Review

Clinical review: Beyond immediate survival from resuscitation – long-term outcome considerations after cardiac arrest

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Abstract

A substantial body of literature concerning resuscitation from cardiac arrest now exists. However, not surprisingly, the greater part concerns the cardiac arrest event itself and optimising survival and outcome at relatively proximal time points. The aim of this review is to present the evidence base for interventions and therapeutic strategies that might be offered to patients surviving the immediate aftermath of a cardiac arrest, excluding components of resuscitation itself that may lead to benefits in long-term survival. In addition, this paper reviews the data on long-term impact, physical and neuropsychological, on patients and their families, revealing a burden that is often underestimated and underappreciated. As greater numbers of patients survive cardiac arrest, outcome measures more sophisticated than simple survival are required.

Introduction

Survival to a particular time after an 'index' cardiac arrest event, as recommended by the Utstein guidelines [1], is the most commonly reported outcome measure for resuscitation, with hospital discharge and 1-year survival often reported. Excessive mortality risk is greatest within the first year after arrest and, after 2 years, approaches that of an age- and gender-matched population [2]. A retrospective review of in-hospital mortality identified neurological injury as the mode of early death in two thirds of out-of-hospital cardiac arrest (OOHCA) patients admitted to intensive care. Cardiovascular death and multi-organ failure death accounted for the remainder [3]. A number of studies have investigated survival rates at greater than 1 year and how survival following OOHCA has changed over time. Such studies suggest that longer-term survival figures are improving [4-7]. This may be due to changes in coronary artery disease patterns, resuscitation practice, and/or subsequent medical intervention.

With greater numbers of patients now surviving for longer periods, survival alone may be an inadequate assessment of resuscitation and post-resuscitation care. A more suitable tool may be assessment of quality of life (QOL) after hospital discharge. This requires an understanding of the psychosocial impact of cardiac arrest and its sequelae on the survivor and associated family members.

The aim of this review is to present the evidence base for interventions and therapeutic strategies that might be offered to patients surviving the immediate aftermath of an OOHCA (excluding components of resuscitation itself) which may lead to benefits in long-term survival. In addition, this paper reviews the data on long-term impact, both physical and neuropsychological, on patients and their families.

Methodology

Search terms recommended by the American Heart Association [8] and International Liaison Committee on Resuscitation (ILCOR) were used. These were used by working parties evaluating evidence for the ILCOR 2005 Consensus statement [9].

An electronic search of the literature by means of PubMed was conducted using MeSH (Medical Subject Heading) main search terms 'heart arrest' or 'cardiopulmonary resuscitation'. Additional terms recommended were 'antiarrhythmia agent', 'glucose', 'hypothermia' or 'induced hypothermia', 'defibril-

ACE = angiotensin-converting enzyme; ADL = activity of daily living; AVID = Antiarrhythmics Versus Implantable Defibrillators; CABG = coronary artery bypass grafting; CASH = Cardiac Arrest Study Hamburg; CIDS = Canadian Implantable Defibrillator Study; CPC = Cerebral Performance Category; DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*; ECG = electrocardiogram; I-ADL = instrumental activity of daily living; ICD = implantable cardiac defibrillator; IES = Impact of Event Scale; ILCOR = International Liaison Committee on Resuscitation; LV = left ventricular; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MMS = mini-mental state; MTH = moderate therapeutic hypothermia; MUSTT = Multicenter Unsustained Tachycardia Trial; OOHCA = out-of-hospital cardiac arrest; OPC = Overall Performance Category; P-ADL = personal activity of daily living; PTSD = post-traumatic stress disorder; QOL = quality of life; ROSC = return of spontaneous circulation; STEMI = ST segment elevation myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

lators, implantable', 'seizures', 'thrombolytic therapy', 'angioplasty', 'coronary artery bypass grafting', and 'ventricular dysfunction'. The primary search identified a total of 4,431 papers. The following search limits were then applied: human, adult, and English language. Application of search limits reduced the initial search to 1,038 articles. Studies were then reviewed for relevance. We excluded papers if they were reviews, case reports, or referred to interventions prior to the return of a spontaneous circulation; 58 papers were identified. Additional papers were obtained from the reference list used by the ILCOR working parties for the 2005 Consensus statement and from a manual search of reference lists from reviewed papers. A total of 73 papers were identified as relevant for inclusion.

Using the search term 'quality of life' and the same primary search terms and limits, we identified 59 articles, of which 27 were relevant. A manual search of reference lists was also conducted, leading to the inclusion of another 13 articles.

Overall, the literature retrieved was somewhat diverse and was not suitable for meta-analysis. Specifically, papers did not consistently report the patient populations in terms of cause of cardiac arrest or whether they occurred in-hospital or out-of-hospital and there was substantial heterogeneity. Thus, the evidence was synthesised into a narrative review.

Overview of long-term mortality

Survival studies performed during the period 1970 to 1985 found a 4-year survival of 40% to 61% [6,10-12]. Investigators (from several countries) examining long-term survival of patients discharged from the hospital following OOHCA have consistently shown an improvement. Pell and colleagues [5] showed that 5-year survival had improved in Scotland over a 10-year period (1991 to 2001) from 64.2% to 76%. This was due to a reduction in the risk of subsequent cardiac death. Part of this improvement was attributed to a higher percentage of patients less than 55 years of age and changes in clinical management after cardiac arrest. The subsequent use of beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, antithrombotic agents, and revascularisation methods had increased over time. The authors also identified the increased use of implantable cardiac defibrillators (ICDs) and changes in smoking habits as reasons for the improvements observed [5]. Similar mortality results for OOHCA have been observed by Cobbe and colleagues [4], also in Scotland, for the period 1988 to 1994, with a 4-year survival rate of 68%. Rea and colleagues [13] found that long-term OOHCA survival in King County, WA, USA, had improved over a 26-year study period (1976 to 2001). Over each 5-year interval, cardiac mortality fell by 21% [13]. Again, the authors identified changes in clinical practice and lifestyle changes as being important. Data published from Olmstead County, MN, USA, from 1990 to 2001 of confirmed ventricular fibrillation (VF) cardiac arrests found a 5-year survival rate of 79% [7]. The higher figures obtained by these authors may reflect an enrolment bias as only patients with a confirmed initial rhythm of VF were included.

In contrast, Engdahl and colleagues [14] have shown no improvement in survival in a Swedish cohort between 1981 and 1998. Notable differences, when compared with data from Scotland, include the proportion of those surviving to hospital discharge with an initial rhythm of VF and the number of patients receiving bystander resuscitation [5]. Pell and colleagues [5] found that almost all (greater than 94%) patients had an initial rhythm of VF or ventricular tachycardia (VT) compared with approximately 80% in the Swedish cohort. The number of patients receiving bystander resuscitation was consistently above 60% in the Scottish cohort compared with approximately 30% in the Swedish study. This lends support to current European Resuscitation Council recommendations on the need for early basic life support [15].

Interventions

Changes in survival represent the culmination of several medical advances that have occurred over the previous two decades. Improvements in primary and secondary prevention of coronary artery disease and changes in resuscitation have all contributed. Interventions shown to improve outcome following return of spontaneous circulation (ROSC) include optimisation of ventricular function immediately after the event, revascularisation, arrhythmia management, and therapeutic hypothermia (Table 1).

Revascularisation is integral to ventricular optimisation and arrhythmia management and will be discussed in conjunction with these interventions. The identification of the risk of ventricular arrhythmias after cardiac arrest by electrophysiological testing can predict long-term outcome. Thus, Wilber and colleagues [16] examined 166 survivors of OOHCA not associated with acute myocardial infarction (MI) and identified, over a mean follow-up of 21 months, a 33% (12/36) cardiac arrest recurrence rate in patients with inducible, but not suppressed, arrhythmias. This was compared with 12% (11/91) in whom inducible arrhythmias had been suppressed by surgery or antiarrhythmic agents [16].

Revascularisation

Cardiac arrest survivors with significant coronary atherosclerotic disease have a 20% chance of VF recurrence at 1 year [17-19]. Of those admitted to hospital immediately after cardiac arrest, almost half have coronary artery occlusion. Furukawa and colleagues [20] showed, in post-arrest patients with chronic coronary artery disease, ventricular arrhythmias unresponsive to therapy to be predictive of higher 2-year mortality. Patients surviving OOHCA often have a reversible ischaemic cause for their cardiac arrest. Ventricular arrhythmias as a cause of cardiac arrest often are associated with myocardial ischaemia. Bunch and colleagues [21] identified that 78% (66/79) of VF

Table 1

Interventions and their effect on outcome

Author(s)	Year	Study type	Population	Number	Intervention	Endpoint	Outcome	Grade of evidence (Table 2)
Revascularisation								
Bendz *et al.* [18]	2004	Prospective, observational	Cardiac arrest with STEMI	40	PCI	In-hospital and 2-year mortality	Favours PCI	3
Borger van der Burg *et al.* [27]	2003	Prospective, observational	Cardiac arrest survivors	142	Surgical or PCI revascularisation	4-year survival	Favours revascularisation	2++
Cook *et al.* [25]	2002	AVID subgroup analysis	Mixed arrest/non-arrest. VF/VT, symptomatic VT. LVEF <0.4	281	Surgical revascularisation	2-year mortality	Reduced mortality in revascularised group. Additive benefit to ICD	2++
Bigger [28]	1997	RCT	IHD, LVEF <0.36, abnormal ECG	900	Surgical revascularisation versus surgical revascularisation + ICD	Mortality	No advantage in ICD group	1+
Spaulding *et al.* [22]	1997	Prospective cohort study	OOHCA survivors	84	PCI	In-hospital mortality	Favours PCI	2+
Every *et al.* [24]	1992	Retrospective, observational	OOHCA survivors	285	Surgical revascularisation	Recurrence of cardiac arrest and mortality	Favours revascularisation	2–
Kelly *et al.* [26]	1990	Retrospective, observational	Post-arrest	50	Surgical revascularisation	Arrhythmia reduction	Reduction in inducible VF only	2–
Kaiser *et al.* [23]	1975	Retrospective, observational	OOHCA survivors	11	Surgical revascularisation	Mortality	Favours revascularisation	3
ICD or antiarrhythmic agents								
Nagahara *et al.* [17]	2006	Case-control	OOHCA survivors	58	ICD	Incidence of malignant arrhythmias	Favours ICD	2–
Bokhari *et al.* [47]	2004	RCT. Subgroup of CIDS study	Sustained VF/VT or cardiac arrest	120	Amiodarone or ICD	Mortality over 11-year follow-up	Favours ICD	1+
Hennersdorf *et al.* [48]	2003	Prospective cohort	OOHCA survivors	204	ICD or antiarrhythmic agent	Mortality over mean follow-up of 5 years	Favours ICD	2+
Connolly *et al.* [46]	2000	Meta-analysis	Mixed arrest/non-arrest ventricular arrhythmias	1,866	ICD versus antiarrhythmic drug	Mortality/arrhythmia	Favours ICD	1–
Kuck *et al.* [45]	2000	RCT	Cardiac arrest	288	ICD versus antiarrhythmic drug	Mortality/arrhythmia	Favours ICD	1–
Connolly *et al.* [44]	2000	RCT	Cardiac arrest-VF/VT/ syncope	659	ICD versus antiarrhythmic drug	Mortality/arrhythmia recurrence	Favours ICD	1–
AVID [43]	1997	RCT	Mixed arrest/non-arrest. VF/VT, symptomatic VT. LVEF <0.4	1,016	ICD versus antiarrhythmic drug	2- and 3-year mortality and arrhythmia occurrence	Favours ICD	1–

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Table 1 (continued)

Interventions and their effect on outcome

Author(s)	Year	Study type	Population	Number	Intervention	Endpoint	Outcome	Grade of evidence [151]
Haverkamp *et al.* [35]	1997	Retrospective, observational	Inducible VF/VT and cardiac arrest survivors	396	Sotalol therapy	1- and 3-year mortality and cardiac arrest occurrence	May not be as effective as ICD	2–
Buxton *et al.* [40]	1999	RCT	IHD and sustained inducible ventricular arrhythmias	754	Antiarrhythmic therapy versus conventional therapy	Cardiac arrest or death from arrhythmia	Favours antiarrhythmic therapy due to ICD	1–
Moss *et al.* [41]	1996	RCT	Previous MI, LVEF <0.35, ventricular arrhythmia	196	ICD versus conventional TX	Mortality	Favours ICD	1–
Wever *et al.* [49]	1995	RCT	Post-cardiac arrest due to old MI	66	ICD versus conventional TX	Mortality, hospital days, interventions	Favours ICD	1–
CASCADE [38]	1993	RCT	OOHCA non-Q wave	228	Amiodarone versus other antiarrhythmics	2-year mortality	Higher survival in amiodarone group	2+
Powell *et al.* [50]	1993	Retrospective, observational	Post-cardiac arrest due to ventricular arrhythmias	336	ICD	Mortality and sudden cardiac death	Favours ICD	3
Crandall *et al.* [51]	1993	Retrospective, observational	Cardiac arrest with no inducible arrhythmia	194	ICD	Mortality and sudden cardiac death	Reduction in sudden cardiac death, no change in overall mortality	3
Hallstrom *et al.* [34]	1991	Retrospective, observational	OOHCA survivors	941	Antiarrhythmic agents	2-year mortality	Increased mortality in patients given prophylactic antiarrhythmics	2–
Moosvi *et al.* [36]	1990	Retrospective, observational	OOHCA survivors with CHD	209	Quinidine or procainamide or no antiarrhythmic therapy	Incidence of sudden death	Increased sudden death in empiric antiarrhythmic therapy	2–
Myerburg *et al.* [37]	1977	Case series	OOHCA survivors	12	Quinidine or procainamide	1-year mortality	Favours antiarrhythmic therapy	3
Therapeutic hypothermia								
Holzer *et al.* [81]	2005	Meta-analysis	Post-cardiac arrest	385	Therapeutic hypothermia	Hospital and 6-month survival and neurological outcome	Favours therapeutic hypothermia	1–
HACA Group [79]	2002	RCT	Post-OOH VF cardiac arrest	275	Therapeutic hypothermia	6-month mortality and neurological outcome	Reduced mortality and better neurological outcome	1+
Bernard *et al.* [69]	2002	RCT	Post-OOH VF arrest	77	Therapeutic hypothermia	Hospital mortality and neurological outcome	Reduced mortality and better neurological outcome	1+

Continued overleaf

Table 1 (continued)

Interventions and their effect on outcome

Author(s)	Year	Study type	Population	Number	Intervention	Endpoint	Outcome	Grade of evidence [151]
Nagao *et al.* [71]	2000	Prospective cohort	OOHCA patients	23	Therapeutic hypothermia	Cerebral performance	Good neurological outcome	2–
Yanagawa *et al.* [77]	1998	Prospective case-control	OOHCA patients	28	Therapeutic hypothermia	Hospital mortality and neurological outcome	Improved survival and neurological outcome	2+
Bernard *et al.* [78]	1997	Prospective case-control	OOHCA patients	44	Therapeutic hypothermia	Hospital mortality and neurological outcome	Improved survival and neurological outcome	2+

AVID, antiarrhythmics Versus Implantable Defibrillators; CASCADE, Cardiac Arrest in Seattle: Conventional Versus Amiodarone Drug Evaluation; CHD, coronary heart disease; CIDS, Canadian Implantable Defibrillator Study; ECG, electrocardiogram; HACA, Hypothermia After Cardiac Arrest; ICD, implantable cardiac defibrillator; IHD, ischaemic heart disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; OOH, out-of-hospital; OOHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; RCT, randomised controlled trial; STEMI, ST segment elevation myocardial infarction; TX, treatment; VF, ventricular fibrillation; VT, ventricular tachycardia.

OOHCA patients surviving to hospital discharge had ischaemic heart disease, with 47% of these presenting with an acute MI. Similar findings have been reported from Göteborg, Sweden, and Glasgow, Scotland [10,14].

Although there is a large body of evidence validating thrombolysis in patients with ST segment elevation myocardial infarction (STEMI), our search revealed no literature specific to a post-cardiac arrest subgroup in whom a spontaneous circulation has returned. Though relatively contraindicated in patients with prolonged cardiopulmonary resuscitation, thrombolysis would not be unreasonable to use in those patients with electrocardiogram (ECG) evidence of recent coronary artery occlusion. Clinical and ECG findings, however, may not predict arterial occlusion, and immediate angioplasty can improve survival to hospital discharge [22]. Angiography can identify the presence of thrombus-associated coronary artery occlusion that may be the cause of cardiac arrest.

Revascularisation may improve survival through myocardial salvage. Bendz and colleagues [18] showed that OOHCA patients with ECG-confirmed STEMI receiving primary angioplasty had a survival rate comparable to a control non-cardiac arrest STEMI group 2 years after hospital discharge. However, the study included only patients with an arrest-to-resuscitation time of less than 10 minutes and thus may have enrolled only those with a higher probability of survival. Unfortunately, no data on the incidence of arrhythmia post-revascularisation were given [18].

Retrospective case series have identified coronary artery bypass grafting (CABG) as a tool in reducing the incidence of recurrent arrest and prolonging survival after STEMI OOHCA [23,24]. Data extracted from the Antiarrhythmics Versus Implantable Defibrillators (AVID) study showed, in 281 patients (presenting with ventricular arrhythmias) who received CABG, an improvement in 5-year survival independent of ICD implantation [25]. A retrospective observational study of 50 post-cardiac arrest patients identified a reduction in inducible arrhythmias following CABG; VF was no longer inducible in all 11 patients who had inducible VF pre-operatively. In contrast, 80% of patients with inducible VT pre-operatively still had the arrhythmia following surgery [26]. Ventricular arrhythmia cardiac arrest survivors with coronary artery disease and non-inducible arrhythmias had a 100% survival rate ($n = 18$) over a 4-year follow-up (range, 1 to 48 months) compared with 87% (18/80) in patients not revascularised with inducible arrhythmias [27]. The CABG Patch trial, a prospective study of 900 patients with a left ventricular ejection fraction (LVEF) of less than 0.36 and ECG abnormalities scheduled for elective CABG who were randomly assigned to ICD or standard medical therapy, found that ICD use conferred no additional survival benefit to patients at high risk of arrhythmia formation [28]. In the control limb, the arrhythmia rate was low, implying that

Table 2

Scottish Intercollegiate Guideline Network: levels of evidence [151]

Level of evidence	Evidence required
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2−	Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytic studies (for example, case reports and case series)
4	Expert opinion

revascularisation reduces the incidence of arrhythmia formation and subsequent death. Revascularisation reduces the incidence of cardiac ischaemia that commonly precedes potentially fatal ventricular arrhythmias [29,30]. However, some patients following CABG may still have malignant arrhythmias. A case series of 23 cardiac arrest survivors discovered that 43% of patients received at least one ICD shock (range, 1 to 22 shocks) over a mean follow-up of 34 months. All patients had received CABG for ischaemia and were non-inducible with programmed stimulation [31].

Not all patients with potentially fatal arrhythmias have operable coronary artery disease. Therefore, revascularisation as a tool for arrhythmia management can be useful only in a specific cohort of patients. Though not specifically described in the post-cardiac arrest population, beta-blockers, aspirin, and statins have all been shown to prolong survival in patients with ischaemic heart disease. Thus, current guidelines produced by a task force representing the American Heart Association and American College of Cardiology state that patients with peri-MI ventricular arrhythmias in whom ischaemia is fully reversed do not require an ICD and that those with ischaemia not fully reversible should receive an ICD [32].

Thus, revascularisation appears to improve survival through a reduction in malignant arrhythmias and, potentially, myocardial salvage. There is currently no evidence supporting the use of thrombolysis in patients post-arrest without electrographic evidence of acute MI. The literature suggests that there should be a greater use of early angiography and electrophysiological testing to identify the presence of reversible ischaemia and the need for revascularisation or the use of ICD or antiarrhythmic agents. Although there is more evidence supporting the use of CABG compared with percutaneous angioplasty, this may be purely historical and requires further assessment.

Pharmacological and electrical rhythm stabilisation

Pharmacological and electrical methods often are employed to prevent the recurrence of arrhythmias, with amiodarone commonly used for arrhythmia prevention [33]. Retrospective studies of antiarrhythmic drug use after cardiac arrest have produced conflicting results [34-37]. The CASCADE (Cardiac Arrest in Seattle: Conventional Versus Amiodarone Drug Evaluation) study, a randomised multi-centre study of 228 patients post-VF confirmed cardiac arrest with electrophysiological evidence of an increased risk of further episodes, showed amiodarone to be superior to other antiarrhythmic agents at preventing VF arrests, sudden cardiac arrest, and ICD triggering episodes at 2, 5, and 6 years after the event [38]. However, the increasing use of ICDs may have a role in reducing long-term mortality, especially the high mortality rate seen in the first year after hospital discharge. Several observational studies have seen an increase in long-term survival and an increase in ICD use over the same time frames [10,13,14]. Pell and colleagues [5] estimated a 5-year mortality reduction if all patients fitting the criteria for ICDs had received them.

The role of ICDs for ventricular arrhythmia management has been proven in randomised controlled trials. The Multicenter Unsustained Tachycardia Trial (MUSTT) prospectively randomly assigned 754 patients (with coronary artery disease, an LVEF of less than 40%, and spontaneous unsustained tachycardia or sustained tachycardia on electrophysiological manipulation) to either antiarrhythmic therapy (pharmacological or electrical) or conventional medical therapy (beta-blockers/ACE/diuretics/aspirin). The mean follow-up was 39 months. A 7% absolute risk reduction of death from arrhyth-

mia or cardiac arrest was found in those randomly assigned to antiarrhythmic therapy. This was solely due to the use of ICDs and not pharmacological therapy [39]. Patients with ICDs not only had fewer cardiac arrests and arrhythmias, but also had improved survival every year for 5 years after enrolment compared with other study patients. Of those assigned to pharmacological agents, only 10% received amiodarone compared with more than 40% receiving class I antiarrhythmic agents. Whether this may have biased the result is uncertain [40]. The MADIT I (Multicenter Automatic Defibrillator Implantation I) study, a prospective randomised trial of 196 patients with inclusion criteria similar to those of the MUSTT study, identified a statistically significant positive outcome for those assigned to ICDs compared with pharmacological agents (54% 2-year reduction in all-cause mortality). The main antiarrhythmic agent in this study was amiodarone [41,42].

Specific to post-cardiac arrest patients, a meta-analysis of three randomised controlled trials (AVID, Canadian Implantable Defibrillator Study [CIDS], and Cardiac Arrest Study Hamburg [CASH]) investigated the role of ICDs versus amiodarone in ventricular arrhythmia reduction and mortality [43-47]. The meta-analysis concluded that there was a 27% reduction in the relative risk of dying (absolute reduction of 3.5% per year) and this was due almost entirely to a 50% reduction in arrhythmic death. The three studies enrolled patients with ventricular arrhythmias, the majority after cardiac arrest. The combined mean follow-up period was 2.3 (± 1.89 standard deviation) years. Patients with an LVEF of less than 35% benefited significantly more from an ICD than those with a greater ejection fraction. The prospective multi-centre CASH study of 288 patients post-cardiac arrest (secondary to sustained ventricular arrhythmias) randomly assigned patients to ICD or amiodarone or metoprolol. The minimum follow-up period was 2 years, with a mean of 57 ± 34 months. Overall mortality rates from all causes were 36.4% in the ICD arm and 44.4% in the antiarrhythmic arm (23% reduction). Although this was not statistically significant, there were fewer sudden deaths in the ICD group; 73% had evidence of coronary artery disease, raising the question of whether revascularisation would have altered the results.

The AVID study was the only one to show a statistically significant difference. The AVID population consisted of patients with documented VF or symptomatic VT, whereas the CASH and CIDS studies were confined to cardiac arrest survivors. More than a third of the AVID study patients were not post-cardiac arrest. There were other significant differences in the inclusion criteria between the three studies. The AVID study, with more than 500 patients in each limb, identified a superior all-cause and arrhythmic death reduction (all-cause deaths 16.5% versus 10%, arrhythmic deaths 7.4% versus 3%, and 27% reduction in all-cause mortality at 2 years). The follow-up period was only 1.5 years as a statistically significant benefit of ICDs led to the early termination of the study. The longest follow-up period described has been 11 years. Patients reported were a subgroup of those enrolled from one centre into the CIDS study. Total mortality was 5.5% per year in the amiodarone group compared with 2.8% in the ICD group. Patients receiving amiodarone had not only a statistically higher mortality but also a greater recurrence of arrhythmias and drug side effects [47]. Similar results have been reported by Hennersdorf and colleagues [48] in Düsseldorf, Germany. This echoes a previous smaller study with a mean follow-up of 27 months [49].

A two-centre retrospective cohort study (Massachusetts/Los Angeles) of 331 OOHCA patients discharged from the hospital identified that 71% had coronary artery disease and reduced ventricular function, 97.6% had a ventricular arrhythmia as the cause of their arrest, and median follow-up was 35 months (range, 1 to 151 months). More deaths (34.3% versus 19.3%) and sudden cardiac deaths (14.4% versus 3.3%) occurred in patients without an ICD. Multivariate analysis identified predictors of cardiac mortality as an LVEF of less than 0.4, absence of ICD, and the presence of inducible VT before hospital discharge. Patients with ICDs had a lower mean follow-up period and less coronary disease, which may have influenced the overall outcome [50]. A retrospective study of 194 survivors of OOHCA with no significant inducible arrhythmias on electrophysiological testing identified that patients receiving an ICD had a lower incidence of sudden cardiac death. However, there was no change in overall mortality compared with those without an ICD. Patients with an ICD were younger and had significantly less coronary artery disease, which may have biased the results [51]. A prospective study of 204 patients post-cardiac arrest identified a significant reduction in mortality in patients (with inducible tachycardia) receiving ICD compared with those receiving antiarrhythmic agents. The mean follow-up period was 57 months [48]. ICDs in conjunction with additional antiarrhythmic agents have been compared with ICD therapy alone. A prospective multi-centre study randomly assigned patients with ICDs to amiodarone and beta-blocker, sotalol, or a beta-blocker (metoprolol, carvedilol, or bisoprolol) for 1 year. Patients had to have sustained VT, VF inducible VT or VF by programmed ventricular stimulation, or cardiac arrest (and an LVEF of less than 40%) as the reason for ICD insertion. The main outcome measure was ICD shock for any reason. Shocks occurred in 38.5% assigned to beta-blocker alone, 24.3% in the sotolol group, and 10.3% in the amiodarone and beta-blocker group. Given that ICD shocks are painful, this may help to improve patient acceptance of the devices [52].

Much of the evidence for arrhythmia management and its influence on long-term survival originated from patients with proven arrhythmias who were not specifically post-cardiac arrest. Although there is less evidence available for post-cardiac arrest patients, the studies available are prospective,

randomised with large populations, and conclude that ICDs are superior to pharmacological agents alone at preventing further arrhythmias and prolonging survival. Although ICDs prevent sudden death, they add a considerable cost impact to patient care and produce painful shocks. Patient selection and, possibly, combined pharmacological therapy are important factors when looking to provide cost-effectiveness. Revascularisation remains an option for a specific subgroup of patients with reversible ischaemia.

Cardiac dysfunction post-arrest

Negovsky [53] described a multi-organ dysfunction syndrome that affects cardiovascular, neurological, pulmonary, and metabolic systems and that occurs after ROSC. Post-resuscitation myocardial dysfunction is now recognised as a separate entity from myocardial stunning secondary to coronary artery occlusion and may lead to a worse prognosis [54]. Patients often require inotropic support following a cardiac arrest for depressed ventricular function; this often reverses within 24 to 48 hours [55-57]. In animal studies, global myocardial stunning has been linked to ischaemia duration, the number and type of defibrillation shocks, and the total dose of epinephrine used during resuscitation [58-63]. A prospective study of transthoracic echocardiography performed 6 hours after ROSC following OOHCA found, on multiple regression analysis, prolonged cardiopulmonary resuscitation, defibrillation, and high-dose epinephrine (greater than 5 mg) to be associated with poor left ventricular (LV) systolic function. Patients with an LVEF of less than 40% had a higher mortality over the course of 60 days after the event and significantly worse neurological outcomes (as assessed by Cerebral Performance Category [CPC] scores, see Table 3). Impaired LV diastolic function, assessed by isovolumetric relaxation times, was associated with non-VF/VT cardiac arrests and was an independent predictor of a poor outcome [64]. Attempts to correct the dysfunction mechanically and pharmacologically may lead to improved long-term outcomes. As yet, however, there is little robust evidence on which to base specific recommendations [65-68].

Therapeutic hypothermia after cardiac arrest

Neurological injury accounts for a high proportion of early mortality in hospital and within the first year after discharge. Mechanisms described include reperfusion injury, production of free radicals and excitotoxic agents, the activation of degenerative enzymes, and reduced cerebral blood flow after arrest [69-73]. Animal studies have shown that mild therapeutic hypothermia (34°C to 36°C) can limit the degree of brain injury by minimising the above processes [74,75]. Some therapeutic benefit is lost if there is a delay (greater than 15 minutes after ROSC) in instituting hypothermia [76].

Human studies have shown that moderate therapeutic hypothermia (MTH) reduces hospital mortality and improves neurological outcome [69,77-80]. Bernard and colleagues [69] randomly assigned 77 post-OOH VF patients to normothermic or MTH (33°C) therapy. Survival to hospital discharge was improved in the MTH group (49% versus 33%) with higher Overall Performance Category (OPC) scores [69] (Table 3). The Hypothermia After Cardiac Arrest Study Group randomly assigned 275 witnessed VF/VT arrest patients to either maintenance of normothermia or MTH (32°C to 34°C) for 24 hours after arrest. Survival at 6 months was higher in the hypothermic group (59%) compared with the normothermic group (45%), with less neurological injury as assessed by CPC scores. Fifty-five percent of all patients in the treatment limb demonstrated a favourable neurological outcome (CPC 1 to 2) at 6 months compared with 39% in the control limb [79]. A subsequent meta-analysis of therapeutic hypothermia in post-VF arrest patients found that the number needed to treat to prevent one unfavourable neurological outcome was 6 (confidence interval, 4 to 13). Although the results are consistent, key differences between the studies used in the meta-analysis include: presenting rhythm, method of cooling, time taken to reach target temperature and duration of hypothermia [81]. To our knowledge, there have been no follow-up studies of long-term (greater than 1 year) neurological outcome of patients treated with post-arrest hypothermia.

Despite the strict inclusion criteria, which may have led to enrolment bias, similar findings have been described in other studies [69,71,78,82]. Hypothermia has now been recommended by ILCOR and adopted into resuscitation guidelines as part of the 'chain of survival'. Although the evidence to date has been primarily from VF OOHCA, ILCOR recommend that it be considered a treatment option for non-VF OOHCA [83]. Adopting therapeutic hypothermia as routine practice, however, has not occurred in some regions. Reasons given include technical difficulty and a perceived lack of evidence [84-87]. Although the evidence to date has been directed at improvements at 6 months to 1 year, it is reasonable to presume a long-term neurological benefit, but further follow-up studies are required to validate this statement.

Glycaemic control

Glycaemic control (80 to 110 mg/dL) in a critically ill population may provide short- and long-term survival benefits and is recommended in the management of patients with sepsis. Though an area of controversy, reducing the incidence of infection appears to account for much of the observed benefit [88,89]. Van den Berghe and colleagues [90] identified mortality benefit in critically ill medical patients managed with strict glycaemic control for a minimum of 3 days. The majority of OOHCA patients would fulfil both criteria and therefore may benefit [90]. Studies examining patients with brain 'injuries', however, are not conclusive. High mean glucose levels in patients with subarachnoid haemorrhage are associated with a poor neurological outcome and increased mortality. The Glucose Insulin in Stroke Trial, which used glucose/insulin/potassium infusions for 24 hours after admission to maintain serum glucose

Table 3

Scoring system

Scoring system	Description
EQ-5D	Five questions on mobility, self-care, everyday activities, pain, and state of mind, each with three possible answers. Total score: 0 to 100. The higher the score, the better the quality of life.
RAND 36	36 questions/statements on physical and emotional health with two to six choices for each question.
15D	15 dimensions with five levels that describe state of health. Patient chooses which best describes their state.
Cerebral Performance Category (CPC)	CPC 1: Conscious. Alert and able to work and lead a normal life. May have minor psychological or neurological deficits. CPC 2: Moderate cerebral disability. Conscious. Sufficient cerebral function for part-time work in sheltered environment or independent activities of daily life. May have hemiplegia, seizures, ataxia, dysarthria, or permanent memory or mental changes. CPC 3: Severe cerebral disability. Conscious. Dependent on others for daily support because of impaired brain function. CPC 4: Coma, vegetative state. CPC 5: Death. Certified brain dead or dead by traditional criteria.
Overall Performance Category (OPC)	OPC 1: Healthy, alert, capable of normal life. Good cerebral performance (CPC 1) plus no or only mild functional disability from non-cerebral organ system abnormalities. OPC 2: Moderate overall disability. Conscious. Moderate cerebral disability alone (CPC 2) or moderate disability from non-cerebral system dysfunction alone or both. Performs independent activities of daily life. May be able to work part-time in sheltered environment but disabled for competitive work. OPC 3: Severe overall disability. Conscious. Severe cerebral disability alone or severe disability from non-cerebral organ system dysfunction alone or both. Dependent on others for daily support. OPC 4: Same as CPC 4. OPC 5: Same as CPC 5.
Activities of Daily Living (ADLs)	Personal ADLs assess bathing, dressing, toilet visit, mobility, continence, and eating. Instrumental ADLs assess cleaning, shopping, cooking, and transportation.
Functional Independence Measure (FIM™)	An 18-point scale scoring from 1 to 7, with 7 being complete independence. Outcomes measured include self-care, sphincter control, transfers, locomotion, communication, and social cognition.
Symptom Checklist 90 Revised score	A 90-item self-report test designed to reflect psychological symptom patterns within the last 7 days.
Impact of Event Scale	A 15-point self-report questionnaire designed to assess current subjective stress for any specific life event.
Post-traumatic Diagnostic Scale	A 49-point self-report-style questionnaire aimed at assisting with the diagnosis of post-traumatic stress disorder.
MMS	A 30 point scale. Results in the range 0-23 indicate disturbance of cognition. Fields assessed are: Orientation, registration, attention and calculation, recall, language
Hospital Anxiety and Depression Scale	Seven questions for anxiety and seven questions for depression with a choice of four answers for each. Scores from 0 to 3 for each question, depending on answer given. The higher the total score, the more likely it is that affective symptoms are present.

between 4 and 7 mmol/L, identified no mortality benefit. This study was underpowered due to slow recruitment [91-93]. The role of glucose control after OOHCA has been difficult to establish due to confounding factors (for example, time to ROSC) [94,95]. A prospective study of 145 patients admitted following ROSC from a witnessed VF arrest examined the association of glucose levels in neurological outcome. Patients receiving insulin or with a history of diabetes were excluded from the study. A significantly better neurological outcome (as assessed by CPC scores) at 6 months was identified in patients with lower median 24-hour glucose levels (146 ± 39 mg/dL interquartile range) compared with those with higher levels (184 ± 88 mg/dL) even after controlling for duration of arrest and lactate levels [96]. A retrospective observational study of 461 OOHCA patients identified, by multivariate analysis, that a glucose level of greater than 10.6 mmol/L within the first 24 hours after admission was associated with significantly higher hospital mortality [97]. A retrospective study of 98 patients identified mean blood glucose as being an independent predictor of survival at 6 months [98]. Whether glycaemic control confers longer survival and neurological benefits is unclear. High glucose levels may be a surrogate marker for the severity of brain injury incurred, reflecting the release of stress hormones (for example, cortisol, glucagon, and epinephrine). A study randomly assigning survivors of OOHCA to tight glycaemic control or no glucose control would, given the current levels of evidence for glycaemic control in critical care studies, be unethical. A sensible approach would be to prevent hyperglycaemia following OOHCA.

Anticonvulsant prophylaxis, thrombolysis, and neurological outcome

Seizure activity after cardiac arrest is common, with observational studies identifying an incidence of up to 36% [99,100]. It is associated with a poor neurological outcome. However, the presence of seizure activity is likely to be the effect of significant cerebral injury. Small animal studies have described a reduction in the neuronal damage after cardiac arrest with lamotrogine and fosphenytoin [101,102]. There are, to date, no human studies examining whether anti-convulsant therapy affects patient outcome in this context.

Small animal studies have demonstrated that peri-arrest thrombolysis can improve cerebral microcirculation flow and electroencephalogram readings immediately after ROSC [103,104]. To date, there are no human studies or case reports of thrombolysis being used after ROSC to improve neurological outcome. Given the level of available evidence, no recommendation can be made for the routine use of thrombolysis or prophylactic anticonvulsant drugs.

Nishizawa and Kudoh [105] studied eight patients after OOHCA and discovered jugular bulb venous blood oxygen saturation altered in direct proportion to changes in mean arterial pressure. Impairment of cerebral autoregulation may be due to cerebral ischaemia accompanying cardiac arrest [105]. Similar results were obtained by Sundgreen and colleagues [106], identifying either a loss or right shift in cerebral autoregulation. Maintaining an appropriate mean arterial pressure may lead to less secondary brain injury. Although these are areas of considerable interest which may provide potential therapeutic avenues, recommendations cannot be made without further research.

Neurocognitive and functional outcome: effects on survivors and families

Gross neurological outcome

When assessing how successful a resuscitation attempt has been, the initial Utstein recommendations focussed on survival at hospital discharge, with function assessed by CPC and OPC at discharge [107-109]. As up to 90% of hospital mortality following OOHCA is attributed to brain injury, this seems an appropriate outcome measure [110].

In Olmstead County, of patients who experienced a VF OOHCA, 145 (72%) patients were admitted alive, 79 (54%) survived to hospital discharge, 75 patients discharged had an OPC score of 1, and 5 patients discharged had a score of 2 (Table 3). Five patients were transferred to a nursing home with an OPC score of 3 to 4 [21]. Engdahl and colleagues [14] found that fewer patients were being discharged home with a CPC score of 1 or 2 over a 20-year period (1981 to 1991, 78%; 1991 to 1998, 63%) and more patients were being discharged to nursing homes and rehabilitation clinics. Such differences may reflect the study populations and community services available. A cause for the increase in patients requiring long-term care may be advances in peri-arrest management, with more patients surviving with what, historically, would have been unsurvivable brain injuries. Importantly, gross neurological outcome may improve with time. Among patients who had a CPC score of 2 at discharge, 77% improved to a CPC score of 1 one year later. Among patients with a CPC score of 3 at discharge, 25% improved to a CPC score of 2 and 4% to a CPC score of 1 one year later [111].

Mortality data give no indication of whether an individual returns to any degree of normal neurological function, and CPC/OPC, as somewhat gross measures, tend not to correlate with QOL as judged by questionnaires and structured interviews. Hsu and colleagues [112] studied 35 patients at an average of 7 months after arrest and found that CPC correlated poorly with QOL. A CPC score of 1 on discharge had a sensitivity of 78%, a specificity of 43%, a positive predictive value of 64%, and a negative predictive value of 60% for a QOL that was the same as or better than before the cardiac arrest [112]. Recent recommended guidelines (from participants of the Utstein Consensus Symposium) for research into in-hospital post-resuscitation care suggest the use of QOL markers as a measure of the effectiveness of care as well as outcome [113]. Three QOL scales are now recommended. These are the EQ-5D, the RAND 36, and the 15D [114-116] (Table 3).

Functional outcome and quality of life

Functional assessment is often made using activities of daily living (ADLs). Two different scales have been described: personal ADL (P-ADL) and instrumental ADL (I-ADL) (Table 3) [117,118]. Survivors of cardiac arrest frequently remain dependent on others for most activities. A prospective cohort study of patients after OOHCA examined ADLs 1 year after cardiac arrest, reporting that 5/26 patients remained dependent [119]. A small retrospective study with an average follow-up of 25 months found that P-ADL was a problem for 3/20 patients and that 7/20 patients were dependent for I-ADLs [120]. Grosvasser and colleagues [121], using a similar scoring system, found that 17/31 patients were dependent when followed up at least 3 years after the event. Lundgren-Nilsson and colleagues [110] assessed ADL using the Functional Independence Measure (FIM™) and the Instrumental Activity Measure (Table 3). They found that 61% were dependent for motor performance and 65% for social cognitive areas when assessed within 2 weeks of their cardiac arrest. The level of dependence fell at 45 days after the event to 43% (motor) and 56% (social cognitive) with no significant improvement between 45 days and 1 year [110].

Another marker of recovery often used is a return to pre-arrest social activities, including employment. The study of Pußwald and colleagues [122] of 12 survivors at a median period of 25 months after hospital discharge found that none

had returned to employment. Grosvasser and colleagues [121] found that only 1 of 31 survivors was back to work 3 years after the cardiac arrest. A retrospective study from San Francisco, CA, USA, found that, of 61 survivors, 36 had been in employment prior to their cardiac arrest. At 6 months, this figure had fallen to 26 and to 16 at 1 year. The largest fall was in those in full-time employment (46% to 18% at 1 year). The mean age of this group was 48 years. The main reasons given for not returning to work were the occurrence of symptoms with exercise, impairment of intellectual function, and approaching retirement age [123]. These findings are similar to those of earlier studies [124,125].

Granja and colleagues [126] used the EQ-5D to assess health-related QOL in 19 survivors at 6 months. Eight were working and six of these had returned to their previous level of activity. Eleven were already retired, with seven returning to previous levels of activity. Those assessed had a 'good' QOL. No significant differences were found when compared with a general critical care control group [126]. A retrospective observational study of OOHCA patients in Rotterdam, The Netherlands, found that 109 (83%) hospital survivors returned questionnaires and had a mean EQ-5D visual analogue scale score of 85/100, representing a good QOL [127]. Thus, the above studies show that, although CPC and OPC scores are often used, they may be insensitive and do not truly reflect functional status.

Memory and cognitive dysfunction

Cognitive impairment is common after cardiac arrest. A study of 25 patients identified that 72% of patients had mild to severe impairment in at least one cognitive area at hospital discharge, with memory being the most common deficit; time to post-arrest wakening was most predictive of longer-term cognitive outcome [128]. A retrospective study of 12 patients with anoxic injury of cardiac origin assessed a median of 25 months after injury found that all had evidence of impairment in areas such as memory, orientation, alertness, and awareness. Three syndromes were identified: severe physical and intellectual impairment, dementia, and amnesic syndrome. Extrapolating this evidence is difficult as all patients had confirmed brain damage and had undergone prolonged rehabilitation, thus are unlikely to be representative of all survivors [129]. A prospective randomised study of 68 OOHCA survivors by Roine and colleagues [130] showed that 48% still had evidence of cognitive impairment at 1 year, the incidence at 3 months being 60% measured with the mini-mental state (MMS) scoring system. Using the MMS scoring system, Sunnerhagen and colleagues [120] found that persisting cognitive impairment was still present at 2 years after the event, with cognitive impairment occurring in 35% of survivors studied. The better result may reflect differences in cardiac arrest populations, population sizes, or length of time since the event. One notable difference between the two studies was the time from arrest to arrival of emergency medical services. Arrival times were shorter in the study of Sunnerhagen and colleagues compared with the population of Roine and colleagues, suggesting that the interval from arrest to commencement of cardiopulmonary resuscitation (and so cerebral perfusion) is important for long-term neurological outcome. Others have found memory and concentration to be still impaired 3 to 4 years after the event compared with control populations [129,131-134]. The above studies all suggest that cognitive impairment, especially concentration, is common after cardiac arrest. Moreover, the studies exclude patients with severe neurological impairment, thus masking the true proportion of impaired survivors. Maximal recovery appears to occur early, with long-term cognitive impairment a real possibility.

Affective disorders

In the early phase after a cardiac arrest, a high prevalence of anxiety and panic symptoms has been described [135,136]. Anxiety, depression, anger, stress, and confusion are highest at hospital discharge. A prospective randomised study examining the effect of nimodipine on neurocognitive sequelae after cardiac arrest found that 69% of all patients surviving to 1 year had depressive symptoms when tested with the Symptom Checklist 90 Revised score (Table 3). Nimodipine had no effect on the cognitive functions tested [130]. O'Reilly and colleagues [137] performed a retrospective case-control study of 27 patients from Scotland who were enrolled within 18 months of their resuscitation and assessed with the Hospital Anxiety and Depression Scale (Table 3). Clinical anxiety and depression were more common in the post-cardiac arrest group compared with the MI control group (30% versus 7% and 15% versus 0%, respectively). Statistical significance was reached only for depression [137]. Reasons for these discrepancies probably lie in the different assessment tools used and the variable and unmeasured level of support and care provided. Whether these symptoms persist in the long term is unclear. Some investigators have reported that affective symptoms tend to decline over the following year, with the greatest reduction reported at 6 months after discharge [123,138,139].

Post-traumatic stress disorder symptoms

One of the core criteria for developing post-traumatic stress disorder (PTSD) is the experiencing of an event that was an actual or perceived threat to life. Serious illness is now included as such an event in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) [140]. In their case-control study, O'Reilly and colleagues [137] found that five (19%) cardiac arrest survivors and two (7%) MI survivors fulfilled DSM-IV criteria for PTSD when assessed by structured clinical interview, the Impact of Event Scale (IES), and a self-reporting questionnaire (Post-traumatic Diagnostic Scale) (Table 3). There was, however, relatively poor agreement between the interviews and self-report diagnoses [137]. A similar-sized study from Munich, Germany, using IES, examined patients 2 to 5 years after the event and found that 8/21 patients had PTSD symptoms

associated with significantly higher scores for depression and anxiety. Patients with PTSD symptoms reported a lack of confidence in the future and low estimates of their mental and somatic condition, tending to report more physical symptoms. Further analysis identified that sedation at illness onset reduced the risk of developing PTSD by fivefold [131]. The mean duration of unconsciousness in those sedated was 618 minutes compared with 92 minutes in those not sedated. The authors speculate that prolonged sedation may inhibit imprinting of painful and adverse stimuli; also, awakening in a more controlled environment may generate more positive emotions.

Neurocognitive and affective disorders in critical illness

Depression, anxiety, and avoidance symptoms are common among patients discharged from general intensive care units [141]. In medical intensive care patients, 33% to 78% of survivors had neurocognitive impairment at 6 months to 1 year. This can still be present 6 years later [142-145]. Suggested mechanisms include hypoxia, hyperglycaemia, and ischaemia. Sedative and analgesic drugs and sepsis may also contribute [146]. Many OOHCA patients spend a significant period of time in a critical care environment. Thus, cognitive and psychological disorders may be, in part, a generic consequence of critical illness rather than the sequelae of the cardiac arrest itself.

Information from qualitative studies

Several qualitative studies have investigated the broader aspects of patient survival from the perspective of the individual and family. Dougherty and colleagues [147] examined this in survivors of OOH VF arrest who then received an ICD. Thirteen survivors and family members were followed up over 1 year after hospital discharge. Using structured questionnaires and interviews, they identified 'domains of concern' and the strategies implemented to cope with these issues. Common areas of concern for partners were the physical and emotional care of the survivor, finding time for their own well-being, relationship changes, understanding ICDs and dealing with shocks, money worries, and communicating with health care providers [138,147]. A study of eight survivors of cardiac arrest with ICDs by Tagney and colleagues [148] from Bristol, UK, reported similar observations. They also found that overprotectiveness of families led to reduced levels of activity and increasing dependence with subsequent loss of confidence. Survivors had concerns over altered body image due to the implanted defibrillator and often concealed symptoms, emotions, and concerns about their ICD from their family. Fear of ICD shocks and possible death may limit physical recovery, including sexual activities [148]. Dougherty and colleagues [147] and Tagney and colleagues [148] found that advice given by health care providers was often technical, with little advice on how to live with an ICD. Sears and colleagues [149] also found that health care providers are often less comfortable dealing with the emotional aspects of ICDs compared with medical issues.

Once the patient is home, strategies are often implemented by partners to make the transition from hospital to home as smooth as possible. Actions employed include arranging and adapting furniture to allow easier use, words of encouragement to help overcome anger and frustration, and increased activity levels and using games to improve memory deficits and help with reorientating the survivor to their environment. Investigators in this field agree that more could be done to prepare and support families in the longer term after hospital discharge. The burden of caring for a survivor can also have a more severe emotional impact. Pußwald and colleagues [122] found that 6 of 12 family members interviewed were clinically depressed, stating concerns over loss of employment in order to be the main carer and financial worries as being important.

Although the above qualitative studies raise important issues, the small size of the samples means that the themes described above may not encompass all the concerns of post-arrest patients. Furthermore, the literature has concentrated on patients post-arrest with ICDs and may not accurately reflect the general post-arrest population.

Conclusion

Longer-term survival following OOHCA is improving. Post-resuscitation management has been highlighted in the European Resuscitation Council guidelines of 2005. The new 'Chain of Survival' for surviving cardiac arrest now places more emphasis on the final link: 'post-resuscitation care to restore quality of life' [150].

Revascularisation, ICDs, and therapeutic hypothermia appear to have had a considerable impact. Revascularisation and ICDs reduce mortality in the long term mainly by arrhythmia management. However, the considerable financial impact of these interventions means that patient selection is all important to ensure cost-effectiveness. The presence of reversible ischaemia with or without inducible arrhythmia needs to be identified early on in the post-resuscitation management phase. There is a strong argument to be made for early angiography in all post-arrest survivors and electrophysiological testing for those patients without reversible ischaemia. Based on the evidence available, angioplasty appears to have a role to play in revascularisation and its role will become more defined with further research into this area.

Therapeutic hypothermia improves short-term survival and gross neurological outcome. However, its impact on longer-term sequelae has yet to be reported. Although there are inconsistencies in the methodologies used in the various studies, the uniformly positive outcomes mean it should be considered for all cardiac arrest survivors irrespective of the causative arrhythmia. It is likely that outcomes will improve as cooling techniques become more sophisticated, allowing for more rapid and controlled cooling and rewarming.

Tight glucose control to date is unproven in OOHCA survivors. However, the evidence available suggests that it may be associated with an improved neurological outcome. Given the recommendations for glycaemic control in the critically ill population, it would seem sensible to apply these to post-cardiac arrest patients until further evidence is available. The potential risk for hypoglycaemia and exacerbating cerebral injury needs to be taken into account.

Although mortality is a useful clinical tool for assessing changes in practice, it does not reveal any information about more subtle outcomes important to the patient and their families. Functional dependency and neuropsychiatric sequelae are common and may be due to the initial insult or a response to the critical illness state. A better understanding of the patients' needs after hospital discharge may lead to an improvement in the level of after-care currently provided. This can be achieved only by ensuring that the research agenda include longer-term outcome reporting and that such reporting be sufficiently sophisticated to encompass a multi-dimensional assessment of quality of survival, impact on families, and future health care needs and costs. In simple terms, producing cohorts of severely damaged survivors is unlikely to be universally regarded as a success.

Competing interests

The authors declare that they have no competing interests.

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