Continuous chest compression cardiopulmonary resuscitation following out-of-hospital cardiac arrest

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Articles appraised

Rea T, Fahrenbruch C, Culley L, et al. CPR with chest compression alone or with rescue breathing. *N Engl J Med* 2010; 363: 423–33.

Svensson L, Bohm K, Castren M, et al. Compression only CPR or standard CPR in out-of-hospital cardiac arrest. *N Engl J Med* 2010; 363: 434–42.

Critical care issue

Out-of-hospital cardiac arrest claims hundreds of thousands of lives each year.¹ Early bystander cardiopulmonary resuscitation (CPR) improves the likelihood of successful resuscitation and favourable outcome.² However, recent guidelines have decreased the emphasis on rescue breathing while promoting continuous chest compression-CPR (CCC-CPR). Continuous chest compression-CPR avoids interruptions in compressions, thereby maximizing cerebral and coronary perfusion.³ Furthermore, avoiding exogenous breaths should lessen positive intrathoracic pressure, thereby increasing cardiac filling.⁴ Taking these factors into account, this technique should improve the delivery of oxygenated blood during circulatory standstill. There may

also be less reluctance on the bystander's part if the technique involves less mouth-to-mouth contact. A previous relatively small randomized controlled trial in humans compared CCC-CPR vs standard CPR with rescue ventilations.⁵ In the July 2010 issue of *The New England Journal of Medicine*, two large-scale prospective randomized controlled trials were published regarding this topic of concern.^{6,7}

Summary and key findings

Rea *et al.* performed a prospective randomized controlled trial in three centres, two in the United States and one in the United Kingdom.⁶ Enrolment occurred from July 2004 to April 2009, and 1,941 of 5,525 eligible patients were enrolled. Nine hundred eighty-one patients were randomized to receive CCC-CPR, and 960 patients were randomized to receive standard CPR with rescue breathing. The primary endpoint was survival to hospital discharge, while secondary outcomes included return of spontaneous circulation and a favourable neurologic status at hospital discharge (defined as a Cerebral Performance Category of 1 [good cerebral performance] or 2 [moderate cerebral disability]). The allotted treatment was given to 76.7% of patients enrolled in the study.

Svensson *et al.* also performed a prospective randomized controlled trial⁷ using the Swedish Emergency Medical Dispatch System. Enrolment occurred from February 2005 to January 2009, and 1,276 of 3,809 eligible patients were enrolled. Six hundred twenty patients were randomized to receive CCC-CPR, and 656 patients were randomized to receive standard CPR with rescue breathing. The primary endpoint was 30-day survival, while

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secondary endpoints included one-day survival, survival to discharge, and survival based on the initial cardiac rhythm. The allotted treatment was given to 81.2% of patients enrolled in the study.

In Rea's study, survival to hospital discharge was not statistically different between groups (12.5% CCC-CPR vs 11.0% standard CPR, 95% confidence interval (CI) -1.4 – 4.4 ; $P = 0.31$). Furthermore, at the end of care by Emergency Medical Services, there was no statistical difference either in the percentage of patients with a pulse (34.8% CCC-CPR vs 31.4% standard CPR, 95% CI -0.8 – 7.6 ; $P = 0.12$) or in the percentage of patients with a favourable neurological status (14.4% CCC-CPR vs 11.5% standard CPR, 95% CI -0.8 – 6.5 ; $P = 0.13$). The authors claimed a trend towards favourable neurological outcome following CCC-CPR, particularly for those with arrest secondary to cardiac cause or those with a shockable arrest.

Similarly, in Svensson's study, 30-day survival was not statistically different between the two groups (8.7% CCC-CPR vs 7.0% standard CPR, 95% CI -1.2 – 4.6 %; $P = 0.29$). The one-day survival was also similar between the two groups (24% CCC-CPR vs 20% standard CPR; $P = 0.18$) as was survival to discharge (19.1% CCC-CPR vs 14.8% standard CPR; $P = 0.16$). There was a trend towards increased survival at discharge, at one day, and at 30 days following CCC-CPR. For patients with witnessed out-of-hospital cardiac arrest, both authors concluded that CCC-CPR was associated with similar or potentially better survival when compared with standard CPR.

Critical appraisal

Current state of the literature and study relevance

For half a century since the formal introduction of CPR, oxygenation and ventilation have been integral to initial resuscitation following cardiac arrest.¹ It has only been in the previous two decades that this method has been challenged. In animal models of ventricular fibrillation and in human observational and cohort studies, CCC-CPR was non-inferior to standard CPR and possibly was superior.^{8–15} Therefore, in 1997, the American Heart Association called for further research.¹⁶ In 2000, Hallstrom *et al.* published the first human randomized trial comparing 241 patients who underwent CCC-CPR vs 279 patients who underwent standard CPR in out-of-hospital cardiac arrest.⁵ Survival to hospital discharge was higher for the CCC-CPR group (14.6 vs 10.4%, respectively) but did not reach statistical significance ($P = 0.18$). The study was also underpowered. For these reasons, the larger multicentre studies of Rea *et al.* and Svensson *et al.* were eagerly anticipated.

Analysis of methodology

The two studies were similar but not identical. Both involved recruitment by emergency medical dispatchers following any call for suspected cardiac arrest. Patients were included if they were unconscious (and not obviously dead) and if the patient had either abnormal or absent breathing. Svensson included only witnessed cardiac arrests, while Rea included cardiac arrests of all-comers. Exclusion criteria for both studies included primary respiratory arrests, evidence of trauma or intoxication, inability of the bystander to receive instructions for CPR (due to either unwillingness or communication difficulty), or arrival of EMS prior to the bystander administering CPR. While Rea's study was performed only in adult patients (>18 yr), Svensson included patients over eight years-of-age. In both studies, dispatchers provided telephone instructions to the bystander to perform either CCC-CPR or standard CPR with rescue breathing (in a ratio of 15:2). In Rea's study, randomization occurred by opening sequentially numbered envelopes that were stratified by the dispatch centre and blocked in sets of ten. In Svensson's study, the allotted treatment was recorded on each data collection sheet and concealed by a slip of paper that was removed upon patient recruitment. The data collection sheets were separated into blocks of 100 sheets with 50 sheets for each instruction randomly allocated by an SPSS random number generator.

In Rea's study, blinded personnel reviewed a standardized data abstraction form and the dispatch audiotape. The neurological status of the patients was determined in two of the three centres, but the personnel who made this determination were not specified. In Svensson's study, emergency medical dispatchers recorded the details of patient demographics and cardiac arrest. Further information was derived later from EMS records and the Swedish national registry. Notably, neurological outcome was not reported. Neither study blinded the EMS staff, dispatcher, or hospital personnel. Neither author specified whether the data analyzers (in contrast to the data collectors) were blinded. Nevertheless, both studies examined primary outcomes that were unequivocal, which should minimize bias. In contrast, Rea's examination of neurological status is open to bias. Data in both studies were analyzed according to protocol and intention-to-treat, and no significant difference was found between CCC-CPR and standard CPR.

Strengths, weaknesses, and external validity

We commend both research groups for conducting large-scale prospective randomized controlled trials to examine mortality following two initial resuscitation strategies.

Both studies were well designed, clinically relevant, and easily understood. The randomization was sound and the patient characteristics and other administered treatments were similar between the two arms. However, as with any such study, there are limitations.

Unfortunately, neither investigator recruited enough patients to meet their sample size calculation. Rea aimed to detect an absolute difference of 3.5% in survival rate with 80% power, which would have required 2,100 patients in each arm. Svensson aimed to detect a 2% difference in mortality with 80% power, which would have required 2,213 patients in each arm. Insufficient enrolment increases the risk of a type II error. Furthermore, approximately one-third of the randomized patients in each study did not fulfill inclusion and exclusion criteria, which reduces generalizability. The investigators deliberately excluded respiratory, toxic, or traumatic causes of cardiac arrest. However, distinguishing these types of cardiac arrests in real time can be difficult for experienced clinicians, much less the lay public.

Neither investigator compared CCC-CPR with the most up-to-date compression-ventilation strategy, because the protocols were designed prior to the 2005 guidelines,¹⁷ which promote a ratio of 30:2 not 15:2. Thus, the standard CPR group received twice as many ventilations, perhaps exaggerating its influence. Both studies can also be criticized for substantial protocol deviations. In Rea's study, almost one in every four patients did not progress to chest compression, and in Svensson's study, more than one in every ten medical dispatchers gave CPR instructions beyond those provided. Perhaps protocol violations are understandable given the stress associated with cardiac arrest and the consequences of failed resuscitation; however, they threaten generalizability. Nevertheless, investigators mitigated the protocol violations by analyzing the data both with intention-to-treat and per protocol analysis.

While survival is a useful and objective endpoint, functional neurological recovery is also important. Svensson *et al.* did not report on neurological outcome, and Rea reported on only two of three centres, which signifies that this endpoint was further underpowered. Questions also remain regarding "hands-only CPR" in prolonged resuscitation and in-hospital cardiac arrest. Both Svensson and Rea studied relatively brief bystander resuscitative efforts. Within minutes, well-equipped and highly trained EMS personnel took over resuscitation. Patients typically have oxygen reserves to tolerate anoxic resuscitation for at least a few minutes. It remains unclear when, if ever, the oxygenation benefit of rescue breaths outweighs the circulatory benefits of uninterrupted chest compressions.¹ Despite these limitations, these two trials have studied the effects of

CCC-CPR in a combined total of more than 3,000 patients on two continents.

Clinical perspective

Regardless of their limitations, these studies are significant, especially considering the millions of patients who receive CPR annually and the tens of thousands of people who are taught these resuscitation techniques. We may prefer studies that show a clear benefit or detriment. However, the conclusion that CCC-CPR is non-inferior is clinically relevant given evidence that the public (and medical personnel) is averse to providing rescue breathing, primarily citing concerns of communicable disease transmission.¹⁷⁻²⁰ Continuous chest compression-CPR simplifies basic life support. It is easier to teach, easier to remember, and easier to perform, especially as a single rescuer.²⁰ Due to its comparative simplicity, this technique is more likely to be performed early on and without interruption. Therefore, while CCC-CPR remains to be studied in the hospital setting or following prolonged anoxic arrest, it has considerable potential to improve outcome. There is little doubt that early CPR saves lives.² In a word, the "why" of CPR has been answered. The current issue is the "how" of CPR, and the question remains: "How" can CPR be performed most successfully, and "how" can bystanders be encouraged to perform CPR based on the best and the most practical evidence?

Conclusions

Two prospective randomized controlled trials have found that CCC-CPR is associated with at least as good a survival rate as CPR with rescue breathing following out-of-hospital cardiac arrest. Results cannot be readily generalized to respiratory arrests; arrests secondary to trauma or toxic ingestions, arrests in young children, or arrests following in-hospital or prolonged arrest. However, "hands-only" CPR could be the preferred method for managing outpatient cardiac arrest because it is easier to teach and more likely to be performed.

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