Survival of 1476 patients initially resuscitated from out of hospital cardiac arrest

Stuart M Cobbe, Kirsty Dalziel, Ian Ford, Andrew K Marsden

Abstract

Objectives—To determine the short and long term outcome of patients admitted to hospital after initially successful resuscitation from cardiac arrest out of hospital.

Design—Review of ambulance and hospital records. Follow up of mortality by "flagging" with the registrar general. Cox proportional hazards analysis of predictors of mortality in patients discharged alive from hospital.

Setting—Scottish Ambulance Service and acute hospitals throughout Scotland.

Subjects—1476 patients admitted to a hospital ward, of whom 680 (46%) were discharged alive.

Main outcome measures—Survival to hospital discharge, neurological status at discharge, time to death, and cause of death after discharge.

Results—The median duration of hospital stay was 10 days (interquartile range 8-15) in patients discharged alive and 1 (1-4) day in those dying in hospital. Neurological status at discharge in survivors was normal or mildly impaired in 605 (89%), moderately impaired in 58 (8.5%), and severely impaired in 13 (2%); one patient was comatose. Direct discharge to home occurred in 622 (91%) cases. The 680 discharged survivors were followed up for a median of 25 (range 0-68) months. There were 176 deaths, of which 81 were sudden cardiac deaths, 55 were non-sudden cardiac deaths, and 40 were due to other causes. The product limit estimate of 4 year survival after discharge was 68%. The independent predictors of mortality on follow up were increased age, treatment for heart failure, and cardiac arrest not due to definite myocardial infarction.

Conclusion—About 40% of initial survivors of resuscitation out of hospital are discharged home without major neurological disability. Patients at high risk of subsequent cardiac death can be identified and may benefit from further cardiological evaluation.

Introduction

Despite pioneering work performed in Belfast¹ and Brighton,² systems of cardiopulmonary resuscitation and defibrillation out of hospital have not been widespread in the United Kingdom until recent years. The development of the automated external defibrillator has enabled ambulance technicians to provide defibrillation without the need for training to full paramedic level.^{3,4}

Automated external defibrillators have been installed in all emergency ambulances in Scotland since 1988-9, and the protocol and immediate outcome of resuscitations undertaken by the Scottish Ambulance Service have been reported.⁵⁻⁷ We determined the short and long term survival of patients after initially successful resuscitation from cardiac arrest out of hospital in Scotland and identified predictors of mortality after discharge from hospital.

Methods

PATIENTS

The study population comprised consecutive patients admitted to a hospital ward after initially successful resuscitation from cardiac arrest by the Scottish Ambulance Service from the introduction of prehospital defibrillation on 1 October 1988 to 30 June 1994. Resuscitation was attempted in 10 081 patients, of whom 1476 (14.6%) were admitted alive to a hospital ward. Resuscitation details were recorded on ambulance service cardiopulmonary resuscitation report forms, and a request was made to the medical records department of the receiving hospital for confirmation of patients' identification details, outcome of admission, and a copy of the discharge summary for patients discharged alive.

Clinical information obtained on patients discharged alive from hospital included any history of myocardial infarction, symptoms preceding collapse, changes on electrocardiography and cardiac enzyme activities after admission, management in hospital and on discharge, and neurological status at discharge.

DEFINITION OF CAUSE OF CARDIAC ARREST

Myocardial infarction covered sequential electrocardiographic changes (new Q waves or ST segment elevation) associated with raised activity of cardiac enzymes to greater than twice the upper limit of normal.

Ischaemia or non-Q wave myocardial infarction—This was transient ST depression or T wave inversion with no new Q wave development, or both; and cardiac enzyme activity raised or within normal range.

Primary ventricular fibrillation meant collapse without new electrocardiographic changes. A previous myocardial infarction, congestive heart failure, left ventricular hypertrophy, or valvar heart disease supported the diagnosis. Cardiac enzyme activity was raised¹ or within normal limits.

Other causes—These were determined as being primarily cardiac or non-cardiac according to available evidence.

DEFINITION OF NEUROLOGICAL STATUS AT DISCHARGE

Normal or mild disability—There was no specific mention of neurological disability at time of discharge, or neurological disability was confined to mild memory loss or mild confusion.

Moderate disability—This indicated more severe persisting neurological abnormality requiring detailed assessment of suitability for home discharge.

Severe disability—Patients were not able to maintain independent existence, requiring long term institutional care.

FOLLOW UP

The period of follow up of patients discharged from hospital was measured from the date of discharge till the date of death or the census date of 30 June 1994. Patients were "flagged" with the registrar general for

Department of Medical Cardiology, Glasgow Royal Infirmary, Glasgow G31 2ER
Stuart M Cobbe, professor of medical cardiology
Kirsty Dalziel, research statistician

Robertson Centre for Biostatistics, University of Glasgow, Glasgow G12 8QQ
Ian Ford, professor of statistics

Scottish Ambulance Service, Edinburgh EH10 5UU
Andrew K Marsden, consultant medical director

Correspondence to: Professor Cobbe.

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Table 1—Management of survivors of cardiac arrest due to underlying heart disease

Treatment and investigation	Total (n = 618)	No (%) of patients receiving treatment or investigation		
		Myocardial infarction (n = 339)	Ischaemia or non-Q wave myocardial infarction (n = 136)	Primary ventricular fibrillation (n = 143)
Thrombolysis on admission	179 (29)	156 (46)	17 (13)	4 (3)
Discharge treatment*:				
Nil	12 (2)	3 (1)	7 (5)	4 (3)
Aspirin	451 (73)	281 (83)	90 (66)	79 (55)
Anticoagulants	37 (6)	20 (6)	7 (5)	11 (8)
β Blocker	173 (28)	112 (33)	44 (32)	19 (13)
Nitrate/calcium channel blockers	167 (27)	95 (28)	42 (31)	30 (21)
Diuretics	210 (34)	105 (31)	35 (26)	72 (50)
Angiotensin converting enzyme inhibitor	124 (20)	58 (17)	14 (10)	51 (36)
Antiarrhythmics	155 (25)	37 (11)	35 (26)	79 (55)
Investigations:				
Exercise electrocardiography	117 (19)	81 (24)	29 (21)	9 (6)
Coronary angiography	80 (13)	27 (8)	29 (21)	24 (17)
Electrophysiology	3 (5)	3 (1)	11 (8)	17 (12)

*Management on discharge was unknown in 15 patients.

Scotland, and vital status at the census date was determined through the registrar general's office. Those with a certified cause of death due to ischaemic heart disease (*International Classification of Diseases*, ninth revision, codes 410 to 414) or other forms of heart disease (codes 415-429) were considered to have died suddenly if the certified place of death was outside hospital or if there was a further ambulance cardiopulmonary resuscitation report indicating a recurrent cardiac arrest. Other causes of cardiac death were classified as "non-sudden" and the remainder of the deaths were designated as non-cardiac.

STATISTICAL ANALYSIS

Continuous variables are presented as median (interquartile range), and differences between grouped data were analysed by the Mann-Whitney U test. Univariate survival analysis was performed on the 680 discharged patients by using the product limit estimate, and Kaplan-Meier survival curves were generated. Comparisons between survival curves were performed by the Mantel-Cox (log rank) test.

A Cox proportional hazards stepwise analysis was performed to assess which factors had independent influence on survival in a subset of 618 patients whose cardiac arrest was due to underlying heart disease and in whom details of clinical management were obtainable. The probability value to enter the model was $P \leq 0.05$. The results of the Cox analysis are presented as hazard ratios with 95% confidence intervals.

Results

COURSE IN HOSPITAL

Of 1476 patients admitted to a ward, 796 died in hospital and 680 were discharged. The median duration of hospital stay in survivors was 10 days (interquartile range 8-15; range 1-379) compared with 1 day (1-4; 0-373) in non-survivors. Of the non-survivors, only 45 (5.7%) and 12 (1.5%) survived in hospital for more than 15 and 30 days, respectively. The median age of survivors was significantly less than that of non-survivors (64 v 67 years, $P < 0.0001$).

The presumed cause of cardiac arrest in the survivors was acute myocardial infarction in 345 (51%), ischaemia or non-Q wave infarction in 139 (20%), primary ventricular fibrillation in 146 (22%), other conditions in 41 (6%), and undetermined in nine (2%). The median age of patients with acute myocardial infarction was 61 (54-68) years compared with 67 (59-72) in both

the ischaemia or non-Q wave infarction and the primary ventricular fibrillation groups ($P < 0.001$).

Neurological status on discharge was normal or mildly impaired in 605 (89%) of the patients, while 58 (8.5%) had moderate disability, 13 (2%) had severe disability, and one was comatose. Neurological status was undetermined in three patients (0.5%). Discharge from the acute hospital was to home in 622 (91%) cases, another acute hospital in 25 cases, a rehabilitation unit in 23, a long stay facility in nine, and a psychiatric unit in one.

Details of clinical management were obtained on 618/630 (98%) patients with cardiac arrest due to underlying heart disease (table 1). Nearly half of the patients with acute myocardial infarction received thrombolytic therapy on admission. The commonest drugs prescribed at discharge were aspirin, diuretics, β blockers, or other anti-ischaemic treatment (nitrates or calcium channel blockers). Amiodarone was the most commonly prescribed antiarrhythmic drug (96/157 (61%)). Only a small minority of patients underwent immediate further investigation by exercise testing, coronary arteriography, or electrophysiological study.

SURVIVAL

Survival was calculated from the date of discharge until the date of death or 30 June 1994, giving a median follow up period of 25 (range 0-68) months. There were 176 deaths during the study period. The median age at

Fig 1—Kaplan-Meier survival curves for 680 patients discharged alive from hospital. Curves illustrate proportion free from sudden cardiac death, any cardiac death, or death due to any cause during follow up. Survival curve for normal Scottish population, adjusted for age and sex, is illustrated by broken line

Table 2—Independent predictors of all cause mortality by Cox proportional hazards stepwise analysis in 618 patients with cardiac arrest due to underlying heart disease*

Variable	Hazard ratio (95% confidence interval)	P value
Age (1 year)	1.04 (1.02 to 1.06)	<0.001
Diuretic or angiotensin converting enzyme inhibitor (yes/no)	2.01 (1.45 to 2.79)	<0.001
Type of arrest (no myocardial infarction/myocardial infarction)	1.60 (1.15 to 2.23)	0.004

*Entry criteria for multivariate analysis, $P < 0.05$.

the initial admission of patients who died during follow up was 68 (interquartile range 60–73) years compared with 62 years (54–69; $P < 0.0001$) in the 504 patients surviving. Death was certified as due to ischaemic or other heart disease in 136 patients (77%), malignancy in 12 (7%), cerebrovascular disease in 10 (6%), and other causes in 18 (10%). Of the 136 cardiac deaths, 81 (60%) were sudden. The proportion of sudden deaths according to the original type of arrest was 31/68 (46%) in the myocardial infarction group, 14/43 (33%) in the ischaemia or non-Q wave myocardial infarction group, and 29/48 (60%) in the primary ventricular fibrillation group.

Figure 1 shows the survival curves for probability of overall survival, freedom from cardiac death, and freedom from sudden death. The overall survival is compared with the normal Scottish population, adjusted for age and sex.⁸ The product limit estimate of overall survival in the patients was 84% at one year, 77% at two years, 73% at three years, and 68% at four years. There was no difference in probability of survival between men and women (data not shown). The association between age and survival was significant ($P \leq 0.0001$, figure 2), the product limit estimates of four year survival being 84%, 74%, 67%, and 48% for

Fig 2—Survival curves of patients aged <55 years ($n = 153$), 55–64 years ($n = 206$), 65–69 years ($n = 129$), and ≥ 70 years ($n = 192$)

Fig 3—Survival curves after discharge according to cause of initial cardiac arrest: acute myocardial infarction ($n = 339$), ischaemia or non-Q wave infarction ($n = 136$), or primary ventricular fibrillation ($n = 143$)

the age categories <55, 55–64, 65–69, and ≥ 70 years, respectively. The unadjusted effect of type of cardiac arrest on total survival was highly significant ($P < 0.001$), indicating a greater probability of survival after acute myocardial infarction than after ischaemia or non-Q wave infarction or primary ventricular fibrillation (fig 3).

The Cox proportional hazards stepwise analysis investigated the effect on mortality of increased age (per 1 year increment), previous myocardial infarction, underlying cause of cardiac arrest, and drug treatment and investigation. As the survival curves for the ischaemia or non-Q wave myocardial infarction and primary ventricular fibrillation groups were virtually identical, the two groups were combined as a “no myocardial infarction” group for this analysis. Table 2 tabulates the results in order of significance. The three variables of sufficient significance to enter the model for all cause mortality were age, use of diuretic or angiotensin converting enzyme inhibitor, and type of arrest (no myocardial infarction *v* myocardial infarction). The three independent predictors identified in the proportional hazards analysis were used to calculate estimates of survival from cardiac death and of overall survival in the specified subgroups (table 3). It can be seen that the three year survival free from cardiac death ranged from 97% to 60% and the overall survival from 92% to 52%. The worst cardiac prognosis was seen in patients receiving diuretics or angiotensin converting enzyme inhibitors who had not suffered a definite myocardial infarction, regardless of age. The best cardiac prognosis was seen in younger patients not receiving diuretics or angiotensin converting enzyme inhibitors, regardless of whether they had suffered a definite myocardial infarction.

The proportional hazards analysis of sudden deaths ($n = 81$) identified only treatment with diuretic or angiotensin converting enzyme inhibitor (hazard ratio 3.25; 95% confidence interval 1.98 to 5.33; $P < 0.001$) and thrombolytic therapy (0.45; 0.25 to 0.85; $P = 0.008$) as independent predictors.

Discussion

The clinical management, investigation, and outcome of survivors of cardiac arrest in this series is probably representative of current British practice. Our results and the previous British study of in hospital resuscitation⁹ indicate that around 40% of patients admitted to a hospital ward after resuscitation can be expected to be discharged alive without major neurological handicap. Prolonged hospital admission was not necessary in most survivors nor did patients who ultimately succumbed in hospital tend to survive more than a few days.

Our results differ from those in previous large, unselected series of survivors of cardiac arrest^{10–13} in having been collected in recent years and over a wide geographical area and range of hospitals. Although comparison of results must be undertaken with caution, it is reassuring to note that the four year survival in the present series (68%) is superior to the 40–61% reported previously^{10–13} in populations of similar median age. Obvious differences in management between the

Table 3—Kaplan-Meier three year survival estimates in subgroups*

Age <64 years	Angiotensin converting enzyme inhibitor or diuretic	Myocardial infarction	No in group	Cardiac deaths (n)	Cardiac survival at 3 years† (%)	Total deaths (n)	Total survival at 3 years (%)
Y	N	N	93	3	97	9	92
Y	N	Y	133	9	93	13	91
N	N	Y	74	11	88	15	82
Y	Y	Y	69	14	78	16	75
N	Y	Y	69	20	68	24	62
N	N	N	107	31	66	42	58
Y	Y	N	43	16	61	20	52
N	Y	N	92	32	60	37	56

*Groups are listed in descending order of cardiac survival. †For calculation of cardiac survival, deaths due to a non-cardiac cause were censored at the time of death.

present and previous series include the widespread use of aspirin and thrombolytic therapy, both of which were independently associated with reduced mortality in the myocardial infarction group (data not shown). The use of β blockers reduces the risk of sudden death after acute myocardial infarction¹⁴ and was associated with reduced mortality in a previous study of survivors of cardiac arrest.¹³ The univariate hazard ratio for treatment with β blockers in the present series was 0.46 (95% confidence interval 0.30 to 0.70), but β blockade was not a significant independent factor in the proportional hazards analysis. The low usage of class I antiarrhythmic drugs compared with previous series may have protected patients from the lethal proarrhythmic effects of these drugs which have been identified in recent years.^{13 15-17}

The apparent paradox that patients sustaining definite myocardial infarction have a better long term prognosis than the "no myocardial infarct" group has been reported previously^{10 18} and was confirmed in this series. The "no myocardial infarct" group comprised patients whose ventricular fibrillation was induced by acute ischaemia or non-Q wave infarction, who have a high risk of recurrent ischaemic events,^{19 20} or who are prone to recurrent re-entrant ventricular arrhythmias usually on the basis of old myocardial infarction, left ventricular dysfunction, or hypertrophy.²¹ The "no myocardial infarction" group was heterogeneous, however, and the prognosis in the younger "no myocardial infarction" group who were not receiving diuretics or angiotensin converting enzyme inhibitors was surprisingly good (table 3).

The management after discharge of the patients who suffered from ischaemia or non-Q wave infarction in the present series did not differ greatly from that of the definite infarction group. Given that the median age of the "no myocardial infarction" patients was 67 years, there may have been reluctance to submit elderly patients to aggressive intervention. Such patients have a high prevalence of severe multivessel coronary disease, however, and the outcome of surgical revascularisation is good.^{22 23}

The appropriate management of the primary ventricular fibrillation group is yet to be clarified by prospective placebo controlled clinical trials. The use of empirical class I antiarrhythmic agents is associated with an increase in mortality¹³⁻¹⁵ and even antiarrhythmic treatment guided by electrophysiological testing seems no better than empirical β blockade²⁴ and is inferior to amiodarone.²⁵ The implantable cardioverter defibrillator is commonly used in the United States for this type of patient²⁶ and seems to reduce the risk of sudden death, although its effects on overall survival are less impressive²⁷ and await confirmation in clinical trials currently under way.^{28 29}

The impact of cardiac failure and left ventricular dysfunction as independent risk factors for overall mortality and risk of recurrent sudden death is evident whether assessed indirectly by the use of antifailure treatment in the present series and the study of Goldstein *et al* in 1985¹² or directly by measurement of left ventricular ejection fraction.²¹ Although left ventricular dysfunction may not be reversible in these patients, a minority may benefit from revascularisation, and there is some evidence of benefit from amiodarone.³⁰

In summary, although advanced age and poor left ventricular function may make further evaluation inappropriate, selected survivors of cardiac arrest without myocardial infarction may benefit from cardiological assessment.

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Conflict of interest: None.

Key messages

- Forty per cent of patients initially resuscitated from out of hospital cardiac arrest are discharged without major neurological disability, and prolonged hospital admission is uncommon
- Nearly 70% of patients discharged after cardiac arrest are alive four years after the event
- Patients whose cardiac arrest is not due to definite myocardial infarction require further cardiological assessment

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Prospective evaluation of eligibility for thrombolytic therapy in acute myocardial infarction

John K French, Barbara F Williams, Hamish H Hart, Susan Wyatt, June E Poole, Christine Ingram, Christopher J Ellis, Miles G Williams, Harvey D White

Abstract

Objective—To determine the proportion of patients presenting with acute myocardial infarction who are eligible for thrombolytic therapy.

Design—Cohort follow up study.

Setting—The four coronary care units in Auckland, New Zealand.

Subjects—All 3014 patients presenting to the units with suspected myocardial infarction in 1993.

Main outcome measures—Eligibility for reperfusion with thrombolytic therapy (presentation within 12 hours of the onset of ischaemic chest pain with ST elevation ≥ 2 mm in leads V1-V3, ST elevation ≥ 1 mm in any other two contiguous leads, or new left bundle branch block); proportions of (a) patients eligible for reperfusion and (b) patients with contraindications to thrombolysis; death (including causes); definite myocardial infarction.

Results—948 patients had definite myocardial infarction, 124 probable myocardial infarction, and nine ST elevation but no infarction; 1274 patients had unstable angina and 659 chest pain of other causes. Of patients with definite or probable myocardial infarction, 576 (53.3%) were eligible for reperfusion, 39 had definite contraindications to thrombolysis (risk of bleeding). Hence 49.7% of patients (537/1081) were eligible for thrombolysis and 43.5% (470) received this treatment. Hospital mortality among patients eligible for reperfusion was 11.7% (55/470 cases) among those who received thrombolysis and 17.0% (18/106) among those who did not.

Conclusions—On current criteria about half of patients admitted to coronary care units with definite or probable myocardial infarction are eli-

gible for thrombolytic therapy. Few eligible patients have definite contraindications to thrombolytic therapy. Mortality for all community admissions for myocardial infarction remains high.

Introduction

Because of the mortality benefit conferred by thrombolytic therapy in acute myocardial infarction¹⁻⁶ strategies must be aimed at delivering treatment to the maximum number of eligible patients presenting to hospital from the general community. The proportion of patients eligible for thrombolytic therapy reportedly varies from 15-16%^{7,8} to 79%.⁹ These figures are affected by whether eligibility is based on admission electrocardiographic and time window criteria or a discharge diagnosis of myocardial infarction. Patients entering thrombolytic trials such as the fourth international study of infarct survival,⁹ which reported 79% utilisation of thrombolytic therapy, may represent only a subset of those who present to general hospitals with suspected myocardial infarction. This is within the range (70-80%) suggested by Ketley and Woods^{10,11} as the likely optimum rate of eligibility for thrombolytic therapy and less than the National Health Service recommended rate (90%).¹² By contrast, some studies reporting low rates of thrombolytic use may have excluded potentially eligible patients—for example, elderly patients, diabetic patients, or patients treated by primary angioplasty.^{7,8}

To determine the eligibility of consecutive, unselected patients with suspected acute myocardial infarction presenting to community hospitals for reperfusion with thrombolytic therapy we prospectively evaluated patients presenting to the four coronary care units in Auckland, New Zealand, in 1993.

Coronary Care Unit,
Green Lane Hospital,
Auckland, New Zealand
John K French, cardiologist
Barbara F Williams, research
nurse
Harvey D White, director of
coronary care and
cardiovascular research

Coronary Care Unit,
North Shore Hospital,
Auckland
Hamish H Hart, physician
Susan Wyatt, research nurse

Coronary Care Unit,
Middlemore Hospital,
Auckland
June E Poole, rehabilitation
nurse
Miles G Williams, cardiologist

Coronary Care Unit,
Auckland Hospital,
Auckland
Christine Ingram, charge
nurse
Christopher J Ellis,
cardiologist

Correspondence to:
Dr John French, Cardiology
Department, Green Lane
Hospital, Epsom, Auckland
1003, New Zealand.

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