# Predictors of inhospital outcome after acute inferior wall myocardial infarction

Jim M H, Chan A O, Tse H F, Lau C P

### ABSTRACT

Introduction: Compared with anterior wall myocardial infarction, inferior wall myocardial infarction is generally regarded as being low risk. The aim of this study was to elucidate the clinical factors affecting its inhospital outcome.

<u>Methods</u>: From January 1997 to March 2006, 546 consecutive patients who suffered from their first inferior wall myocardial infarction were recruited for the study. The demographic, clinical, electrocardiographical and angiographical characteristics, treatment and medications, complications and inhospital deaths were subjected to univariate analysis. The factors that had a p-value of less than 0.1 were included for multivariate logistic regression analysis. A pvalue of less than 0.05 was considered significant. The impact of thrombolysis on clinical outcome in various high-risk patient subsets was also examined.

Cardiac Medical Unit, Grantham Hospital, 125 Wong Chuk Hang Road, Hong Kong

Jim MH, MD Associate Consultant

Gastroenterology and Hepatology Centre, Hong Kong Sanitorium, 2 Village Road, Happy Valley, Hong Kong

Chan AO, MD, PhD Director

University Department of Medicine, University of Hong Kong Pok Fu Lam Road, Hong Kong

Tse HF, MD, PhD Professor

Lau CP, MD Honorary Clinical Professor

**Correspondence to:** Dr Man-Hong Jim Tel: (852) 2518 2619 Fax: (852) 2518 8558 Email: jimmanh2002 @yahoo.com Results: An advanced age of more than 74 years, female gender, lateral wall extension, complete atrioventricular block, bundle branch block, and cardiac free-wall rupture were found to be independent predictors of inhospital mortality, whereas the use of thrombolysis was associated with a favourable outcome. On the other hand, right ventricular infarction and precordial STsegment depression are not predictive of poor outcome. In addition, thrombolysis reduced inhospital mortality in patients with an age above 64 years, male gender, lateral wall extension, haemodynamically-significant right ventricular infarction and complete atrioventricular block.

<u>Conclusion</u>: In inferior wall myocardial infarction, independent predictors of poor inhospital outcome are advanced age, female gender, lateral wall extension, complete atrioventricular block, bundle branch block and cardiac free-wall rupture. The use of thrombolysis is generally beneficial, especially in those of the high-risk subsets. Keywords: acute myocardial infarction, inferior wall myocardial infarction, myocardial infarction, right ventricular infarction, thrombolysis Singapore Med | 2009;50(10):956-961

## INTRODUCTION

Inferior wall myocardial infarction (MI) is generally regarded as being low risk, compared with anterior wall MI. The reported inhospital mortality rate ranges from 11% in the pre-thrombolytic  $era^{(1)}$  to 3.5%–9% in the thrombolytic era,<sup>(2-4)</sup> which is about half that of anterior wall MI. Some authorities have questioned the role of thrombolysis in the treatment of patients with inferior wall MI due to the small size of the infarct.<sup>(5,6)</sup> Various demographical, clinical and electrocardiographical (ECG) characteristics and therapeutic interventions have been established as independent predictors of clinical outcomes in acute MI. Whether these factors are equally applicable to inferior wall MI is uncertain. Furthermore, right ventricular (RV) infarction, precordial ST-segment depression and complete atrioventricular (AV) block have also been identified as the three high-risk subsets in inferior wall MI.<sup>(7)</sup> The purpose of this study was to elucidate the factors that determine the inhospital mortality of patients with inferior wall MI using multivariate logistic regression analysis, and to determine the effect of thrombolysis in various high-risk subsets.

#### **METHODS**

From January 1997 to March 2006, 546 consecutive patients who were admitted to our Coronary Care Unit with a discharge diagnosis of inferior wall MI were retrospectively enrolled into the study. Patients with a prior history of MI were excluded. In general, patients who presented for < 12 hours were subjected to thrombolysis in the absence of any contraindication, whereas patients who had delayed presentations (> 12 hours) or contraindications, were managed conservatively. From 2001 onwards, thrombolysis-eligible patients who were admitted within office hours (i.e. 0800–1700 hours) were treated with primary angioplasty after an assessment by the interventional cardiologists. Left ventricular ejection fraction (LVEF) was routinely measured by means of transthoracic echocardiography at Day 1 or 2. The patients'

Table	Ι.	Clinical	characteristics	and	outcome	of	546
conse	cut	ive patie	ents suffering fro	m in	ferior wall	MI.	

Clinical characteristics	No. (%) of patients (n = 546)
Age* (years)	65.3 ± 13.0
Female	144 (26.4)
Ever-smoker	296 (54.2)
Diabetes mellitus	167 (30.6)
Hypertension	249 (45.6)
Hyperlipidaemia	249 (45.6)
Symptom onset < 6 hours	390 (71.4)
Symptom onset > 24 hours	57 (10.4)
Lateral wall extension	122 (22.3)
Right ventricular infarction	181 (33.2)
Atrial infarction	9 (1.6)
Left ventricular ejection fraction*	47.6 ± 11.8
Peak CPK level* (U/L)	2,741 ± 2,198
First-degree AV block	114 (20.9)
Second-degree AV block	25 (4.6)
Complete AV block	70 (12.8)
Atrial fibrillation	98 (17.9)
Ventricular tachycardia/fibrillation	38 (7.0)
Bundle branch block	37 (6.8)
ST depression of $\geq 1.0 \text{ mm in V}_3$	258 (47.3)
Thrombolysis	281 (51.5)
Primary angioplasty	58 (10.6)
Angiotensin-converter enzyme inhibitor	369 (67.6)
Beta-blocker	308 (56.4)
Statins	291 (53.3)
Glycoprotein IIb/IIIa inhibitors	32 (5.9)
Re-infarction	21 (3.8)
Cardiac free wall rupture	15 (2.7)
Acute pulmonary oedema	19 (3.5)
Intracranial bleeding	I (0.2)
Inhospital mortality	69 (12.6)
One-year mortality among survivors	39 (8.2)

\* expressed as mean and standard deviation

CPK: creatinine phosphokinase; AV: atrioventricular

clinical characteristics were then analysed with respect to inhospital mortality. This study was approved by the local ethical advisory board.

Inferior MI was defined as typical chest pain lasting longer than 30 minutes, a ST-segment elevation of  $\geq$  1.0 mm in  $\geq$  two inferior leads, and more than a two-fold increase in the serum creatinine phosphokinase level. Lateral wall extension was identified by the concomitant presence of a ST-segment elevation of  $\geq 1.0$  mm in any one of the lateral leads (I, aVL, V5, or V6). Atrial infarction was defined as a concomitant PR-segment depression of  $\geq 1.2$  mm in the inferior leads.<sup>(8)</sup> Precordial ST-segment depression was defined as a ST-segment depression of  $\geq 1.0$  mm in the lead V3 measured at 80 ms from the J point. Cardiogenic shock was defined as a blood pressure of  $\leq$  90/60 mmHg with evidence of decreased organ perfusion, or one which required inotropic support. Haemodynamically-significant RV infarction was defined as a ST-segment elevation of  $\geq$  1.0 mm in the lead V<sub>4R</sub> in ECG, and associated with

Table II.The angiographic results of patients with inferior wall MI.

Angiographical results	No. (%) of patients (n = 369)		
RCA-dominant	319 (86.4)		
Infarct-related site and artery			
Proximal RCA	149 (40.4)		
Distal RCA	132 (35.8)		
Proximal LCx	16 (4.3)		
Distal LCx	50 (13.6)		
Unidentified	22 (6.0)		
Multi-vessel disease	204 (55.3)		

RCA: right coronary artery; LCx: left circumflex

either cardiogenic shock or a LVEF  $\leq 40\%$ . Cardiac freewall rupture was defined as a haemodynamic collapse or sudden death due to electromechanical dissociation that was associated with pericardial effusion on transthoracic echocardiography. Acute pulmonary oedema was defined as pulmonary congestion in the chest radiograph with an oxygen requirement of more than 50%, or a requirement of positive airway pressure ventilation or mechanical ventilation. Multivessel disease was defined as the presence of lesions  $\geq 50\%$  of the diameter stenosis in  $\geq$ two major coronary arteries.

The measurements were presented as mean  $\pm$  one standard deviation for continuous variables, and absolute number or percentage for categorical variables. Univariate analysis was first performed to identify plausible factors affecting inhospital mortality, such as demography, risk factor profiles, features of infarct, ECG changes and arrhythmias, treatment strategy and medications, complications, angiographic results, and clinical outcome, using either the two-sided Student's *t*-test or Pearson  $\chi^2$ test, as appropriate. Any variables with a p-value of < 0.1was subjected to multivariate logistic regression analysis to determine the predictors of inhospital mortality. A pvalue of < 0.05 was considered statistically significant. The analysis was performed by using the Statistical Package for Social Science version 15.0 (SPSS Inc, Chicago, IL, USA).

#### RESULTS

The clinical profiles of all the patients are summarised in Table I. Most patients (> 70%) presented within six hours of the symptom onset. Thrombolytic therapy remains the principal treatment strategy adopted in our hospital. The inhospital mortality was 12.6%. The one-year all-cause mortality among the survivors was 8.2%. Coronary angiography was performed in 369 (67.6%) patients. The angiographic findings are listed in Table II. The results of the univariate analysis of factors affecting the inhospital mortality are summarised in Table III. RV infarction

Factor	Odds ratio	p-value
Age $\geq$ 75 years	3.369	0.000*
Female gender	1.789	0.029*
Ever-smoker	0.594	0.056
Diabetes mellitus	1.224	0.456
Hypertension	1.314	0.286
Hyperlipidaemia	0.332	0.000*
Lateral wall extension	2.702	0.000*
Right ventricular infarction	1.399	0.232
Haemodynamically-significant right ventricular infarction	2.974	0.000*
Atrial infarction	5.697	0.005*
Onset of symptom < 6 hours	0.638	0.108
Onset of symptom > 24 hours	2.234	0.020*
Second-degree AV block	0.812	0.702
Complete AV block	3.314	0.000*
Atrial fibrillation	3.110	0.000*
Ventricular tachycardia/fibrillation	4.276	0.000*
Bundle branch block	2.759	0.009*
ST depression in V <sub>3</sub>	1.067	0.712
Left ventricular ejection fraction $\leq 35\%$	5.702	0.000*
Thrombolysis	0.546	0.020*
Primary angioplasty	0.220	0.024*
Re-infarction	3.659	0.004*
Cardiac rupture	32.552	0.000*
Acute pulmonary oedema	6.861	0.000*
Cardiogenic shock	16.029	0.000*
Multivessel disease	1.126	0.878

 Table III. Univariate analysis of the factors affecting inhospital mortality.

\* p-value is significant

AV: atrioventricular

was not associated with a worse outcome. However, haemodynamically-significant RV infarction strongly predicted a poor clinical outcome. Multivariate logistic regression analysis showed that advanced age  $\geq$  75 years, female gender, lateral wall extension, complete AV block, bundle branch block, the absence of thrombolysis and cardiac free-wall rupture were independent predictors of elevated inhospital mortality (Table IV).

The efficacy of thrombolysis according to age group and gender is shown in Table V and Fig. 1. The use of thrombolytic therapy was associated with a significant decrease in mortality in patients aged  $\geq 65$  years (12.8% vs. 26.8%, p = 0.0042) compared with those not receiving reperfusion therapy. However, this benefit was not seen in patients aged < 65 years (5.3% vs. 6.3%, p = 0.75). In addition, a decrease in mortality by thombolysis was only demonstrable in men (9.3% vs. 16.8%, p = 0.047), but not in women (12.5% vs. 23.8%, p = 0.17).

A significant reduction in inhospital mortality was observed in patients with lateral wall extension (16.9%

Table IV. Independent predictors of inhospital mortality after multivariate logistic regression analysis.

Independent predictor	Odds ratio	D-value	
	(95% confidence interval)		
Advanced age $\geq$ 75 years	3.47 (0.978–1.105)	0.015	
Female gender	4.20 (0.06-0.987)	0.048	
Lateral wall extension	4.65 (0.054-0.523)	0.002	
Complete AV block	3.94 (0.061-0.785)	0.013	
Bundle branch block	5.35 (0.030-0.712)	0.013	
Thrombolysis	0.12 (1.611-339.755)	0.021	
Cardiac free-wall rupture	38.5 (0.000–0.145)	0.02	

AV: atrioventricular

vs. 38.5%, p = 0.0225), haemodynamically-significant RV infarction (19.4% vs. 63.2%, p = 0.0026) and complete AV block (14.3% vs. 45.2%, p = 0.0072), after the administration of thrombolysis. There was no difference in the baseline demographics between patients except in the former category. No beneficial effect was seen in patients with bundle branch block (Table VI).

## DISCUSSION

Advanced age has been consistently shown to be related to an unfavourable short-term prognosis in acute MI.<sup>(9)</sup> The elderly patients are more likely to be female, and have more comorbidities. In addition, they are less likely to receive reperfusion therapy or adjunctive pharmacotherapy.<sup>(10,11)</sup> Gurwitz et al reported a progressive decrease in the use of thrombolytic therapy with increasing age.<sup>(12)</sup> Physicians are reluctant to prescribe thrombolysis to elderly patients as they frequently have delayed presentation, unknown time symptom onset, relative contraindications to thrombolytic agent(s) and a higher bleeding risk. Gurwitz et al also reported the underuse of beta-blockers in the elderly.<sup>(13)</sup> Nevertheless, advanced age was found to be an independent predictor of inhospital mortality after the adjustment of these confounding factors.<sup>(14)</sup> Similar findings were observed in our study. Increasing age was associated with female gender, delayed presentation of > 24 hours, less revascularisation therapy and use of betablocker, and higher inhospital mortality (Fig. 2). We also found that patients aged  $\geq 65$  years showed significant mortality benefits from thrombolysis. Thus, careful selection of patients for thrombolysis in the elderly may be justified.

Women aged < 75 years have about a two-fold increase in inhospital death compared with their male counterparts,<sup>(15)</sup> although this difference in mortality disappeared above 75 years of age. The female gender is more frequently associated with diabetes mellitus and cardiogenic shock, and less likely to receive revascularisation therapy and beta-blocker.<sup>(16,17)</sup> In



**Fig. I** Bar chart shows the comparison of inhospital mortality in patients who were treated with thrombolysis or conservatively in different age and gender groups.



Fig. 2 Bar chart shows the distribution of gender, time of presentation, use of revascularisation therapy and beta-blocker, and inhospital mortality across the various age groups.

this study, the female gender was associated with advanced age, delayed presentation of > 24 hours, less revascularisation therapy, infrequent use of beta-blocker and higher inhospital mortality (Fig. 3). These associations accounted for the relative lack of benefit of thrombolysis on mortality in female compared with male patients.

Bundle branch block is a marker of both unfavourable short- and long-term clinical outcomes, as described by Go et al in a study involving nearly 300,000 patients with acute MI.<sup>(18)</sup> Patients with bundle branch block are generally older and have more comorbidities. In our study, none of the patients were on beta-blocker before admission. Its presence is associated with an increase in inhospital deaths with an odds ratio (OR) of 5.35, compared with an approximate OR of 1.7 in other studies involving inferior MI patients.<sup>(19,20)</sup> In this study, thrombolysis has not been shown to be beneficial in this subset of patients, probably due to the small patient number.

Berger and Ryan identified three high-risk subsets



**Fig. 3** Bar chart shows the gender difference in the distribution of time of presentation, treatment received and inhospital mortality.

BB: beta-blocker; PCI: percutaneous coronary intervention

in inferior wall MI: complete AV block, precordial STsegment depression and RV infarction.<sup>(7)</sup> In our study, complete AV block predicted inhospital death with an OR of 3.94, and thrombolysis has been observed to reduce the inhospital mortality by nearly 70%. Its association with a poor inhospital outcome has already been widely reported.<sup>(21,22)</sup> The increased inhospital death is probably related to its association with a larger infarct size. While precordial ST depression is generally accepted as an indicator of concurrent posterior ischaemia and larger infarct size,<sup>(23)</sup> mortality impairment has not been universally demonstrated,<sup>(24)</sup> as in this study. Precordial ST depression indicates posterior wall ischaemia and can be caused by a distal left circumflex artery occlusion, which usually leads to a relatively small territory of infarct. Sometimes, a proximal dominant right coronary artery occlusion (larger infarct) causes precordial ST-segment elevation, which cancels out the presumed ST-segment depression.<sup>(25)</sup> Lateral wall extension has been found to be an independent predictor of mortality with an OR of 4.65 in this study. It has been reported to be associated with larger infarct size(26) and occlusion of a "mega-artery" in the literature.<sup>(27)</sup> The use of thrombolysis in this high-risk subset of patients has been associated with an improved outcome in this study.

RV infarction has not been shown to be an independent predictor of mortality, probably due to the low absolute inhospital mortality as compared with the control group in this study. The diagnosis of RV infarction does not necessarily imply severe RV functional impairment. In fact, only about one-fourth of patients with RV infarction are haemodynamically compromised in the literature.<sup>(28)</sup> If only the latter is considered, the short-term prognosis is very poor (36% inhospital mortality). This subgroup comprises about one-third of all RV infarction in this study. This sub-classification is sound because it takes

	No. (%) of patients w	No. (%) of patients with inhospital mortality		Odds ratio	
	Thrombolysis	Conservative			
Age (years)					
< 65	7/132 (5.3)	4/64 (6.3)	0.7515	0.8400	
≥ 65	19/149 (12.8)	38/142 (26.8)	0.0042*	0.4000	
Gender					
Men	21/226 (9.3)	21/125 (16.8)	0.047*	0.5073	
Women	7/56 (12.5)	19/80 (23.8)	0.1666	0.525	

Table V. Age and gender differences in the beneficial effect of thrombolysis on inhospital mortality.

\* p-value is significant

Table VI. The	effects of	thrombol	vsis on	patients in	the	high-risk subsets.

High-risk subset	Thrombolysis	Conservative	p-value
Lateral wall extension, total no.	71	39	
No. (%) of male patients	55 (77.5)	19 (48.7)	0.0029*
Mean age $\pm$ standard deviation (years)	61.2 ± 13.6	65.5 ± 13.6	0.028*
No. (%) of inhospital mortality	12 (16.9)	15 (38.5)	0.0225*
Haemodynamically-significant right ventricular infarct, total no.	31	19	
No. (%) of male patients	22 (71.0)	10 (52.6)	0.2191
Mean age $\pm$ standard deviation (years)	67.8 ± 11.1	70.0 ± 11.6	0.5129
No. (%) of inhospital mortality	6 (19.4)	12 (63.2)	0.0026*
Complete atrioventricular block, total no.	35	31	
No. (%) of male patients	26 (74.3)	18 (58.1)	0.1969
Mean age ± standard deviation (years)	66.4 ± 11.2	70.7 ± 11.4	0.1289
No. (%) of inhospital mortality	5 (14.3)	14 (45.2)	0.0072*
Bundle branch block, total no.	23	10	
No. (%) of male patients	19 (82.6)	6 (60.0)	0.2054
Mean age $\pm$ standard deviation (years)	70.3 ± 10.7	71.1 ± 10.8	0.8379
No. (%) of inhospital mortality	7 (30.4)	2 (20.0)	0.6859

\* p-value is significant

into account the functional importance or the sequel of the right coronary artery occlusion (reduced LVEF  $\leq$ 40% and cardiogenic shock). An improved outcome has been observed after thrombolysis in this high-risk patient subset. Conversely, the prognosis is dismal if a conservative approach is adopted.

Thrombolysis within the therapeutic window is a therapy of proven survival benefit in acute MI.(2-4) However, its role in the treatment of inferior MI remains controversial. The mortality reduction is only modest in most of the large trials<sup>(3,4,29)</sup> and a meta-analysis.<sup>(30)</sup> Several factors contribute to this observation. First, inferior MI is relatively low risk compared with anterior wall MI. As a result, a large number of patients are required to demonstrate a survival benefit. Second, the therapeutic window is short (< six hours) for inferior  $MI^{(5)}$  (vs. < 12 hours for anterior wall MI). Thus, a reduced or an absence of benefit is observed in earlier studies which recruited a significant number of patients presenting between six and 12 hours. Finally, right coronary artery has a lower patency and higher re-occlusion rate, compared with the left anterior descending artery after thrombolysis.<sup>(31)</sup> In our study, thrombolysis is found to be an independent predictor of improved inhospital mortality with an OR of 0.54; this is especially useful for those high-risk patient subsets.

This retrospective study comprised 546 consecutive patients who presented to a regional hospital with inferior wall MI. The inhospital mortality and one-year mortality among the hospital survivors was 12.6% and 8.2%, respectively. The multivariate logistic regression analysis showed that an advanced age of  $\geq$  75 years, female gender, lateral wall extension, complete AV block, bundle branch block, an absence of thrombolytic therapy and cardiac free-wall rupture are independent predictors of inhospital mortality. The use of thrombolysis has been observed to improve the short-term outcome in high-risk subsets, such as the elderly, male gender, lateral wall extension, haemodynamically-significant RV infarction and complete AV block.

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