

## **Factors Affecting in-Hospital Mortality of Acute Myocardial Infarction**

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**(Received 17 Dec 2008; accepted 9 May 2009)**

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### **Abstract**

**Background:** Acute myocardial infarction (AMI) is one of the most common causes of morbidity and mortality. Considering immense socioeconomic damages of growing AMI in developing countries we estimated prognostic value of major risk factors of AMI to predict probable In-hospital AMI mortality.

**Methods:** In a cohort survey from June 2004 to March 2006, 1798 patients hospitalized with proven AMI entered into two groups: Survived (patients discharged alive) and Expired (patients expired during hospitalization due to AMI). We evaluated relationship of 17 risk factors including age, sex, smoking, opium usage, hypertension, diabetes mellitus (DM), dyslipidemia, Killip class, existence of Q wave, ST segment elevation, bundle branch blocks (BBB), involved surface of heart, mean left ventricular ejection fraction (LVEF), mitral valve regurgitation (MR), and serum level of Troponin I and CKMB, with patients' survival and expiry by using chi square test, T test and multivariate logistic regression analysis. P value  $\leq 0.05$  was considered significant.

**Results:** There were 1629 (90.6%) survived and 169 (9.4%) expired patients. Factors significantly affected in-hospital mortality of AMI include: age ( $P < 0.001$ ), femaleness ( $P < 0.001$ ), smoking ( $P < 0.001$ ), Killip class  $> II$  ( $P < 0.001$ ), hypertension ( $P = 0.036$ ), DM ( $P < 0.001$ ), bundle branch block ( $P < 0.001$ ), Moderate to severe mitral regurgitation ( $P < 0.001$ ), lower Mean LVEF ( $P < 0.001$ ), and lower mean serum concentration of CKMB and Troponin I ( $P < 0.001$ ). Mortality was significantly higher in anterolateral infarction.

**Conclusion:** Mean age  $> 69.01$  yr, femaleness, Killip class III & V, hypertension, DM, moderate to severe MR, anterolateral AMI, bundle branch block and higher serum concentration of CKMB & Troponin I are associated with higher In-hospital post-AMI mortality.

**Keywords:** *Acute myocardial infarction, Prognosis, In-Hospital mortality*

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### **Introduction**

Acute myocardial infarction (AMI) is one of the most common and critical causes of global hospitalization due to its morbidity and mortality (1). Some patients expire at admission, some expire during hospitalization period (due to arrhythmia or cardiogenic shock) and some expire after discharge because of reoccurrence of AMI or its adverse outcomes like congestive heart failure, etc. Considering growing occurrence of AMI (especially in young people) in developing countries (2-3) and immense socioeconomic damages secondary to its adverse consequences (first 24 h In-hospital mortality is 7% for ST elevated AMI,

2.4% for non-ST elevated AMI, and 11.8% for undetermined AMI; and 30 d mortality rate rise to 8.4%, 3.5% and 13.3% for ST elevated, Non-ST elevated and undetermined AMI respectively (4)), it is wise to estimate prognostic value of several major risk factors of AMI in order to predicting probable In-hospital AMI mortality. Thus, we will be able to treat high-risk patients better. There are few surveys that evaluated some of those risk factors (not all of them) in order to presenting a model for management of such high-risk patients (5). Data on current cardiovascular risk management and patients' lifestyle are severely needed to identify gaps and determine spe-

cific targets for improvement of cardiovascular patients care, and to examine underlying factors and tailor relevant interventions (6).

Therefore, the aim of this study was to evaluate prognostic value of as many risk factors as possible.

## Materials and Methods

### Study patients

This retrospective cohort survey was conducted in Tehran Heart Center through extracting patients' data from Ischemic Heart Disease database from June 2004 to March 2006. Thus, 1798 patients hospitalized with proven AMI were selected. AMI diagnosed in a clinical and paraclinical setting (based on European Society of Cardiology/American College of Cardiology definition of myocardial infarction (7)). These patients were assigned to two groups. Group A (survived) consisted of patients admitted for proven AMI and discharged alive and group B (expired) consisted of patients admitted for proven AMI and expired during hospitalization time because of AMI or its adverse outcomes.

Ethical issues were accepted by ethics committee of Tehran Heart Center. All patients read and signed an "informed consent" form at the beginning of hospitalization declared they are satisfied with application of their anonymous data for research purposes.

There were 17 risk factors including patients' age, sex, active or current smoking (according to CDC definition (8), opium usage (oral, intravenous or exhalative), existence of systemic hypertension (according to Joint National Committee sixth report (9), clinically measured), diabetes mellitus (according to American Diabetes Association guideline (10) or a documented positive history) and dyslipidemia (according to the updated Framingham guidance (11) or a documented positive history), Killip class (evaluated clinically), existence of Q wave, ST segment elevation, right and left bundle branch blocks (RBBB and LBBB) and involved surface of heart (determined with ECG recording), mean left ventricular ejection fraction (LVEF)

(EF < 45%, severe EF < 30%) and mitral valve regurgitation (MR) (proven by echocardiography), and serum level of heart enzymes Troponin I (>0.8 µg/L according to kit reference value, assessed by Biomerieux kit with enzyme-linked fluorescent assay (ELFA)) and CKMB (>35 mg/dL according to reference interval of Tehran Heart Center, assessed by Diagnostica kit (Germany) with immunoinhibition method).

### Statistical analysis

Relationship of above-mentioned risk factors with patients' survival and expiry, chi square test, *t* test and multivariate logistic regression analysis was assessed by software SPSS. *P* value ≤ 0.05 was considered significant. Finally we performed a multivariate logistic regression analysis and included age, sex, smoking and opium usage, hypertension, diabetes mellitus, dyslipidemia, Killip classes, BBB, ejection fraction and MR to calculate their prognostic power. In this study 5 risk factors including number of preceding AMI, heart rate at admission, duration of QRS complex at EKG and serum level of Homocysteine and Lipoprotein A remained undetermined.

## Results

The profile of variables is shown in Table 1. There were 1629 patients (90.6%) in group A and 169 patients (9.4%) in group B. Demographic findings show that survived and expired patients' mean age were 61.91 and 69.01 yr old respectively. Mean age was significantly older in group B (*P* < 0.001).

Killip class evaluation showed that patients with Killip class I, II, III and IV were 86.4%, 11.8%, 1.3% and 0.5% respectively within group A. Frequency of Killip class I, II, III and IV were 33.8%, 20%, 20% and 26.2% respectively within group B. Difference between four classes of Killip indicated that class I was significantly more frequent in group A, but class III and IV were significantly more frequent in group B (*P* < 0.001). Calculation of mortality rate within Killip classes showed that mortality within class I, II, III and IV

were 3.8%, 14.7%, 57.4% and 81.8% respectively (Fig. 1).

Inspection of ECG records revealed that there were no significant difference between frequency of Q wave and ST segment elevation group A and B ( $P$  value for Q wave was 0.68 and for ST elevation was 0.15). In the other hand, there was a significant difference between frequency of bundle branch block (BBB) within group A and B. ( $P < 0.001$ ) (Fig. 2). Frequency of involvement of heart surfaces and their related incidence of In-hospital AMI mortality showed that anterolateral MI (V5-V6 leads) accompanied with highest mortality (15.4%) in comparison with anterior MI (V1-V4 leads) (10.8% of them expired), inferior MI (II, III and AVF leads) (6.9% of them expired), lateral MI (I and AVL leads) (9.1% of them expired), posterior MI (11.1% of them expired) (Fig. 3). We ignored less frequent involved surfaces (including Right ventricular, apical, septal, inferoseptal, posterolateral and inferobasal) that made no difference between groups.

Mean LVEF was 46.1% in group A and 29.62% in group B. This difference was significant ( $P < 0.001$ ). MR assessment showed that no MR, trivial MR and mild MR are significantly more frequent in group A, while moderate to severe MR are more prevalent in group B ( $P < 0.001$ ). Mean serum level of CKMB in group A and B was 80.68 ( $\pm 2.20$ ) mg/dL and 101.10 ( $\pm 8.22$ ) mg/dL respectively. It was significantly higher in patients within group B ( $P = 0.006$ ). Mean serum level of Troponin I in group A and B was 8.72 ( $\pm 0.31$ )  $\mu\text{g/L}$  and 11.70 ( $\pm 1.18$ )  $\mu\text{g/L}$  respectively. It was significantly higher in patients within group B ( $P = 0.004$ ).

Result of multivariate logistic regression analysis showed that relative risk of LVEF  $\leq 30\%$  was 2.72 to 8.56 (confidence interval 95% with Odds ratio 4.83, and  $P < 0.001$ ), and relative risk of Killip classification was 3.26 to 10.16 (confidence interval 95% with Odds ratio 5.76, and  $P < 0.001$ ). MR showed a trend risk with Odds ratio 1.84 and  $P = 0.063$ .

**Table 1:** Frequency of risk factors and predictors of in-hospital mortality after acute myocardial infarction. All risk factors are shown as percent except for Mean serum CKMB and Mean serum Troponin which their scaling measurements are shown in their relevant rows

Risk factors	Survived group (%)	Expired group (%)	P value
Sex			
Male	74.89	61.53	<0.001
Female	24.61	38.46	
Smoking	32.2	17.4	<0.001
Opium usage	9.9	8	0.044
Hypertension	43.3	51.8	0.036
Diabetes mellitus	37.1	47.3	<0.001
Dyslipidemia	48.1	44.1	0.1
Q wave	44.8	43.2	0.68
ST elevation	52.5	46.7	0.15
BBB	4.3	17.2	<0.001
Mean LVEF	46.1	29.62	<0.001
MR			
Mild	26.5	15.4	<0.001
Moderate	6.4	11.8	
Severe	1.4	5.9	
Mean serum CKMB*	80.68 mg/dL	101.10 mg/dL	0.006
Mean serum Troponin	8.72 $\mu\text{gr/L}$	11.70 $\mu\text{gr/L}$	0.004

\*CKMB, Creatine kinase, cardiac isoenzyme

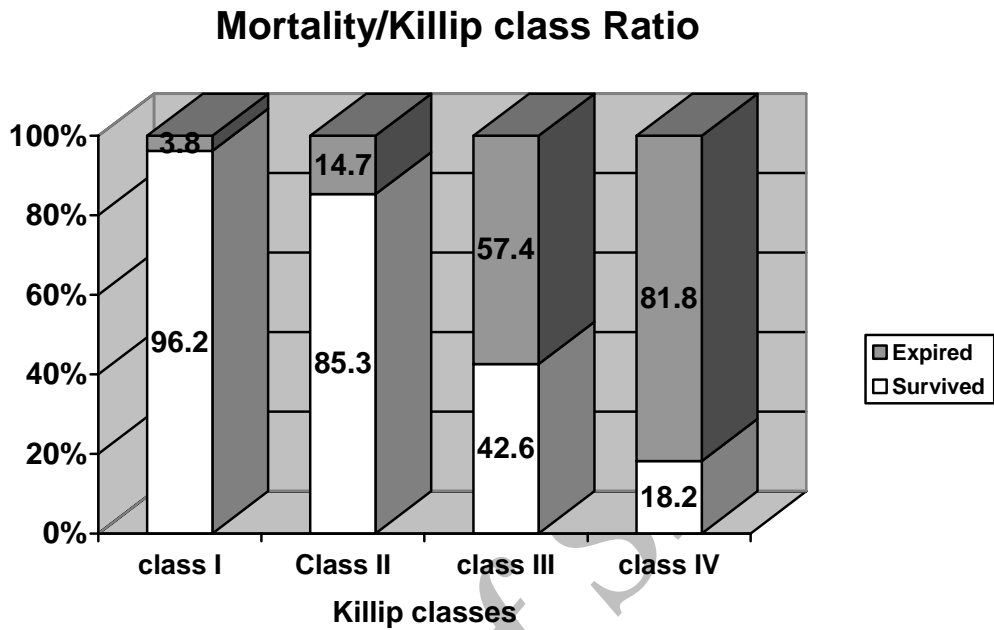


Fig. 1: Mortality rate within different Killip classes within survived and expired groups

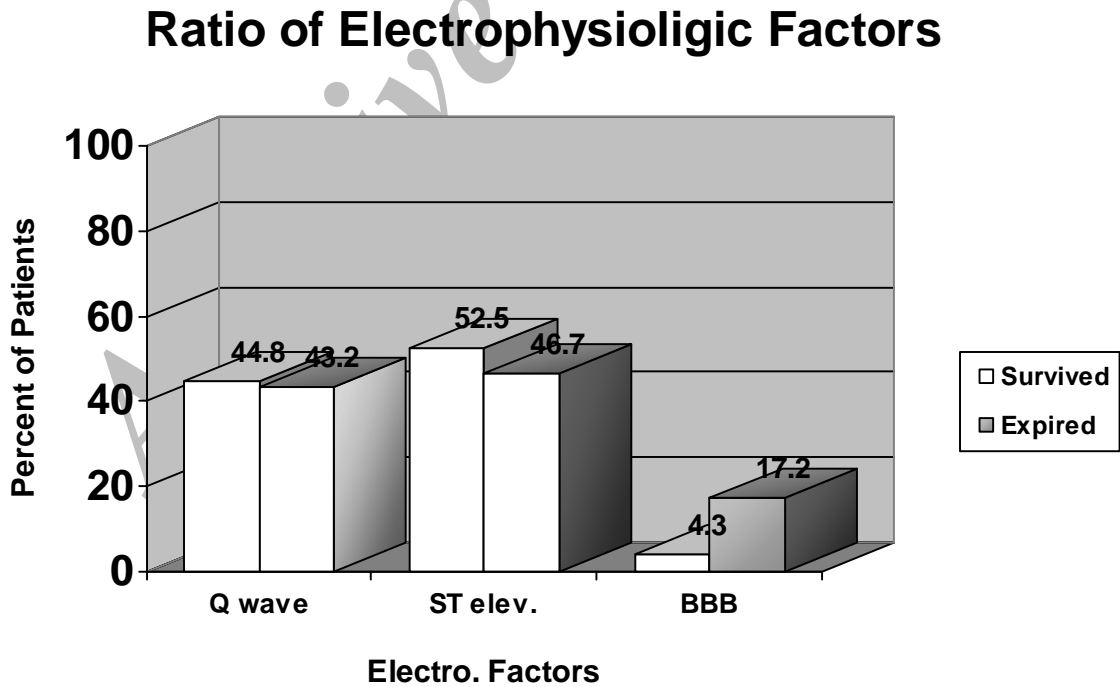


Fig. 2: Ratio of Electrophysiologic factors within survived and expired groups

### Mortality/type of MI Ratio

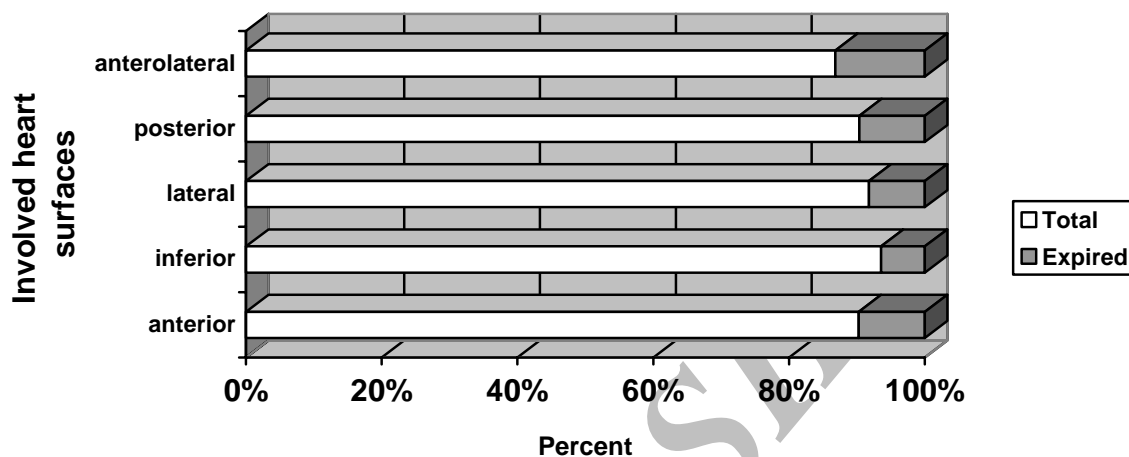


Fig. 3: Mortality of acute myocardial infarction according to affected heart surface

#### Discussion

Since the incidence of AMI mortality has shown no decrease and mean age of AMI has decreased in developing countries (2-3) and burden of its socioeconomic damages to both patients and health system is heavy, it is reasonable to estimate value of several predictor risk factors of In-hospital AMI mortality.

Findings of this survey show that female gender is a risk factor for In-hospital AMI mortality, despite lesser prevalence of coronary artery disease (CAD) including AMI in females than males. It seems that females are more resistant to developing CAD, but if they are involved they are more susceptible to most adverse consequences. Previous studies have determined gender differences of post-hospital mortality indicated no difference between male and females (12). The expired patients' mean age was older than that of survived patients. It is in accordance with manifestation of more severe CAD in older patients. Meanwhile, expired patients' mean age was 69.01 yr old that conforms to a preceding study estimated mean age 70 yr old (13, 14). Current smokers and opium users were greatly and a little more frequent respectively within survived patients. It

seems contradictory. Performing multivariate logistic regression analysis demonstrated that smoking and addiction had no protective effect on survived patients. This analysis showed that expired patients with smoking or opium usage died in younger ages than similar survived patients (i.e. patients with smoking or opium usage), thus smoker and opium-user patients within survived group are appeared protected against In-hospital AMI death because of their younger age. Our analysis implied that patients with smoking and opium usage expire at the younger age, thus smokers and addict patients within survived patients pretend such a paradoxical finding. In other words: we have two groups: expired patients (a combination mostly of smokers and addict patients who expired at younger age), and survived patients (a combination of smokers, non-smokers, addict and non-addict patients). If we compare these two groups regardless of their combination, it looks like that survived "older" patients are commonly more smoker and addict. We should notice that smoking and opium usage expired patients at younger age.

Diabetes mellitus (DM) was a very greater risk factor than hypertension in group B that conforms to well-known macrovascular adverse outcomes

of DM and also to Fournier et al (15), but as a matter of fact improvement of macrovascular prognosis of DM is better obtained with tight control of blood pressure and dyslipidemia rather than tight control of blood sugar. Our findings frankly showed not such correlation with In-hospital AMI mortality because our study showed that DM itself is the most powerful single risk factor for patients' expiry; it means control of DM (i.e. control of blood sugar) immensely reduces the risk of In-hospital AMI mortality. A survey by Tzung-Dau Wang et al has showed that improvement of dyslipidemia amends LVEF (16) and decreases CKMB serum level (17). As is clearly deduced, Killip class III and IV are expired patients' important companions (a very high incidence (3)). Our findings conform to Vincent S. Degeare et al. (18) that have demonstrated prevalence of Killip class III in In-hospital AMI mortality as 19%; in addition showed higher Killip class (III and IV) was associated with older age, history of DM and lower LVEF. Calculation of mortality within Killip classes demonstrated that the highest mortality rate in descending order lies within class IV, III, II and I. Mortality was significantly greater within classes II, III and IV in comparison with class I. Thus, presence of Killip classes II, III and IV are with greater risk of In-hospital AMI mortality (see the end of discussion for further clarification).

Our study indicates that presence of BBB is an electrocardiographic risk factor. It is reasonable that some electrophysiologic abnormalities (especially BBB that is a dramatic dangerous abnormality) increase risk of fatal arrhythmias. Concerning involved surfaces of heart and location of involvement the most mortality was seen in anterolateral involvement, perhaps due to probable left anterior descending artery (LAD), left circumflex artery (LCX) or left main coronary artery (LMCA) involvement. It is approximately equal to Fournier et al which suggested anterior AMI (they regarded V1-V6 leads) is associated with greater risk of AMI mortality (15).

Low LVEF is a well-known prognostic predictor for In-hospital AMI mortality (9, 19-20). Our

study indicates that mean LVEF lesser than or equal to 30% (severe CHF) is a strong risk factor for In-hospital AMI mortality. There was no remarkable CHF within group A patients (mean LVEF>45%, no CHF). Absence of MR, and trivial or mild MR are associated with patients' survival, while moderate to severe MR are risk factors for In-hospital AMI mortality. We considered no MR, trivial and mild MR a single category because they made no significant difference neither for calculation of correlation nor in multivariate logistic regression analysis. These findings conforms to Feinberg et al (21) that demonstrated mild MR (29%) is associated with increased AMI mortality (especially after adjustment for age, gender, DM, systemic hypertension, Killip class  $\geq$ II, and LVEF  $\leq$ 40%). As is seen, mild MR is more frequent than moderate and severe MR within survived patients.

According to our findings, more serum level of CKMB and Troponin I rises, more probable mortality occurs. It is explained by as is serum level rising, as extent of injury. The cut points for CKMB and Troponin I are subject to be determined. It is in accordance with Kanna et al. (22) that demonstrated Troponin level as a powerful predictor of In-hospital AMI mortality.

Interpretation of multivariate logistic regression analysis documented that Killip class and LVEF are in descending order most powerful predictors and MR is a trend predictor for In-Hospital AMI mortality. We used multivariate logistic regression analysis again without including Killip class and it showed LVEF and DM were most powerful predictors (relative risk 1.28 to 2.60, confidence interval 95% with Odds ratio 1.84, and  $P= 0.01$ ). We could interpret it since patient's Killip class is clinical resultant of all underlying risk factors, taking Killip class in account omit all risk factors from model. Therefore pure effect of LVEF and DM was revealed in absence of Killip class.

Since several risk factors which some of them are proven predictors like number of preceding AMI, heart rate at admission, duration of QRS complex were not among our evaluated risk factors, it

is proposed the whole definite or probable predictors will be evaluated in a new trial for introduction of a new scoring model that predicts In-hospital AMI mortality. These risk factors (some of them are novel) include heart rate at admission, number of preceding proven AMI, alcohol consumption, ratio of peak E-wave velocity to flow propagation velocity (assessed by color M-mode Doppler echocardiography) and serum concentration of patients' BUN, Homocysteine and Lipoprotein A. It maybe useful to take number of involved coronary vessels in accounts.

In conclusion, our data demonstrate that female gender, age over 69 yr old, smoking and opium usage, presence of diabetes mellitus and systemic hypertension, Killip class II, III and IV, presence of right and left bundle branch blocks, anterolateral AMI, low LVEF (<30%), presence of moderate to severe MR, and higher serum concentration of CKMB and Troponin I are associated with increased In-hospital AMI mortality, but only Killip class and LVEF (and somewhat MR, as a trend) are independent prognostic predictors for In-hospital AMI mortality.

### **Acknowledgements**

This study was funded by Clinical and Experimental Research Unit, Tehran Heart Center hospital, Tehran University of Medical Sciences, Iran. We should thanks Dr MA Boroumand MD, head of Pathology and Clinical Laboratory department of Tehran Heart Center for granting data about measurement of CKMB and Troponin I, and also staff of database recording section of Clinical and Basic Research department of Tehran Heart Center for their decisive recordings.

The authors declare that there is no conflict of interests.

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