Indian J Physiol Pharmacol 2012; 56(1) : 21–27

EJECTION FRACTION AT THE FIRST ATTACK OF MYOCARDIAL INFARCTION AND POSTINFARCTION SURVIVAL IN SOUTH INDIAN POPULATION

NIVEDITA NANDA[1]*, SANAT KUMAR SEN[1] AND MARK C. AROKIARAJ[2]

Departments of [1]Biochemistry and [2]Cardiology, Pondicherry Institute of Medical Sciences, Pondicherry – 605 014

(Received on March 7, 2011)

Abstract : Ischemic heart disease is estimated to be the most important cause of mortality by the end of 2020 world wide despite sufficient improvement in health care. It has several modifiable and few non modifiable prognostic variables. Therefore, we analyzed the data of all patients admitted for the first time for acute myocardial infarction (MI) and evaluated the long term modifiable prognostic variables retrospectively. We did not find any difference in the age, blood pressure, hematological and several biochemical parameters between patients who survived and those who expired in 4 years of follow up. Our study revealed that in the expired group patients, the mean admission heart rate, ejection fraction, serum urea and creatinine levels were higher and bicarbonate level was lower compared to survived group patients at the first attack of MI. Also, despite the less incidence of myocardial infarction in females, the percentage of cardiac death was higher in female MI patients. We suggest from our retrospective analysis that MI patients with higher heart rate, altered renal function and metabolic acidosis should be rigorously followed up and special counseling should be provided to old age female patients for better prognosis and survival.

Key words : myocardial infarction, ejection fraction, acidosis, female patients

INTRODUCTION

Myocardial infarction (MI) is the one of the commonest causes of morbidity and mortality in men and women worldwide (1, 2). MI is so common in developing countries such as India, by 2007 32% death were due to ischemic heart disease (IHD) alone (3). In India it has become the leading cause of death (4). Although a new epidemic, it has become a major health issue and mortality burden is expected to double by 2015 (5). According to the mortality estimate in Tamilnadu itself IHD related death is 36% (6). It is associated with few non modifiable (7) and several modifiable risk factors (7, 8,

*Corresponding Author : Dr. Nivedita Nanda, Department of Biochemistry, Pondicherry Institute of Medical Sciences, Pondicherry – 605 014, India; Email : drnivedita@pimsmmm.net

9). A drastic rise in the stressful yet sedentary life style, food intake rich in high energy and fat, smoking, lack of physical activities leading to obesity has led to the sharp rise in incidence of cases even in developing countries (10). Despite sufficient improvement in health care, ischemic heart disease is estimated to be the most important cause of mortality by the end of 2020 world wide (2).

The patients who survive the first attack of acute myocardial infarction are susceptible to heart failure, recurrence of angina, re-infarction, arrhythmias, and sudden cardiac death. Most deaths occur in the first six months after infarction (10). Advancing age is the most important non-modifiable prognostic factor for long-term prognosis (11) whereas the left ventricular function assessed clinically or quantified as either ejection fraction or end-systolic volume is the most important modifiable factor (10).

An ejection fraction less than 30% is reported to be a major risk factor for cardiac death and re-infarction, in the first year after myocardial infarction (12). Apart from ejection fraction, there are several other modifiable prognostic factors such as decreased heart rate variability, cigarette smoking, hypercholesterolemia, and diabetes mellitus etc. in a Spanish report it was found that the admission plasma glucose and first fasting blood glucose levels can predict the adverse outcome of acute coronary syndrome patients (13). Similarly, a report from Netherlands suggests that an impaired baseline renal function can add to the prognostic risk after first myocardial infarction (14). Similar works done in and Canada and USA showed that serum urea and creatinine levels are powerful indicators of post discharge mortality especially among the old aged cardiovascular patients and patients with systolic dysfunction respectively (15, 16). So, identification of these adverse prognostic factors can help in risk stratification and further modification of treatment regimen (1). However, similar reports on the predictive value of various biochemical or hematological parameters on cardio vascular mortality and survival after first attack of MI are missing in Indian studies.

Therefore, we wanted to assess the long-term (from 2006 to 2009) prognostic variables of cardiac death in MI cases. Hence, we retrospectively analyzed the recorded data (the biochemical and hematological parameters and cardiac markers at the time of admission) of MI patients admitted to Pondicherry Institute of Medical Sciences (PIMS) from 2006 to 2009.

MATERIALS AND METHODS

The cardiac marker enzymes, biochemical and hematological parameters of forty six MI cases admitted to PIMS from the period of 2006 to 2009 were collected. MI was confirmed based on their clinical features, ECG recordings and cardiac marker enzymes. The physiological parameters at the time of admission such as age, heart rate, systolic and diastolic blood pressures and respiratory rate were also noted down.

All biochemical parameters were estimated in the clinical biochemistry lab using commercial kits adapted to autoanalyser. Glucose estimation was by glucose oxidase peroxidase method (Enzopak;

Reckon Diagnostics, India), and Troponin I estimation was by rapid sensitive immunochemistry method (Biomed, India). The cardiac enzymes used as markers of MI such as total CK, CK-MB and LDH were assessed by kits from Enzopak (Reckon Diagnostics, India). Lipid profile parameters such as total cholesterol, triglyceride and HDL cholesterol were analyzed by using kits from Siemens (Siemens; Siemens Health Care Diagnostics Inc. USA). Sodium, potassium and chloride were assessed in a semi automated electrolyte analyzer (Ilyte, India). Total cell count, hemoglobin and packed cell volume were analyzed using commercial kits (Transasia, India) adapted to automated coulter (Sysmex XT 1800i, USA). ESR was evaluated by Wintrobe's method. RBC, platelet count, MCV, MCH and MCHC were determined from peripheral smear. PT-INR was evaluated using commercial kits (Tulip diagnostics, India).

Statistical analysis of data

The data are expressed as Mean±SD. Comparison between the two groups was done by Student's *t* test for parametric data and by Mann Whitney test for non-parametric data. Correlation between parameters was done by Pearson's correlation analysis. The p values less than 0.05 was considered significant.

RESULTS

The patients were divided into two groups. The first group was survived group consisting of patients who survived till 2009 and expired group consisted of patients who did not survive. The physiological parameters and ejection fractions are depicted in Table I while biochemical and hematological parameters are shown in Table II and III respectively.

The gender ratio showed that the male gender was predominant in survived group while percentage of female gender was more in the expired group. There was no difference in the admission age. There was no difference in the systolic and diastolic blood pressures and respiratory rate (Table I). However the admission heart rate was significantly higher in the expired group. Also the severity of myocardial dysfunction as assessed by the ejection fraction in ECHO was significantly higher in the expired group (Table I).

Admission values of urea (P<0.01) and creatinine (P<0.05) were significantly higher in the survived group. There was no difference in any other biochemical parameters and cardiac enzymes among the

TABLE I: Physiological parameters at the time of first admission of old MI patients: comparison of patients who survived versus who expired within 3 years of first attack.

	Survived (n=26)	*Expired (n=20)*
Females	6/26(23%)	7/17(41%)
Males	20/26(77%)	10/17(59%)
Age (Years)	57.34±13.05	64.05±7.24
HR (per min)	80.69±12.17	96.44±20.30**
SBP (mm Hg)	128.91±18.51	122.00±23.75
DBP (mm Hg)	81.00±11.06	75.46±16.46
Respiratory rate (per minute)	28.75±5.96	28.42±11.63
EF (%)	49.16±9.00	35.62±8.45*

Data presented as mean±SD. Analysis done by student's unpaired *t* test. *P<0.05 and **P<0.01; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; EF: ejection fraction.

TABLE II: Cardiac markers, enzymes and lipid profile at the time of first admission for old MI patients: comparison of patients who survived versus who expired within 3 years of first attack.

	Survived (n=26)	*Expired (n=20)*
FBS(mg/dL)	133.60±40.39	161.00±62.64
Urea (mg/dL)	29.64±17.63	63.21±44.68**
Creatinine (mg/dL)	1.34±0.77	2.29±1.80**
Troponin I positive (> 1 ng/mL)	12/26(46%)	7/17(41%)
CK (U/L)	233.10±160.00	551.77±312.49
CKMB (U/L)	68.35±35.31	97.27±57.74
LDH (U/L)	264.33±106.61	324.33±119.7
TC (mg/dL)	182.70±56.84	179.42±42.14
TG (mg/dL)	152.70±46.21	109.20±34.62
HDL (mg/dL)	36.60±6.22	34.80±6.83
LDL (mg/dL)	112.70±53.38	118.00±24.70
VLDL (mg/dL)	27.88±4.80	22.00±7.07
Na^+ (mM/L)	136.66±3.81	136.26±6.61
K^+ (mM/L)	4.21±0.58	4.76±1.19
Cl^- (mM/L)	101.23±6.12	100.88±7.37
$HCO3^-$(mM/L)	24.89±4.48	20.50±4.48*

Data presented as Mean±SD. *P<0.05 when analysis done by student's unpaired *t* test and ##P<0.01 when analysis done by Mann Whitney non parametric test.

TABLE III: Hematological parameters at the time of first admission for MI patients in survived and expired groups.

	Survived (n=26)	*Expired (n=20)*
Hb (g/dL)	12.39±3.52	11.33±2.87
PCV (%)	34.80±14.82	25.28±15.23
ESR (mm/1 hr)	50.10±8.73	104.66±16.00
PT-INR	1.40±0.34	1.10±0.14
RBC (millions/mm^3)	4.60±0.62	3.98±0.80
Platelet (lakhs/mm^3)	2.80±0.63	2.46±1.17
MCV (fL)	90.03±4.46	88.15±8.26
MCH (pg)	30.50±2.27	29.90±1.14
MCHC (g/dL)	34.00±1.86	34.05±2.59

Data presented as Mean+SD. Analysis done by student's unpaired *t* test.

2 groups (Table II). Also there was no difference in any of the hematological parameters (Table III). The ejection fraction was positively correlated with platelet count in the expired group of patients (Table IV).

TABLE IV: Correlation of ejection fraction (EF) of MI patients in survived group and expired group with platelet count and heart rate (HR).

	Survived group		*Expired group*	
	r	*P*	*r*	*p*
Platelet count	–0.94	0.067	–0.773	0.024
HR	–0.06	0.870	0.685	0.09

P<0.05 was considered significant.

DISCUSSION

In our study we found the admission age of survived group to be higher. However, this difference was not statistically significant. This could be due to a small sample size. Male gender is recognized as a risk factor for coronary artery disease below the age of 45 (17). In our study also the male cases were predominant in the survived group with an incidence of 77% and females were only 23%. However, it was surprising to note that the female gender percentage increased (41%) in the expired group. As the mean age for both the groups was higher than 45 yrs, the risk of MI is same for both the gender. Nevertheless, the increased percentage of female patients in expired group suggests that either female gender are more susceptible to cardiac death from re-infarction or they are paid less attention in our society in terms of health care especially in the old age in India.

The admission fasting blood sugar level was more than 126 mg/dl for both the groups. However, there was no statistical difference between the groups. DM is already an

established risk of MI (18). However, in our previous study we had reported an increased fraction of non diabetic and pre diabetic patients in MI cases in our area (19). Acute MI is an extremely stressful situation. So it is associated with release of higher level of stress hormones such as cortisol, catecholamines which have insulin antagonistic action can increase the blood glucose level. This could be the reason why the admission glucose value was higher in both the groups. It has been reported that among the non-diabetic patients with acute myocardial infarction, those with higher admission blood glucose had higher rates of death, re-hospitalization for heart failure, and re-hospitalization for non-fatal re-infarction (20). Hence, the importance of detection of higher admission value of plasma glucose should be taken seriously for a better prognosis during the subsequent period of follow up.

The percentage of troponin I positive case was almost equal in both the groups. There was no difference in the levels of CK, CK-MB and LDH. However, the severity of myocardial dysfunction as assessed by the ejection fraction in ECHO was significantly lower in the patients of expired group suggesting that gross reduction in left ventricular function at the time of admission itself is an indicator of poor prognosis. Previous reports suggest EF less than 0.3 which would be roughly 30% to be a risk factor for cardiac death and re-infarction (12), and in our study it was within the range of 27% to 43% in the expired group.

There was no difference in the admission lipid profile and electrolyte values. Conversely, the admission values of urea ($P<0.01$) and creatinine ($P<0.05$) were significantly higher in the survived group. There was no difference in any of the hematological parameters (Table III). This suggests that cardiac dysfunction was mostly accelerated in the expired group of patients due to early deterioration of their renal functions.

Despite the absence of difference in hematological parameters, there was a significantly negative correlation between the ejection fraction and platelet count in the expired group (Table IV). This correlation was not significant in the survived group. It is a well known fact that platelets play an important role in thrombosis as well as in acute ischemic coronary syndrome (17). In a previous report low platelet count was found to be associated with MI and peripheral artery disease patients (18). In contrast we found platelet count to be within the normal range in both the groups of our study. Despite this platelet count was negatively correlated with their left ventricular dysfunction (EF). To the best of our knowledge, this has not been reported earlier. An earlier report suggests increased platelet reactivity to be associated with poor prognosis in the MI survivors (19). It indicates that MI patients with higher platelet count and MI patients with normal platelet count but higher platelet reactivity also would be vulnerable to left ventricular dysfunction which just might be the case in our patients' group. Unfortunately there was no assay done on platelet reactivity in these patients so we do not have any direct data supporting our observation.

The mean bicarbonate value was lower in expired patients group compared to

survived patients (Table III). The base deficit indicates that patients in the expired group had metabolic acidosis at the time of their first attack of MI. Previous reports suggest that the lack of tissue perfusion and increased oxygen demand in MI leads to lactic acidosis and more often it is associated with cardiogenic shock. Severe acidosis itself can lead to ventricular arrhythmias (20). Acidosis per se can worsen fibrin polymerization and further strengthens the clot (21). Normally acidosis initiates hyperventilation to expel the excess acid as carbon dioxide in these MI patients as a compensatory mechanism. The patients who fail to expel the acids out by such physiological compensatory mechanisms would go through a prolonged period of metabolic acidosis which further can aggravate their condition.

From our study, we conclude that in Indian population, those MI patients whose admission values are associated with low ejection fraction, high platelet count or high platelet reactivity and acid base imbalance indicating acidosis are more vulnerable to cardiac death. Even when they survive the first attack of MI they have to be monitored more aggressively as part of their follow up. Also we propose that the old aged Indian female MI patients are more susceptible to cardiac death compared to male patients. Hence special attention and counseling should be provided to them and their family members to ensure better prognosis and a prolonged life span.

REFERENCES

1. Biaglehole R, Irwin A, Prentice T. The world health report: 2004: Changing history. WHO: Ed Biaglehole R. 2004; 120–124.
2. Murry CJ, Lopez AD. Global comparative assessments in the health sector; disease burden, expenditures and intervention. Geneva: WHO, 1994.
3. Mukherjee AK. Prediction of coronary heart disease using risk factor categories. *J Ind Med Assoc* 1995; 93: 312–315.
4. Ghaffar A, Reddy KS, Singhi M. Burden of non-communicable diseases in South Asia. *BMJ* 2004; 328: 807–810.
5. Gupta R. Escalating coronary heart disease and risk factors in South Asians. *Indian Heart J* 2007; 59: 214–217.
6. Gupta R, Misra A, Pais P, Rastogi P, Gupta VP. Correlation of regional cardiovascular disease mortality in India with lifestyle and nutritional factors. *Int J Cardiol* 2006; 108: 291–300.
7. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998; 97: 1837–1847.
8. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. *Diab Care* 2004; 27: 1047–1053.
9. Jensen G, Nyboe J, Appleyard M, Schnohr P. Risk factors for acute myocardial infarction in Copenhagen, II: Smoking, alcohol intake, physical activity, obesity, oral contraception, diabetes, lipids, and blood pressure. *Eur Heart J* 1991; 12: 298–308.
10. Woo KS, White HD. Factors affecting outcome after recovery from myocardial infarction. *Ann Rev Med* 1994; 45: 325–339.
11. Rich MW, Bosner MS, Chung MK, Shen J, McKenzie JP. Is age an independent predictor of early and late mortality in patients with acute myocardial infarction ? *Am J Med* 1992; 92: 7–13.
12. de Cock CC, Visser FC, van Eenige MJ, Roos JP. Short-term and long-term prognosis after myocardial infarction: prognostic value of coronary anatomy and left ventriculography. *Int J Cardiol* 1989; 24: 197–209.
13. Vivas D, Gracia-Rubira JC, Gonzalez-Ferrar JJ, et al. Prognostic value of first fasting glucose

measurement compared with admission glucose level in patients with acute coronary syndrome. *Rev Esp Cardiol* 2008; 61: 458–464.

14. Hillege HL, van Gilst WH, van Veidhuisen DJ, et al. Accelerated decline and prognostic impact of renal function after myocardial infarction and the benefits of ACE inhibition: the CATS randomized trial. *Eur Heart J* 2003; 24: 412–420.
15. Smith GL, Shlipak MG, Havranek EP, et al. Serum urea nitrogen, creatinine, and estimators of renal functions. *Arch Intern Med* 2006; 166: 1134–1142.
16. Jose P, Skali H, Anavekar N. Increase in creatinine and cardiovascular risk in patients with systolic dysfunction after myocardial infarction. *J Am Soc Nephrol* 2006; 17: 2886–2891.
17. James IC. Executive summary of the third report of the national cholesterol education programme (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel III). *JAMA* 2001; 285: 2486–2497.
18. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA* 1979; 241: 2035–2038.
19. Nanda N, Sen SK, Arokiaraj MC, Sripradha R, Roma R, Pattegar K. Fraction of non diabetic and prediabetic population in myocardial infarction: a retrospective analysis. *Ind J Physio Pharmacol* 2009; 53: 334–340.
20. Otten R, Kline-Rogers E, Meier DJ. Impact of pre-diabetic state on clinical outcomes in patients with acute coronary syndrome. *Heart* 2005; 91: 1466–1468.
21. Metha P, Metha J. Platelet function studies in coronary artery disease: evidence for enhanced platelet microthrombus formation activity in acute myocardial infarction. *Am J Cardiol* 1979; 43: 757–760.
22. Fagher B, Sjögren A, Sjögren U. Platelet counts in myocardial infarction, angina pectoris and peripheral artery disease. *Acta Med Scand* 1985; 217: 21–26.
23. Trip MD, Cats VM, van Capelle FJ, Vreeken J. Latelet hyper-reactivity and prognosis in survivors of myocardial infarction. *N Engl J Med* 1990; 31 322: 1549–1554.
24. Pilcher J, Nagle RE. Acid base imbalance and arrhythmias after myocardial infarction. *Br Heart J* 1971; 33: 536–532.
25. Engstrom M, Schott U, Roner B, Reinstrup P. Acidosis impairs the coagulation: a thrombo-elastographic study. *J Truma* 2006; 61: 624–628.