The 2005 European Guidelines for cardiopulmonary resuscitation: major changes and rationale

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ABSTRACT
During the 2005 International Consensus Conference on Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care Science, a rigorous evidence-based evaluation process was conducted. The consensus reached during that Conference constituted the basis of the current CPR guidelines of the European Resuscitation Council (ERC), published in December 2005. Those guidelines included many important changes, made on the basis of emerging evidence. For example, the compression-ventilation ratio for CPR in non-intubated patients was increased from 15:2 to 30:2 and a strong recommendation to minimize interruptions in chest compression was issued in order to maximise organ perfusion. Energy levels for monophasic defibrillation were increased and specific energy levels for biphasic defibrillation have been recommended, in order to maximise the efficacy of the first shock. New timing of defibrillation shocks is now advised: the three-stacked shock sequence has been replaced by high-energy single shocks followed by two-minute cycles of CPR, in order to reduce CPR interruptions. Timing for administration of drugs has been adapted to the new shock sequence and the advanced life support (ALS) universal algorithm has been modified. Some controversial topics are still a matter of investigation and debate, including the use of therapeutic hypothermia in non-shockable cardiac arrests, the efficacy of a period of CPR before defibrillation in long-lasting cardiac arrests, and the chest-compression-only CPR for first responders of out-of-hospital cardiac arrests.

Key words: Heart arrest - Cardiopulmonary resuscitation - Advanced cardiac life support - Life support systems - Defibrillators - Anti-arrhythmia agents - Hypothermia - Guidelines.

In the past several years, the evidence underlying the practice of cardiopulmonary resuscitation (CPR) has undergone a rigorous evaluation process, which was concluded during the 2005 International Consensus Conference on CPR and Emergency Cardiovascular Care Science. The consensus reached during that conference constituted the basis of the current CPR guidelines of the European Resuscitation Council (ERC). The revision process produced relevant changes in the recommended sequence of actions during resuscitation. The present paper focuses on the changes most likely to have important implications in current clinical practice.

Compression-ventilation ratio
In non-intubated patients, chest compressions and ventilations cannot be performed simultaneously; therefore, CPR requires periodic interruptions of chest compressions to give ventilations. Until 2005, the recommended chest compression-ventilation ratio in the CPR sequence was 15:2. However, in experimental cardiac arrest with a
15:2 compression-ventilation ratio, the interruption of chest compressions to give two ventilations was associated with a significant decrease of coronary perfusion pressure, which lasted for the majority of the following chest compression cycle. Other experimental studies in animals have shown that continuous chest compressions are associated with better haemodynamics and survival compared to standard CPR, while any interruption in chest compressions was associated with a reduced recovery of spontaneous circulation (ROSC) and survival, as well as increased postresuscitation myocardial dysfunction. In humans, a retrospective spectral analysis of the ventricular fibrillation (VF) waveforms recorded during resuscitation attempts showed that interruption of CPR was associated with a decreased probability of defibrillation success. In summary, chest compressions should ideally never be interrupted in order to obtain optimal hemodynamics during CPR. However, uninterrupted chest compressions may eventually cause insufficient ventilation and reduced arterial oxygenation.

The best solution may be represented by a compression-ventilation ratio, ensuring both minimal interruption of chest compressions and sufficient ventilation. In animal models of cardiac arrest, high compression-ventilation rates (100:2, 50:2 and 50:5) did not show any significant advantage over the conventional 15:2 ratio, especially in terms of arterial oxygenation and survival rates. However, the 30:2 ratio was associated with a significantly shorter time to ROSC and a greater systemic and cerebral oxygenation than continuous chest compressions. Moreover, a theoretical mathematical model suggests that a compression-ventilation ratio of 30:2 would provide the best blood flow and oxygen delivery.

For all these reasons, a 30:2 ratio is now the recommendation for adult CPR when the patient has not yet been intubated. After an advanced airway (e.g. tracheal tube or laryngeal mask) is placed, the patient can be ventilated without pausing during chest compressions to give ventilations (i.e., CPR can be “asynchronous”). As a general recommendation, interruptions of chest compressions should be reduced as much as possible.

Chest compression-only CPR

Chest compression-only CPR has some advantages: it is easier to teach and perform, and it ensures maximal hemodynamic efficiency. Additionally, the lay rescuer may be unwilling to perform mouth-to-mouth ventilation.

However, chest compression-only CPR has some limitations. In an animal model of asphyxial cardiac arrest, CPR with continuous chest compressions was associated with higher pulmonary edema than CPR consisting of both compression and ventilation. Animal studies on non-asphyxial cardiac arrest demonstrated that chest compression-only CPR can be initially equivalent to chest compression with ventilation, but is quickly associated to arterial desaturation within two minutes.

In humans, a randomised trial on telephone instruction in CPR showed that in lay rescuers, chest compression-only CPR can be at least as efficient in terms of survival rates as conventional CPR when the emergency medical system response is fast (mean response time 4 minutes). Conversely, another observational study showed that compression-only CPR obtains higher survival rates than no CPR, but lower survival rates than conventional CPR.

In conclusion, CPR with both ventilation and compression remains the standard technique according to the 2005 ERC Guidelines. Compression-only CPR is recommended for those rescuers unwilling or not trained to perform airway and breathing manoeuvres.

In contrast with this recommendation, the SOS-KANTO study, published after the release of the 2005 Guidelines and performed on 4,068 adults witnessing out-of-hospital cardiac arrests, concluded that compression-only resuscitation resulted in a higher proportion of favourable neurological outcomes than conventional CPR. This study was performed in a subgroup of patients with apnoea and shockable rhythm, and whose resuscitation had been started within 4 min. Moreover, no evidence of benefit from the addition of mouth-to-mouth ventilation was demonstrated in any subgroup. On the basis of these results, revision of the 2005 ERC guidelines and recommendation of cardiac-only resuscitation for all arrests of presumable cardiac origin has been advocated.
Defibrillation: energy levels, waveforms and number of defibrillating shocks

One of the major improvements in recent years in the treatment of cardiac arrest has been represented by the advent of biphasic defibrillation. Biphasic defibrillation has similar or higher success rates than monophasic defibrillation by using equal or lower energy levels\textsuperscript{14-16} This also implies a lower risk of myocardial electrical damage\textsuperscript{17} and the possibility to build smaller, lighter defibrillator machines.

Several defibrillation waveforms exist, although none were undoubtedly superior to the others in terms of ROSC or survival to hospital discharge. For this reason, no specific defibrillation waveform – either monophasic or biphasic – is recommended in the current guidelines.\textsuperscript{1} Both monophasic and biphasic defibrillation are considered to be acceptable to terminate ventricular fibrillation or pulseless ventricular tachycardia (VF/VT), although lower energy levels can be used for biphasic defibrillation.

Energy level for the first shock

The policy in the current guidelines is to maximise the efficacy of the initial defibrillating shock, in order to reduce the duration of cardiac arrest and to avoid both myocardial electrical damage and prolonged interruptions of CPR due to repeated shocks. Human studies demonstrate that successful defibrillation can be obtained within the first shock in more than 90\% of the cases.\textsuperscript{16} The majority of human clinical studies on biphasic defibrillation\textsuperscript{18-20} used initial energy levels ranging from 100 to 200 J. Neither human clinical nor laboratory studies have demonstrated evidence of a significantly greater benefit or harm from any energy level currently used. Regarding monophasic defibrillation, one hospital study\textsuperscript{21} demonstrated that energy levels of 300-320 J show a trend towards greater initial shock success rates than levels of 200-240 J and similar first shock success rates compared to higher (400-440 J) energies.

For the first shock, the current guidelines\textsuperscript{1} recommend a biphasic shock energy level of 150-200 J, except for the rectilinear biphasic waveform, where a 120 J energy level is considered acceptable. The recommended energy level for monophasic shocks is 360 J.

Energy level and timing for the subsequent shocks

The principle of increasing the energy level for subsequent shocks if the previous shock was unsuccessful appears reasonable. Current guidelines\textsuperscript{1} recognise this principle and indicate that escalating biphasic energies up to 360 J is acceptable for shock-refractory VF/VT. A multicenter randomised trial, published after the release of the 2005 guidelines, confirmed that out-of-hospital cardiac arrests escalating biphasic energy shocks have higher success rates than fixed-energy biphasic shocks.\textsuperscript{22} As far as monophasic defibrillation is concerned, the recommended energy for the first shock (360 J) is already maximal and represents the upper energy limit of the majority of existing defibrillator machines. Thus, increasing monophasic energy is not recommended for persistent VF/VT.

One of the most relevant changes introduced in the 2005 guidelines is the different timing of defibrillating shocks for shock-refractory VF/VT and their relationships with CPR. Clinical observational studies have shown that interruption of CPR manoeuvres to deliver defibrillating shocks may cause deterioration of CPR hemodynamics and reduction of the probability of shock success.\textsuperscript{5} While previous guidelines recommended the administration of stacked sequences of three shocks followed by one minute of CPR for the treatment of refractory VF/VT, current guidelines recommend only a single shock followed by immediate resumption of CPR for two minutes (Figure 1). This change was due to the following reasons: 1) a stacked 3-shock sequence would cause interruption of CPR for a prolonged length of time; 2) in clinical studies, the second and the third shock do not add much to the cumulative defibrillation success of a 3-stacked sequence; in fact, the vast majority of successful defibrillation attempts occurs at the first shock of the sequence\textsuperscript{16, 23} (Table I); 3) provision of CPR may increase the probability of success of the following defibrillation attempts, especially when resuscitation is delayed.\textsuperscript{24} No published human or animal studies have compared a one-shock protocol with a three-stacked shock.
sequence for any outcome. Further research on this topic is needed.

Differently from previous recommendations, the current 2005 guidelines recommend immediate resumption of CPR for two minutes after shock delivery, without any rhythm or pulse check. This decision was made in order to minimise interruption of CPR, and is based on evidence indicating that only in a minority of cases is a palpable pulse present immediately after a successful shock, due to mechanical myocardial stunning. In this context, the current guidelines recommend immediate resumption of CPR after a shock, without any rhythm or pulse check. This decision was made in order to minimise interruption of CPR, and is based on evidence indicating that only in a minority of cases is a palpable pulse present immediately after a successful shock, due to mechanical myocardial stunning (Table I).

Adrenaline and other vasopressors

The rationale of the administration of adrenaline and other vasopressors during CPR is to improve the coronary and cerebral perfusion pressure by increasing peripheral vascular resistances and redirecting blood from the splanchnic and cutaneous-muscular districts to the heart and brain. The inotropic effect is not the primary aim for adrenaline use during cardiac arrest, since other vasopressors with little or no effect on cardiac contractility (vasopressin) have been used in cardiac arrest with similar survival rates.

Although vasopressors are commonly considered the mainstay of drug treatment in cardiac arrest, there is still no placebo-controlled trial demonstrating any positive effect on survival to hospital discharge. Despite this lack of evidence, the current guidelines indicate that the continued administration of vasopressors in cardiac arrest is reasonable.

Adrenaline is the most commonly used vasopressor in cardiopulmonary resuscitation. The recommended adrenaline dosage is 1 mg i.v. every 3-5 minutes (in practice, 1 mg every two 2-minute cycles of CPR). The suggested time for administering adrenaline varies depending on the underlying cardiac rhythm. For non-VF/VT rhythms (i.e., asystole and pulseless electrical activity [PEA]) there is consensus on immediate use of adrenaline, the use of this drug for VF/VT rhythms is more controversial. In fact, adrenaline, as a beta-adrenergic stimulator, could induce tachyarrhythmias due to its chronotropic and bathmotropic effects.

**Table I.** Percentage of shock success after biphasic defibrillation.

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<th>VF interruption</th>
<th>ROSC</th>
<th>Immediate palpable pulse after shock</th>
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<tbody>
<tr>
<td>1st shock</td>
<td>83.6%</td>
<td>21.8%</td>
<td>2.5%</td>
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<tr>
<td>2nd shock</td>
<td>7.5%</td>
<td>10.7%</td>
<td></td>
</tr>
<tr>
<td>3rd shock</td>
<td>4.8%</td>
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Data from 481 out-of-hospital cardiac arrests treated using biphasic defibrillation according to the ILCOR 2001 guidelines: percentages of immediate electrical success (VF interruption), recovery of spontaneous circulation (ROSC) and immediate post-shock recovery of palpable pulse are reported (from Rea et al.23).

**Figure 1.** The sequence of CPR, defibrillation shocks and administration of drugs for persistent VF/VT according to the European Resuscitation Council (ERC) Guidelines for adult advanced life support.
effects, and could increase myocardial oxygen consumption after ROSC because of its inotropic effect, leading to myocardial ischemia.

Current guidelines put more emphasis on early defibrillation and on the maintenance of good-quality CPR rather than on adrenaline use for the initial treatment of VF/VT arrests. The administration of adrenaline should be considered only if VF/VT persists after two unsuccessful cycles of defibrillation and CPR, and it should be given immediately prior to the third shock (Figure 1).

Vasopressin has been used as an alternative to or in conjunction with adrenaline. It has some potential advantages, as it is a pure vasopressor and exerts no beta-agonist inotropic or chronotropic action. Although early experiences were encouraging, results of clinical trials and of two metaanalyses showed that in humans vasopressin has no relevant advantage over adrenaline. The limited availability of vasopressin in many European countries further discourages its use. The current European Resuscitation Council guidelines for advanced life support do not recommend vasopressin for the treatment of cardiac arrest.

Antiarhythmics

Despite no definitive evidence that antiarrhythmic therapies increase survival at hospital discharge from cardiac arrest, there is some evidence that they improve short-term survival when cardiac arrest is caused by VF/VT rhythms. In two randomised controlled clinical trials carried out in the out-of-hospital setting, the administration of amiodarone (300 mg i.v. 29; 5 mg kg^{-1} i.v. 30) to patients in cardiac arrest with refractory VF/VT improved survival in hospital admission when compared to placebo or lidocaine 1.5 mg kg^{-1} i.v. 30. In both of these studies, the antiarrhythmic therapy was administered if VF/VT persisted after at least three shocks, which had been given using the previously recommended three-stacked shock protocol. There are still no data on the use of amiodarone after a single shock. The current ERC guidelines recommend the administration of amiodarone 300 mg i.v. immediately before the fourth shock if VF/VT persists after three shock-CPR cycles (Figure 1).

Since lidocaine showed a lower short-term survival benefit when compared to amiodarone, its use is not recommended as a first-line drug, but should be considered at a dose of 1 mg kg^{-1} i.v. as a second choice drug for shock-refractory VF/VT if amiodarone is not available. Lidocaine should not be used if amiodarone has already been given, since both drugs exert an antagonistic effect on the duration of action potential: a shortening for lidocaine due of Na-channel blocking action; a prolongation for amiodarone due to K-channel blocking action.

Therapeutic hypothermia

In 2002, two distinct randomised controlled trials demonstrated that mild therapeutic hypothermia (32-34 °C) administered during the first 12-24 hours after VF cardiac arrest improves both survival and neurological recovery. The study population included almost exclusively out-of-hospital cardiac arrests and only VF rhythms, making the extrapolation of these results to in-hospital cardiac arrests and non-VF/VT rhythms difficult. A small clinical study with a retrospective control group showed improved outcome after therapeutic hypothermia in comatose survivors of out-of-hospital non-VF/VT cardiac arrest. An additional study using a historical control group demonstrated improved neurological outcomes in comatose survivors of asystolic/PEA cardiac arrest, although these patients were all out-of-hospital cardiac arrests and the results have been presented only in abstract form. Based on these studies, the current ALS guidelines recommend mild therapeutic hypothermia (cooling to 32-34 °C) for 12-24 hours in all comatose survivors of out-of-hospital cardiac arrest when the initial recorded rhythm was ventricular fibrillation. Cooling should be initiated as soon as possible. The use of therapeutic hypothermia should be considered in comatose survivors of out-of-hospital non-VF/VT cardiac arrest or after in-hospital cardiac arrest.

Both external and internal cooling techniques have been used to induce therapeutic hypothermia and both could be considered acceptable. Intravascular cooling enables a more precise induction and maintenance of target temperature but has not been clearly demonstrated to benefit sur-
vival. Thus, no specific cooling technique has been recommended as a first choice.

CPR before defibrillation

Until 2005, immediate defibrillation was the standard recommendation for all VF/VT cardiac arrests, and defibrillation was prioritised over CPR. Recent evidence has challenged this policy. In animal studies of VF lasting ≥5 min, CPR before defibrillation improved haemodynamics and survival rates. In a before-and-after study, and in a randomised trial conducted on adult out-of-hospital VF/VT, 1.5-3 min of CPR performed by healthcare professionals before attempted defibrillation improved both ROSC and survival rates when the response interval (ambulance dispatch to arrival) and time to defibrillation was ≥4-5 min. Analysis of the VF frequency spectrum in cardiac arrest patients demonstrated that three or more minutes of CPR improved the VF frequency, thus increasing the chance of successful defibrillation.

These results were not confirmed by another randomized trial in adults with out-of-hospital VF/VT, in which 1.5 min of paramedic CPR before defibrillation did not improve ROSC or survival to hospital discharge. Some limitations of this study could partially explain the lack of beneficial evidence. In fact, the study was underpowered and CPR was administered according to the previous guidelines, with a 5:1 ratio, so chest compression was frequently interrupted to ventilate, which could have warranted an insufficient myocardial perfusion, thus reducing the beneficial effect of cardiac compression on myocardial metabolism. The issue of “compression first vs shock first” is included in 2005 ERC guidelines among controversial topics. Current guidelines recommend a period of 1.5-3 min of CPR before attempting defibrillation in adults with out-of-hospital cardiac arrest when the ambulance arrival time is known to be longer than 4-5 min. There are insufficient data to determine whether this recommendation should be applied to in-hospital cardiac arrest.

Conclusions

Based on recent evidence, several changes have been introduced in the international guidelines for the management of cardiac arrest. Major changes concerned the compression-ventilation ratio for CPR in non-intubated patients, energy levels and timing of defibrillation shocks, timing for administration of adrenaline and amiodarone. For some topics, including therapeutic hypothermia in non-VF/VT rhythms, CPR before defibrillation and chest compression-only CPR, controversy still exists. Further studies to provide more definitive evidence are warranted.

References

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