

Therapeutic Addressal of Post-Myocardial Infarction Ventricular Tachycardia: Implantable Cardiac Defibrillator Versus Medical Therapy

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Abstract

Objective: Sudden death due to the occurrence of sustained ventricular arrhythmia (VA) is the main contributor to total mortality in these high-risk post-Myocardial infarction (MI) patients, accounting for about 40% of all deaths. We aimed to assess long term follow up of patients with prior MI and Left Ventricular dysfunction (LVD) undergoing automatic implantable cardioverter-defibrillator (AICD) insertion for primary and secondary prophylaxis. *Methods:* All patients who had prior MI and LVD with symptomatic Ventricular Tachycardia (VT) or patients who underwent electrophysiological studies for inducing VT during 2000 to August 2013 were included for the retrospective analysis. Age, gender, clinical features, addictions, LVEF, survival, recurrence of arrhythmia, recurrence of symptoms and hospitalization for congestive heart failure (CHF), device therapy, were considered for the analysis. *Results:* In our study we had age matched patients with male predominant patient population. We found that Holter study was less predictive than electrophysiological study in detecting VT in patients with MI and LVD. It was found to have 15% survival benefit in AICD group. There was increased hospitalization in AICD group compared to Non-AICD group. Recurrence of arrhythmia and syncope was lower in AICD group whereas hospitalization due to CHF was higher in AICD patients. *Conclusions:* Our study shows that the implantation of a defibrillator in patients with a prior MI and LVD, with symptomatic or inducible VA on electrophysiological study has survival benefit, with increased incidence of hospitalization which can be attributed to Device therapy, CHF and morbidity due to longer life.

Keywords: Post MI; Ventricular Tachycardia; LV Dysfunction; Syncope; AICD.

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Reprints Requests

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Received on 14.09.2017,
Accepted on 25.09.2017

Introduction

Total mortality and sudden cardiac death (SCD) after acute myocardial infarction (MI) have significantly decreased in recent years, as a result of advanced therapy [1]. Nevertheless, there is a subgroup of patients with recent MI which remains at high risk of dying in the first months to two years after hospital discharge (overall mortality rate 20% at 2 years) [2]. Sudden cardiac death due to the

occurrence of sustained ventricular arrhythmia (VA) is the main contributor to total mortality in these high-risk post-MI patients, accounting for about 40% of all deaths [3]. It therefore crucial to identify and protect patients with prior MI who are prone to serious VA during follow-up, in order to reduce both SCD and all-cause mortality.

Sudden cardiac death can be identified by electrophysiology (EP) study using programmed electrical stimulation for ventricular tachycardia (VT)

induction protocol [4,5]. Patients who have monomorphic VT on EP study have high incidence of SCD. Syncope is known to be associated with arrhythmic episodes appropriately treated by ICDs. In present study, we compared two groups of patients with prior myocardial infarction and left ventricular dysfunction (LVD) who underwent EP study for VT induction or with symptomatic VT, requiring automatic implantable cardioverter-defibrillator (AICD) insertion versus those patients who were advised AICD but continued to be on medical management. We aimed to assess long term follow up of patients with prior MI and LVD undergoing AICD insertion for primary and secondary prophylaxis for assessing survival benefit, recurrence of symptoms, recurrence of arrhythmia, hospitalization for Congestive heart failure (CHF), VT, syncope, device therapy.

Materials and Methods

This was a retrospective study extended from year 2000 to 2013 at AIMS, Kochi. Data was collected from the records of medical record data and registers of patients undergoing EP study for inducible VT and newly enrolled patients during the study period. Follow up of patients with ICD was included during their regular visits. Patients who lost the follow up either due to death, change of place or non-compliance to the treatment were excluded from the study and mail or telephonic confirmation of data was recorded.

The study patients according to inclusion criteria were divided into two arms.

1st Group (ICD Group)

Included patients with prior myocardial infarction, LVD and symptomatic or inducible VT on EPS who underwent ICD implantation for primary or secondary prevention of SCD.

2nd Group (Non-ICD Group)

Included patients with prior myocardial infarction, LV dysfunction and symptomatic or inducible ventricular tachycardia on EPS who were advised ICD implantation for primary or secondary prevention of SCD, but were on medical therapy for social or medical reasons.

Electrophysiological Study

The protocol for EPS included delivery of 1, 2, and 3 ventricular extra stimuli at 2 right ventricular sites

at two different trains of pacing cycle lengths to induce ventricular tachyarrhythmia/ VF. The end point was the induction of sustained (duration ≥ 30 seconds) ventricular tachycardia or fibrillation or completion of the protocol. The patients were seen at 1 and 3 months after discharge and then every 6 months. Hospitalisation for recurrence of symptoms, VT or VF episodes, occurrence of CHF and other causes were studied. A full interrogation of the device in order to determine the status of the ICD generator and leads was done. The mode of delivered therapy (shocks or antitachycardia pacing) was recorded for every episode as well as and the number of therapeutic attempts of each mode. Inappropriate therapy was declared if antitachycardia pacing or shocks were given for a rhythm other than VT or ventricular fibrillation. Appropriate therapy was divided into effective or ineffective, according to the success in converting the tachycardia. Antiarrhythmic drug therapy was prescribed either before or after the implant.

Statistical Analysis

Categorical data was expressed as rates, ratios and percentages and the comparison was done using chi-square test. Continuous data was express as mean \pm standard deviation (SD). This was done with respect to the benefit of implantable cardiac defibrillator in patients who were advised ICD for inducible ventricular tachycardia over patients who were advised ICD but were on medical therapy.

Results

A total of 68 patients were included in the study as per inclusion criteria. Age, gender, comorbidities, type of MI, results of holter and EPS, echocardiographic parameters, coronary angiograms. Revascularization status and modality of revascularization, survival, hospitalization and recurrence of arrhythmias or syncope were studied in both the groups. Also were noted Device therapy and related complications. The age of the patients included in the study ranged from 27 to 80 years. Majority of patients 38 % in AICD group and 44% in medically managed group were in the age group of 61-70 years.

Most of the included patients were males 96% in AICD group whereas medically managed group had no female patients. Smoking was present in 62% patients in AICD group and 83% in non-AICD group. Hypertension was major risk factor and was seen in

64% patients in AICD group and 52% in non-AICD group. All the included patients were on drugs for hypertension. Most common drugs used were ACEI or ARBs (53%) for hypertension management.

Diabetes was absent in 62% patients in AICD group and 65% Non-AICD group. History of Anterior wall MI was given in 60% and 48% whereas pure inferior wall was involved in 29% and 48% patients in AICD and non-AICD group respectively. In this study beta-blockers were mainstay of drug treatment and was given to 98% in AICD group and 91% in non-AICD group, Digoxin was prescribed to 31% and 17% in respective groups. Coronary angiogram was done for all patients, 36% patient had triple vessel disease in AICD group, requiring revascularization whereas 39% were found to have recanalised vessels in non-AICD group.

In this study revascularization was done in 69% patients in AICD group, whereas it was seen that 52% patients in non-AICD group did not require revascularization. In small number of the patient revascularization was not possible and hence was left alone for medical management.

In patients in whom revascularisation was attempted, 58% was complete and 42% was partial in AICD group whereas it was found to be complete in 35% and partial in 65% patients in non-AICD group. Revascularization using PTCA was achieved in 04 (17.3%) and CABG in 04 (17.3%) patients in non-AICD group whereas revascularization with PTCA was higher 13 (28.8%) and CABG in 18 (40%) patients in AICD patients.

Holter study results showed 73% patients in AICD group and 74% patients in non-AICD group had normal study. Most common type of VT induced was

SMVT seen in 62% and 91% patients in AICD group and non-AICD groups respectively. In AICD group, 9% patients were detected to have VF during VT induction. VT was unstable in 69% and 65% patients in AICD and non-AICD groups respectively.

Regarding AICD therapy 22% patients were successfully reverted to sinus rhythm using ATP therapy and 20% patients received appropriate shock. Around 13% patients received both ATP with defibrillation. Inappropriate shock was delivered in 04 (8.8%) patients whereas 02 (4.4%) patients had unsuccessful ATP delivery for reversal of VT. No major device complications were found in 84% patients, whereas pocket infection was seen in 7% patients.

All-cause mortality in the study group was found to be 20% patients in AICD group and 35% patients in non-AICD group. Out of 09 deaths among AICD group, 05 were due to cardiac cause and 03 were due to non-cardiac cause whereas out of 08 deaths among non-AICD group, 04 were due to cardiac cause and 02 were due to non-cardiac cause, rest 03 patients died outside hospitalization and hence cause of death was unknown.

In 87% patients in AICD and 74% non-AICD group did not have recurrence of Syncope or presyncope after the initial presentation. The most common indication for hospitalisation in AICD group was for recurrence of VT (31%) followed by device therapy (27%) and CHF (9%) whereas recurrent VT and CHF constituted 13% each in Non-AICD group. Recurrent VT occurred in 38% patients in AICD group, whereas in 52% patients in non-AICD group arrhythmia could not be detected.

Table 1: Baseline Characteristics

Sr. No.	Characteristics	AICD	Non - AICD	P - Value
1	Study Population (No.)	45 (100%)	23 (100%)	
2	Age (Mean Years)	63.36 + 9.7	61.0 + 11.1	0.981
3	Male	43 (95.6%)	23 (100%)	0.789
	Female	02 (4.4%)	00 (0.0%)	
4	Smoking	28 (62.2%)	19 (82.6%)	0.149
5	Alcohol	27 (60.0%)	17 (73.9%)	0.386
6	Diabetes Mellitus	17 (37.8%)	08 (34.8%)	1.000
7	Hypertension	29 (64.4%)	12 (52.2%)	0.474
8	FBS (in Mg/Dl)	114.7 + 27.5	122.3 + 63.3	0.720
9	Urea (in Mg/Dl)	33.9 + 17.6	27.0 + 9.0	0.485
10	LDL (in Mg/Dl)	83.13 + 33.9	83.9 + 17.7	0.881
11	HDL (in Mg/Dl)	38.6 + 6.5	39.1 + 7.3	0.396
12	Triglyceride (in Mg/Dl)	123.4 + 65.5	131.8 + 62.1	0.511
13	LVEF (%)	32.2 + 6.3	33.4 + 6.1	0.882
14	LV IDD (in Mm)	63.0 + 5.7	61.3 + 7.6	0.720

Table 2:

Studies	All-Cause Mortality	
	AICD (%)	Non AICD (%)
OUR STUDY	20.0	35.0
MADIT	15.7	38.6
MADIT - II	14.2	19.8
MUSTT	25.0	32.0
BOKHARI ET AL.	26.0	46.6
CHAN ET AL.	13.9	19.7
ERMIS ET AL.	20.9	40.6

Table 3:

	AICD N=45	NON-AICD N=23
All Cause Mortality	09 (20%)	08 (34.8%)
Occurance of CHF	09 (20%)	07 (30.4%)
Recurrence of PRE Syncope or Syncope	06 (13.3%)	06 (26.1%)
Hospitalisation	24 (53.3%)	11 (47.8%)

Table 4:

Study	1 Year Survival	5 Year Survival
SINGH et al	98%	
RAPS study		
HOFFMANN et al.	98%	89%
Beth Israel study		
Lin et al	98%	87%
Cedars- sinai study, NY		
Our study	98%	93%

Discussion

The implantable cardiac defibrillator was introduced into practice in 1980 and several studies have reported the ability of this device to terminate ventricular fibrillation automatically. In this study the implantation of defibrillator improves survival among patients with prior myocardial infarction and left ventricular ejection fraction of 0.40 or less. As compared with conventional medical therapy group, defibrillator has lower incidence of death due to arrhythmia.

The two groups were age matched. The prescribed medications, including beta-blockers, had no discernible effect on the survival benefit derived from the defibrillator in this population. Our study had patients with mean age of 61.11±11.1 in Non-ICD group whereas AICD group had 63.36±9.7. Similarly MADIT trial included patients with mean age 64±9, comparable results were seen in MADIT II and MUSTT trials [6-8]. Majority of patients in this study were males (100% in non-AICD and 96% in AICD group). Similarly most trials reported male predominant study population. In a study by MacFadden et al, AICD related complications were more often in women than men. Our study had 82.6%

smokers in non-ICD and 62.2% AICD group. This result was comparable to incidence reported by other studies like MADIT and MADIT II.

The incidence of hypertension was 52.2% in non-ICD and 64.4% in AICD group. Diabetes Mellitus was 34.4% in Non-ICD and 37.8% in AICD group. Whereas MADIT reported 35% and 48% hypertensive patients in Non-AICD and AICD group and MADIT II trials had 53% in both groups. In study by Meyborg Mura et al, 45.1% were diabetics [9]. Similarly AVID trial reported lower incidence of Diabetes (25% in defibrillator group and 24% in antiarrhythmic group) whereas hypertension was reported in 55% and 56% patients respectively [10].

We included patients who had prior MI or recent MI >3 weeks before enrollment. Majority of patients had STEMI (88.9%) in AICD group and 95.7% in non-AICD group. Other studies included coronary artery disease patients but also had comparable incidence of MI in MUSTT trial and slightly lower incidence in MADIT II trial. Among 25 patients in the Non-AICD group, 91.3 % were given beta-blockers, and 87% were prescribed Amiodarone. In AICD group beta-blocker was prescribed in 98% patients and amiodarone in 68.9% patients. The commonest beta-blocker used was Carvedilol. Digitalis was used in 17.4% and

31.1% in Non-AICD and AICD group respectively, which was much underused as compared to other studies. Other trials report lower use of beta-blockers except MADIT II which had higher use of beta-blockers (70%) in both groups. MUSTT trial reported 26% patients discharged on Amiodarone. Amiodarone has mild antiadrenergic properties. Beta-blockers are often used to control rate of atrial fibrillation, thus preventing inappropriate shocks. Previous studies have reported that anti-arrhythmic drugs therapy guided by Holter as well as EPS did not improve survival. We reported that 56% in non-AICD and 67% in AICD group had serum Urea levels >25 mg/dl. As per our study, patient had renal cause related death in 2 patients. Other studies have lower incidence of elevated serum urea as reported in MADIT (21% and 22%) and MADIT II (29% and 32%) in Non-AICD and AICD trials respectively. The MADIT-II investigators revealed that factors such as hospitalization for heart failure or coronary events, elevated blood urea nitrogen levels, and poor NYHA functional class were reliable indicators of appropriate AICD firing.

Our study included patients with LVEF <40%. The average LVEF was 32.2 ± 6.3 in AICD group and 33.48 ± 6.1 in non-AICD group. LVEF has also been found to be associated with tachycardia acceleration and occurrence of syncope and proarrhythmia at follow-up in the Syncopal SMVT group in a study by Mauricio Abello et al [11]. In SCD-HeFT, the ejection-fraction threshold for entry into the trial was 35%, but the enrolled patients had a median ejection fraction of 25%, with an interquartile range of 20 to 30% [12]. A subgroup analysis of participants who had ejection fractions higher than 30% suggested no benefit from AICD therapy. A similar trend was seen in the MADIT and MADIT II study populations.

In this study revascularization was done in 68.9% in AICD group and 34.8% non-AICD group. Revascularization using PTCA was achieved in 17.3% and CABG in 04 (17.3%) patients in non-AICD group whereas revascularization with PTCA was higher 13 (28.8%) and CABG in 18 (40%) patients in AICD patients. It was also studied that revascularization was more complete in 57.8% in AICD group and much lower in Non-AICD group, which itself can be cause of persistent ischemia and strata for developing recurrent ventricular arrhythmias. MADIT II reported 56% and 58% patients in AICD and medical therapy group underwent CABG, whereas coronary angioplasty was done in 45% and 42% patients in respective groups.

EPS was performed without complications in majority of patients. We included patients who had

induced VT on EPS and SMVT was induced in 62.2% patients in AICD group and 91.4% patients in non-AICD group. SMVT is known to be common VT in ischemia heart disease patients and has more morbidity in these group of patients. Holter was less informative and reported to be normal in 73.4% and 72% in AICD and Non-ICD groups respectively. The MUSTT investigators demonstrated a statistically significant higher mortality rate among patients who had inducible ventricular arrhythmias on EPS. Such patients are more likely to develop new reentrant circuits, which could account for the higher-than-expected rate of VT even in those patients who displayed normal EPS at some point in time.

We studied survival as our primary endpoint to assess long term benefits of AICD insertion. There were 09 (20%) deaths in AICD group and 08 (35%) in non-AICD group. Patients assigned to receive the defibrillator had a much lower rate of death from primary arrhythmia than patients assigned to conventional therapy. It is noteworthy that there were more deaths from non-arrhythmic causes in the defibrillator group, possibly reflecting inaccuracy in classifying the cause of death. Though the results were not statistically significant but trend towards survival benefit is found. Total deaths in both groups were 17, of which 9 (20%) deaths in AICD group and 08 (35%) in non-AICD group.

MADIT II included Myocardial infarction with LVEF < 30% and randomized 1232 patients without prior EPS and studied all-cause mortality as primary endpoint. They reported 14.2% deaths in ICD group whereas 19.8% in medically managed group. MADIT II trials had 31% reduction in the risk of death in defibrillator group compared with conventional medical therapy. In contrast, MADIT trial survival rate improved within the few months after the implantation of the device, MADIT II had showed survival benefit after nine months after device implantation. The mortality rate in the conventional-therapy group was high (32 percent at two years), but it was consistent with that previously reported for a similar group of patients with inducible or non-suppressible ventricular tachycardia. MADIT trial reported 24 months mortality being 32% whereas AVID trial which had ICD inserted for secondary prophylaxis reported 24% mortality at 24 months. The CABG-patch trial had 18% mortality in defibrillator group [13]. In observational studies by Chan et al., Bokhari et al. and Ermis et al., the all-cause mortality was reported to be 13.9%, 26.0% and 20.9% in AICD group respectively [14-16].

We reported incidence of syncope/presyncope in both groups to be 26.1% in non-AICD group and 13.3%

in AICD group. Despite the high frequency of recurrent ventricular tachycardia, recurrent syncope is avoided presumably due to the rapid delivery of effective AICD therapy. Although specific references to the rate of recurrence of syncope in AICD recipients are scarce, data from other authors suggest a higher incidence of syncope as compared to our patients [17-20].

Ba"nsch et al. reported an actuarial incidence of syncope in the recipients of AICDs of 15% at 2 years [21]. Their population included 52% of patients with AICDs that did not allow antitachycardia therapy and discharges were initially adjusted to maximum energy. Kou et al. found a 9% recurrence of syncope at a mean follow-up of 16 months and 16% at 35 months, respectively, in a series of 180 patients who received an AICD after aborted sudden death or a history of syncope/ pre-syncope and documented ventricular tachycardia [22]. In all of these reports, high energy shocks were the only or predominant mode of therapy. Our therapeutic approach shows that a sizeable portion of ventricular tachycardia episodes could be successfully treated by antitachycardia pacing alone 10 (20.8%). Furthermore, failure of antitachycardia pacing or acceleration secondary to antitachycardia pacing was infrequent. Back-up shock therapy was necessary in only 09 episodes (18.8%).

In our study, hospitalization was not required in 21 (46.7%) and 15 (52.2%) patients in AICD and non-AICD group respectively. Among hospitalized patients, 31.1% were hospitalized for VT and 27.1% for device therapy in AICD group, whereas 13.0% patients were admitted due to CHF and VT equally in non-AICD group. Defibrillator shocks might contribute to recurrent hospitalizations and myocardial injury.

The non-AICD group may have arrhythmia which may go undetected due to various reasons and hence is under reported. The multicenter prospective report by the Slow VT Study Group in 2005 indicated that the incidence of slow VT in ICD recipients is relatively high, approaching 30%. In MADIT II trial new or worsened heart failure was slightly more frequent in defibrillator group than medically managed group.

In our study, 38 (83.6%) patients did not have any major complications. Pocket infection was commonest and seen in 03 (6.6%) patients while lead related problems was seen in 04 (8.8%) patients.

In other 53 studies including randomised control trial as well as observational study conducted at various places (Appendix Table 2, available at www.annals.org) showed that frequency of

postimplantation complications included 148 (1.4%) device malfunction, 161 (1.5%) lead problems, 76 (0.6%) implant site infections and 711 (5.8%) inappropriate shocks [23].

Limitations

We had small sample size to study the statistical significance. This was a non-randomized retrospective study. The study population had discrepancy in terms of types of ICDs implanted as well as the duration of follow up in the two groups – which may have significant impact on the final outcomes. Radiofrequency ablation as definite therapy for VT was not done in majority of patients. Most of the AICDs were of older generation where ATP during charging was not available for therapy.

Conclusion

Our study shows that the implantation of defibrillator in patients with prior myocardial infarction and left ventricular dysfunction, with symptomatic or inducible ventricular tachyarrhythmia on electrophysiologic study have a trend towards survival benefit, compared to similar group of patients on medical follow up. However, AICD group has more incidence of hospitalization due to Device therapy (appropriate and inappropriate) and complications.

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