Original Article

Sudden cardiac death early after ST elevation myocardial infarction with and without severe left ventricular dysfunction

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ABSTRACT

Introduction: There is high incidence of SCD in the early period following STEMI. We compared the temporal patterns and predictors of SCD amongst patients with LVEF ≤35% and LVEF >35%.

Methods: Data from STEMI patients was prospectively collected. SCD cases formed the study cohort and were categorized into 2 groups based on their LV function.

Results: There were 929 patients (mean age 55 ± 17 years) with a follow up of 41 ± 16 months. 154 pts (16.6%) had LVEF ≤35% (Group A, LVEF-29.9% ± 6%) and 775 pts had LVEF >35% (Group B, LVEF – 49% ± 14%). The two groups were similar with respect to sex distribution, age, prevalence of hypertension, and mean period of presentation. They differed in incidence of anterior wall MI (77.2% vs 55%), reperfusion (69% vs. 75%), prevalence of diabetes (50.6% vs 42%), and medication non-compliance (34% vs. 13%). The total SCD was 78 [Gp A, 25 (16.2%); Gp B, 53 (6.8%); p < 0.001]. The temporal cumulative SCD related mortality in the 2 groups was 1st month (8% vs. 4% p = 0.075), 3 months (14% vs. 5%, p < 0.001), 6 months (17% vs. 5%, p < 0.001), 1 year (18% vs. 6%, p < 0.001), at end of follow up (27% vs. 8%, p < 0.001). Multivariate predictors of SCD were medication compliance in the first month, and severe LV dysfunction with medication compliance beyond 1st month.

Conclusion: The incidence of SCD is high in first month after STEMI, irrespective of LV function. The number of SCD is higher in Group B patients. Algorithms to assess risk of SCD in early post STEMI period are urgently needed.
1. Introduction

Acute myocardial infarction (MI) constitutes the commonest cardiovascular substrate for sudden cardiac death (SCD). It has been observed that there is a clustering of SCD cases in the early post MI period and we found in an earlier study that a significant proportion of SCD occur in the first month following ST elevation myocardial infarction (STEMI) event. This report is designed to compare the temporal patterns and predictors of sudden death amongst the STEMI patients with and without LV dysfunction.

2. Methods

The patient population was obtained from a large tertiary cardiac care centre. The methodology and patient characteristics have been previously described. Briefly, patients admitted with acute STEMI were entered into a predesigned data base and follow up data was collected over a 3 year period. Deaths were classified as cardiovascular deaths (CVDs), non-cardiovascular or unclassifiable. CVDs were further classified as sudden or non-sudden. Classification of deaths was done by two independent monitors and resolved by an adjudicator in case of conflict. This study was approved by the institutional ethics committee.

3. Definitions

For the purpose of this study we used the following definitions which were used in our earlier study.

1. CVD: Deaths related to heart failure, ischemia, recurrent infarction, arrhythmic and non-arrhythmic sudden deaths, and cerebrovascular accidents.
2. SCD: CVD was defined as sudden if it was: (A) a witnessed death that occurred within 60 min from the onset of new symptoms unless a cause other than cardiac was obvious; (B) an unwitnessed death (<24 h) in the absence of pre-existing progressive circulatory failure or other causes of death; or (C) death during attempted resuscitation.
4. Compliance with medications: Patients who took at least beta blockers and antiplatelet drugs.

4. Statistics

Statistical analyses were performed using MedCalc for Windows, V.12 – 1993e2011 (MedCalc Software, Mariakerke, Belgium). Discrete variables were presented in percent and continuous variables as mean ± 6 standard deviation (SD). Chi-square test was done to compare discrete variables and t-test was done to compare continuous variables. Cumulative event rates were calculated with the use of the Kaplan–Meier method. Multivariate analysis was performed using the Cox proportional-hazards regression. Event times for all patients were measured from the time of admission.

5. Results

There were 929 patients (765 male and 164 female) with STEMI followed up for a mean period of 41 ± 16 months. Their mean age was 55 ± 17 years (Female: 60 ± 11 years; Male: 54 ± 18 years). Patients were categorized into 2 groups based on their pre-discharge LV function assessment. Patients with LV ejection fraction (LVEF) ≤35% (n = 154) constituted group A, while those with LVEF >35% (n = 775) were included in group B. The demographic characteristics of these two cohorts are summarized in Table 1. The two groups were comparable with respect to age and sex distribution and presentation time, but the proportion of anterior wall MI and diabetes mellitus, incidence of reperfusion were higher in cohort A. Non-compliance with evidence based medication was significantly higher in cohort A compared to cohort B (34% & vs. 13%, p < 0.001).

At the end of follow up the total mortality was 62 (40.3%) in group A and 97 (12.5%) in group B (p < 0.001). Of these, the number of patients who were adjudicated to have died due to SCD were 25 (16.2%) and 53 (6.8%) respectively (p < 0.001). The temporal profile of SCD is shown in Fig. 1. The cumulative SCD related mortality in group A was 12% (8%) in the 1st month, 15% (14%) in the first 3 months, 17% (17%) in the 1st 6 months, 18% (18%) in the first year and 25% (27%) at the end of follow up. The corresponding numbers in group B were 34%(4%), 34%(5%), 36%(5%), 42%(6%) and 53%(8%) respectively [p = 0.075, <0.001, <0.001, <0.001, <0.001 respectively.] In both the groups most of the SCD cases occurred in the first month. This is apparent by the fact that 12 out of total 25 SCD in Group A and 34 out of total 53 SCD in Group B occurred in this period (p = 0.186).

The effect of various factors influencing the occurrence of SCD was analyzed over time. Table 2A and B show the effect of predictive factors in the first month and beyond following STEMI. During the first month, univariate analysis demonstrated LV dysfunction, diabetes mellitus, absence of reperfusion and revascularization, non-compliance with

### Table 1 – Demographic characteristics (n = 929).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A (n = 154)</th>
<th>Group B (n = 775)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:Female</td>
<td>127:27</td>
<td>638:137</td>
<td>0.3331</td>
</tr>
<tr>
<td>Mean age</td>
<td>57.92 ± 20 yrs</td>
<td>54.95 ± 20 yrs</td>
<td>0.0534</td>
</tr>
<tr>
<td>Diabetes</td>
<td>80 (50.6%)</td>
<td>325 (42%)</td>
<td>0.0111</td>
</tr>
<tr>
<td>Hypertension</td>
<td>88 (55.7%)</td>
<td>401 (52%)</td>
<td>0.1103</td>
</tr>
<tr>
<td>Reperfused</td>
<td>106 (69%)</td>
<td>584 (75%)</td>
<td>0.0454</td>
</tr>
<tr>
<td>Revascularized</td>
<td>56 (36%)</td>
<td>309 (40%)</td>
<td>0.2164</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>122 (77.2%)</td>
<td>428 (55%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time of presentation</td>
<td>4.46 ± 4</td>
<td>3.96 ± 3</td>
<td>0.0815</td>
</tr>
<tr>
<td>Mean LVEF</td>
<td>29.9% ± 6%</td>
<td>49% ± 14%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non-compliance</td>
<td>53 (34.4%)</td>
<td>104 (13.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>with evidence based medication</td>
<td></td>
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</tr>
</tbody>
</table>
medication and female sex to be predictors of SCD, however multivariate analysis revealed only non-compliance with medication to be a significant predictor of SCD. In contrast, after 1 month, univariate predictors of SCD were presence of severe LV dysfunction, absence of reperfusion and revascularization, female sex and lack of compliance to evidence based medication. Multivariate analysis narrowed these predictors to severe LV dysfunction and lack of compliance to medications.

6. Discussion

SCD constitutes 10% of total mortality in India with acute coronary events being the commonest etiology.2 It remains the most unpredictable catastrophic clinical event in post STEMI patients. The risk is high in the initial period following acute MI but continues to exist in patients with remote MI and LV dysfunction. While implantation of ICD has been proven to provide safety from SCD in the latter group of patients, this strategy has not been found useful in tackling the arrhythmic mortality in the early period. This inference was drawn from the DINAMIT trial where ICD in early post MI period (6–40 days) in patients with LVEF ≤35% and autonomic impairment showed no mortality benefit at 1 year (7.5% vs. 6.9%).3 It was found that non-arrhythmic deaths resulting from worsening ventricular function from increased shocks in addition to cardiac rupture and pump failure negated the beneficial effect of defibrillators. It is to be highlighted that this and other ICD studies focused on the presence of severe LV dysfunction for risk stratification.

This study has 2 important observations. Firstly, most of the SCD cases post STEMI occur in the 1st month and presence of severe LV dysfunction alone cannot be relied upon to stratify risk in this period. This is shown by the fact that in the first month, SCD related mortality was statistically not different in the 2 groups. Secondly, the SCD burden is higher in the group with better LV function, as seen by the fact that in this period 34 out of 46 SCD occurred in this group. Being numerically the larger group, the SCD numbers are logically more in this cohort, though the proportion of SCD in patients with LVEF ≤35% is higher. Both these facts have significant clinical implications. It has been shown in our earlier study and by other groups that mortality and SCD are more common after MI in the first few months. Data from the western world show that early revascularization particularly by primary PCI and use of evidence based medications have contributed to progressive decline in mortality during this period.4–12 Unfortunately these positive trends have not percolated to India and other similar nations.1 This is also evident in our results which show that in the early post MI period compliance to evidence based medications was the only factor by

<table>
<thead>
<tr>
<th>Predictor</th>
<th>b</th>
<th>SE</th>
<th>Wald</th>
<th>Exp(b)</th>
<th>95% CI of Exp(b)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF ≤ 35%</td>
<td>0.4379</td>
<td>0.3446</td>
<td>1.6150</td>
<td>0.6454</td>
<td>0.3296–1.2637</td>
<td>0.2038</td>
</tr>
<tr>
<td>Non-compliance with evidence based medications</td>
<td>5.5381</td>
<td>0.7365</td>
<td>56.5405</td>
<td>254.1959</td>
<td>60.4551–1068.8184</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Absence of reperfusion or revascularization</td>
<td>0.1955</td>
<td>0.3031</td>
<td>0.4158</td>
<td>1.2159</td>
<td>0.6732–2.1959</td>
<td>0.5191</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.2834</td>
<td>0.3328</td>
<td>0.7247</td>
<td>1.3276</td>
<td>0.6937–2.5406</td>
<td>0.3946</td>
</tr>
</tbody>
</table>

Fig. 1 – Kaplan-Meyer survival curves of sudden cardiac death free survival in Group A (LVEF ≤ 35%) compared with Group B (LVEF > 35%) show that the curves are parallel till the first month following which they start diverging. The right panel is a magnified version of the initial portion of the graph. This figure shows that there is no difference in the occurrence of SCD between the two cohorts in the first month after STEMI (p = 0.37), while the incidence increases in the Group A after this period and continues till end of follow up (p < 0.0001).
multivariate analysis that predicted SCD. Beyond this period predictably severe LV dysfunction was the only factor influencing occurrence of SCD. These results demonstrate that focusing on LV function alone in the early post MI period may result in under recognizing a number of potential SCD cases. The number of SCD in the group B is not insignificant and there exists a strong case for evolving risk stratification strategies for patients with relatively preserved LV function in this period. There has been active work in this area and we may expect robust SCD risk predictors in the early post MI population in the near future. Zaman et al. used electrophysiological studies following primary PCI to recommend ICD implantation. They were successful in showing a mortality reduction at 12 months by employing this strategy in a select subgroup of patients with LVEF <40%. This study however did not include patients with better LV function.13 Echocardiographic parameters like global longitudinal strain have been explored as markers of SCD in both preserved and impaired LV function and this parameter did not only risk stratify the patients with good LV function for SCD risk, but also identified patients with significant LV dysfunction who were not at high SCD risk.14 There is data showing value of some cardiac biomarkers in predicting myocardial fibrosis and mortality in heart failure population. These and other biomarkers may be investigated as components of risk stratification algorithms.15 In the present times where extended loop recorders (ELR) are available which can non invasively record cardiac rhythms, it may be useful to employ them in early post MI period. There could be increased role for external wearable defibrillators in select group of patients. Another clinically relevant observation that emerges in this report is the consistent correlation of SCD and compliance with evidence based medications throughout the study period. This fact assumes importance when seen in the background of PURE study where there was gross under usage of evidence based medications for secondary prophylaxis in patients from low income countries.16 There is hence considerable wisdom in prioritizing health care resources to ensure early reperfusion and effective compliance with medications. This would certainly be a cost effective strategy to combat SCD in India.

7. Limitations of the study

This is a single center study with relatively small number of SCD. The follow up was not regulated by a protocol. However, this presents a real life practice scenario which is representative of contemporary Indian practice.

8. Conclusions

Patients with STEMI are at increased risk of SCD in the 1st month irrespective of presence of severe LV dysfunction and in terms of absolute numbers, SCD is higher in patients with preserved LV function. There is a need to evolve risk stratification algorithms beyond LV function this period.

Conflicts of interest

All authors have none to declare.

REFERENCES


