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Outcome and factors associated with mortality in patients admitted to ICU following cardiac arrest

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Abstract

***Aims*: Review the short and medium term outcome of all cardiac arrest patients admitted to the ICU, determine the factors associated with mortality, and review the rate and outcome of patients receiving mild therapeutic hypothermia.**

***Methods*: Retrospective review the medical records of all patients admitted to ICU following cardiac arrest between January 2000 and December 2007.**

***Results*: The 175 patients admitted to ICU after cardiac arrest constituted 1.4% of all ICU admissions. Ninety three patients (53.1%) survived to ICU discharge, 69 patients (39.4%) survived to hospital discharge, 61 patients (34.9%) survived to one year, and 48 patients (27.4%) had favorable neurological outcome, as determined by the Glasgow-Pittsburg Cerebral Performance Category one or two, at one year. The multivariate regression model showed that duration of resuscitation, admission APACHE II score and coronary angiogram/percutaneous coronary intervention were significant factors associated with hospital mortality.**

***Conclusion*: Our data suggest that the provision of post resuscitation care in ICU produces a significant percentage of high quality survivors. Factors predictive of hospital mortality include duration of resuscitation, APACHE II score and the appropriate use of coronary angiogram/percutaneous coronary intervention.**

Introduction

Cardiac arrest has a poor survival and is a major cause of death worldwide. The average hospital survival rate is only 5-10% for out of hospital cardiac arrest (1,2) and 5-20% for in hospital cardiac arrests. (3-5) Successful resuscitation requires a coordinated sequence of activities that include early activation of emergency services, early cardiopulmonary resuscitation, rapid defibrillation, advanced life support and proper early post-resuscitation care. The last link, post-resuscitation care, should ideally take place in the Intensive Care Unit (ICU). Until recently, few studies had reported survival rates for the sub-group of cardiac arrest patients subsequently admitted to an ICU. In the UK Intensive Care National Audit and Research Centre Case Mix Program Database (6) which covered the period December 1995 to November 2005, post cardiac arrest patients accounted for 5.8% of all admissions to the 174 ICUs in the database. Of these, 42.9% survived to leave the ICU, and 28.6% survived to acute hospital discharge. The few other ICU studies of cardiac arrest have also reported hospital survival rates of between 30 and 60%. (7-10) Asian outcome data in this group of patients who receive post resuscitation care

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in ICU are however, lacking. Given the relatively poor prognosis of this group of patients, identifying predictors of successful outcome after post-arrest care in ICU may assist the process of selection of patients for admission. It also allows more accurate prognostic estimation, an important factor when communicating to family and surrogate decision makers.

The outcome of successfully resuscitated patients is mainly determined by the extent of hypoxic ischemic brain injury suffered at the time of the arrest. Two randomized but unblinded clinical trials, (11,12) and a subsequent meta-analysis (13) show improved survival and better neurological outcome in adults who remain comatose after initial resuscitation from out-of-hospital ventricular fibrillation arrest, and who were cooled within hours after the initial resuscitation. According to recent international guidelines, induction of mild hypothermia to 32-34 degrees for 12-24 hours is recommended for all comatose survivors of out of hospital VF arrests. (14) Although the clinical evidence is weak, it has also been suggested that hypothermia may be also beneficial for non-VF cardiac arrests and in-hospital arrests. (15)

We conducted a retrospective audit in our ICU, aiming to review the outcomes and factors associated with mortality in patients admitted to the ICU after cardiac arrest, and also to evaluate our practice and the outcome of therapeutically induced hypothermia.

Methods

Patients

This retrospective audit was conducted in a 22-bed medical-surgical ICU of a University teaching hospital in Hong Kong. The audit period was from January 2000 to December 2007. The audit population included all patients admitted to the ICU after a cardiac arrest. Patients were included if they had received cardiopulmonary resuscitation (defined as delivery of chest compressions) within 24 hours of admission to the ICU.

Data collection

All data were collected by retrospective review of patient's hospital records, resuscitation record, outpatient follow up records and hospital death registries. The following parameters were collected for each patient: age, sex, in hospital or out-of-hospital cardiac arrest, initial ECG arrest rhythm, co-morbidities, resuscitation duration, cause of the arrest, thrombolysis or percutaneous coronary intervention, and implementation of therapeutic hypothermia (TH). Severity of illness was assessed using the APACHE II score. (16) The following complications were documented: pneumonia, sepsis, arrhythmias, and seizures. The primary outcomes were hospital survival and one year outcome using the Glasgow-Pittsburgh Cerebral Performance Categories (CPC). (17) CPC 1 indicates essentially total recovery (conscious and alert patient, able to work and to lead a normal life). Patients with CPC 2 have moderate disability (conscious, able to work at least part-time, and independent for their daily life activities, with or without neurologic manifestations such as hemiplegic, seizures, ataxia, dysarthria, dysphasia or permanent memory or mental changes). CPC 3 indicates severe disability (conscious, but fully dependent on others for daily support because of severely impaired cognitive function; these patients are discharged to institutions or long-term rehabilitation facilities). Patients with CPC 4 are in vegetative state, and CPC 5 indicates death. Outcome was assessed by reports of neurologic examinations made just before hospital discharge and at out-patient clinics. Good outcome was defined as CPC 1 or 2 at one year. Secondary outcomes of interest included ICU survival, and ICU and hospital length of stay.

For the patients who had been treated with TH, additional data were obtained. These data included time to achieve hypothermic, duration of cooling, temperature achieved, methods of cooling, time to re-warming and any complications including bleeding, cold diuresis, arrhythmias, infection or electrolyte disturbance. A major bleeding event is defined as one requiring blood or blood product transfusion or needing surgical intervention to stop the bleeding.

Statistics

Analyzes were performed using SPSS version 15.0 for Windows. Continuous data were expressed as median and interquartile range, and were compared using the Mann-

Whitney U-test and Kruskal-Wallis H-test. Categorical data were compared with chi-square tests. The candidate predictors of hospital mortality were initially assessed by means of univariate analysis of demographic and clinical variables, and the variables with a p value of <0.10 were included in a multivariate (modified Poisson) regression model to estimate the relative risk of factors associated with hospital mortality. (18) All p-values are based on a two-tailed test of significances. p-values<0.05 were considered significant.

Results

Patient characteristics

During the 8 year audit period, 175 patients were admitted to ICU after cardiac arrests, and this constituted 1.4% of all ICU admissions (**Figure 1**). The median age was 64 years (IQR 51-75) and the median duration of resuscitation prior to return of spontaneous circulation (ROSC) was 10 minutes (IQR 5-20 minutes). The majority of patients (64%) were admitted after in-hospital arrest, and these patients had shorter duration of resuscitation than those admitted after out-of-hospital cardiac arrests [8 min (IQR 5-15) vs 17 min (IQR 10-28), p<0.001]. Patients admitted with in-hospital arrest were also older [68-year-old (IQR 57-76) vs 54-year-old (IQR 45-55), p<0.001], had more asystole/PEA arrests (84.8% vs 50.8%, p<0.001), and more often had non-cardiac causes of arrest (65.2% vs 44.4%, p=0.031), compared to patients suffering out-of-hospital arrests.

The initial rhythm was VT/VF in 48 patients (27.4%). A comparison of patients with VT/VF arrest and those with non-VT/VF arrest is shown in **Table 1** (**Tables 1a** and **lb**). Patients with VT/VF arrests were younger, more often had a cardiac/ischemic cause of arrest, location of arrest was more often out of hospital, and had a lower mean APACHE II score.

Post-resuscitation care

All patients admitted to the ICU received mechanical ventilation. Acute myocardial infarction was the cause of arrest in 55 patients (31%). Nine patients (5.1%) received thrombolysis, and 23 patients (13.1%) underwent percutaneous coronary intervention (PCI). Altogether 33 patients (19%) were treated with TH. The first patient treated with hypothermia was admitted to the ICU in December 2002. From then onwards, an increasing proportion of patients were treated with hypothermia (**Figure 1**).

The implementation of hypothermia was decided by the treating physician. Compared to normothermic patients, patients treated with TH were younger, had more out of hospital arrests, more VT/VF arrests, a lower APACHE II score, and more often had a cardiac/ischemic cause of arrest (**Table 1**).

Implementation of TH

Central temperature was monitored with nasopharyngeal probes. All patients were cooled by non-invasive surface cooling, namely ice packs and forced air cooling blankets. In 2 patients, cooling was induced by infusion of 1.5 liters of cold intravenous saline (4 ^{o}C). During cooling, 32 out of 33 patients were sedated and 31 out of 33 patients paralyzed to prevent shivering and increase the efficiency of surface cooling. All the patients who were sedated and paralyzed during hypothermia were monitored with 4-channel bedside EEG to exclude seizure activity. Re-warming was passive in all patients.

The median time from ROSC to achieving hypothermia was 6.8 (IQR 4.5-9.4) hours and the median time from the start of cooling to achieving hypothermia was 4.5 (IRQ 3.3-6.8) hours. The mean duration of cooling was 24 (IQR 16-24) hours, and in all patients, the temperature achieved was 32-33 degrees. The median time from termination of cooling to achieving normothermia was 6.8 (IQR 5.0 to 10.3) hours.

No major side effects were observed with hypothermia. Oozing from the intravascular catheter insertion sites was reported in 5 patients. All were successfully treated with local compression. There were no major bleeding events documented. Six patients received both TH and percutaneous coronary intervention. All these six patients received aspirin, clopidigrel and abciximab (glycoprotein IIb/IIIa inhibitor), but no serious bleeding was observed in this group. Pneumonia was equally prevalent in patients who were cooled and not cooled, and were mostly attributed to aspiration (**Table 2**). The incidence of arrhythmias was also similar in both groups (**Table 1**).

Outcome

Table 1 shows the outcome of all patients admitted to the ICU after cardiac arrest from 2000 to 2007. Of the whole group of 175 patients, 93 patients (53.1%) survived to ICU discharge, 69 patients (39.4%) survived to hospital discharge, 61 patients (34.9%) survived to one year, and 48 patients (27.4%) had favorable neurological outcome, as determined by CPC, at one year.

The median length of ICU stay was 4 days (IQR 2-6 days) and median length of hospital stay was 11 days (IQR 4-24 days). Survivors had a longer length of ICU [(4 (3-7) vs 3 (2-6) days, p<0.001] and longer hospital stay [20 (13-33) vs 11 (4-24) days, p<0.001] than non-survivors (**Table 1**). Survivors also had a shorter duration of resuscitation, higher frequency of acute myocardial infarction, higher incidence of coronary intervention procedures, and were more often cooled (**Table 1**). Of the patients with favorable neurological outcome at one year, two had persistent myoclonic seizures.

The multivariate regression model showed that duration of resuscitation, APACHE II score and coronary angiogram/percutaneous coronary intervention were significant factors associated with hospital mortality. TH was not a significant factor associated with survival after adjusting for other factors in the model (**Table 2**).

Discussion

This audit showed that patients admitted to a tertiary referral ICU in Hong Kong after cardiac arrest have good short and medium term survival rates. More than 50% survived to leave the ICU, 39% survived to acute hospital discharge and 27% survived to one year with good neurological outcome. The survival rates are comparable with those reported internationally, (6-10) however, this good outcome is in a select group of post-arrest patients. Both Asian and international data have shown that the rate of hospital survival after cardiac arrest is low. (1-5) Because of these low survival rates, coupled with scarce ICU resources, many of these patients may not have been admitted to the ICU for post-arrest care. Previously published data from the same hospital indicate that only 13.3% of all patients suffering from in-hospital cardiac arrest were subsequently admitted to the ICU. (5) This may account for the observation that post-cardiac arrest patients accounted for only 1.4 % of all ICU admissions. Another possible consequence of the restrictive admission policy is selection bias. Because admission to the ICU was determined on the basis of likely medical benefit, the relatively high survival rate and good outcome in patients admitted to the ICU post arrest reported in this audit is possibly the result of selection of those patients most likely to survive.

The multivariate regression model showed that coronary angiogram/percutaneous coronary intervention was associated with reduced hospital mortality. A recent study also showed that emergency percutaneous coronary intervention could improve outcome in patients with ST-elevation myocardial infarction complicated by out- of-hospital cardiac arrests. (19) The study data suggests that cardiopulmonary resuscitation, followed by systematic early mechanical revascularization and circulatory support may represent a successful strategy for patients who develop cardiac arrest after myocardial infarction. These patients may also deserve priority for ICU admission, as their outcome and therefore benefit from ICU care is likely to be better. TH may also retain its beneficial effects even in patients who develop cardiogenic shock. (20) Other factors predictive of hospital mortality include duration of resuscitation and the patient's severity of illness (measured by APACHE II score). Duration of resuscitation could be considered in assigning priority for ICU admission, however, as APACHE II score can only be determined after 24h, its use should be restricted to the assessment of prognosis once the patient is in the ICU.

After adjusting for other factors in the regression model, hypothermia was no longer a significant factor associated with survival. This may be related to the relatively small number of patients who received TH in our audit. During the audit period, only 18.3% of all post-resuscitation patients admitted to the ICU were treated with hypothermia. It was not possible to ascertain with accuracy reasons for excluding patients from TH because of the retrospective nature of our data, but there are several possibilities related to current clinical indications for the institution of TH. These include the necessity for coma, concerns of establishing TH in the presence of an unstable hemodynamic state or progressive metabolic acidosis, severe systemic infection, pre-existing coagulopathy and established multiple organ failure. Other reasons include pre-arrest morbidities with a decision to restrict aggressive care, or the restriction of the use of TH for the tightly selected patient group of out of hospital VF arrests.

An important concern has been the presumed potential for TH to cause serious adverse events, in particular bleeding, infections and arrhythmia. This concern did not materialize in our audit. The incidence of arrhythmias and pneumonia was similar in patients who were or were not cooled, and we did not observe any major bleeding episodes. Although there is experimental evidence that TH can adversely affect hemostasis, (21-25) the risk of significant bleeding during TH appears very low. (26) Very few bleeding complication have been reported in large clinical trials of TH, including those involving patients following cardiac arrest, trauma and neurosurgery. (11,12,27,28) Complications such as cardiovascular instability, coagulopathy, hyperglycemia, increased plasma amylase, cold diuresis, hypophosphatemia and hypomagnesaemia are relatively easy to treat in the ICU and can be reduced by careful monitoring and meticulous intervention. (27)

In terms of resource utilization, additional costs related to hypothermia are few. When introducing TH in our practice, we used a simple surface cooling method and hastened cooling with cold intravenous fluids. (29,30) These methods were effective, noninvasive and are already commonly used to control excessive fever in our ICU. The requirement for sedation and paralysis may be expected to prolong ICU stay, however, our data showed that the adoption of TH did not prolong either ICU stay or hospital stay. One study recently showed that TH can shorten ICU stay in survivors after out-of-hospital cardiac arrest. (31) Overall, it appears that the costs of TH are modest and the improved outcome demonstrated in randomized controlled trials using TH, suggests a beneficial cost-effectiveness ratio.

The interpretation of data from this audit is limited by its retrospective nature, and the relatively low number of patients ultimately receiving TH. This limited the robustness of associations related to the effects of hypothermia on the major outcomes. Strengths of our audit include the duration and completeness of follow up after cardiac arrest, and the ability to determine functional outcome.

Conclusion

Our data suggest that the provision of post resuscitation care in ICU produces a significant percentage of high quality survivors. Factors predictive of hospital mortality include duration of resuscitation, APACHE II score and the appropriate use of coronary angiogram/percutaneous coronary intervention. These patients may deserve priority for ICU admission. TH for post-arrest patients was successfully implemented in our ICU, although the enrollment rate after its introduction as a routine intervention was only about 40% and could possibly be improved. Although multivariate analysis did not demonstrate a strong association between TH and mortality, the relatively low cost of the intervention and high quality data from randomized controlled trials showing benefit, it remains a desirable therapeutic intervention.

Table 1. Data of all cardiac arrests admitted to ICU from 2000-2008

Table 1a

	All patients n=175	VT/VF n=48	Non VT/VF n=127	*p*
Age (median, IQR)	64 (51-75)	56 (45-66)	67 (54-77)	0.002
Sex (male)	101 (57.7%)	34 (70.8%)	67 (52.8%)	0.031
Out of hospital arrests	63 (36%)	31 (64.6%)	32 (25.2%)	<0.001
Resuscitation duration (in min) (median, IQR)	10 (5-20)	12 (7-20)	10 (5-20)	0.295
APACHE II	33 (28-40)	28 (27-32)	35 (30-42)	<0.001
AMI/arrhythmias as cause of arrest	74 (42.3%)	37 (77.1%)	37 (29.1)	<0.001
Thrombolysis	9 (5.1%)	4 (8.3%)	5 (3.9%)	0.260
CC/PCI	23 (13.1%)	13 (27.1%)	10 (7.9%)	0.002
Myoclonus post arrest	30 (17.1)	7 (14.6%)	23 (17.1%)	0.659
Therapeutic hypothermia	33 (18.9%)	21 (43.8%)	12 (9.4%)	<0.001
ICU survival	93 (53.1%)	32 (66.7%)	61 (48.0%)	0.029
Hospital survival	69 (39.4%)	28 (58.3%)	41 (32.3%)	0.003
One year survival	61 (34.9%)	25 (52.1%)	36 (28.3%)	0.004
Good neuro outcome at one year	48 (27.4%)	20 (41.7%)	28 (22.0%)	0.009
ICU length of stay (median days, IQR)	4 (2-6)	3.5 (2-6)	4 (2-7)	0.973
Hospital length of stay (median, IQR)	11 (4-24)	13.5 (6-23)	10 (4-25)	0.565
Tracheotomy	37 (21%)	7 (14.6%)	30 (23.6%)	0.219

Table 1b

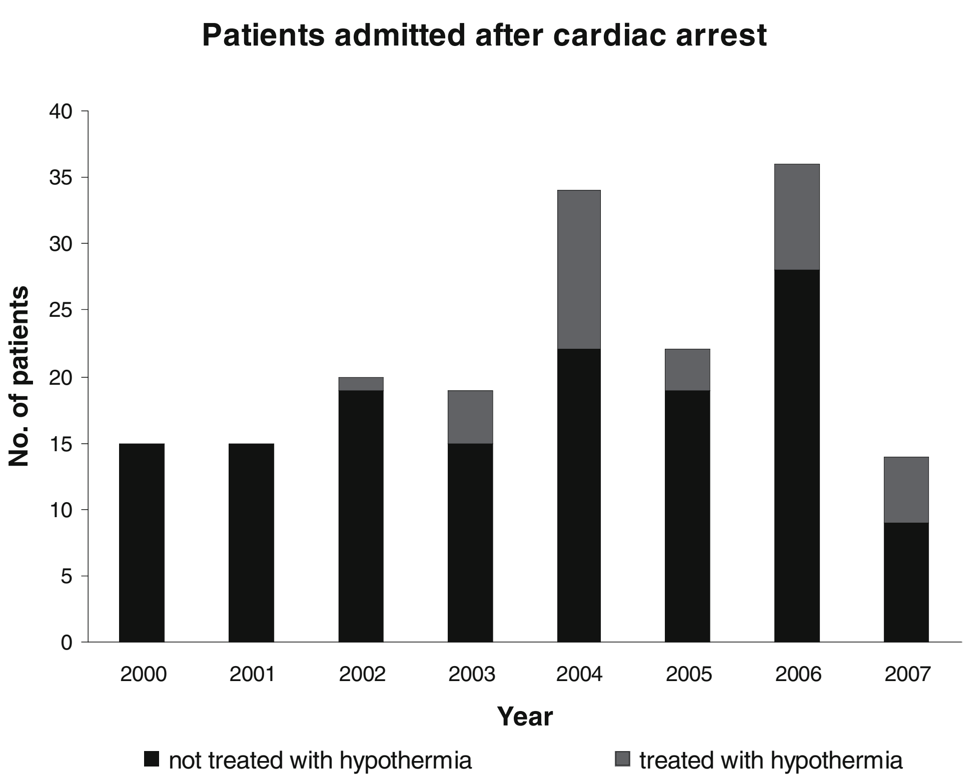
	In hospital arrest n=112	Out of hospital arrest n=63	*p*
Age (median, IQR)	68 (57-76)	54 (45-66)	<0.001
Sex (male)	60 (53.6%)	41 (65.1%)	0.154
Initial rhythm VT/VF	17 (15.2%)	31 (49.2%)	<0.001
Resuscitation duration (in min) (median, IQR)	8 (5-15)	17 (10-28)	<0.001
APACHE II	35 (30-43)	31 (27-34)	<0.001
AMI/arrhythmias as cause of arrest	39 (34.8%)	35 (55.6%)	0.031
Thrombolysis	7 (6.3%)	2 (3.2%)	0.492
CC/PCI	12 (10.7%)	11 (17.5%)	0.246
Therapeutic hypothermia	12 (10.7%)	21 (33.3%)	<0.001
Myoclonus post arrest	18 (16.1%)	12 (19.0%)	0.678
ICU survival	61 (54.5%)	32 (50.8%)	0.652
Hospital survival	41 (36.6%)	28 (44.4%)	0.309
One year survival	36 (32.1%)	25 (39.7%)	0.326
Good neuro outcome at one year	31 (27.7%)	17 (27.0)	0.917
ICU length of stay (median days, IQR)	3 (2-7)	4 (2-6)	0.583
Hospital length of stay (median, IQR)	12.5 (5-28)	8 (3-19)	0.052
Tracheotomy	26 (23.2%)	11 (17.5%)	0.371

Table 2. Factors associated with hospital mortality

Factors associated with hospital mortality	Relative risk (95%CI)	*p*
Therapeutic hypothermia given (vs no hypothermia)	0.80 (0.54 to 1.19)	0.27
Male (vs female)	0.86 (0.71 to 1.05)	0.15
AMI/arrhythmia as cause of arrest (vs non AMI/arrhythmia)	0.86 (0.66 to 1.11)	0.24
Initial rhythm VT/VF (vs non VT/VF)	1.03 (0.75 to 1.42)	0.86
Resuscitation duration ≥10 min (vs <10 min)	1.28 (1.04 to 1.59)	0.02
APACHE score (per unit)	1.03 (1.01 to 1.04)	<0.001
Coronary angiogram/PCI (vs none)	0.08 (0.01 to 0.58)	0.01

Legend: AMI=acute myocardial infarction; PCI= percutaneous coronary intervention

Figure 1. Number of patients receiving TH over the audit period



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