Abstract

Introduction: Myocardial infarction (MI) is a well-recognized clinical entity with a worldwide distribution. The World Health Organization defines MI as a diagnosis when two of the following triad is present: clinical symptoms (i.e.: typical chest pain), cardiac enzyme elevation and ECG changes. In the United States alone, 1.5 million cases of MI occur per year. The overall prevalence of coronary heart disease in India was between 32-45/1000 people in different communities, and the prevalence of MI varied between 10-15/1000 people. Infarction has previously been classified as transmural if ST elevation or Q waves were observed in ECG or sub-endocardial if typical chest pain, creatine phosphokinase (CPK) enzyme elevation, and ST-T wave changes occurred in the absence of new Q waves. However, on pathological examination, most infarctions involve the subendocardium and some transmural extension is common even in the absence of Q waves on ECG. Thus a more appropriate classification was devised, based on the presence or absence of Q waves. The well-established risk factors for MI include old age, male gender, smoking, diabetes, hypertension, hypercholesterolemia and the presence or family history of ischemic heart disease. Previous studies...
have shown a higher incidence of non-Q wave MI in the elderly and females. Several studies looked at differences between the two types of infarction regarding prevalence of hypertension, smoking, diabetes, hypercholesterolemia and family history of ischemic heart disease. None found any difference in the distribution of these risk factors between the two types of infarctions. Stone et al, however reported an increased frequency of diabetes in people suffering non-Q wave infarctions. The Framingham study reported a higher incidence of hypertension in non-Q wave myocardial infarction group. A history of hypertension remains predictive of adverse outcome, particularly short-term mortality. For patients less than 65 years of age, hypertension is a moderate risk factor for long term mortality. Diabetic patients had a higher mortality at 28 days post MI. Cigarette smoking did not show a quantitative relationship with the severity of the acute infarction in terms of short and long term mortality.

The prognosis after myocardial infarction depends on the infarct size, as demonstrated by the CK levels in blood, left ventricular function, and the use of thrombolytic therapy. Studies have shown that patients with non Q wave MI suffered smaller infarcts, as reflected by lower CPK levels, and higher post MI left ventricular ejection fraction. People suffering Q wave infarction usually experience higher in hospital mortality. However there is no difference in long term survival when compared to non-Q wave MI. This is controversial, and studies showing no difference regarding in hospital mortality, and reduced long term survival for non Q wave infarctions have also been reported. It has been shown that the total in hospital and 6 month mortality was lower in patients younger than 50 years than those above 50 years. In one study, gender did not affect in-hospital and three-year mortality rates. Other studies have demonstrated a higher short-term mortality in women but similar long-term mortality.

Existing literature holds much controversy regarding the prognosis of patient with Q wave and non Q wave infarctions. Therefore, we conducted this study to compare the in hospital mortality, mortality at 1 year and the time to death in association with the various risk factors proven to have a role in myocardial infarction.

Materials and Methods

Patients
A retrospective cohort of patients admitted at the Aga Khan: University Hospital (AKUH), a tertiary care hospital between January 1, 1994 and December 31, 1997 with a diagnosis of MI was eligible for inclusion in the study. A total of 1596 patients were identified by the indexing and coding department AKUH, of whom 272 died in hospital while 1324 were discharged. Patients were excluded from the study if they had a prior MI, a preexisting left bundle branch block on ECG, history of prior revascularization (i.e. coronary artery bypass grafting and coronary angioplasty) and if telephone contact was not possible. Patients were telephoned in order to determine their survival status until 1st Jan 1999. The final study sample included 420 patients of whom 80 died in hospital while 340 survived their hospital stay and were interviewed via phone.

Congestive heart failure was taken as documented by the attending physician and/or diffuse bilateral rales on chest auscultation and/or evidence of pulmonary edema on chest X-ray and/or presence of S3 on auscultation. A cardiologist (AA) using the Minnesota code criteria determined the type of infarct for Q-wave MI.

Data management and analysis
The SPSS software package was used for data entry and analysis. Age was categorized into quartiles and used in subsequent analysis. Patients with Q-wave MI were compared with those suffering non Q-wave MI with regard to demographic and clinical variables. The student’s t-test or chi-square test was used as appropriate.

In-hospital mortality, mortality at 1 year follow-up and time to death during follow-up were the three outcome variables used in this study. Unadjusted relationship of infarct type (i.e. Q-wave or non Q-wave) with in-hospital mortality and mortality at 1 year was assessed by simple logistic regression. Univariate logistic regression was used to identify potential confounding factors from gender, sex, history of hypertension, diabetes mellitus, smoking and family history of ischemic heart disease. Factors related with the three outcome variables were incorporated multivariable analysis (P 0.2). The final models for ‘in-hospital mortality’ and ‘mortality at 1 year’ were selected through backward stepwise procedure and included factors which were significantly (P <0.05) related to these outcome variables.

Unadjusted survival experience over the study duration was estimated using the Kaplan Meier method to discharge were examined using Cox proportional hazard model. The independent variables considered were the same as for in-hospital mortality and mortality at 1 year.

**Results**

Table 1 describes the baseline characteristics of patients presenting with Q wave and non Q wave MI. Patients with Q-wave MI were significantly more likely to have family history of ischemic heart disease (p = 0.026), higher mean CK (p < 0.0001) and receive thrombolytic therapy (p<0.001). The two groups however, did not differ significantly in age, gender, history of smoking, history of diabetes, history of hypertension and congestive heart failure in hospital (Table 1).
In-Hospital Mortality
Eighty patients died during the course of their hospital stay. Amongst 269 patients who suffered Q wave MI, 64 (23.8%) died whereas only 16 (10.6%) out of 151 patients suffering from non-Q wave MI expired, during their hospital stay.

The final multivariable logistic regression model for in-hospital mortality (Table 2)
demonstrated that age, smoking and infarct type significantly affected outcome. After adjusting for confounders, it was seen that Q-wave MI patients were more likely to suffer from in-hospital mortality than non-Q wave MI patients (adjusted OR = 2.76, 95% CI 1.5 - 5.01, p 0.001). Smoking had a protective effect on in-hospital mortality (adjusted OR = 0.24, 95% CI 0.12 - 0.48, p <0.001). Patients over 67 year of age had increased likelihood of dying during hospital stay compared to patients aged 49 years (adjusted OR = 3.81; 95% CI: 1.54-9.47, p = 0.004).

**Mortality at 1 Year**
One year after experiencing their first MI, 103 patients died. This constituted 77(28.6%) of patients with Q wave MI and 26 (17.2%) of patients with non-Q wave MI. The final multivariate logistic regression model (Table 3)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted odds ratio (95% CI)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td><strong>Type of Infarct</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q wave</td>
<td>2.76</td>
<td>(1.50 - 5.01)</td>
</tr>
<tr>
<td>Non-Q wave</td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td><strong>Smoking history</strong></td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.24</td>
<td>(0.12 - 0.48)</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥67 yrs</td>
<td>3.81</td>
<td>(1.54 - 9.47)</td>
</tr>
<tr>
<td>59 - 66 yrs</td>
<td>2.40</td>
<td>(0.94 - 6.16)</td>
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<td>50 - 58 yrs</td>
<td>1.68</td>
<td>(0.64 - 4.39)</td>
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<td>≤49 yrs</td>
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demonstrated that age, smoking and infarct type, significantly affected 1-year mortality. Patients with Q-wave infarction experienced increased mortality at 1 year follow-up than patients with non-Q wave infarctions (OR = 2.04; 95% CI 1.21-3.43, p = 0.0076). Smoking had a protective effect on 1 year mortality (OR 0.34, 95% CI: 0.19-0.6, p = 0.0002). Patients aged 59-66 years were 2.95 times more likely to die within 1 year compared to patients 49 years (adjusted OR = 2.95, 95% CI: 1.23-7.06, p = 0.015). Patients >.67 years of age had an even higher odds of dying within 1 year after first MI (adjusted OR = 5.18; 95% CI: 2.22-12.1, p = 0.0001).

**Time to death following hospitalization**

The median time to death following the diagnosis of MI was 6 days. Median survival time of the patients who died after suffering from non-Q wave MI and Q-wave MI was 61 days and 4 days respectively (Figure).
Figure. Kaplan-Meier survival curves of time-to-death following a first Q-wave (n=269) and non-Q-wave (n=151) myocardial infarction among patients presented at the Aga Khan University Hospital, Karachi, January 1, 1994 - December 31, 1997.

The final multivariate Cox proportional hazard model (Table 4)
demonstrated that age, smoking, revascularization and infarct type, significantly affected time to death following diagnosis of MI. After adjusting for confounders, the relationship between infarct type and time to death was marginally significant (adjusted RH = 1.45, 95% CI: 0.98-2.13, p = 0.06). Revascularization (adjusted RH = 0.18; 95% CI: 0.08-0.42, p = 0.0001) and smoking history (adjusted RH 0.43, 95% CI: 0.28-0.67, p = 0.0002) prolonged survival following first diagnosis of MI among the study subjects. Patients above 67 years were 2.1 times more likely to die during the total follow-up period than patients below 49 years (adjusted RH = 2.1; 95% CI: 1.2-3.8, p = 0.01).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted relative hazard (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Infarct</td>
<td></td>
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<tr>
<td>Q wave</td>
<td>1.45 (0.98 - 2.13)</td>
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<td>Non-Q wave</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Yes</td>
<td>0.43 (0.28 - 0.66)</td>
<td>0.0002</td>
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<tr>
<td>No</td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td>Revascularization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.18 (0.08 - 0.42)</td>
<td>0.0001</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥67 yrs</td>
<td>2.09 (1.16 - 3.78)</td>
<td>0.01</td>
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<tr>
<td>59 - 66 yrs</td>
<td>1.55 (0.84 - 2.87)</td>
<td>0.16</td>
</tr>
<tr>
<td>50 - 58 yrs</td>
<td>1.14 (0.59 - 2.15)</td>
<td>0.69</td>
</tr>
<tr>
<td>≤49 yrs</td>
<td>1.00</td>
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Gender and Family history of IHD tested significant in univariate analysis but were proven to be insignificant (p>0.05) in multivariate analysis and hence were not included in the multivariate model.
Discussion

This data demonstrates important differences in baseline characteristics and clinical outcome between patients presenting with first Q wave and non-Q wave MI. Majority of the risk factors associated with MI did not show a statistically significant difference in their distribution between Q wave and non-Q wave MI. This is consistent with data from previous studies\textsuperscript{10,11} Coll et al\textsuperscript{12} showed that patients with non Q wave MI were significantly younger. On the other hand Nicod et al observed that patients with non-Q wave MI were significantly older\textsuperscript{7}. However he had excluded patients in whom location of infarct could not be determined.

Stone et al observed more diabetics in the group of patients with non-Q wave MI\textsuperscript{8}. In our study sample, family history of IHD was found more frequently in patients with Q wave MI. A higher CK peak value was also found in Q wave vs non-Q wave MI. This is consistent with previous studies\textsuperscript{23,24}. The biological rationale underlying this observation is that patients with non-Q wave MI\textsuperscript{8}'s often exhibit partial coronary occlusion in the infarct territory. On the other hand, patients with Q wave MI’s often have total coronary artery occlusion in the infarct territory. This leads to increased infarct size and thus higher peak CK levels\textsuperscript{33,34}.

Multivariate analysis indicates that Q wave MI patients have higher in-hospital mortality than non-Q wave MI patients, with a similar trend being observed for 1 year mortality. This finding corroborates the results of many recent studies\textsuperscript{19,20,25,26}. Regarding long term mortality, patients with Q wave MI exhibited marginally increased mortality than patients with non-Q wave MI (OR = 1.45, 95% CI 0.98 - 2). However, much controversy surrounds this issue, since literature is available suggesting that Q wave and non Q wave MI patients have similar short term\textsuperscript{20} and long term survival\textsuperscript{8}. However, it should be noted that these studies also included patients with previous MI\textsuperscript{8,21} used only univariate analysis\textsuperscript{21} and excluded a subgroup of patients having antero-inferior MI\textsuperscript{8}.

Smoking had a beneficial effect on survival in in-hospital mortality. This finding is supported by previous literature\textsuperscript{34}. The biological rationale for this effect is that smokers develop occlusive coronary thrombi at an earlier stage of atherosclerosis than in non-smokers. Thus, left ventricular function is relatively well preserved following MI in smokers, owing to the less advanced stage of coronary atherosclerosis. Hence, in-hospital mortality is lower in smokers compared to non-smokers. However, smokers tend to suffer a higher frequency of reinfarctions, which reduces their long-term survival\textsuperscript{34}. The results show a protective effect of smoking on mortality at 1-year follow up as well as for time to death following discharge from hospital. This may be explained by the limited follow-up period of this study.

Patients over 67 years of age had increased risk of dying than patients below 50 years of age for in hospital mortality, 1-year mortality and early death following discharge. This is supported by Mocetti et at\textsuperscript{29} who also showed a higher in hospital and 6 month mortality in patients above 70 years.

In conclusion, patients with first Q-wave MI had a worse prognosis than patients with non Q wave MI. Hence they warrant a closer follow-up and aggressive risk reduction measures. Additional planned prospective studies are needed to evaluate whether early aggressive intervention may beneficially modify the natural history of this disease.

Limitations of the study

Although multivariate analysis was used to adjust for prognostic factors affecting survival after MI (Q wave v/s. non Q-wave), medications given to patient after hospital discharge could modify the long-term outcome. Such data was not reliably available for many subjects and were therefore, not included in the analysis. Records did not contain adequate data for quantifying time lag between symptom onset and hospital presentation of MI patients. Therefore, the peak CK levels may not be a reliable estimate
of the actual infarct size in these patients. Another limitation of the study was that the cause of death could not be ascertained on telephonic interview. For that reason, all cause mortality was used.

References