Medical Science



TREATMENTS AND OUTCOMES OF CARDIAC ARRHYTHMIAS AFTER MYOCARDIAL INFARCTION: A PROSPECTIVE, FOLLOW UP STUDY IN A TERTIARY- CARE HOSPITAL

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ABSTRACT

Purpose: Cardiac arrhythmias after acute myocardial infarction (AMI) are associated with significant mortality and morbidity. There is little epidemiological data from India on patients developing cardiac arrhythmias as a complication of AMI. We recorded the patterns, treatments and predictors of post-AMI arrhythmias in the hospital. We also determined the outcomes at six months and assessed the predictors of mortality using multivariate logistic regression.

Results: We recruited 202 AMI patients, of whom 102 (50.5%) developed arrhythmia. The commonest arrhythmias were blocks (59, 57.8%) ventricular arrhythmias (31, 30.4%) and atrial arrhythmias (17, 16.7%). Older age (OR 1.07, 95% CI 1.04, 1.10, p<0.0001) and increased heart rate (OR 1.02, 95% CI 1.01, 1.04, p=0.005) were predictors of arrhythmias. Of 102 patients with arrhythmia, 92 (90.2%) received specific treatments and 10 (9.8%) were conservatively managed. Beta blockers were used in 69 (67.6%) patients followed by amiodarone (22, 21.6%) and calcium channel blockers (21, 20.6%). Among those with arrhythmias, 14 (13.7%) died at six months. A lower ejection fraction at presentation (OR 0.86, 95% CI 0.78, 0.95, p=0.003) was a significant predictor of mortality.

Conclusion: Older age and increased heart rate were significant predictors of arrhythmias and a lower ejection fraction was a predictor of mortality. A larger, multicentre study is required to understand the epidemiology of the disease in India and to assess the predictors and outcomes of post-AMI arrhythmias. This will help in better management of patients in the post infarction period and to improve outcomes.

KEY WORDS: Acute myocardial infarction, arrhythmias, India.

Introduction

The focus of disease has drastically shifted from communicable to noncommunicable diseases in India, the major cause of this shift being a rapid increase in patients with cardiovascular disease (CVD). What was initially thought to be a disease of prosperous, developed countries has become a major cause of mortality in middle and low- income nations. Within India, the disease is has a spread encompassing the urban and rural populations and is only expected to rise in the next few years. (Prabhakaran et al., 2016; Fuster, 2014; Narain at al., 2011) Ischemic heart disease and stroke have emerged as the two major diseases under the umbrella of CVD. (Prabhakaran et al., 2016) The recent increase can be attributed to better clinical diagnosis, more health care facilities, greater survival, and aging of the population. (Ahmad, 2005) The mean age for first AMI is lower in South Asian countries (53.0 years) compared to other countries (58.8). (Joshi, 2007) It is now known that about 90% of patients with AMI develop some form of cardiac arrhythmia during or immediately after the event. The risk of serious arrhythmias like ventricular fibrillation is greatest in the first hour and declines thereafter.(Adgey et al., 1968; Al-Khatib et al., 2002; Goldberg et al., 1992)

The bulk of evidence on post- infarction cardiac arrhythmias comes from Western studies and there are no data from India to date. We conducted this study to fill this gap in data. The objective of our study was to determine the demography, presentation, patterns, treatments and predictors of post myocardial infarction- cardiac arrhythmias in a tertiary care setting in India. We also sought to assess the outcomes in these patients at six months and determine the predictors of mortality.

Materials and methods

We conducted a prospective follow-up study at the Coronary Care Unit at St. John's Medical College and Hospital, Bangalore, a tertiary care centre in South India between January 2011 and June 2012. The study was approved by the local ethics committee and written informed consent was obtained from all patients prior to recruitment. We recruited consenting patients with acute myocardial infarction (AMI) and classified them into 2 groups. Group I were AMI patients who did not develop arrhythmia and group II were AMI patients who developed arrhythmia as a complication. Patients treated elsewhere and referred to this hospital for further management without adequate and reliable information on prior treatments received were excluded.

We calculated details on patient demographics, prescription treatments and the investigations carried out. At 6 months, we collected data on treatments and outcomes.

We summarized descriptive data as mean and medians and recorded crude rates of treatments and outcomes. We compared categorical variables using Chisquared tests and continuous variables using Student's t- test. Medians were compared using the Mann-Whitney U test. For comparison of categorical variables over time, we used the McNemar's test. To assess the determinants of arrhythmias, we used multivariable logistic regression analysis. The dependent variable was development of arrhythmia and independent variables were patient characteristics (age, sex, socio-economic status), time to reach hospital from onset of symptoms, risk factors (diabetes, hypertension, previous myocardial infarction, smoking, blood pressures, ejection fraction, and heart rate). To determine the predictors of mortality at 6 months, we again performed multivariable logistic regression analysis. The dependent variable was death at 6 months. In addition to the above independent variables, we included type of arrhythmia, treatments given in hospital and procedures performed. We report the adjusted odds ratios (with their 95% confidence intervals) for these analyses. In all analyses, a p value <0.05 was considered significant. Statistical analyses were performed using SPSS version 16.

Results

In a 13-month period (January 2011- December 2011), we recruited 202 patients. Of these, 100 had AMI only and 102 patients had AMI with arrhythmia. Table 1 depicts the baseline characteristics of patients. The overall mean SD age was 60.7 (13.55) years. Patients in the AMI with arrhythmia group were older than AMI only patients (64.6 vs. 56.7 years, p < 0.001). More patients in the AMI with arrhythmia group had a history of myocardial infarction as compared to the AMI only group (24.5% vs. 9%, p < 0.003). The mean duration of stay in hospital for all patients was 7.7 (SD 4.73) days.

Table 2 depicts the different type of arrhythmias. There were 18 different arrhythmias. Among the 102 patients, 78 (76.5%) developed one arrhythmia and 24 (23.5%) developed two or more arrhythmias during the course of the hospital stay. The commonest arrhythmias was conduction blocks, seen in 59 (57.8%) patients, about one- third of patients [31 (30.4%)] had ventricular arrhythmia, 17 (16.7%) developed atrial arrhythmia and 2 (2%) developed AV- nodal arrhythmia with a junctional rhythm. The commonest ventricular arrhythmia was ventricular tachycardia (VT), seen in 13 (12.7%) patients.

Table 3 depicts the pharmacological treatments. Overall, 32 (15.8%) patients received thrombolytic therapy. All patients received dual antiplatelet (aspirin and clopidogrel), 129 (63.9%) received angiotensin-converting enzyme inhibitors (ACE inhibitors), 127 (62.9%) received beta blockers, 98 (48.5%) received furosemide and 61 (30.2%) received spironolactone. ACE inhibitor use was

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greater in the AMI only group as compared to AMI with arrhythmia group (75% vs. 52.9%, p=0.001). Use of other drugs was similar in the two groups. Figure 1 depicts the different treatments in cardiac arrhythmias.

In the AMI with arrhythmia group, 92 (90.2%) received treatment for arrhythmia and 10 (9.8%) did not receive any treatment for their arrhythmias. Drug treatment was given to 91 (89.2%) patients. Beta blockers were given to 69 (67.6%) patients, amiodarone to 22 (21.6%), calcium channel blockers to 21 (20.6%), atropine and digoxin to 12 (11.8%) each. Non- pharmacological treatments were given to 28 (27.5%) patients. Among them, 17 (16.5%) patients received DC cardioversion, 5 (4.9%) received carotid sinus massage, 5 (4.9%) received temporary pacing and 4 (3.9%) received patients.

We performed univariate analysis, followed by a multivariable logistic regression analysis to assess the determinants of arrhythmias. In the univariate analysis, age, socio- economic status (SES) and pulse rate were found to be significant determinants. Older patients (OR 1.7, 95% CI 1.04, 1.10, p < 0.001) and these with a higher pulse rate were more likely to develop arrhythmia (OR 1.02, 95% CI 1.1, 1.04, p = 0.005).

At 6 months in this group, 7 (6.9%) died in hospital, 4 (3.9%) had a non-fatal cardiac arrest and 1 (1%) had a recurrent MI. Table 4 shows the outcomes of patients with AMI and arrhythmias.

Among the total 202 patients AMI, 14 (6.9%) died in the hospital, 7 in each group. Among 95 patients discharged from the AMI with arrhythmia group, betablockers were the most commonly prescribe anti-arrhythmic medication [71 (74.7%) patients], followed by calcium channel blockers [14 (14.7%)] and amiodarone [10 (10.5%)].

Discussion

There is little literature available from India on post- infarction cardiac arrhythmias and their management in the hospital. This study was done in those who developed cardiac arrhythmias after an episode of acute myocardial infarction (AMI). We assessed patient demographics, patterns of arrhythmias, the drug treatments and the rates of major outcomes at discharge and at six months.

Studies have shown that the incidence of conduction disturbances have not changed before and after the use of thrombolytics, but the incidence of complete heart block (CHB) has declined. (Go et al., 1998; Wong et al., 2006; Newby et al., 1998). As compared to large studies conducted in the United States, the rates of RBBB and LBBB in our study were higher. This could just be a play of chance as a result of our much smaller sample size. (Go et al., 1998) Many studies have shown a wide variation in the incidence of atrial tachyarrhythmias in the periinfarction period (6 to 20%) (Goldberg et al., 1990; Scmidtt et al., 2009) The rates observed in our study fell in this range. The rates of atrial fibrillation and paroxysmal supra- ventricular tachycardia (PSVT) also fell within the ranges quoted by previous studies (Jons et al., 2011; Wong et al., 2000; Ganz and Friedman, 1995). Coming to the ventricular arrhythmias, previous studies showed that after an event of AMI, VT is less common than VF. We noted a higher incidence of patients with VT compared to VF (11.8% vs. 7.8%). This could be due to two reasons. Firstly, it could be as a result of a high proportion with a previous myocardial infarction (24.5% patients), as a healed myocardial scar predisposes to VT during an attack of myocardial infarction. Another reason could be a higher mortality in AMI patients with VF due to sudden cardiac death (SCD) before presentation to the hospital. The data from such patients cannot be collected.

Our study found that older age and higher heart rate were predictors for arrhythmias. The association between older age and arrhythmias has been documented in the past. (Pirzada et al., 2009) On the other hand, the association between heart rate and arrhythmias seems uncertain, with studies showing arrhythmias occurring in patients with both low and high heart rates. A meta- analysis showed that lower heart rate at admission (weighted mean difference - 4.02 beats/ minute) was a risk factor for primary VF after AMI. (Gheeraert et al., 2006) Another study by Ohlow showed a higher risk of ventricular arrhythmias with heart rate greater than 100 beats/ minute. (Ohlow et al., 2012)

Treatments in this study largely complied with the American College of Cardiology and American Heart Association (ACC/AHA) guidelines. In accordance with the guidelines, atropine bolus was given for symptomatic bradyarrhythmias and complete heart block. Patients with partial, asymptomatic blocks like RBBB, LBBB and bifascicular blocks were not given any treatment. Literature shows that post- infarction atrial tachy-arrhythmias must be actively controlled as it can increase the oxygen demand, leading to exacerbation of myocardial ischemia. Recommendations for initial treatment are rate control, beta blockade is considered for unstable patients. (Antman et al., 2004; Antman et al., 2008; Epstein et al., 2008; Fuster et al., 2011) The drugs used for rate control in our study were intravenous (IV) beta blockers and intravenous verapamil, which agreed with the recommended guidelines. Most patients with were hemodynamically stable, hence DC cardioversion was not used. For rate control and maintenance of sinus rhythm, amiodarone was given. The 2004 ACC/AHA guidelines (Antman et al., 2004) recommend the following sequence for PSVT: Carotid sinus massage, intravenous adenosine, intravenous beta blockade with metoprolol or esmolol, and intravenous digoxin. Patients in our study were

treated in accordance with the guidelines. The CAST studies showed that treatment of ventricular premature beats (VPBs) with antiarrhythmic drugs did not improve either short- or long-term outcomes; with some drugs, the mortality increased. (Echt et al., 1991) Hence the recommendations suggest that no treatment should be given for the suppression of asymptomatic VPBs. (Antman et al., 2004; Antman et al., 2008; Epstein et al., 2008; Fuster et al., 2011) In compliance with the guidelines, isolated cases of ventricular premature contractions and ventricular trigemini received only beta- blockers as therapy for acute MI. No specific anti- arrhythmic therapy was instituted. Unstable VT was considered a lifethreatening emergency and was treated according to ACLS protocols. (Neumar et al., 2010) The 2010 AHA guidelines gave weak recommendation for the use of intravenous lidocaine to the treat of recurrent sustained VT. In our study 13 (12.7%) patients presented with AMI and ventricular tachycardia during the study period. Among these patients 6 (5.9%) patients received amiodarone andinfusion followed by oral maintenance dose. Lignocaine bolus and infusion doses (as recommended) were used in 2 patients refractory to amiodarone treatment. Electrical cardioversion using DC current was done in 8 (7.8%) patients. The amount of current given ranged from 150- 300 Joules. Lastly, going by the guidelines, among the 10 (9.8%) patients with ventricular fibrillation (VF), half received amiodarone (infusion and maintenance) and 1 patient received lidocaine (bolus IV and infusion). Unsynchronized electrical cardioversion using DC current between 150-300 Joules was done for 8 (7.8%) patients.

The multivariable logistic regression analysis showed that ejection fraction was a significant predictor of mortality [OR 0.86, 95% CI (0.78, 0.95), p = 0.003]. As the ejection fraction increased, mortality was less likely to occur. Left ventricular systolic function is known to be a strong predictor for development of post-myocardial infarction arrhythmias. (Goldberg et al., 2008; Bigger et al., 1984) Lower values of LV ejection fraction (LVEF < 40%) are known to be better predictors of mortality due to arrhythmias in the post- infarction period than 24- hour ECGs. There are many studies that show the association between lower ejection fraction and development of arrhythmias, as well as its association with increased mortality. Robert J. Goldberg et al reported lower ejection fraction for that patients who developed ventricular fibrillation as compared to patients who did not develop VF. (Goldberg et al., 2008) The GUSTO-1 study noted that depressed ejection fraction was associated with a higher risk of sustained VT and VF (P <0.001). (Newby et al, 1998) Bigger et al reported a 2.5 times increase in risk of death in patients with LVEF <30% due to ventricular arrhythmias after myocardial infarction (Bigger et al., 1984)

In our study, patients who died soon after admission to the hospital could not be included. Also due to the small sample size, our study was underpowered to determine the effects of arrhythmia on outcomes with a greater degree of precision. In conclusion, a larger study that is regionally, or better still nationally representative study can reliably explore the patterns and determinants of the outcomes of arrhythmias in the post-infarction period. It will provide important data in this less-known area in medicine. More studies from different health- care setups in India (primary, secondary and tertiary care hospitals) on cardiac arrhythmias would reliably assess the burden, management and determinants of outcomes of cardiac arrhythmias in India.

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Parameter		Overall (202)	AMI only (100)	AMI with arrhythmia (102)	p- value	
Age Mean (SD)		60.7 (13.55)	56.7 (12.94)	64.6 (13.04)	p < 0.001	
Sex (%)	Male	139 (68.8)	68 (68.0)	71 (69.6)	0.805	
Distance to hospital Kms (IQR)		10 (5- 31.3)	10 (5- 38.8)	8 (4.8-30)	0.327	
Socio- economic status (%)	Rich	8 (4)	2 (2.0)	6 (5.9)	0.003	
	Upper middle	74 (36.6)	26 (26.0)	48 (47.1)	0.005	
	Lower middle	78 (38.6)	45 (45.0)	33 (32.4)		
	Poor	42 (20.8)	27 (27.0)	15 (14.7)		
Origin of patients	Rural	4 (2)	1 (1.0)	3 (2.9)	0.516	
	Semi- urban	31 (15.3)	17 (17.0)	14 (13.7)		
	Urban	167 (82.7)	82 (82.0)	85 (83.3)		
H/o Smoking	Never	123 (60.9)	59 (59.0)	64 (62.7)	0.313	
	Former	29 (14.4)	12 (12.0)	17 (16.7)		
	Current	50 (24.8)	29 (29.0)	21 (20.6)		
H/o Alcohol consumption	Never	144 (71.3)	69 (69.0)	75 (73.5)	0.375	
	Former	19 (9.4)	8 (8.0)	11 (10.8)		
	Current	39 (19.3)	23 (23.0)	16 (15.7)		
Time to primary treatment Hours (IQR)		12 (2.9-72)	12 (3-48)	12 (2.4-72)	0.840	
Co- morbidities	HTN	129 (63.9)	68 (68.0)	61 (59.8)	0.225	
	DLP	121 (59.9)	69 (69.0)	52 (51.0)	0.009	
	Diabetes	113 (55.9)	54 (54.0)	59 (57.8)	0.582	
	Previous MI	34 (16.8%)	9 (9)	25 (24.5)	0.003	
Key investigations	Angiogram	94 (46.5)	49 (49.0)	45 (44.1)	0.487	
	Angioplasty without stent	5 (2.5)	2 (2.0)	3 (2.9)	0.667	
	Angioplasty with stent	58 (28.7)	26 (26.0)	32 (31.4)	0.399	
	CABG	2 (1.0)	2 (2.0)	0 (0.0)	-	
Type of AMI (%)	STEMI	98 (48.5)	48 (48.0)	50 (49.0)	0.372	
	NSTEMI		104 (51.5)	52 (52.0)	52 (51.0)	
Pulse rate Mean (SD)		88.6 (24.01)	84.60 (14.53)	92.6 (30.33)	0.022	
Systolic BP Mean (SD)		133.4 (28.62)	139.6 (27.56)	126.8 (28.39)	0.002	
Diastolic BP Mean (SD)		84.6 (15.39)	87.7 (15.65)	81 (14.38)	0.003	
Ejection fraction Mean (SD)		46 (14.16)	47.5 (12.89)	44.4 (15.25)	0.159	
Patients with $EF < 40\%$; n (%)		58 (28.7)	25 (25.0)	33 (32.3)	0.188	
Duration of stay in days Mean (SD)		7.7 (4.73)	6.3 (4.03)	9.1 (4.96)	p<0.001	

Abbreviation key: AMI- Acute myocardial infarction; SD- Standard deviation; IQR- Interquartile range; H/o- history of; HTN- Hypertension; DLP- Dyslipidemia; CABG- Coronary artery bypass graft; STEMI- ST segment elevation myocardial infarction; NSTEMI- non ST segment elevation myocardial infarction; BP- Blood pressure; EF- Ejection fraction.

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Type of arrhythmia		Number of arrhythmias	Number of patients (102)	Total arrhythmias (129)
	Supraver	ntricular arrhythmias (39)		
Sinus tachyc	ardia	16 (15.7)	16 (15.7)	16 (12.4)
Sinus bradyc	ardia	4 (4.0)	4 (4)	4 (3.1)
Atrial arrhythmia	PSVT	5 (4.9)	17 (16.7) 17	17 (13.2)
	Flutter	2 (1.8)		
	Fibrillation	10 (9.8)		
Nodal arrhythmia (junctional rhythm)		2 (2.0)	2 (2)	2 (1.6)
	Condu	action disturbances (59)		
LBBB		12 (11.8)	59 (57.8)	59 (45.7)
RBBB		15 (14.7)		
Bifascicular block		5 (4.9)		
Left hemiblock		5 (4.9)		
1 st degree heart block		5 (4.9)		
2 nd degree heart block		1 (1.0)		
Complete hear	Complete heart block			
	Ventri	cular arrhythmias (31)		
Ventricular premature complexes 4 (4.0)		4 (4.0)	31 (30.4)	31 (24.0)
Ventricular bigemini		2 (1.8)		
Ventricular trigemini		2 (1.8)		
Ventricular tachycardia		13 (12.7)		
Ventricular fibr	illation	10 (9.8)		
Combination of an	rhythmias1	-	24 (23.5)	-

¹ This row depicts the number of patients who had a combination of ≥ 2 arrhythmias from same or different classes

Abbreviation key: PSVT- Paroxysmal supraventricular tachycardia; LBBB- Left bundle branch block; RBBB- Right bundle branch block

Drug Thrombolysis		Overall (202)	AMI only (100)	AMI with arrhythmia (102)	p- valu
		32 (15.8)	18 (18.0)	14 (13.7)	0.405
		Thrombolytic :	agents		
Thrombolysis drug	STK	22 (10.9)	11 (11.0)	11 (10.8)	0.333
	Tenecteplase	6 (3.0)	5 (5.0)	1 (1.0)	
	Reteplase	4 (2.0)	2 (2.0)	2 (2.0)	
		Antiplatelet a	8		
Aspirin		202 (100)	100 (100)	102 (100)	-
Clopidogrel		202 (100)	100 (100)	102 (100)	-
		Other drugs actin	g on CVS		
Beta blocker		127 (62.9)	69 (69.0)	58 (56.9)	0.074
Carvedilol		22 (10.9)	10 (10.0)	12 (11.8)	0.687
ACE inhibitor		129 (63.9)	75 (75.0)	54 (52.9)	0.001
ARB		26 (12.9)	12 (12.0)	14 (13.7)	0.714
Nitrate		42 (20.8)	22 (22.0)	20 (19.6)	0.675
Spironolactone		61 (30.2)	29 (29.0)	32 (31.4)	0.713
Furosemide		98 (48.5)	43 (43.0)	55 (53.9)	0.120
Calcium channel blocker		35 (17.3)	14 (14.0)	21 (20.6)	0.216
Trimetazidine		55 (27.2)	21 (21)	34 (33.3)	0.049
Nicorandil		52 (25.7)	22 (22.0)	30 (29.4)	0.228
		Hypolipidemic	agent		
Statin		178 (88.1)	85 (85.0)	93 (91.2)	0.175
	L. C.	Anti- coagulant	drugs		
Heparin		44 (21.8)	25 (25.0)	19 (18.6)	0.273
Enoxaparin		131 (64.9)	61 (61.0)	70 (68.6)	0.256
Dalteparin		20 (9.9)	12 (12.0)	8 (7.8)	0.323
Fondaparinux		8 (4.0)	5 (5.0)	3 (2.9)	0.453
Warfarin		11 (5.4)	2 (2.0)	9 (8.8)	0.033
	I_	Anti- diabetic	drugs		
Metformin		17 (8.4)	7 (7.0)	10 (9.8)	0.473
Regular insulin		91 (45.0)	41 (41.0)	50 (49)	0.252
Premixed insulin		9 (4.5)	3 (3.0)	6 (5.9)	0.321
NPH (Intermediate- acting) insul	n	62 (30.7)	29 (29.0)	33 (32.4)	0.605
		Miscellaneous	drugs		
Proton pump inhibitor		160 (79.2)	79 (79.0)	81 (79.4)	0.943
Ondansetron		57 (28.2)	29 (29.0)	28 (27.5)	0.807
- acetylcysteine		33 (16.3)	18 (18.0)	15 (14.7)	0.527

Abbreviation key: AMI- Acute myocardial infarction; STK- Streptokinase; ACE inhibitor- Angiotensin converting enzyme inhibitor; ARB- Angiotensin receptor blocker; NPH- Neutral Protamine Hagedorn insulin; CVS- Cardiovascular system

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Table 4: Outcomes in hospital at	1 month and at 6 months in nationts who d	lovelaned arrhythmias after AMI

Outcome	In hospital (102)	From discharge to 1 month (95) ¹	From 1 month to 6 months (90) ²	Total (102) ³
CCF	0 (0.0)	2 (2.1)	1 (1.1)	3 (2.9)
Stroke	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.0)
Recurrent MI	1 (1.0)	1 (1.1)	3 (3.3)	5 (4.9)
Non- fatal cardiac arrest	4 (3.9)	0 (0.0)	0 (0.0)	4 (3.9)
Death	7 (6.9)	3 (3.1)	4 (4.4)	14 (13.7)

¹At the first follow- up at 1 month, 2 patients were lost to follow up

² At the second follow- up at 6 months, 5 patients were lost to follow- up ³ Overall 7 patients were lost to follow- up

Abbreviation list: AMI- Acute myocardial infarction; CCF- Congestive cardiac failure; recurrent MI- recurrent myocardial infarction