INDIAN HEART JOURNAL 66 (2014) 569–573

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ihj

Original Article

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

Nishad Chitnis [a], *Sudhindra Vooturi* [b], *B. Hygriv Rao* [c,*]

[a] *Cardiologist, Dept. of Cardiology, Krishna Institute of Medical Sciences, Hyderabad 500003, India*

[b] *Physiotherapist and Statistician, Dept. of Physiotherapy, Krishna Institute of Medical Sciences, Hyderabad 500003, India*

[c] *Director Pacing & Electrophysiology, Dept. of Cardiology, Krishna Institute of Medical Sciences, Hyderabad 500003, India*

ARTICLE INFO

Article history:
Received 25 August 2014
Accepted 17 October 2014
Available online 14 November 2014

Keywords:
Sudden cardiac death
STEMI
LV dysfunction
India
First month

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.

* *Corresponding author*. Tel.: +91 40 27725000.
E-mail address: hygriv@hotmail.com (B. Hygriv Rao).

http://dx.doi.org/10.1016/j.ihj.2014.10.416

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.[1] This report is designed to compare the temporal patterns and predictors of sudden death amongst the STEMI patients with and without severe 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.[1] 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]

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.
3. Severe LV Dysfunction: LV ejection fraction ≤35%, assessed by 2D Echocardiogram by standard methods.
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 ($p \leq 0.001$). Of these, the number of patients who were adjudicated to have died due to SCD were 25 (16.2%) and 53 (6.8%) respectively ($p \leq 0.001$). 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 ($n = 929$).

Characteristic	Group A ($n = 154$)	Group B ($n = 775$)	p Value
Male:Female	127:27	638:137	0.3331
Mean age	57.92 ± 20 yrs	54.95 ± 20 yrs	0.0534
Diabetes	80 (50.6%)	325 (42%)	0.0111
Hypertension	88 (55.7%)	401 (52%)	0.1103
Reperfused	106 (69%)	584 (75%)	0.0454
Revascularized	56 (36%)	309 (40%)	0.2164
Anterior MI	122 (77.2%)	428 (55%)	<0.0001
Time of presentation (in hours)	4.46 ± 4	3.96 ± 3	0.0815
Mean LVEF	29.9% ± 6%	49% ± 14%	<0.0001
Non-compliance with evidence based medication	53 (34.4%)	104 (13.4%)	<0.0001

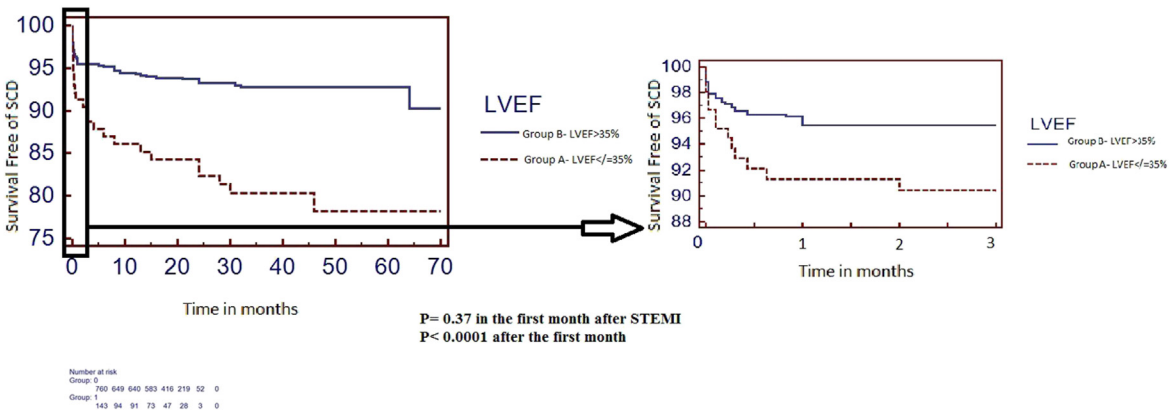

Fig. 1 – Kaplan-Meyer survival curves of sudden cardiac death free survival in Group A (LVEF ≤ 35%) compared with Group B (LVEF > 35%) show that the curves are parallel till the first month following which they start diverging. The right panel is a magnified version of the initial portion of the graph. 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 ($p < 0.0001$).

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 2A – Predictors of sudden cardiac death in the first month after STEMI multivariate analysis.

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

Table 2B – Predictors of sudden cardiac death beyond one month following STEMI multivariate analysis.

Predictor	*b*	SE	Wald	Exp(b)	95% CI of Exp(b)	*p*
LVEF ≤ 35%	1.5061	0.3677	16.7792	4.5091	2.2015–9.2356	<0.0001
Non-compliance with evidence based medications	3.6924	0.7629	23.4230	40.1420	9.0675–177.7106	<0.0001
Absence of reperfusion or revascularization	0.6306	0.3863	2.6648	1.8788	0.8845–3.9906	0.1026
Female sex	0.3077	0.4368	0.4960	1.3602	0.5803–3.1884	0.4813

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 etal 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

1. Rao BH, Sastry BKS, Korabathina R, Raju KP. Sudden cardiac death after acute ST elevation myocardial infarction: insight from a developing country. *Heart Asia*. 2012:83–89.
2. Rao BH, Sastry BK, Chugh SS, et al. Contribution of sudden cardiac death to total mortality in India – a population based study. *Int J Cardiol*. 2012 Jan 26;154:163–167.
3. Hohnloser SH, Kuck KH, Dorian P. Prophylactic Use of an implantable Cardioverter–defibrillator after acute myocardial infarction. *N Engl J Med*. 2004;351:2481–2488.
4. Seghieri C, Mimmi S, Lenzi J, et al. 30-day in-hospital mortality after acute myocardial infarction in Tuscany (Italy): an observational study using hospital discharge data. *BMC Med Res Methodol*. 2012;12:170.
5. Dorsch MF, Blackman DJ, Greenwood JP, et al. Primary percutaneous coronary intervention for acute ST elevation myocardial infarction – first year's experience of a tertiary referral centre in the UK. *Clin Med*. 2008;8:259–263.
6. Adabag AS, Therneau TM, Gersh BJ, et al. Sudden death after myocardial infarction. *JAMA*. 2008 (5);300:2022–2029.
7. Bigger JT, Fleiss JL, Kleiger R, et al. The relationships among ventricular arrhythmias, left ventricular dysfunction, and mortality in the 2 years after myocardial infarction. *Circulation*. 1984;69:250–258.
8. Myerburg RJ, Kessler KM, Castellanos A. Sudden cardiac death: structure, function, and time-dependence of risk. *Circulation*. 1992;85:I-2–I-10.
9. Hohnloser SH, Gersh BJ. Changing late prognosis of acute myocardial infarction: impact on management of ventricular arrhythmias in the era of reperfusion and the implantable cardioverter-defibrillator. *Circulation*. 2003;107:941–946.
10. Abildstrom SZ, Ottesen MM, Rask-Madsen C, et al. Sudden cardiovascular death following myocardial infarction: the importance of left ventricular systolic dysfunction and congestive heart failure. *Int J Cardiol*. 2005;104:184–189.

11. Piccini JP, Zhang M, Pieper K, et al. Predictors of sudden cardiac death change with time after myocardial infarction: results from the VALIANT trial. *Eur Heart J*. 2010;31:211–221.
12. Israel CW. Mechanisms of sudden cardiac death. *IHJ*. 2014;66:S10–S17.
13. Zaman S, Narayan A, Thiagalingam A, et al. Significance of repeat programmed ventricular stimulation at electrophysiology study for arrhythmia prediction after acute myocardial infarction. *Pacing Clin Electrophysiol*. 2014 Jul;37:795–802.
14. Ersbøll M, Valeur N, Andersen MJ, et al. Early echocardiographic deformation analysis for the prediction of sudden cardiac death and life-Threatening arrhythmias after myocardial infarction. *J Am Coll Cardiol Img*. 2013;6:851–860.
15. Januzzi Jr JL, Peacock WF, Maisel AS, et al. Measurement of the interleukin family member ST2 in patients with acute dyspnea: results from the PRIDE (Pro-Brain Natriuretic Peptide Investigation of Dyspnea in the Emergency Department) study. *J Am Coll Cardiol*. 2007 Aug 14;50:607–613.
16. Yusuf S, Islam S, Chow CK, et al. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. *Lancet*. 2011;378:1231–1243.