Cardiac arrest survivors need urgent percutaneous intervention

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In this article, we address the potential benefits of immediate coronary angiography in the management of patients with out-of-hospital cardiac arrest (OHCA), in whom coronary occlusion is the most likely aetiology.

Incidence of out-of-hospital cardiac arrest

The incidence of OHCA in Europe and the United States is estimated to be 1 to 2 per 1000 population annually.[1] In Sydney, Cheung and colleagues found that the age-standardised incidence of OHCA was 52.6 events per 100 000 person-years.[2] Ischaemic heart disease is responsible for up to 70% of cases, while structural heart disease (myocarditis, hypertrophic cardiomyopathy and arrhythmogenic right ventricular dysplasia) accounts for 10%, and events in structurally normal hearts (Brugada syndrome, long QT syndrome and pre-excitation) for another 10%.

Coronary artery disease, with or without myocardial infarction, is by far the most common background to sudden cardiac death in the Western world. In a Queensland study of ambulance attendance to cardiac arrest, resuscitation was attempted in 52% of cases and, of these, 74% had a cardiac aetiology.[3] Coronary thrombus or plaque disruption is found in more than 50% of cases of sudden death, and severe coronary disease has been reported in up to 94% of cases of sudden cardiac death.[4,5] Unfortunately, a lethal ventricular arrhythmia may be the first symptomatic manifestation of heart disease in as many as 50% of patients who experience sudden cardiac death.[6] In addition, although there has been a reduction in overall cardiac mortality worldwide, the percentage of cardiac deaths that are sudden has actually increased to almost 50%.[7] Sudden cardiac death can occur as a result of ventricular fibrillation, pulseless ventricular tachycardia, pulseless electrical activity (PEA) or asystole. Ventricular fibrillation and pulseless ventricular tachycardia are responsible for about 35% of all out-of-hospital episodes of sudden cardiac death, and have been the rhythms most commonly associated with this event.[8] However, there has been an increase in the proportion of sudden cardiac death caused by PEA, with reports of up to 70% in one US series.[9]

The survival chain of cardiac arrest

Survival after OHCA depends on a sequence of events termed "the chain of survival", which involves rapid access to emergency medical care, cardiopulmonary resuscitation (CPR), defibrillation, and advanced care.[10,11] In most places, survival rates range from 3% to 10%, because the chain of survival is not promptly implemented, although with the increasing availability of early defibrillation the rates are improving, with survival of up to 40%.[12] However, a study from Sydney in 2004–2005 showed that survival following OHCA remains very poor. In this study of 2011 episodes of OHCA, survival at 28 days, 90 days and 1 year was 12.6%, 12.2%, and 11.5%, respectively.[3] Survival was highest when the electrocardiogram (ECG) at presentation showed ventricular fibrillation. There is a great potential for improving these poor survival percentages.

Given the high mortality, attempts have been made to address each aspect in the chain of survival to improve the speed and accuracy of treatment. A German study from 1981–1997 found success in some areas, such as a shortening of the median interval from collapse until defibrillation from 9 minutes to 6 minutes, and an increase in the proportion of patients receiving bystander CPR from 14% to 28%.[7] Nevertheless, the proportion of patients discharged alive from hospital increased from 16% to 29% in 1993, but thereafter decreased to 13% in 1997. Thus, new strategies are clearly needed to improve the outcomes in such patients.

Importance of time from symptom onset to reperfusion

According to guidelines from the American Heart Association and American College of Cardiology, primary angioplasty is the preferred reperfusion therapy for acute myocardial infarction (AMI) if it can be performed in a timely fashion by high-volume operators in a high-volume institution.[13] Mortality after AMI is strongly related to the time from symptom onset to reperfusion. This relationship is well recognised for fibrinolytic therapy, but more recently has been noted for primary angioplasty by Keeley and Grines.[14] They showed that 30-day mortality was 3.3% when the delay to primary angioplasty was less than 20 minutes, but 6.7% when the delay was 60–75 minutes. De Luca and colleagues showed in a sample of over 1000 patients that the cumulative survival of patients treated with primary angioplasty increased from 94% to more than 98% at 1 year if reperfusion was achieved within 2 hours of symptom onset compared with those treated between 4 and 6 hours.[15] Extrapolation of these figures reveals that there is an absolute mortality penalty of 1% at 30 days for every 22 minutes of delay in the time to reperfusion.

Can system changes improve time to reperfusion?

There is a strong case for establishing regional heart centres where patients are treated by high-volume operators in high-volume centres.

Spaulding and colleagues showed that outcome after emergency angioplasty was related to the volume of procedures performed in the hospital. For hospitals where fewer than 400 angioplasties were performed per year, the mortality was 8.4%, whereas for those where more than 400 were performed, the mortality was 6.7%.[12] The authors concluded that patients with AMI, cardiogenic shock and OHCA were best treated in high-volume institutions. Nallamothu et al, on behalf of the National Registry of Myocardial Infarction Investigators, similarly showed that the relative risk of in-hospital death was reduced by 36% in hospitals in the highest quartile for volume of primary angioplasties for AMI.[16] These hospitals had a median door-to-balloon time of 99.6 minutes, compared with 118.3 minutes for the hospitals in the lowest quartile. A similar relationship exists for operator volume, in that outcomes in the management of AMI are better when the procedures are performed by more experienced operators. Practice makes perfect.

Patients who are at highest risk benefit most from a reduction in the door-to-balloon time. The study by McNamara et al looked at data from 29 222 patients with ST-elevation myocardial infarction (STEMI) who presented within 6 hours of symptom onset. In the high-risk patients, in-hospital mortality was reduced from 10% to 4.2% if the door-to-balloon time was less than 90 minutes compared with > 150 minutes.[17]

Unfortunately, even in the best institutions, time from symptom onset to hospital admission is between 106 and 183 minutes, while door-to-balloon time is between 90 and 171 minutes (Prague-1,[18] Prague-2[19] and National Registry of Myocardial Infarction Investigators [NRMI]-4[20] trials). In US hospitals, fewer than 5% of AMI patients have a door-balloon time less than 90 minutes (NRMI-4 study).[21]

The impact of field triage

We have reported previously our experience with a system of field triage in northern and western Sydney and its impact on time to reperfusion, infarct size and mortality.[22] The study involved a prospective registry of 301 patients with AMI who called an ambulance. They were either taken to the nearest emergency department (ED) for triage, or underwent a 12-lead ECG in the ambulance and were triaged directly to the cardiac catheter laboratory of a regional heart centre for percutaneous coronary intervention (PCI) (field-triage group). The time from symptom onset to hospitalisation was 110 minutes in both groups. However, the time from symptom onset to reperfusion was 253 minutes in the ED-triage group and 150 minutes in the field-triage group. The door-to-balloon times were 116 and 30 minutes, respectively. Infarct size was reduced by field triage, as was mortality at 30 days (1.9% compared with 7.3%). Similar numbers of patients sustained cardiac arrest before reperfusion in the two groups (5% and 6%).

We consider it likely that the reduction in infarct size and mortality related to the 100 minutes of saved time of coronary occlusion in the field-triage group. Three other studies have shown similar benefits of field triage. A Canadian study showed a hospital mortality of 1.9% after field triage, compared with 8.9% with ED triage. In that study, 60% of the ED-triage group received fibrinolysis.[23] Bjorklund and colleagues showed a 43% reduction in adjusted mortality after field triage,[24] while Ortolani and colleagues showed that field triage reduced mortality in patients with cardiogenic shock from 40% to 13.8%.[25]

Gersh and Anderson describe a two-phase relationship between ischaemic time and outcome after coronary occlusion.[26] There is an early phase up to 180 minutes from symptom onset where the relationship is very steep, such that a 60-minute delay can increase mortality by 20%. After this time, the relationship is much less steep, in that a 60-minute delay increases mortality by only 2%. The key to patient treatment is to establish reperfusion in the first 180 minutes from coronary occlusion if possible.

This objective is unlikely to be achieved without a radical change to the "system" of patient management, so that triage to the cardiac catheter laboratory is made in the field rather than in the ED.

What are the consequences of delayed reperfusion?

The consequences of delayed reperfusion after coronary occlusion were investigated in the Occluded Artery Trial.[27] This study randomised 2166 patients with total coronary occlusion to coronary angioplasty 3–28 days after coronary occlusion to or medical therapy. All patients had an ejection fraction < 50% and were deemed to be at high risk of future events.

The composite primary end-point of death, myocardial infarction or New York Heart Association grade IV heart failure occurred in 17.2% of the PCI group and 15.6% of the medical-treatment group. There was even a trend to excess reinfarction in the PCI group. Delayed reperfusion had no beneficial effect on long-term mortality. Clearly, this has implications regarding the management of survivors of OHCA. Deferring reperfusion until the extent of neurological impairment has been established will deny the survivors a chance of long-term myocardial salvage and freedom from the consequences of heart failure.

Selection of patients for immediate reperfusion

Determining which patients with coronary occlusion and OHCA may benefit from emergency angiography and/or PCI remains controversial, with several studies attempting to address the question. In a retrospective observational registry study, Garot el al looked at cardiac-arrest patients who underwent urgent angiography in Paris between 1995 and 2005. All patients had STEMI and were taken to the cardiac catheter laboratory regardless of neurological status on arrival in the ED.[28] Of the 186 patients, cardiac arrest was preceded by a known typical chest pain in 66% of patients. The mean interval between the onset of cardiac arrest and arrival of a first responder was 6.2 minutes, whereas external defibrillation was performed within 12.6 minutes. Return of spontaneous circulation was obtained within 20.8 minutes after cardiac arrest, and the mean interval between the onset of AMI and admission to the cardiac catheter laboratory was 190.7 minutes. Coronary angiography showed a recent coronary occlusion (TIMI grade 0 or 1) in 138 patients, and a severe coronary lesion (> 75% stenosis) in the remaining 48. Stent implantation to the culprit lesion of the infarct-related artery was successful in 87% of patients. Of the 186 patients enrolled, 103 (54%) were discharged alive, and 89 (86%) had good cerebral function. This in-hospital survival rate is very similar to that observed in patients presenting with AMI complicated by cardiogenic shock.[29]

The data suggest that urgent angiography is indicated in patients who present with STEMI complicated by cardiac arrest. Further support for this approach comes from a recent study from Texas, which demonstrated that urgent angiography was one of the factors that improved survival in cardiac arrest patients after introduction of a system with integration of medical and emergency services.[30]

More difficult to determine is the appropriate strategy for patients who present with cardiac arrest and no evidence of STEMI on the ECG. Spaulding et al attempted to answer this question with a prospective trial in which patients with cardiac arrest were sent directly to the cardiac catheter laboratory without need for clinical or ECG data indicating a cardiac cause for the arrest.[31] Successfully resuscitated patients were included in the study if they were aged between 30 and 75 years and were previously leading a normal life, and if the sudden cardiac arrest occurred within 6 hours of the onset of symptoms, and there was no obvious non-cardiac cause of cardiac arrest. Eighty-five patients were included in the study, with a mean age of 55 years, mostly men. Of these, 72% had ventricular fibrillation, and 33% had chest pain reported before the arrest. The first ECG after return to sinus rhythm showed ST segment elevation in 42%, ST segment depression in 9%, left bundle branch block in 21%, and non-specific or normal ST and T patterns in 26%. Coronary artery occlusions were found in 40 patients (48%), and percutaneous transluminal coronary angioplasty was attempted in 37 and was successful in 28. A further 20 patients (33%) had clinically significant coronary artery lesions with no acute occlusion. Of the remaining 24 patients, 17 (20%) had normal coronary arteries, and seven (8%) had insignificant disease.

Clinical and ECG data, analysed by multivariate logistic regression, demonstrated only ST-segment elevation (OR, 4.3; 95% CI, 1.6–2; $P = 0.004$) and chest pain before the arrest (OR, 4.0; 95% CI, 1.3–10.1; $P = 0.02$) as independent predictors of acute coronary occlusion. However, nine patients who presented with no ST-segment elevation or chest pain were found to have coronary artery occlusion.

Thirty-two patients (38%) survived to discharge, 30 of whom had no, or minimal, neurological complications. Independent predictors of survival were absence of the need for inotropic drug treatment during transport (OR, 3.6; 95% CI, 1.1–11.8; $P = 0.03$) and successful coronary angioplasty (OR, 5.2; 95% CI, 1.1–24.5; $P = 0.04$)

This study highlights several important points. Firstly, it demonstrates the high prevalence of acute coronary artery occlusion in OHCA survivors. Secondly, there is potential for improved outcome with immediate PCI when indicated. Finally, acute coronary artery occlusion is difficult to predict in survivors of OHCA on the basis of clinical and ECG data alone. This final observation is not surprising, given the fact that ST elevation occurs in less than 50% of infarcts, and that the use of additional QRST variables only marginally improves the detection of AMI.[32]

Conclusions

Acute myocardial infarction is the major cause of OHCA. There is clear evidence that early reperfusion reduces mortality in AMI patients without cardiac arrest, particularly if field triage to the cardiac catheter laboratory is used. Patients with OHCA and coronary occlusion also appear to benefit from an invasive strategy. We speculate that, for these patients, routine use of field triage to the cardiac catheter laboratory could reduce the delay to coronary reperfusion to the lowest ever reported. Unfortunately, clinical and ECG characteristics are poor at predicting which patients require intervention. The evidence is strong for patients with ST elevation and suggestive for patients with preceding chest pain.

Furthermore, as early recognition of coronary or non-coronary causes of OHCA can result in profoundly different therapeutic strategies, immediate coronary angiography could be warranted on this basis alone.

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