BRIEF REVIEW

Approaches to modern management of cardiac arrest

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The major determinant in survival of patients with out-of-hospital ventricular fibrillation (VF) is the delay to defibrillation. Since the first report of survival from out-of-hospital VF¹ there has been a natural progression to make defibrillation more accessible. This trend has been aided by the development of automatic external defibrillators.

Public access defibrillation

The time delay to defibrillation can be reduced by five minutes if performed by a first responder to the cardiac arrest rather than by the usual paramedic service.² In a review of five controlled trials in which emergency medical technicians were taught to defibrillate, odds ratios for improved survival ranged from 3.3 to 6.9.³ Emergency medical technicians were taught to recognise cardiac arrhythmias and to operate a manual defibrillator in four trials; an automatic external defibrillator was used in the remaining trial.

The validity of emergency medical technicians using automatic external defibrillators has also been tested in controlled trials.⁴⁻⁶ There were no significant differences in hospital admission or discharge rates for patients with cardiac arrest treated by emergency medical technicians (trained to recognise VF) using either a manual defibrillator or an automatic external defibrillator. However, the delay to the first shock was significantly shorter in the automatic external defibrillator group.

Successful use of automatic external defibrillators by emergency medical technicians has raised the possibility of these devices being used by minimally trained individuals. Automatic external defibrillators have already been used successfully by family members of survivors of out-of-hospital cardiac arrest⁷ and by security staff at large public gatherings.⁸ The use of these devices by the lay public could reduce further the time to defibrillation.

Several issues concerning the widespread dissemination of automatic external defibrillators for public use need to be discussed. It is essential that automatic external defibrillators have a very high specificity for shockable rhythms. Inappropriate delivery of direct current (DC) shocks has been reported.⁹⁻¹⁰ Such instances may have important medical and legal implications. Non-electrocardiographic sensors therefore have a role in independent confirmation of cardiac arrest before a shock is

delivered. One of the earliest automatic external defibrillators used a breath detector to confirm indirectly the lack of blood flow to the brain.¹¹ This sensor was subsequently abandoned because of the delay in delivery of a DC shock, probably as a result of agonal respiration.¹² The impedance cardiogram also confirms pulselessness due to cardiac arrest.¹³

The optimum strategy for deployment of an automatic external defibrillator must be identified. As most arrests occur in the home it remains to be proved that a policy of placing automatic external defibrillators in public places will have a major impact on overall survival from cardiac arrest. Furthermore, can the public retain the skills required to use an automatic external defibrillator over a prolonged period of time? This issue was examined in two reports at the recent meeting of the American Heart Association. In one report, police officers were trained to use an automatic external defibrillator. Their skills were tested by written and practical examination.¹⁴ Although written performance declined over a three month period, their skill in the use of an automatic external defibrillator remained satisfactory. In the other study, Cummins *et al* found that three quarters of individuals who received training in the use of automatic external defibrillators omitted one or more critical steps required for their correct use two to four months after training.¹⁵ They suggest that the process needs to be simplified. There are issues of cost and cost effectiveness. The cost of automatic external defibrillators is likely to decrease. However, the cost of deployment and maintenance must be considered—for example, in a shopping mall where there may be less than one cardiac arrest per annum. This issue was examined in a decision analysis model presented at the recent meeting of the American Heart Association.¹⁶ The potential cost effectiveness of standard emergency medical services was compared with that of emergency medical services with public access defibrillation. The difference between the two services was calculated using input data from published studies and fiscal databases as US\$36 302 per quality adjusted life-year. The authors concluded that the incremental cost effectiveness of public access defibrillation was similar to that of other common medical treatments.

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Determinants of successful defibrillation

Successful defibrillation is influenced by the time to defibrillation and transthoracic impedance. The delay to defibrillation can be reduced by automated external or transtelephonic defibrillation. High transthoracic impedance can be overcome by current based defibrillation, assuming that pad size, position, and application to the chest wall are correct.

Outcome may also be influenced by the waveform used in transthoracic defibrillation. A biphasic waveform requires less energy than a monophasic waveform for successful defibrillation by internal cardioverter defibrillators (ICDs).¹⁷ Several studies in the electrophysiological laboratory have examined the biphasic waveform in human transthoracic defibrillation. Greene *et al* found that the Gurvich biphasic waveform delivering a mean energy of 171 J was superior to the Edmark waveform delivering a mean energy of 215 J for successful conversion of ventricular tachycardia and VF.¹⁸ Bardy *et al* compared two truncated biphasic waveforms with a damped sine waveform for transthoracic defibrillation in patients undergoing ICD testing.¹⁹ All waveforms were equally efficacious but the two biphasic waveforms delivered less energy (115 J and 130 J compared with 200 J). In a larger multicentre study Bardy *et al* compared the 130 J truncated biphasic waveform with a 200 J damped sine wave monophasic waveform in 294 patients undergoing ICD testing.²⁰ The first shock efficacy rates were 86% for each waveform. Interestingly, the ST segments measured 10 seconds after the shock were significantly less displaced with the biphasic waveform. Internal biphasic shocks in animals are associated with less injurious effects on myocardial oxidative metabolism and haemodynamic performance than are monophasic shocks.²¹

There are limited data on the use of biphasic waveforms for defibrillation of patients with out-of-hospital VF. White and Gliner²² recently reported their experience of a 150 J impedance compensated, biphasic truncated exponential waveform in 12 consecutive patients with out-of-hospital VF. All episodes of VF (n = 55) were successfully converted by three or fewer shocks. Furthermore, the biphasic shocks were equally efficacious in patients with high or normal transthoracic impedance.

These reports are encouraging but larger studies of patients with out-of-hospital VF are required. Biphasic waveforms are expected to lead to the development of smaller, more portable defibrillators with possibly less injurious myocardial effects.

Antiarrhythmic drugs in resuscitation

Traditionally, lignocaine has been recommended as an adjuvant treatment for VF resistant to DC shocks. More recently, the European Resuscitation Council issued guidelines indicating that lignocaine should be administered at a late stage in the management of VF.²³

The reason for this change in protocol is based partly on animal experiments in which lignocaine increased the defibrillation thresh-

old (DFT).²⁴⁻²⁷ However, this effect was not seen in other studies.²⁸ A possible explanation for these conflicting results may relate to the use of anaesthetic agents. These drugs may interact with lignocaine, thereby raising the DFT.²⁷⁻²⁹ Kerber *et al* reported that lignocaine increased the DFT more in dogs anaesthetised with pentobarbitone (up to 60%) than in dogs anaesthetised with chloralose (10–20%).²⁷ Natale *et al* investigated the effects of lignocaine on the DFT in 36 pigs anaesthetised with halothane and in eight pigs anaesthetised with barbiturates.²⁹ Lignocaine had no effect on the DFT in pigs anaesthetised with halothane but there was a significant increase in the DFT in those anaesthetised with barbiturates.

While it is difficult to translate experimental results to the clinical setting, two studies have examined the effects of lignocaine on the DFT in internal defibrillation in humans.³⁰⁻³¹ Echt *et al* found that energy requirements for defibrillation did not increase when the plasma concentration of lignocaine was less than 5 µg/ml (therapeutic range 1.2–5.5 µg/ml).³⁰ There was a rise in energy requirements, however, at higher plasma concentrations. In a second study lignocaine did not alter the energy requirements for internal defibrillation.³¹ Lake *et al* reported a beneficial effect of lignocaine with regard to energy and current on the DFT in a randomised placebo controlled trial of 20 patients undergoing myocardial reperfusion with coronary artery bypass grafting.³²

Unfortunately, there has not been a randomised placebo controlled trial of lignocaine in the cardiac arrest setting. In a randomised trial comparing lignocaine with adrenaline in VF resistant to one DC shock lignocaine resulted in a greater incidence of asystole but there was no difference in the proportion of patients resuscitated or in the number of survivors.³³ A large retrospective study of 1212 patients examined the effects of lignocaine on survival from witnessed out-of-hospital VF.³⁴ Survival to discharge in patients given lignocaine did not increase, but there was a highly significant restoration of spontaneous circulation ($p < 0.001$) and hospital admission rate (38% v 18%; $p < 0.01$).

Amiodarone has been regarded as a special case. Animal studies have shown a decrease in the DFT when amiodarone is administered intravenously, and an improved response to defibrillation in resistant VF. Cardiac arrest data are encouraging.³⁵ Amiodarone was given by intravenous bolus with or without infusion to 14 patients with refractory or recurrent ventricular tachycardia or VF. The average duration of these resuscitation attempts was 75 minutes. Eleven patients regained a stable rhythm and eight survived to hospital discharge.³⁵ Results of the randomised placebo controlled ARREST trial were presented at the recent meeting of the American Heart Association (Kudenchuk PJ, 70th scientific sessions, AHA, Orlando, Florida, November 1997). A bolus of amiodarone was administered intravenously after three unsuccessful DC shocks. Survival to hospital was significantly increased. The hospital discharge rate did not increase

but the study was not powered to detect a difference. Hypotension and bradycardia increased in the amiodarone treated group but both were regarded as reversible.

Antiarrhythmic drugs are used as a last chance treatment in the European Resuscitation Council guidelines.²³ However, evidence supports administration of class III agents as adjuncts to defibrillation earlier in resuscitation (Kudenchuk PJ, 70th scientific sessions, AHA).³⁶ Results of the ARREST trial showed that amiodarone administered after three failed DC shocks has beneficial effects on defibrillation. Furthermore, bretylium tosylate, which was used as a first line drug for cardiopulmonary arrest in a randomised placebo controlled trial was associated with an improved resuscitation rate.³⁶ Class I agents have been avoided on the basis of an experimental increase in DFT.²⁴⁻²⁷ This finding, however, may be related to the anaesthetic regimen.²⁷⁻²⁹ Furthermore, extrapolation of these results to the substrate of ischaemic heart disease may not be valid.

There is no evidence of increased energy requirements for transthoracic defibrillation with lignocaine administration in humans, nor is there evidence of a worsened outcome. A retrospective study showed that lignocaine is associated with a significantly increased restoration of spontaneous circulation and hospital admission rate.³⁴ However, controlled prospective studies of lignocaine and other antiarrhythmic drugs in VF resistant to DC shocks are essential.

Adrenaline

Coronary and cerebral blood flow during closed chest cardiopulmonary resuscitation (CPR) decrease to levels far below those which are necessary to meet metabolic demands of the heart and brain.³⁷ Adrenergic agonists have been used in the management of cardiac arrest since beneficial effects of adrenaline were found in an animal model of CPR.³⁸ Adrenergic agonists increase aortic diastolic blood pressure and coronary perfusion pressure and improve cerebral and coronary blood flow during CPR.³⁸⁻³⁹ These positive haemodynamic effects, however, are at the expense of decreased blood flow to other vital organs⁴⁰ and higher doses induce a pattern of myocardial injury known as contraction band necrosis.⁴¹ Adrenaline does not reduce energy requirements for defibrillation in animals with normal hearts.⁴² Indeed, β adrenergic stimulation may increase the DFT⁴³ and promote ventricular arrhythmias.⁴⁴ Four large randomised trials have compared high dose and standard dose adrenaline in patients with cardiac arrest.⁴⁵⁻⁴⁸ In total more than 3000 patients were studied: the results are very consistent. In one study restoration of spontaneous circulation was significantly increased in patients given high dose adrenaline.⁴⁷ None of the studies, however, found an increase in the hospital discharge rate with high dose adrenaline.

The question remains as to whether there is any therapeutic benefit even with standard dose adrenaline. Unfortunately, there are no randomised placebo controlled trials of stand-

ard dose adrenaline in patients with cardiac arrest. However, two studies suggest that standard dose adrenaline has no significant effect on hospital discharge after cardiac arrest.⁴⁹⁻⁵⁰ The effects of standard dose adrenaline were assessed in a large retrospective analysis of 1360 patients with witnessed out-of-hospital VF.⁴⁹ Some emergency medical staff were authorised to give standard doses of adrenaline during the observational period. Adrenaline was given to 35% of patients and was associated with a significantly greater rate of restoration of spontaneous circulation and hospital admission. However, there was no significant difference in hospital discharge rates between the two groups. Woodhouse *et al* compared high dose (10 mg) and standard dose (1 mg) adrenaline with placebo in patients with cardiac arrest.⁵⁰ There was no significant difference in immediate survival or hospital discharge between patients given standard dose adrenaline and placebo.

In patients without cardiac arrest even standard dose adrenaline is associated with significant adverse effects. Doses of 1 and 5 mg cause severe pain and pulmonary oedema.⁵¹ A minimal lethal dose of 4 mg given subcutaneously and a maximum tolerated dose of 7-8 mg were reported in a series of 15 patients suffering from adverse effects of adrenaline.⁵² Adrenaline can also cause sustained ventricular arrhythmias.⁵³

Buffers in cardiac arrest

Metabolic acidosis rapidly ensues in total circulatory arrest. Traditionally, bicarbonate has been part of all resuscitation protocols. In the 1980s, however, theories suggested that sodium bicarbonate might worsen the outcome from cardiac arrest. It was argued that bicarbonate exacerbated intracellular acidosis, and caused hyperosmolarity with a consequent reduction in coronary perfusion pressure and a left shift in the oxygen dissociation curve, impairing oxygen release in the tissues. These arguments were rebutted in a review by Narins and Cohen⁵⁴ entitled "Bicarbonate therapy for organic acidosis: the case for its continued use".

Dr Weil *et al* originally postulated that tissue perfusion rather than alveolar hypoventilation is the limiting factor in elimination of carbon dioxide during the very low flow state of CPR.⁵⁵ Administration of bicarbonate would therefore cause release of carbon dioxide which would accumulate in the tissues, penetrate the cells, and exacerbate intracellular acidosis.⁵⁵ However, the combination of bicarbonate administration and adequate CPR does not result in paradoxical acidosis.⁵⁶ Furthermore, initial experimental evidence that bicarbonate exacerbated intracellular acidosis was based on a study in which animals were given a massive dose of 10 mmol/kg bicarbonate after 20 minutes of CPR.⁵⁷ Other workers using more physiological doses did not find a deterioration in acidosis⁵⁸⁻⁵⁹ or a biphasic response in which intracellular pH initially worsens for a short time before improvement.⁶⁰

Experiments have been reported in which bicarbonate causes a reduction in cardiac output and coronary perfusion pressure.^{61, 62} These findings were challenged by Bleske *et al* who argued that the doses used in the earlier studies were much larger than those in clinical practice (1 mEq/kg).⁶³

There is one placebo controlled trial of buffers in patients with cardiac arrest. There was no improvement in outcome with Tribonat, a buffer that does not produce carbon dioxide. Koster,⁶⁴ however, emphasised that the dispatch response time was short (mean 5.8 minutes) and that the degree of acidosis was not very profound in either group.⁶⁴ Additionally, the confidence interval of the odds ratio was wide and was consistent with survival with Tribonat by approximately 40%.

In the absence of a definitive study, administration of buffers should be limited to arrests with proven severe acidosis or after prolonged resuscitation (given blindly); or associated with hyperkalaemia or tricyclic antidepressant overdose.

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