

Cardiopulmonary resuscitation before defibrillation in the out-of-hospital setting: a literature review

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ABSTRACT

Background Many studies over the past decade have investigated delaying initial defibrillation to perform cardiopulmonary resuscitation (CPR), as it has been associated with increased rates of restoration of spontaneous circulation and/or survival. Since 2006, a number of studies have investigated these procedures. The objective of this study was to undertake a literature review examining the commencement of CPR before defibrillation in the out-of-hospital setting.

Methods A literature review was undertaken using the electronic medical databases Ovid Medline, EMBASE, CINHAL Plus, Cochrane Systematic Review and Meditext, from their commencement to the end of June 2011. Keywords used in the search included: CPR, defibrillation, ventricular fibrillation, VF, EMS, EMT, paramedic, emergency medical service, emergency medical technician, prehospital, out-of-hospital and ambulance. References of relevant articles were also reviewed.

Findings Of the 3079 articles located, 10 met the inclusion criteria. The results of these studies showed conflicting results. All retrospective studies (n=6) indicated a benefit in performing pre-shock CPR on patients with ventricular fibrillation for durations between 90 and 180 s. Conversely, all randomised controlled trials demonstrated no benefit from providing CPR before defibrillation compared with immediate defibrillation for return of spontaneous circulation, neurological outcome and/or survival to hospital discharge. However, none of the studies reported evidence that CPR before defibrillation is harmful.

Conclusion Conflicting evidence remains regarding the benefit of CPR before defibrillation. The establishment of a consistent timeframe of chest compressions before defibrillation in the out-of-hospital setting will provide uniformity in standards in clinical practice and education and training.

In 2007, over 9500 people died of a cardiac arrest in Australia.¹ This accounts for approximately 7% of the overall number of deaths that occur in Australia annually. Data from Rural Ambulance Victoria and the Metropolitan Ambulance Service in Victoria, Australia, revealed that paramedics attended 8978 cardiac arrests from January 2002 to December 2003.²

There is strong evidence suggesting that high quality cardiopulmonary resuscitation (CPR), regardless of whether it is performed by healthcare professionals, improves survival rates from cardiac arrest, and increases the likelihood of return of spontaneous circulation (ROSC).^{3–6} Analysis of the ventricular fibrillation (VF) waveform of both

automated and manual CPR by Box *et al*⁷ revealed that CPR increases the likelihood of successful defibrillation for patients in VF. It has been shown that pauses in pre-shock CPR as short as 3–27 s decrease the mean probability of ROSC by approximately 23%, underlying the importance of CPR in the resuscitation effort.⁸

Despite evidence that CPR has a positive effect during cardiac arrest, there is widespread debate and an emerging body of knowledge on the impact of a period of CPR before defibrillation of patients in VF/pulseless ventricular tachycardia (VT), and whether it has a positive effect on the likelihood of survival to hospital discharge, the rate of ROSC and the rate of favourable neurological outcomes. Many studies over the past decade have investigated delaying initial defibrillation to CPR as it has been associated with increased rates of ROSC and/or survival and/or favourable neurological outcomes.^{9–14}

It is hypothesised that by providing CPR before defibrillation this will improve the cellular status of the myocardium in the hope of increasing the likelihood of successful defibrillation.¹⁵ This also causes changes in the VF waveform such as increases in frequency and coarseness of the VF wave form, which is considered to improve the likelihood of successful defibrillation.¹⁵ In addition, this is believed to have a greater benefit for patients who have a response time of more than 4–5 min by emergency medical services (EMS) personnel.^{9–11 14}

The Australian Resuscitation Council electrical therapy for adult advanced life support guidelines (2010),¹⁶ recognised that the results of clinical studies assessing the effectiveness of CPR before defibrillation rather than a strategy of immediate defibrillation were inconsistent. Since 2006 there have been numerous studies on the strategy of CPR before defibrillation for patients found in VF/pulseless VT, with results still proving to be inconsistent on whether this strategy offers any benefits to patient outcomes. However, there have been no reports of adverse effects on patient outcomes as a result of CPR being administered before defibrillation in the out-of-hospital setting.

Overall, to the best of our knowledge, there is only a handful of high quality randomised controlled trials on the benefits of CPR administration before defibrillation in the out-of-hospital setting. Considering the benefits that CPR has overall on patients in cardiac arrest, further investigation is warranted. Further investigation would enable clarity for paramedics on the role of pre-shock CPR, and will assist in the creation and implementation of standardised guidelines for out-of-hospital cardiac arrests (OHCA). Extended investigation on the role of pre-shock CPR will also

provide educational consistency between higher education institutions and the out-of-hospital sector. In other words, this consistency will reduce the likelihood of paramedic students being taught different approaches, which is currently the case.¹⁷ Standardised teaching of paramedics allows the discipline to maintain 'best practice' in line with contemporary changes in evidence-based practice, and the removal of potentially harmful and out-of-date practice.

The International Liaison Committee on Resuscitation recently recommended that defibrillation should not be delayed for CPR as there is inconsistent evidence to support or refute a delay in defibrillation.¹⁸ However, this does not exclude the option of a period of CPR before the initial defibrillation. If CPR is to be performed before the initial defibrillation, it is still unclear how long this period of CPR should be before defibrillation attempts. In a recently published article by Stiell *et al*,¹⁹ it was found that there was no difference in outcomes for patients who received 30–60 s of CPR and those who received 180 s of CPR before defibrillation.

The objective of this study was to undertake a literature review examining the commencement of CPR before defibrillation in the out-of-hospital setting.

METHODS

A literature review was undertaken using the electronic medical databases Ovid Medline, EMBASE, CINHALL Plus, Cochrane Systematic Review and Meditext from their commencement to the end of November 2010.

The search strategy used the following MeSH terms and keywords: CPR, defibrillation, ventricular fibrillation, VF, EMS, EMT, paramedic, emergency medical service, emergency medical technician, prehospital, out-of-hospital and ambulance. These search terms were used individually or in combination. The reference list of retrieved articles was reviewed to ascertain whether articles were missed during the initial search process.

Articles were included if they reported on the use of CPR on patients in VF/pulseless VT before defibrillation in the out-of-hospital setting. Articles were excluded if they were not in English, not featuring human subjects, or were letters to the editor.

RESULTS

The search located 3079 articles; initially 11 publications met the inclusion criteria. Further analysis of these articles revealed that one of the 11 articles was focused on first-responding fire fighters and did not mention EMS or paramedic personnel²⁰ and was subsequently excluded. This left 10 articles to be reviewed,^{7–15 21} which are summarised in supplementary table 1 (available online only). Table 1 includes the National Health and Medical Research Council's evidence hierarchy.

DISCUSSION

It was difficult to draw solid conclusions from the reviewed studies, as the majority of studies were predominately low-level studies and were performed on relatively small study sizes. Several studies were able to demonstrate that the administration of CPR before defibrillation had positive effects on patient outcomes when EMS response times were greater than 4–5 min, however, those studies failed to obtain sufficient participant numbers to power the studies adequately. This could have potentially affected the external validity of the results obtained.

Table 1 National Health and Medical Research Council evidence hierarchy: designations of 'levels of evidence' according to type of research question

Level	Intervention
1	A systematic review of level II studies
2	A randomised controlled trial
3 (I)	A pseudo-randomised controlled trial (ie, alternative allocation or some other method)
3 (II)	A comparative study with concurrent controls: non-randomised, experimental trial, cohort study, case-control study, interrupted time series with a control group
3 (III)	A comparative study without concurrent controls: historical control study, two or more single-arm studies, interrupted time series without a parallel control group
4	Case series with either post-test or pre-test and post-test outcomes

The available literature suggests that further randomised controlled trials are required to produce more conclusive evidence on whether there is any benefit for patients when CPR is commenced before defibrillation in the out-of-hospital setting.

Increased survival to hospital discharge

Several studies demonstrated that patients who received CPR before defibrillation showed an increased rate of survival to hospital discharge when EMS personnel response times were greater than 4–5 min. In a pseudo-randomised trial by Cobb *et al*,¹¹ it was found that the overall survival rate improved from 24% to 30% ($p=0.04$). The majority of this increase in survival rate occurred in patients who had a response time of more than 4 min (17% vs 27% $p=0.01$).¹¹ A randomised trial by Wik *et al*¹⁴ revealed that survival to discharge for patients with a response time of over 5 min showed an improvement from 4% to 22% ($p=0.006$). In a similar trial, Jacobs *et al*¹³ revealed an 18% improvement in survival to hospital discharge in the subgroup of patients in whom response times were more than 5 min. However, the interpretation of this result should be treated with caution as the CI was wide with the lower value also being close to the null (CI 1.61 to 34.3).¹³ All three of the trials were limited by potential issues with confounding variables influencing the results. The study by Cobb *et al*¹¹ was limited by a significant disparity between the size of the control cohort ($n=639$) and the intervention cohort ($n=478$). Whereas the study by Wik *et al*¹⁴ was limited by a relatively small control ($n=96$) and intervention ($n=104$) cohort with 250 participants being required in each cohort for the study to be powered sufficiently, which means the study was potentially underpowered. This was a similar issue that Jacobs *et al*¹³ encountered, with their study also being underpowered by failing to recruit the required number of patients, 390 in total; they recruited and analysed 256 patients (control $n=137$ vs intervention $n=119$). In a study conducted by Hayakawa *et al*,¹² an increase in favourable neurological outcomes was demonstrated; however, there was no change in survival rates to hospital discharge as expected (37% for defibrillation first vs 38% for CPR before defibrillation; $p=0.929$), casting doubt over the generalisability of the results obtained by Cobb *et al*¹¹ and Wik *et al*.¹⁴

In a meta-analysis of randomised controlled trials by Meier *et al*²¹ there was an indication that CPR before defibrillation for patients who have an EMS response time of over 5 min does improve outcomes for patients who have OHCA. However, the results were considered to be statistically not significant. This perhaps warrants further randomised controlled trials that focus on patients with an EMS response time of over 5 min.

Increase in favourable neurological outcomes

In a non-randomised trial conducted by Hayakawa *et al*,¹² it was shown that patients who received CPR before defibrillation showed an increase in favourable neurological outcomes for patients at 30 days post-OHCA (28% vs 14%; $p=0.04$), and 1 year post-OHCA (26% vs 11%; $p=0.03$). Similar increases were found by Cobb *et al*,¹¹ with 23% of patients receiving CPR before defibrillation having a favourable neurological outcome, compared with 17% of patients who received defibrillation. However, both of the studies conducted by Cobb *et al*¹¹ and Hayakawa *et al*¹² were limited by not obtaining sufficient participant numbers to power the studies adequately, neither Cobb *et al*¹¹ nor Hayakawa *et al*¹² included statistical power analyses. The study conducted by Hayakawa *et al*¹² was also limited by the overall small study size, and on average patients who were in the control group initially received an average 2.3 min of CPR before first defibrillation, which may have possibly skewed the results.

Increase in the rate of achievement of ROSC

The only trial to show any increase in the rate of ROSC was a randomised trial conducted by Wik *et al*.¹⁴ The trial showed that patients with a response time of more than 5 min who received CPR before defibrillation had a 20% increase in the achievement rate of ROSC when compared with patients who had a response time of over 5 min and received defibrillation first (58% vs 38% $p=0.04$). If CPR before defibrillation has a positive effect on the likelihood of the achievement of ROSC when EMS response times are more than 5 min (average EMS response times are approximately 12 min),¹⁵ there are significant potential gains for patients treated for OHCA by EMS personnel.

The benefits of CPR before defibrillation in terms of ROSC is further substantiated by Jennings *et al*,² when only 20% (1790 from 8978) of all OHCA attended to by Rural Ambulance Victoria and the Metropolitan Ambulance Service were bystander witnessed in Victoria, Australia. This further underlines the importance of early CPR and defibrillation, with increasing emphasis now being placed on the availability and use of automated external defibrillators (AED) by members of the public. Manufacturers of AED devices need to consider this issue of CPR before defibrillation and take into account the possible benefits of a period of CPR before defibrillation, regardless of patient downtime, to prevent increased complications in the application and use of an AED. Consideration of the recent International Liaison Committee on Resuscitation changes in resuscitation guidelines, which recommend not delaying initial defibrillation for CPR, is also required. There is also a need for issuing concise voice prompts by the AED to enhance the resuscitation effort and reduce pauses in pre-shock CPR.²²

No effects on rate of survival to hospital discharge, or favourable neurological outcome, or increase in the rate of achievement of ROSC

Challenging the previously mentioned studies, several studies and a meta-analysis of randomised controlled clinical trials indicated there was no increased survival to hospital discharge, no increased rate of achievement of ROSC, and no increase in favourable neurological outcomes from performing CPR before defibrillation.^{9 13 21}

Jacobs *et al*¹³ and Baker *et al*⁹ concluded in their randomised controlled trials that there was little, if any, benefit in terms of increased survival to discharge, increased rate of favourable neurological outcomes and an increased rate of ROSC for

patients who received CPR before defibrillation. The study by Jacobs *et al*¹³ did not achieve the participant numbers to power the study adequately, which could have altered the results that were obtained. Furthermore, in the study conducted by Jacobs *et al*¹³ there was a significantly lower than expected survival rate from OHCA (4.7% compared with a previously obtained OHCA survival rate of 10%). Furthermore, the ambulance service where the study by Jacobs *et al*¹³ took place did not provide inotropic support post-ROSC, which may have influenced survival rates. Moreover, a more recent study examining the effect of inotropes on patient survival to hospital discharge by Jacobs *et al*²³ found that the use of out-of-hospital inotropes improved the likelihood of achieving ROSC.

A meta-analysis of randomised controlled trials conducted by Meier *et al*²¹ was unable to uncover current evidence to support the concept that CPR before defibrillation increases the rate of survival to hospital discharge, the rate of achievement of ROSC, or increases the rate of favourable neurological outcomes for patients who have OHCA. We speculate that this was possibly due to the small number of participants enrolled in each randomised trial, and due to the fact that only four randomised trials were included in the meta-analysis resulting in a small pool of participants.

A randomised controlled trial conducted by Jost *et al*²⁰ was initially excluded due to the study being focused on first responding fire fighters. However, results showed that patients who received CPR before defibrillation had similar survival to hospital discharge rates (13.3% for CPR first vs 10.6% for defibrillation first; $p=0.19$), and a similar rate of ROSC (47.0% for CPR first vs 48.6% for defibrillation first; $p=0.65$). As previously mentioned, the study by Jost *et al*²⁰ was excluded because it was focused on first responder fire fighters and not EMS or paramedic personnel. However, this does indicate that this might be an area for further investigations in the future; particularly as first responder fire fighters have a well-established system in Melbourne, Victoria, Australia. In a study conducted by Boyle *et al*,²⁴ it was shown that a first responder's programme run by the Metropolitan Fire and Emergency Services Board could decrease response times and time to resuscitative efforts, which could have positive benefits on patient outcomes.

Optimal time for CPR to be performed before defibrillation

From all the studies analysed in this review, the amount of time that CPR was performed varied in each study, from 90 s to 3 min.^{9 11–14 21} The only paper offering an optimal time frame for which CPR should be performed before defibrillation was by Bradley *et al*,¹⁰ which recommended between 45 s and 195 s of CPR before a defibrillation attempt.

As previously mentioned, it has been shown that pauses in pre-shock CPR as short as 3 s decrease the mean probability of ROSC by approximately 23%.⁸ As CPR continues to be performed there is a noticeable decrease in the quality of CPR that is being performed by EMS personnel,²⁵ which could lead to a more widespread use of automatic CPR devices. In a study by Box *et al*⁷ it was shown that automated CPR was statistically more likely to increase the frequency and coarseness of VF, which could increase the likelihood of a successful reversion outcome.

All of the articles reviewed in this study were limited by the uncontrolled quality of CPR, which potentially may have affected the results that were obtained in each study. As mentioned previously, there is strong evidence that high quality CPR improves survival rates from cardiac arrest, and increases the likelihood of ROSC.^{5 6} It should also be noted that none of

articles reviewed provided any details of post-ROSC care, which may have influenced the results reported in each article.

This study is potentially limited as we may have missed some articles due to a lack of hand searching of the non-electronic and grey literature and we did not include non-English articles. Another issue that arose was that several studies failed to reach participant numbers to power the studies adequately, which may have altered the results obtained. A few of the trials that were examined had unforeseeable and unpreventable protocol changes during the trial period, which could have impacted the results obtained.

CONCLUSION

Currently there is conflicting evidence for the support of CPR before defibrillation in OHCA. There is a need for further large, multicentre, randomised control trials to determine if there is any benefit of CPR before defibrillation. The establishment of a consistent timeframe of chest compressions before defibrillation in the out-of-hospital setting will provide uniformity in standards in clinical practice and education and training. These studies should focus on patients who have an EMS response time of more than 4–5 min because this patient subgroup appears to be the group that will most likely benefit from CPR before defibrillation.

Competing interests None.

Contributors All authors were responsible for the study idea and helped write the paper.

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