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## **$\beta$ -blockers in Post ST Elevation Myocardial Infarction Patient with Low Left Ventricular Systolic Function: A Retrospective Study at Shahid Gangalal National Heart Centre, Kathmandu, Nepal**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Author CMA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SR, DP, NS, BB, AB, PG, ST participate in the designed the study, performed the statistical analysis, wrote the protocol, managed the analyses of the study. All authors read and approved the final manuscript.*

**Original Research Article**

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### **ABSTRACT**

**Aims:** Despite well developed guidelines in the management of ST elevation myocardial infarction with low left ventricular ejection fraction,  $\beta$ -blockers remain an underutilized therapy. We aim to assess the adherence of  $\beta$ -blocker use during the discharge in Shahid Gangalal National Heart Centre, Kathmandu, Nepal.

**Study Design:** Retrospective, Observational study.

**Place and Duration of Study:** Department of cardiology, Shahid Gangalal National Heart Centre, Kathmandu, Nepal. Between January 2012 to December 2012.

**Methodology:** Medical records of 160ST elevation myocardial infarction patients with left ventricular ejection fraction  $\leq 40\%$  and discharged from our centre were retrospectively reviewed regarding the use of  $\beta$ -blocker.

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**Results:** Among the 160 patients, 112 (70%) were males and 48 (30%) were females, mean age was  $59.1 \pm 13.4$  years. Anterior wall myocardial infarction followed by extensive anterior wall was the common in patient with low left ventricular ejection fraction after ST elevation myocardial infarction. Only in 67.5% patients  $\beta$ -blockers were prescribed. Metoprolol tartrate was the most commonly used  $\beta$ -blocker.

**Conclusion:**  $\beta$ -blocker use in patients ST elevation myocardial infarction patients with low left ventricular ejection fraction in our study is comparable to international studies. We still need some more effort to improve our prescription rate.

*Keywords:* ST elevation myocardial infarction; low left ventricular ejection fraction;  $\beta$ -blocker; guidelines.

## 1. INTRODUCTION

According to updated statistics, cardiovascular disease is the first cause of death both in United States and worldwide. In particular, the Global Burden of Disease study classified ischemic heart disease as the leading cause of global mortality, accounting for 1.4 million deaths in the developed world and 5.7 million deaths in developing regions [1]. Compared with post MI patients without left ventricle dysfunction (LVD) patients with LVD have an even worse prognosis [2]. Approximately 50% of the patients with LVD don't have symptoms of heart failure (HF), despite being asymptomatic; they remain at similar risk as patients with symptoms of HF [3].

The benefit of  $\beta$ -blockers for secondary prevention has been established in numerous trials conducted in the pre-reperfusion era and appears to be greatest for patients with MI complicated by HF, LVD, or ventricular arrhythmias [4]. Despite of compelling evidence and recommendations,  $\beta$ -blockers remain an underused therapy in the post MI patients [2]. We aim to analyse the use of  $\beta$ -blocker in post ST elevation myocardial infarction (STEMI) patients with low left ventricular ejection fraction (LVEF).

## 2. MATERIALS AND METHODS

It is a retrospective, single centre study, performed at Shahid Gangalal National Heart Centre, Bansbari, Kathmandu, Nepal. Among 495 ST elevation myocardial infarction patients, 171 patients whose LVEF was  $\leq 40\%$  and discharged from our centre in between January 2012 to December 2012 were retrospectively reviewed regarding the use of  $\beta$ -blocker therapy. Eleven patients were excluded as seven patients had various degree of heart block and others were treated with amiodarone. Performa was designed to collect patient information which included; age, gender, diabetes, dyslipidemia (based on Lipid profile after admission), hypertension based on history and on blood pressure measurement), smoking, left ventricular function (based on echocardiograph, way of reperfusion (Thrombolysis, Primary Percutaneous coronary intervention (PCI)). The study protocol was approved by the Ethics Committee of Shahid Gangalal National Heart Centre.

Cardiovascular risk factors were defined according to American College of Cardiology Key Data Elements and Definitions for Measuring the Clinical Management and Outcomes of Patients with Acute Coronary Syndrome.

1. Smoking: History confirming cigarette smoking (regularly smokes one or more cigarettes per day)
2. Dyslipidemia: History of Dyslipidemia diagnosed and/or treated by physician or meets the criteria of National Cholesterol Education Program:
  - a. Total cholesterol (TC) greater than 5.18mmol/l; or
  - b. Low-density lipoprotein (LDL) greater than or equal to 3.37mmol/L; or
  - c. High-density lipoprotein (HDL) less than 1.04mmol/L.
3. Hypertension (HTN): defined as blood pressure  $\geq 140/90$ mmHg or on treatment.
4. Diabetes (DM): defined as a fasting glucose  $\geq 7.1$ mmol/L or on treatment.

All the variables were entered into the Statistical Package for Social Sciences software, version 14 (SPSS Inc) for data analysis. Descriptive statistics were computed and presented as means and standard deviations for continuous variables like age and LVEF, categorical variables were reported in percentages for the gender, hypertension, diabetes mellitus, dyslipidemia.

### 3. RESULTS AND DISCUSSION

A total of 160 patients were included in this study. Table 1 shows the demographic and clinical characteristics of the studied cohort. The mean age was  $59.1 \pm 13.4$  years. Of the total number of patients included in the study, 112 (70%) were males and 48 (30%) were females. Among the patient smoking was the common conventional risk factor followed by HTN and dyslipidemia. Only close to 25% patients underwent reperfusion therapy. Table 2 shows the mean LVEF, heart rate, systolic blood pressure(SBP) and diastolic blood pressure(DBP) at admission and discharge.

**Table 1. Demographics**

<b>Demographics</b>	<b>n=160</b>	<b>%</b>
HTN	95	59.3
DM	58	36.3
Dyslipidemia	73	45.6
Smoker	101	63.1
Primary PCI	17	10.6
STK	25	15.6
COPD	6	3.75

**Table 2. Baseline characteristics**

<b>Baseline characteristics</b>	
LVEF	$32.1 \pm 6.5\%$
Heart rate	$76.7 \pm 7.7$ bpm
SBP at admission	$124.1 \pm 25.1$ mmHg
DBP at admission	$81.6 \pm 17.5$ mmHg
SBP at discharge	$105.9 \pm 15.0$ mmHg
DBP at discharge	$69.8 \pm 9.5$ mmHg

As shown in Table 3 anterior wall MI followed by extensive anterior wall was the common in patient with low LVEF after STEMI.

As shown in Table 4 most of the patients were prescribed with aspirin, clopidogrel, statins, ACEI/ARB.

As shown in Table 5 Metoprolol tartrate is the most commonly used  $\beta$ -blocker.

**Table 3. STEMI distribution**

<b>STEMI</b>	<b>n=160</b>	<b>%</b>
Anterior	67	41.8
Extensive anterior	44	27.5
Anteroseptal	15	9.3
Inferior	11	6.8
Inferior posterior	7	4.3
Anterior Inferior	4	2.5
Inferior lateral	4	2.5
Inferior posterior lateral	4	2.5
Inferior with RV	2	1.2
Lateral	2	1.2

**Table 4. Medication used**

<b>Medication used</b>	<b>N=160</b>	<b>%</b>
Aspirin	160	100
Clopidogrel	157	98.1
Statins	156	97.5
ACEI	112	70
ARB	20	12.5
Nitrates	63	39.3
$\beta$ -blocker	108	67.5
Spirolactone	80	50

**Table 5. Types of  $\beta$ -blocker used**

<b>Types of <math>\beta</math>-blocker used</b>	<b>n=108</b>	<b>%</b>
Metoprolol tartrate	86	79.6
Metoprolol succinate	9	8.3
Carvedilol	10	9.3
Bisoprolol	2	1.9
Nevibolol	1	0.9

Among the 52 patient in whom  $\beta$ -blocker were not used three had BP of less than 90/60mmHg, six had history of chronic obstructive pulmonary disease (COPD), considered as contraindication for  $\beta$ -blocker therapy.

Based on the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction [5], Oral  $\beta$ -blockers should be initiated in the first 24 hours in patients with STEMI who do not have signs of HF, evidence of a low output state, increased risk for cardiogenic shock, or other contraindications to use of oral  $\beta$ -blockers (PR interval more than 0.24 seconds, second- or third-degree heart block, active asthma, or reactive airways disease). They should be continued during and after hospitalization.

AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and Other Atherosclerotic Vascular Disease [6]: 2011 Update states that  $\beta$ -blocker should be used in all patients with left ventricular systolic dysfunction (ejection fraction  $\leq 40\%$ ) with heart failure or prior myocardial infarction, unless contraindicated. The Use should be limited to carvedilol, metoprolol succinate, or bisoprolol, which have been shown to reduce mortality.

$\beta$ -blockers reduce myocardial workload, and thus oxygen demand, via a reduction in heart rate and blood pressure. They reduce catecholamine levels, decrease myocardial ischemia and limit infarct size, and may prevent the development of definite infarction in acute coronary syndrome patients. Early use of  $\beta$ -blockers in Acute Myocardial Infarction has been shown to reduce the incidence of supraventricular and malignant ventricular arrhythmias, reduce the use of other anti-arrhythmic medications, decrease chest pain symptoms, and decrease sudden cardiac death and early and late re-infarction [7]. These may be the reason of reduction in mortality in STEMI patients when treated with  $\beta$ -blockers.

From the molecular level G protein-coupled receptor kinase 2 (GRK2) a protein is involved in the desensitization and down regulation of G protein-coupled receptors, such as the  $\beta$ -adrenergic receptor, GRK2 increases quickly after STEMI and  $\beta$ -blockers are able to reduce GRK2 levels [8]. It can explain the reason of  $\beta$ -adrenergic receptor up regulation and the reduction of mortality by  $\beta$ -blocker in STEMI patients with low LVEF.

Despite of evidence and clear recommendations,  $\beta$ -blockers remain an underutilized therapy in the post-STEMI period. Only less than half of MI patients are prescribed  $\beta$ -blockers in the chronic setting [9,10]. It is surprising and somewhat disappointing that 30% to 50% of patients with STEMI still fail to receive those agents [11]. A systematic review with meta regression analysis of  $\beta$ -blockade after MI found that  $\beta$ -blockers were used in less than half of eligible patients[12] their studies have reported lower rates of  $\beta$ -blocker use 34.0% at discharge [12]. Additionally, some patients are treated with agents whose long-term use has not been shown to be effective [13].

In our study 67.5% of the patient post MI with low LVEF was treated with  $\beta$ -blockers, which is better than the second National Registry of Myocardial Infarction. In this registry data from 1674 participating hospitals throughout the United States from 1994 to 1998 were analyzed. In only 48% patients with HF post MI were given  $\beta$ -blocker at the time of discharge [14]. In a study done in Malaysia showed that patients receiving  $\beta$ -blockers was 93.1% among those with EF  $\geq 40\%$  vs. 80.4% among patients with EF  $< 40\%$  [15]. However, the numerical percentage of patients with EF  $< 40\%$  or heart failure who received  $\beta$ -blockers was much higher compared to two studies which ranged from 12.4% [16] to 21.0% [17].

Though there is little evidence that a class effect exists, however, and every effort should be made to utilize those specific agents and doses demonstrated to be effective in randomized clinical trials. It is critical to initiate and maintain long term this evidence-based, guideline-recommended, life-prolonging therapy [13]. In clinical practice many patients are initiated and discharged with  $\beta_1$ -selective agents despite their failure to demonstrate significant improvement in long-term survival after MI [18,19]. Implementation of evidence-based therapy may prompt consideration of switching patients from  $\beta_1$ -selective blockers to evidence-based nonselective  $\beta$ -blockers [13].

In our study Metoprolol tartrate is the commonly prescribed before the discharged though it is not the recommended. Our practice of switching it with evidence-based  $\beta$ -blocker is usually done.

Though only nine (5.6%) patients had contraindication to  $\beta$ -blocker therapy, almost in 95% patient we could use the  $\beta$ -blocker safely. Only in 67.5% patients  $\beta$ -blocker was used, remaining 21.2% without contraindication were deprived of evidence based medicine. Physician reluctance to use  $\beta$ -blockers after acute MI may be related to:(1) a perceived decline of benefits due to the introduction of anti platelet agents, ACE inhibitors, statins, and revascularization procedures; (2) concerns about safety in patients with heart failure (HF), COPD, diabetes mellitus, and/or old age; (3) side effect profile; and (4) perceived lack of benefit in non–ST-elevation acute coronary syndrome [20].

Our study has number of limitation as it is a single centre study conducted in small number of patients without a long term follow up.

#### **4. CONCLUSION**

Though  $\beta$ -blockers use in STEM patients with low LVEF in our study is comparable to international studies, we still need some more effort to improve our prescription rate.

#### **CONSENT**

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

#### **ETHICAL APPROVAL**

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

#### **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

#### **REFERENCES**

1. Gaetano Santulli. Epidemiology of Cardiovascular Disease in the 21st Century: Updated Numbers and Updated Facts. *JCvD*. 2013;1:1-2.
2. Gregg C. Fonarow. Comprehensive Adrenergic blockade post myocardial infarction left ventricular dysfunction. *Cardiol Clin*. 2008;26:79-89.
3. Wang TJ, Levy D, Benjamin EJ, et al. The epidemiology of "asymptomatic" left ventricular systolic dysfunction: implications for screening. *Ann Intern Med*. 2003;138:907-16.
4. Freemantle N, Cleland J, Young P, et al. Beta Blockade after myocardial infarction: Systematic review and meta regression analysis. *BMJ*. 1999;318:1730–7.
5. Patrick T. O'Gara, Frederick G. Kushner, Deborah D. Ascheim, Donald E. Casey, Jr, Mina K. Chung, James A. de Lemos, et al. 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. *JACC*. 2013;61:e78–140.
6. Smith SC Jr, Blair SN, Bonow RO, et al. AHA/ACC Scientific Statement: AHA/ACC guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update. A statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*. 2001;104:1577–1579.

7. Anna Kezerashvili, Kevin Marzo, Joshua De Leon. Beta Blocker Use After Acute Myocardial Infarction in the Patient with Normal Systolic Function: When is it "Ok" to Discontinue? *Current Cardiology Reviews*. 2012;8:77-84.
8. Gaetano Santulli, Alfonso Campanile, Letizia Spinelli, Emiliano Assante di Panzillo, Michele Ciccarelli, Bruno Trimarco, Guido Iaccarino. G protein-coupled receptor kinase 2 in patients with acute myocardial infarction. *Am J Cardiol*. 2011;107(8):1125-30
9. Krumholz HM, Radford MJ, Wang Y, et al. National use and effectiveness of beta-blockers for the treatment of elderly patients after acute myocardial infarction: National Cooperative Cardiovascular Project. *JAMA*. 1998;280:623–629.
10. Bradford WD, Chen J, Krumholz HM. Under-utilisation of beta-blockers after acute myocardial infarction: pharmaco-economic implications. *Pharmacoeconomics*. 1999;15:257–268.
11. Yacov Shacham, Eran Leshem-Rubinow, Arie Roth. Is Long-term beta-blocker therapy for myocardial infarction survivors still relevant in the era of primary percutaneous coronary intervention? *IMAJ*. 2013;15:770-774.
12. Gottlieb SS, McCarter RJ, Vogel RA. Effect of beta-blockade on mortality among high-risk and low-risk patients after myocardial infarction. *N Engl J Med*. 1998;339(8):489-97.
13. Gregg C. Fonarow role of beta-blockers for the post-myocardial infarction patient with left ventricular dysfunction. *Journal of Managed Care Medicine*. 2006;9(4):11-17.
14. Wu AH, Parsons L, Every NR, et al. Hospital outcomes in patients presenting with congestive heart failure complicating myocardial infarction: A report from the Second National Registry of Myocardial Infarction (NORMI-2). *J Am Coll Cardiol*. 2002;40:1389-94.
15. Ong WM, Che Zuraini S, Wan Azman WA, Rajasuriar R. Utilization of beta blockers post-myocardial infarction. *Med J Malaysia*. 2013;68:58-63.
16. Gottlieb SS, McCarter RJ, Vogel RA. Effect of beta-blockade on mortality among high-risk and low-risk patients after myocardial infarction. *N Engl J Med*. 1998;339(8):489-97.
17. Viskin S, Kitzis I, Lev E, et al. Treatment with beta-adrenergic blocking agents after myocardial infarction: From randomised trials to clinical practice. *J Am Coll Cardiol*. 1995;25(6):1327-32.
18. ISIS-1 Collaborative Group. Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: ISIS-1. First International Study of Infarct Survival Collaborative Group. *Lancet*. 1986;2:57-66.
19. Lopressor Intervention Trial Research Group. The Lopressor Intervention Trial: multicentre study of metoprolol in survivors of acute myocardial infarction. Lopressor Intervention Trial Research Group. *Eur Heart J*. 1987;8:1056-1064.
20. Mihai Gheorghide, Sidney Goldstein. b-Blockers in the post-myocardial infarction patient. *Circulation*. 2002;106:394-398.

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