning the physical activities that people do as part of their everyday lives (see PDF, Supplemental Digital Content 3, http://links.lww.com/SIH/A562, which contains the written informed consent and IPAQ). Self-reported height and weight were asked to every participant and body mass index (BMI) was calculated.

Study Group and Test

Participants were randomized with an allocation ratio of 1:1:1:1 to one of the following 4 study techniques: 30 compressions and 2-second pause (30c2s), 50 compressions and 5-second pause (50c5s), 100 compressions and 10-second pause (100c10s), or continuous chest compressions without any interruptions (compression only). In addition to compression-only protocol, which is the standard, and 30c2s, which mirrors the recommended sequence by guidelines, we choose the 100c10s, as it was already used by Min et al,[19] and 50c5s as it was half of the protocol used by Min et al[19] and it was easy to remember by the participants. The participants were asked to carry out an 8-minute performance according to the randomized technique on the Laerdal Resusci Anne QCPR manikin, connected to the QCPR software, without any type of feedback or help. They were also asked to count themselves the seconds of pause allowed in each protocol. We chose single-rescuer CPR for 8 minutes considering the mean time of EMS intervention on an OHCA and the fact that approximately 70% of OHCA occurs at home, where it is more probable that the bystander is alone, as confirmed by the evidence present in literature.[3,4,15–18,26] The recording continued for 8 minutes even if participants were not able to finish the protocol scheme because of fatigue or other reasons; the percentage scores were calculated on the compressions performed and the seconds up to the end of the 8 minutes were counted as a pause. The whole 8-minute test was video recorded by an investigator and reviewed, at the end of the study, by the steering committee to ensure participants were not assisted during the test. The position to perform the test was with the manikin on the floor and the trainee kneeled beside it, as also for the 1-minute test.

Outcomes

The primary outcome was the percentage of compressions with correct depth (at least 5 cm) among the groups.[12] Secondary outcomes were the percentage of correctly released compressions, the percentage of compressions with correct hand position, the percentage of compressions with adequate rate (between 100 and 120 compressions per minute), the interruptions with a length of more than 10 seconds (pauses were considered as 10-second pause up to 10.5 seconds and 11-second pause if 10.51 seconds or longer), and the percentage of time where compressions were given [chest compression fraction (CCF)]. All the end points were evaluated considering the whole 8-minute performance carried out by each participant. All the variables were registered by the Laerdal QCPR software. We selected "depth of chest compression" as primary outcome, because evidence suggested that it is associated with patients' survival and functional outcome[27,28] and also because it is the parameter, which is most affected by rescuer's fatigue.[29,30]

Statistical Analysis, Randomization, Blinding

We calculated the sample size necessary to assess the superiority of each chest compression technique compared with "compression-only" technique based on unpublished results of a pilot trial on 20 volunteers. The percentage of compressions with correct depth, the primary outcome for this study, for each technique was found to be 66.5% for "compression only," 84.7% for 30c2s, 91.7% for 50c5s, and 81.7% for 100c10s, with a 90% power at a 2-tailed significance level of 5%. We also assumed a 20% increase in the sample size to take into account potential dropout. The calculated number of participants for each technique was 138, for a final sample of 552 subjects.[31]

The enrolled participants were allocated in one of the study groups using a randomization in blocks (approximately 18 subjects for each technique) to balance the allocation in each center/group, using a list created with a web resource.[32] Sealed opaque envelopes were generated by a collaborator, independent of the study, and were opened by each subject after the 1-minute test and given the informed consent form signed.

During the BLS/AED courses, investigators were blinded to allocation group.

Main descriptive statistics, as mean and standard deviation or median and interquartile range, were used to describe all the variables collected during the study. The χ^2 test was used to evaluate differences between categorical variables, whereas either 1-way analysis of variance or Student *t* test was used to evaluate differences in continuous variables. If the condition of normality was not met, an analogous nonparametric test (Mann-Whitney or Kruskal-Wallis test) was used. In case of multiple comparisons, Bonferroni correction was applied and then the level of statistical significance was reported to 0.05.

Because the outcome "percentage of compressions performed with correct depth" was scaled as 0 or 1, we performed a fractional logistic regression using age, sex, BMI, and level of physical activity (low, intermediate, and high) as independent variables.

The *P* value of 0.05 was considered significant. All the statistical analyses were performed using Stata Version 15. No interim analysis was planned.

Details about data extraction and monitoring can be found in Supplemental Digital Content 1 (which contains the protocol and statistical analysis plan).

RESULTS

Participants

Of the 2154 people who participated in the BLS/AED courses, 576 were enrolled in the study. Fifty nine (11.4%) were excluded from the analysis, as in 48 cases, the 1-minute CPR test was not correctly recorded because of technical reasons and, in 11, the registration of the 8-minute test incidentally failed (Fig. 1). These dropout participants were distributed among all the centers.

Of the 517 participants {median age, 28 [interquartile range (IQR), 23–41] years; 163 women [31.5%]}, 129 were randomized to 30c2s, 50c5s, and 100c10s groups (25% for each protocol), and 130 (25.1%) to the compression-only protocol. Individual characteristics of participants were evenly distributed among the groups (Table 1). More information regarding age distribution among the protocols is presented in Supplemental Digital Content 4 (see Table, Supplemental Digital Content 4, presenting age distribution).

Primary Outcome

The percentage of compressions with correct depth differed significantly among the 4 groups [30c2s, 96% (61.3–99.4); 50c5s, 96% (63–100); 100c10s, 92% (55–100); compression only, 79% (29.1–100%); χ^2 = 12.37; *P* = 0.006; Table 2; Fig. 2]. Post hoc comparison showed a statistically higher rate of compressions with correct depth for 30c2s versus compression only (*P* = 0.02) and for 50c5s versus compression only (*P* = 0.003), but there was no significant difference between 100c10s and compression only (*P* = 0.07).

Secondary Outcomes

The CCF was significantly higher in the compression-only group compared with all other groups (*P* < 0.001). There was a statistically significant difference in the number of interruptions of chest compressions lasting more than 10 seconds among the groups, but post hoc analysis revealed that 100c10s was the only protocol with a rate higher than compression only (*P* < 0.001; Table 2).

There was no significant difference among the groups in percentage of correctly released compressions and percentage of compressions with adequate rate, although it was possible to see a lower percentage in the 30c2s group (Table 2). No difference was found among the groups regarding percentage of compressions with correct hand position (Table 2).

Fractional Logistic Regression Model

Fractional logistic regression model revealed differences in primary outcome among protocols {30c2s vs. compression only, odds ratio [OR] = 2.12 [95% confidence interval (CI) = 1.40–3.20] and 50c5s vs. compression only [OR] = 2.09 [95% CI = 1.36–3.23], respectively}. A statistically significant association was found between the percentage of compressions with correct depth and sex [male vs. female, OR = 3.94 (95% CI = 2.85–5.45)] and with BMI [OR 1.11 (95% CI = 1.06–1.17); Table 3].

DISCUSSION

To the best of our knowledge, this is the largest randomized manikin study (and the first on laypeople) carried out to date evaluating the efficacy of different CPR protocols with intentional interruptions in comparison with compression-only technique.

The main finding of our study was that CPR protocols consisting in 30c2s and 50c5s produced a significantly higher percentage of compressions performed with correct depth

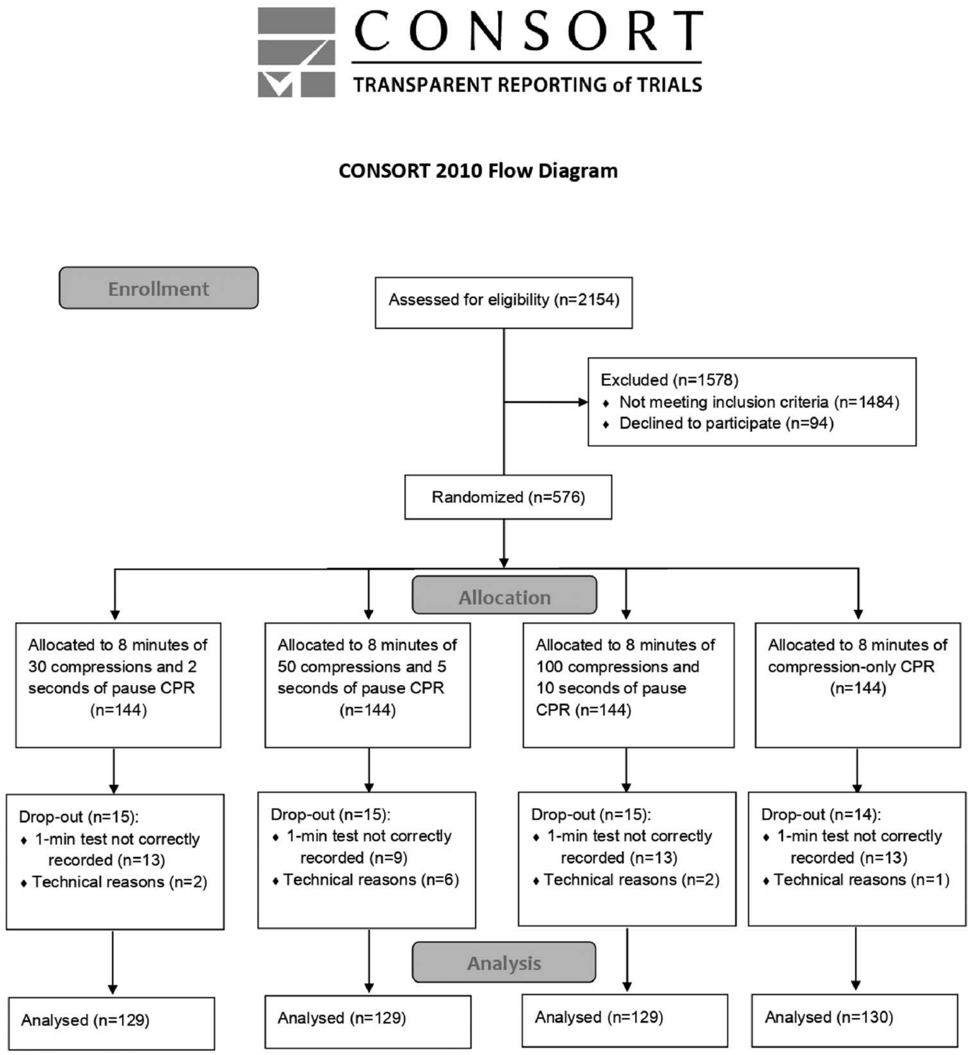

FIGURE 1. The Consolidated Standards of Reporting Trials flow diagram of the study.

than did CO-CPR. Our result is in line with other evidences that highlighted that CO-CPR leads to a worse quality of chest compressions, especially regarding compression depth, compared with standard CPR, in which 30 compressions alternate with 2 ventilations.[33,34] Moreover, our finding is consistent to that of Min et al,[19] who demonstrated that incorporating an interruption to take a rest during CO-CPR, and not to ventilate, increases the percentage of chest compressions performed with correct depth. However, contrary to our study, they found that a protocol alternating 100 chest compressions with 10 seconds of pause was the best in terms of CPR quality, although this protocol was not superior to CO-CPR in our population. This difference can be explained considering that the population in that study was very different from ours, as they enrolled only highly trained emergency medical technician trainees with experience in real cardiac arrest treatment,

TABLE 1. Comparison of the Anthropometric Characteristics and the Level of Physical Activity Among the Groups

	30c2s (n = 129)	50c5s (n = 129)	100c10s (n = 129)	Compression Only (n = 130)	*P*
Age, y*	27 (23.0–42.0)	30 (24.0–41.0)	27 (23.0–42.0)	28 (23.0–39.0)	0.76
Male	82 (23.2%)	97 (27.4%)	91 (25.7%)	84 (23.7%)	0.15
Height, cm*	174 (167.0–180.0)	176 (170.0–180.0)	175 (170.0–180.0)	175 (169.0–180.0)	0.31
Weight, kg*	73 (65.0–83.0)	74 (68.0–80.0)	73 (62.0–83.0)	72 (64.0–82.0)	0.78
BMI, kg/m^2*	23.9 (21.6–26.1)	23.9 (21.6–26.0)	23.5 (21.5–26.8)	23.7 (21.8–25.8)	0.91
Level of physical activity†					0.42
Low	13 (10.4%)	16 (13.8%)	11 (8.8%)	15 (11.9%)	
Intermediate	48 (38.4%)	37 (31.9%)	36 (28.8%)	48 (38.1%)	
High	64 (51.2%)	63 (54.3%)	78 (62.4%)	63 (50%)	

*Numerical data are expressed as a median value with interquartile range (IQR).
†Missing data in 25 participants (4.8%).

TABLE 2. Comparison of the Percentage of Compressions With Correct Depth, Percentage of Correctly Released Compressions, Percentage of Compressions With Correct Hand Position, Compression Rate, Chest Compression Fraction, and Number of Interruptions of More Than 10 Seconds Among the Groups

	Group				*P*			
	30c2s (n = 129)	50c5s (n = 129)	100c10s (n = 129)	Compression Only (n = 130)	Overall	30c2s vs. c-o*	50c5s vs. c-o*	100c10s vs. c-o*
Percentage of compressions with correct depth	96 (61.4–99.4)	96 (63.0–100.0)	92 (55.0–100.0)	79 (29.1–99.0)	0.006	0.023	0.003	0.07
Percentage of correctly released compressions	98 (85.0–100.0)	99 (91.0–100.0)	98 (90.0–100.0)	98 (88.0–100.0)	0.54			
Percentage of compressions with correct hand position	100 (89.0–100.0)	100 (91.0–100.0)	100 (96.0–100.0)	100 (91.0–100.0)	0.95			
Percentage of compressions with adequate rate	71 (34.9–91.9)	81 (46.0–96.8)	88 (48.5–97.9)	83.2 (45.0–96.0)	0.051			
Chest compression fraction, %	87.5 (83.5–90.8)	83.5 (80.6–86.0)	84.4 (82.3–86.7)	100 (97.7–100)	<0.001	<0.001	<0.001	<0.001
No. interruptions of more than 10 s	0 (0.0–0.0)	0 (0.0–0.0)	4 (2.0–6.0)	0 (0.0–0.0)	<0.001	>0.9	0.382	<0.001

Data are presented as median (IQR). "c-o" is for compression only.
*Post hoc analysis.

although we enrolled only laypeople, a population more representative of those being the first to encounter OHCA victims. Moreover, the sample size was smaller compared with our study, and the number of interruptions lasting more than 10 seconds in the performance was not evaluated.

Another parameter recently introduced as part of those suggested to achieve high-quality CPR is CCF, the proportion of time spent performing chest compressions during a resuscitation. The importance of this parameter, however, has remained unclear for years since, although most studies agree in highlighting that a higher CCF value is associated with better outcome.[35,36] However, other studies show evidence of an inverse correlation between survival and CCF.[27] This may be explained by a higher CCF value causing more rescuer fatigue leading to a decrease in chest compression quality, especially depth.[37] This highlights the importance of not only reducing interruptions to the minimum but also respecting other parameters of CPR quality. In our study, the compression-only protocol produced a higher CCF value compared with other protocols, but all 4 protocols were greater than 80%, which is the cutoff value for optimal outcome recommended by a recent consensus statement from the American Heart Association.[13]

Another important aspect is the duration of the interruptions of chest compressions. Guidelines stress that interruptions during CPR must be minimized and should last no longer than 10 seconds, as they can negatively affect the outcome.[12] In our study, the median number of interruptions of chest compression lasting more than 10 seconds was zero for 30c2s, 50c5s, and compression-only, whereas 100c10s was the only protocol with a higher number with respect to compression only. A possible explanation is that laypeople tend to underestimate the real duration of the seconds; therefore, they tend to exceed the limit of 10 seconds.

Regarding the other parameters that contribute to high-quality CPR,[13] there were not any differences for the percentage of compressions performed with adequate rate among the groups. In addition, the median percentage of correctly released compressions and the median percentage of compressions performed with correct hand positions were in line with guidelines recommendations, as both tend to 100% in all 4 protocols.

In addition to the protocols 30c2s and 50c5s, male sex and higher BMI were independently associated with a higher probability to increase the percentage of compressions with correct depth. This finding is consistent with previous studies that demonstrated a role of anthropometric variables on CPR

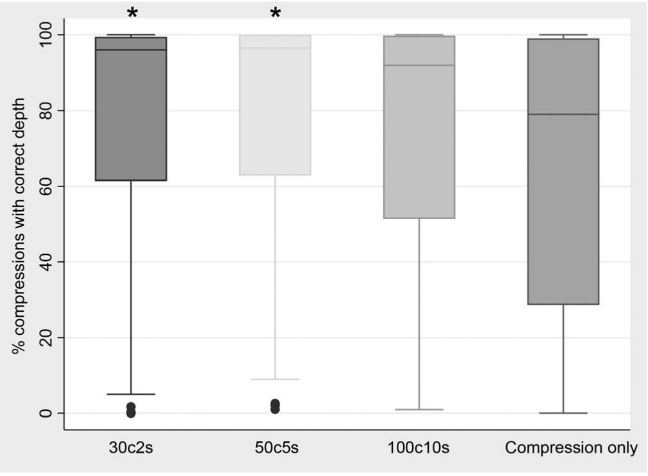

FIGURE 2. Percentage of compressions with correct depth. Data are represented as median with IQR. *Statistically significant difference respect to compression only.

TABLE 3. Fractional Logistic Regression Model

	Fractional Logistic Regression for Percentage of Compressions With Correct Depth	
	OR (95% CI)	P
Sex (male vs. female)	3.94 (2.85–5.45)	<0.001
Age, y	0.99 (0.98–1.01)	0.831
BMI, kg/cm^2	1.11 (1.06–1.17)	<0.001
Protocols		
Compression only	1	
30c2s	2.12 (1.40–3.20)	<0.001
50c5s	2.09 (1.36–3.23)	0.001
100c10s	1.41 (0.93–2.15)	0.100
Level of physical activity		
Low	1	
Intermediate	1.29 (0.79–2.11)	0.304
High	1.51 (0.94–2.40)	0.083

The dependent variable is the percentage of compressions with correct depth. The independent variables are sex, age, BMI, protocols, and level of physical activity. The OR of each protocol is calculated with respect to the compression-only protocol. The level of physical activity (low, intermediate, and high) was defined according to the IPAQ.

quality.[38,39] On the other hand, the level of physical activity calculated with IPAQ was not related with the primary outcome. This could be the starting point for further studies, as no information is available on this topic involving laypeople.

The results of our study, considering the context of previous literature, suggest that 30c2s and 50c5s may lead laypeople to perform CPR with a higher percentage of chest compressions with correct depth compared with compression only, during an 8-minute scenario and maintaining the other parameters of high-quality CPR within the values suggested by the guidelines. This could have interesting practical consequences in CPR training and recommendations for laypeople.

Strength and Limitations

The strength of this study is the randomized, multicenter design, with prospective registration and prepublished protocol. Moreover, we used a validated and reliable method to measure CPR performance during tests (QCPR),[21–23] which were video recorded for quality control.

Our study has limitations. Firstly, it was a study performed on manikins. Although we asked participants to perform an 8-minute test, which is close to the mean time to intervention of EMS in Europe, our findings should be confirmed in a "real world" setting to evaluate benefit on patients' outcome. Secondly, our study population consisted on relatively young laypeople who performed well at a BLS/AED course immediately before the performance. We preferred to select only people who reached the "advanced CPR performer" level at the 1-minute final test to reduce the risk of bias because of heterogeneity of individual CPR quality. However, this may limit the generalizability of our findings.

In addition, height and weight were self-reported by the participants, so an incorrect report of this measurement may have affected our results.

Another limitation is that no information on the precourse level of training and basaline fatigue of the participants are available. Despite the 1-minute final test may have helped reduce bias related to these issues, differences among the groups regarding these characteristics may have been present.

Lastly, we decided not to exclude the participants who did not manage to perform the full 8-minute test. In these cases, the time without compression were considered as interruptions and the lengths in seconds were measures. However, only 5 participants interrupted the compression for more than 40 seconds, whereof 4 for more than 60 seconds. Considering the small number of participants with relevant interruptions, it is unlikely that this has affected the overall results.

CONCLUSIONS

In a simulated scenario of OHCA performed by well-trained laypeople, 30c2s and 50c5s were superior to the compression-only technique in terms of percentage of chest compressions with adequate depth, with no significant impact on compression rate and chest recoil. Further studies are needed to evaluate the impact of these findings on patients' outcome.

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