Early Invasive Revascularisation for Patients Critically Ill After Acute Myocardial Infarction: Impact on Outcome and ICU Resource Utilisation

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ABSTRACT

Objective: *To assess the value of early invasive revascularisation for the initial management of critically ill patients after acute myocardial infarction in the daily practice of a University-affiliated referral hospital and to gauge the impact of such a strategy on the intensive care unit.*

Patients and Methods: *A prospective observational study on all patients admitted to the Royal North Shore hospital who had acute pulmonary oedema and/or shock prior to acute angiography for acute myocardial infarction from January 1st, 1998 to December 31st, 2001.*

Results: *During the study period 846 patients with acute myocardial infarction had coronary artery angiography, 139 had acute pulmonary oedema and/or shock prior to angiography. The average age was 70 years, 65% of whom were male. Approximately 70% of these patients were admitted to the intensive care unit and coronary artery bypass surgery was performed on 38%. Of those patients admitted to the intensive care unit, 95% required mechanical ventilation, 81% required inotropic support and 50% required intra-aortic balloon counterpulsation. In-hospital mortality was 32%, 6 weeks mortality was 38% and 6 month mortality was 42%.*

Conclusions: *Our results confirm the benefit of early invasive revascularisation for critically ill patients after acute myocardial infarction although a substantial amount of intensive care unit resources and cardiothoracic surgical expertise were required.* (**Critical Care and Resuscitation 2003; 5: 258-265**)

Key words: Acute myocardial infarction, cardiogenic shock, angiography, revascularisation

The management of cardiogenic shock following acute myocardial infarction (AMI) remains one of the challenges facing intensive care physicians today. Recently there has been a change in treatment of these patients as an understanding of the pathophysiology has prompted the focus to shift to coronary artery reperfusion. Initially this was attempted with thrombolytic agents, although the widespread use of these agents has not been associated with a substantial improvement in mortality for critically ill patients.[1]

Recent studies show a survival advantage when invasive procedures are utilised to open or bypass blocked coronary vessels.[2] By 1999 the American Heart Association guidelines were advocating early invasive revascularisation for specific groups of patients,[3] and in the same year the results of the SHOCK trial (SHould we emergently revascularise Occluded Coronaries for cardiogenic shocK) showed a trend to benefit for patients with cardiogenic shock treated with an invasive strategy.[4] In the GRACE multinational registry study, coronary artery stenting was the most powerful predictor of hospital survival (odds ratio 3.99, 95% CI 2.41 to 6.62).[5] In 2003, a meta-analysis of 23 randomised controlled trials found

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an improvement in mortality, recurrent ischaemia and major complications when this strategy was used in all patients with AMI.[6] However, an invasive strategy has not always been associated with improved survival in patients with cardiogenic shock,[7,8] prompting Boersma *et al*, to state "whether these results can be applied and translated into daily practice remains unclear".[9]

Improvement in mortality is unlikely to come from the revascularisation procedure alone. Patients with shock and acute pulmonary oedema following AMI require haemodynamic and respiratory support that can only be provided in an intensive care unit (ICU). The majority of patients in the SHOCK trial were supported with inotropic therapy, mechanical ventilation and intra-aortic balloon counterpulsation (IABP). This is labour intensive and can place a large and unpredictable load on hospital resources. On the other hand, some patients may dramatically improve after angioplasty and may not require intensive care management. In this instance an interventional strategy may reduce the ICU workload. To determine the net effect of the use of an early invasive revascularisation strategy, all patients who are likely to need ICU care, either because of shock or acute pulmonary oedema would have to be assessed. As yet no study has addressed these issues.

A prospective observational study was performed to understand the effect that an early invasive revascularisation strategy has had on an ICU resource utilisation in terms of volume, length of stay and outcome and to assess the benefit, or otherwise, of this strategy.

PATIENTS and METHODS

The Royal North Shore hospital is a 544 bed University-affiliated referral hospital in Sydney, Australia. It provides services for a local population of approximately 300,000 and serves as the specialist referral centre for a population of 1.3 million people. Patients may be referred from up to 80 km away for interventional cardiac procedures. At this institution an invasive protocol has been operational since 1997,[10] providing a 24 hour service, mandating early coronary angiography and angioplasty plus or minus stenting to achieve TIMI 3 flow in patients with AMI and cardiogenic shock as soon as possible after hospital arrival. Cardiac surgery is performed urgently if percutaneous coronary artery angioplasty is not possible technically and if coronary artery reperfusion is otherwise indicated.

Detailed data were collected on all patients who had acute coronary angiography for suspected myocardial infarction presenting either, a) acutely to the principal hospital after an AMI or cardiac arrest, b) for rescue procedure after failed thrombolysis at another hospital or c) as a referral from another hospital with ongoing chest pain, cardiac arrest or shock. All patients were followed-up by telephone interview after discharge.

To assess the effects on ICU utilisation, we reviewed not only patients with cardiogenic shock after AMI but all who might normally require ICU admission including those unstable patients with acute pulmonary oedema. To identify all patients with AMI who presented in shock or pulmonary oedema, we reviewed the database for patients who were initially classified as Killip class III or IV,[11] prior to angiography, as well as all patients who were admitted to the ICU. The medical records were reviewed to ensure acute pulmonary oedema (defined as chest X-ray evidence or basal crepitations associated with respiratory distress, tachypnoea, hypoxia or the need for mechanical ventilation) or shock (defined as systolic BP < 90 mmHg not due to drugs, arrhythmia or hypovolaemia or the need for inotropic or vasopressor support) were documented prior to angiography. Figure 1 illustrates how the final group was compiled.

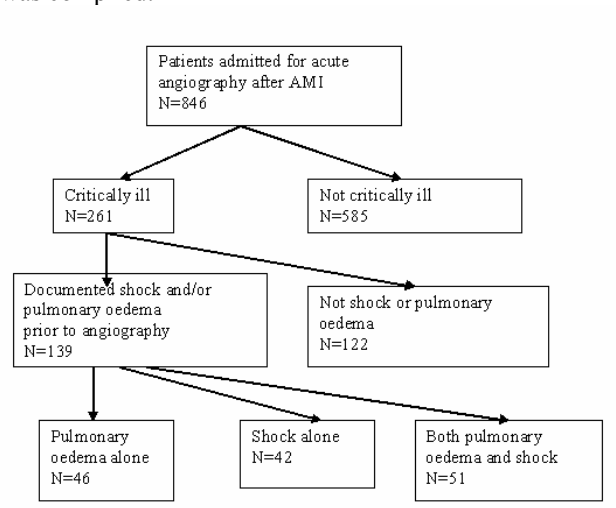

Figure 1. Study profile

We recorded the patient's clinical state at presentation (e.g. shock and/or acute pulmonary oedema), co-morbidities (e.g. previous myocardial infarction, hypertension, diabetes, previous coronary artery bypass grafting, previous stroke), reason for referral (e.g. primary angioplasty, rescue angioplasty, non-ST elevation myocardial infarction or post-cardiac arrest) and peak creatine phosphokinase isoenzyme MB and troponin T levels. We calculated an APACHE II score based on the worst figures available prior to angiography. Missing data were recorded as zero. All

patients were followed-up to determine the interventions performed (e.g. angiography, angioplasty or angioplasty and stent implantation) and the use of coronary artery bypass surgery.

We collected data on the number of patients admitted to ICU, length of stay, ICU mortality and interventions performed (e.g. mechanical ventilation, inotropic support and intra-aortic balloon counterpulsation). Outcome data were collected including in-hospital mortality, hospital length of stay and follow-up at 6 weeks and 6 months.

Statistical analysis

Data were expressed as mean ± SD and median if appropriate. Comparisons between means were performed using the unpaired t-test or ANOVA for continuous data and chi squared analysis of contingency tables for categorical data. A logistic regression analysis was performed to assess the factors associated with mortality. Approval from the Northern Sydney Area Health Service Ethics Committee was obtained to record data and patients gave informed consent for follow-up by telephone.

RESULTS

From January 1st, 1998 until December 31st, 2001, a total of 846 patients underwent angiography for suspected acute myocardial infarction. Of this group, 139 were critically ill with shock and/or acute pulmonary oedema prior to angiography.

Demographic data for the critically ill group (table 1): The patients were mostly middle-aged males who had numerous co-morbidities and were usually previously independent before suffering extensive myocardial damage. Because of the complexity of their illness and need for rapid intervention, APACHE II data were sometimes incomplete and the scores may have underestimated the severity of illness.

Interventions and overall mortality (table 2): On average, 8 hours elapsed from the onset of chest pain to the achievement of TIMI 3 flow. Most patients required ICU admission and approximately 40% required acute coronary artery bypass surgery largely because of diffuse or severe left main stem coronary artery disease. Mortality figures for the whole group were: in hospital (32%), 6 weeks (38%) and 6 months (42%), indicating severity of illness, co-morbidities and age of the cohort. Figure 2 illustrates how the patients were directed through the system and the outcome of the groups.

Survivors versus non-survivors (table 3): Non-survivors were older, more likely to have comorbidities, had higher Apache II scores and required admission to ICU more often with extensive haemo-

Table 1. Demographic data

	Overall (n=139)
Age (years ± SD)	70.2 +/- 11.8
Sex	
Male	91 (65.5%)
Female	48 (34.5%)
Reason for admission	
Primary angioplasty	66 (47.5%)
Cardiac arrest	20 (14.4%)
Failed lysis	53 (38.1%)
Co-morbidity	
Previous AMI	31 (22.3%)
Diabetes	24 (17.3%)
Hypertension	61 (43.9%)
Stroke	15 (10.8%)
Previous CABG	20 (14.4%)
Normal abode	
Home	132 (95%)
Institution	5 (3.6%)
Unknown	2 (1.4%)
Functional state	
Active	115 (82.7%)
Impaired	19 (13.7%)
Unknown	5 3.6%)
APACHE II	
Before angiography	16.2 (± 8.2)
Peak cardiac enzymes	
CKMB (ug/L)	406 ± 841 (n=73)
Troponin T (ug/L)	8.4 ± 13.9 (n=96)

AMI = acute myocardial infarction, CABG = coronary artery bypass graft, CKMB = creatinine phosphokinase (MB isoenzyme)

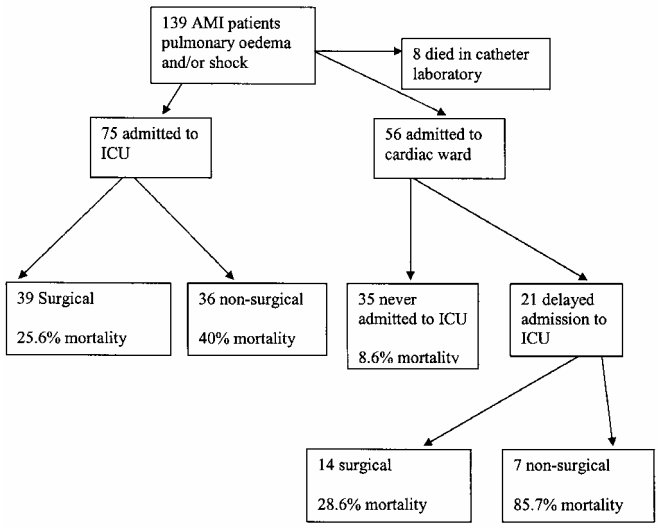

Figure 2. Study outcome

dynamic support. Multiple logistic regression analysis showed that the conditions associated with non-survival were: increased age ($p < 0.001$), higher APACHE score ($p = 0.015$) and diabetes ($p = 0.044$).

Table 2. Procedures and outcomes

	Overall (n=139)
Procedures	
Angiography only	63
Angioplasty	13
Angioplasty and stenting	63
Time from chest pain to notification	
Mean ± SD (minutes)	337 ± 327
Median (minutes)	250
Time from notification to TIMI 3 flow	
Mean ± SD (minutes)	145 ± 117
Median (minutes)	111
Surgery	
Total	53
CABG	51
MVR	2
Intensive care unit	
Admission	97 (69.8%)
LOS in days (mean ± SD)	7.6 ± 8.8
ICU mortality	29 (29.9%)
ICU interventions	
Mechanical ventilation	92 (94.8%)
Mean duration ± SD (days)	5.6 ± 8.0
Inotropic support	79 (81.4%)
Mean duration ± SD (days)	5.1 ± 5.1
Median duration (days)	4
IABP	49 (50.5%)
Mean duration ± SD (days)	3.9 ± 3.1
Median duration (days)	3
Hospital outcomes	
Hospital mortality	45 (32.4%)
Hospital LOS in days (mean ± SD)	11.2 ± 10.8
6 weeks (134 followed up)	
Mortality	51 (38%)
6 months (126 followed up)	
Mortality	53 (42%)

LOS = length of stay, CABG = coronary artery bypass graft, MVR = mitral valve replacement, ICU = intensive care unit, IABP = intra-aortic balloon pump

Results according to clinical state (Table 4): Patients with both pulmonary oedema and shock had higher Apache II scores, required ICU admission more often, and had higher mortality in hospital, at 6 weeks and 6 months (Table 3).

Effect of transfer from another hospital within the region (table 5): Patients presenting initially to another hospital compared with patients presenting directly to our hospital had a non-significant increased incidence of previous AMI (14% versus 28.9%, $p = 0.08$), previous coronary artery surgery (10.9% versus 17.8%, $p = 0.32$), higher troponin T levels (6.1 ug/L versus 12.2 ug/L, $p = 0.14$) and were more likely to have both pulmonary oedema and shock ($p = 0.015$). The average time from chest pain to TIMI 3 flow in the transferred patients was twice that of the primary presenting patients (658 minutes versus 332 minutes). Despite this these patients had similar mortality rates of: in-hospital (29% versus 33%, $p = 0.68$), 6 weeks (36% versus 35%, $p = 0.9$) and 6 months (41% versus 37%, $p = 0.7$). Transferred patients were more likely to have had failed thrombolysis (51% versus 4%, $p < 0.05$) and less likely to be presenting for primary thrombolysis (16% versus 77.5%, $p < 0.05$).

Time to achieve TIMI 3 flow (table 4): We compared the two groups of patients in whom TIMI 3 flow was achieved in more or less than 6 hours. As the delay was often due to transfer time or initial use of thrombolysis in the referring hospital, the 'reasons for admission' were usually different. "Greater than 6 hour" patients had more co-morbidities and higher troponin T levels on admission. Nevertheless, despite this, the mortality rates at each interval were similar.

DISCUSSION

Until recently, the incidence of severe cardiac dysfunction after AMI and its associated mortality have not changed. In particular, the incidence of cardiogenic shock after AMI has been stable over time at about 7 - 10%.[2] The traditional teaching has been that the mortality of cardiogenic shock in the setting of AMI is between 60 and 80%.[12] Killip and Kimball attempted to understand the clinical features of myocardial dysfunction that were predictive of outcome after AMI,[11] and the clinical classification they described provided a useful tool for risk stratification in these patients. They described Class III patients as patients with "rales over greater than 50% of the lung fields (frequently pulmonary edema)" and Class IV as patients in "shock", observing a mortality of 44% and 80 - 100% in Class III and IV patients, respectively. Recent studies have confirmed the utility of this classification in predicting outcome with one study reporting 30 day mortality rates of 35% and 67% in class III and IV patients, respectively.[12] Our results confirm that these easily recognised clinical features are still associated with increased mortality.

Forrester *et al*, classified patients according to haemodynamic variables and found increasing mortality with increasing haemodynamic disturbance.[13] They used data from the pulmonary artery floatation catheter to grade patients in one of

four groups; reporting a 2.2% mortality in patients with a pulmon-ary artery occlusion pressure (PAoP) < 18 mmHg and cardiac index (CI) > 2.2 L/m^2/min (Group I), a 10.1% mortality in patients with a PAoP > 18 mmHg and CI > 2.2 L/m^2/min (Group II), a 22.4% mortality in patients with a PAoP < 18 mmHg and CI < 2.2 L/m^2/min (Group III) and a 55.5% mortality in patients with a PAoP > 18 mmHg and CI < 2.2 L/m^2/min (Group VI).

Since these studies there have been major improvements in the management of AMI patients although the widespread use of thrombolysis has been associated with only a small improvement in the mortality of cardiogenic shock.[1]

The use of an invasive revascularisation strategy for the management of all AMI patients has been supported by a meta-analysis.[4] Such a strategy has been recommended for critically ill patients with AMI,[14,15] although there is some doubt as to the applicability of these results to normal clinical practice.[9]

Table 3. Data for survivors compared with non-survivors

		Survivors (n= 94)	Non-survivors (n= 45)	p
Age in years (mean ± SD)		67.8 ± 12.6	75.1 ± 8.3	< 0.05
Co-morbidity	Previous AMI	16 (17%)	15 (33.3%)	< 0.05
	Diabetes	14 (14.9%)	10 (22.2%)	0.284
	Previous CABG	11 (11.7%)	9 (20%)	0.192
APACHE II	Prior to angiography	14.8 ± 7.7	18.9 ± 8.9	< 0.05
Peak cardiac enzymes	CKMB (ug/L)	423 ± 968 (n = 54)	358 ± 254 (n = 19)	0.327
	Troponin T (ug/L)	8.8 ± 14.4 (n = 62)	7.5 ± 13.1 (n = 33)	0.326
Time from chest pain to TIMI 3 flow (minutes) (mean ± SD)		479 ± 294	486 ± 388	0.718
Intensive care unit	Admission	63 (67%)	34 (75.6%)	0.305
	LOS in days (mean ± SD)	6.8 ± 6.1	9.2 ± 12.3	0.092
	Inotropic support	48 (76.2%)	32 (94.1%)	< 0.05
	IABP	29 (30.9%)	21 (61.8%)	0.069

CKMB = creatinine phosphokinase (MB isoenzyme), CABG = coronary artery bypass graft, AMI = acute myocardial infarction, IABP = intra-aortic balloon pump, LOS = length of stay

Table 4. Data for patients with pulmonary oedema, shock and both pulmonary oedema and shock

		Pulmonary oedema (n=46)	Shock (n=42)	Shock and pulmonary oedema (n=51)	ANOVA or Chi square of trend
APACHE II	Prior to angiography	12.7 (± 6.5)	17.0 (± 8.7)	18.6 (±8.4)*	
ICU	admission	30 (65.2%)	25 (59.5%)	42 (82.4%)	p < 0.05
	LOS average (days) (mean ± SD)	4.1 ± 3.5	9.4 ± 12.8	9.2 ± 8.2 **	
	ICU mortality	7 (23.3%)	8 (32%)	15 (35.7%)	p = 0.21
Hospital outcomes	Hospital mortality	11 (23.9%)	10 (23.8%)	24 (47.1%)	p < 0.05
6 weeks	Mortality	11/43(25.6%)	12/40(30%)	28/51(55.9%)	p < 0.05
6 months	Mortality	12/41(29.3%)	12/36(33.3%)	29/49(59.2%)	p < 0.05

* pulmonary oedema alone compared with the other two groups was associated with a significantly lower APACHE II score (p< 0.05)
**only " Shock and pulmonary oedema" compared with "Pulmonary oedema" alone was associated with a significantly longer intensive care unit length of stay (p< 0.05). LOS = length of stay, ICU = intensive care unit.

Table 5. Patients with either more or less than 6 hours from onset of chest pain to TIMI 3 flow

		Less than 6 hr (n= 59)	Greater than 6 hr (n= 66)	p
Presenting hospital	RNSH	42 (71.2%)	17 (25.8%)	< 0.05
	Other	17 28.8%)	49 (74.2%)	< 0.05
APACHE II (average ± SD)	Prior to angiography	16.6 ± 8.5	15.7 ± 8.3	0.275
Clinical state at presentation	Pulmonary oedema	20 (33.9%)	21 (31.8%)	0.805
	Shock	18 (30.5%)	19 (28.8%)	0.833
	Pulmonary oedema and shock	21 (35.6%)	26 (39.4%)	0.664
Peak cardiac enzymes	CKMB (ug/L)	237 ± 278 (n = 28)	540 ± 1097 (n = 40)	0.051
	Troponin T (ug/L)	6.9 ± 13.0 (n = 40)	10 ± 13.5 (n = 44)	0.143
ICU	Admission	37 (62.7%)	48 (72.7%)	
ICU Interventions	Mechanical ventilation	37 (100%)	43 (89.6%)	0.776
	Inotropic support	29 (78.4%)	40 (83.3%)	0.198
	IABP	20 (33.9%)	26 (54.2%)	0.525
Hospital outcomes	Hospital mortality	20 (33.9%)	22 (33.3%)	0.946
	Hospital LOS (days) (average ± SD)	10.4 ± 10.6	10.3 ± 9.8	0.999
6 weeks	Mortality	22/58 (37.9%)	25/64 (39%)	0.898
6 months	Mortality	23/55 (41.8%)	26/60 (43.3%)	0.869

The SHOCK trial investigators found an improvement in mortality with an invasive strategy that did not reach statistical significance at 6 months and 1 year (63.1% versus 50.3% and 66.4% versus 53.3%, respectively).[4] In 2001, another review from the SHOCK trial registry described 150 patients with AMI who were managed initially with thrombolysis ± intra-aortic balloon pump and 152 patients in whom revascularisation was mandated within 6 hours. This review reported a 13.2% absolute reduction in 1 year mortality with early revascularisation (relative risk for death of 0.72 with 95% CI of 0.54 to 0.95).[16] In this registry of patients, 83% of the survivors at one year were in NYHA group I or II.[17] Several other small studies have confirmed these results and suggest that sicker patients benefit most from the invasive strategy.[18,19]

The effect that implementing such a strategy on ICU resources has not been evaluated, in spite of the fact that ICU level care is integral to the management of these patients. If an invasive strategy is the gold standard for management of critically ill patients after AMI, it is important to understand the effects on the ICU workload and investigate whether a reasonable outcome is achieved in a standard practice of a metropolitan hospital with a large referral base. The use of large prospective databases to review results of new therapies has been advocated as an important step in the widespread implementation of these new therapies.[20] Our study was devised to assess these issues and review applicability of recent evidence to our region.

We chose to arrange our critically ill patients into 3 groups, akin to the Forrester *et al*, groups II, III and IV, to understand more fully the associations with mortality and to guide ICU admission. We chose groups that could be clearly identified, prior to angiography, as potentially needing ICU support. We found that the presence of shock and pulmonary oedema indicated more severe dysfunction and significantly increased mortality at all time periods after ICU discharge.

The mortality rates in our study for the patients with shock were 36.5% in-hospital, 44% at 6 weeks and 48% at 6 months, which compare favourably with these contemporary reports, confirming that good results can be achieved in a "real world" setting and compares favourably with that in other studies. In the SHOCK trial, 6 month mortality was 50.3% in the invasive strategy group,[4] and in a more recent report the in-hospital mortality was 46.4%.[16]

However, in the Edep and Brown study,[21] the in-hospital mortality was 56%, and the 30 day mortality in the Berger *et al*,[22] and the Urban *et al*, study of, 66.2% and 69% respectively,[7] reveal that higher mortality rates have been reported.

The inclusion of patients with acute pulmonary oedema in our study extends the work by Wu *et al*,[23] who noted that while many people have reported the outcomes for patients with cardiogenic shock complicating AMI, patients with congestive heart failure also have increased mortality. They found an incidence of heart failure of 19.1% and an associated in-hospital mortality of 21.4%. The non-randomised SHOCK trial registry patients reported an in-hospital mortality rate of 60.8% for patients with left ventricular failure.[4] Our study demonstrates that patients with acute pulmonary oedema complicating AMI, have a significant mortality and will also require ICU management in the setting of an early invasive revascularisation strategy.

What has not been examined by previous studies has been the effect of implementing an early invasive revascularisation strategy on the ICU facilities. Previous reports have concentrated on the angiographic procedure and have neglected to review the ICU contribution in the management of these critically ill patients. Patients in the SHOCK trial required high levels of intervention to achieve their results, with 99% requiring inotropic support, 86% IABP support and 88% requiring mechanical ventilation. In this study 37.5% required urgent coronary artery bypass grafting.[4] The results of our study were similar, with approximately 70% of the patients with signs of myocardial dysfunction requiring ICU admission (a total of 737 ICU days), 81% of whom required inotropic support, 50.5% required IABP support (191 days on aortic counterpulsation) and 95% required mechanical ventilation (515 ventilator days). In our study, 36.7% of the patients required urgent coronary artery bypass grafting.

Approximately 25% of patients improve after TIMI 3 flow of the culprit vessel is achieved and some of these patients may be able to be managed in a coronary care unit. In our study, a high mortality occurred if these patients are later required to be admitted to the ICU (unrelated to coronary artery bypass grafting Figure 2).

Brodie *et al*, recorded no difference in 30 day mortality and 6 month ejection fraction in a group of unselected patients who were transferred from other hospitals after AMI and who had delayed treatment times.[24] However, when they repeated the study they found that the time delay was critical to the outcome of sicker patients.[25] In-hospital mortality was 31% and 62% in patients with shock in whom time to reperfusion was < 3 hours and ≥ 6 hours, respectively. On the other hand, our data are consistent with the recommendation that invasive strategies should be performed "in high volume centres",[3] and that transfer to a large referral centre is associated with better outcomes.[26] One recent study examined the impact of transferring patients to specialist centers and found that transfer for angiography was superior to on-site fibrinolysis provided the transfer took less than 2 hours,[27] another study found that coronary stenting was superior to fibrinolysis independent of the time-to-treatment intervals with the benefit increasing with increasing time from symptom onset.[28]

In our study neither transfer nor "times from pain to TIMI 3 flow" of less or greater than 6 hours correlated with survival. The apparent lack of a time threshold indicates that in our setting there is sufficient time to plan the transfer, prepare the patient and communicate with the ICU team.

Nevertheless, our study was a non-randomised, non-controlled observational study and may not reliably compare with other studies. There also remains the possibility of selection bias. For example, the sickest patients may have died before transfer, be selected for transfer or excluded from transfer and so not be included in our analysis. However, consistent with recent studies, we believe that an acute invasive strategy for the management of critically ill patients after AMI is a worthwhile undertaking for a metropolitan, regional hospital. We found that an early invasive revascularisation strategy for critically ill patients with AMI is associated with good outcomes, although this requires the input of specialist ICU resources. Those patients who are admitted to ICU require high levels of support including inotropic agents, invasive monitor-ing, mechanical ventilation and intra-aortic balloon counterpulsation. From our data, there also appears to be time for consultation with the ICU team and safe transfer from peripheral hospitals without jeopardising patient care.

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