

A Nested Case-Control Assessment Determining Emerging Risk Factors in Patients of Acute Myocardial Infarction

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Abstract

Aim: To determine the risk factors associated with patients of acute myocardial infarction.

Materials and methods: This study was a nested case-control was carried out to determine risk factors associated with AMI in the Department of Medical Cardiology, Indira Gandhi Institute of Cardiology, Patna, Bihar, India. Cases from the cohort of patients with in-hospital AMI identified and compared with controls. The study duration was one year.

Results: Case patients had a mean (SD) age of 65.5 (11.0) years and control individuals had a mean (SD) age of 65.5 (11.0) years. Variables associated with an increased risk of in-hospital AMI included being married, a history of coronary artery disease, prior myocardial infarction, peripheral vascular disease, elevated heart rate.

Conclusion: Factors associated with an increased risk of in-hospital AMI included history of atherosclerosis, traditional atherosclerotic risk factors, and markers of physiological stress. Additional research to define risk reduction and optimal treatment strategies of in-hospital AMI are needed to address this common and high-risk condition.

Keywords: risk factors, acute myocardial infarction

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Introduction

Most studies of acute myocardial infarction (AMI) epidemiology and treatment have focused on patients who experience the onset of AMI outside of the hospital. Insights from these studies have informed risk factors and optimal treatment of AMI, which have led to subsequent reductions in AMI incidence and mortality. [1-2] It is increasingly recognized that AMI also occurs among patients already hospitalized for other

conditions. [3-4] Insights on AMI occurring during hospitalization are limited.

Patients with in-hospital ST-segment elevation myocardial infarction (STEMI) have been shown to experience delays in revascularization and worse short-term outcomes when compared with patients experiencing STEMI onset in the outpatient setting. [5-8] Although these comparisons have identified potential

treatment gaps in the care of in-hospital STEMI, [9] less is known about the patient characteristics and long-term outcomes associated with in-hospital AMI. Additionally, prior studies have compared in-hospital AMI outcomes with those of individuals with outpatient onset AMI who survive to hospital admission, potentially biasing comparisons of patient characteristics and outcomes. [10-11] Finally, STEMI reflects less than 25% of all myocardial infarctions and few studies of in-hospital AMI have included non-ST-segment elevation myocardial infarctions (NSTEMI). [12-13] Little is known about the full spectrum of in-hospital AMI.

Patients who survive an acute myocardial infarction (AMI) are at high risk of major cardiovascular events following discharge, although risk may vary considerably between patients. Lifestyle changes, quality of care, and treatment with guideline-directed medical therapy after AMI are all important for secondary prevention. Patient characteristics are also associated with risk of cardiovascular events.

Identification of these characteristics would better inform patients, families, and physicians about the risk of cardiovascular events following discharge and help ensure intensive follow-up and risk factor modification. Efforts to identify risk factors have focused on the period immediately after initial hospitalization for AMI and have not provided a longer-term perspective. Moreover, studies on long-term outcomes after an AMI predominately focus on mortality. [14-18]

Moreover, coronary artery disease tends to emerge earlier in life, and thus mortality rate ratios are greatest in the youngest South Asians compared with other ethnic groups. [5, 6] However, acute myocardial infarction in young South Asians has not been extensively studied, and most of the existing data are on migrant South Asian populations.

Material & Methods:

This study was a nested case-control was carried out to determine risk factors associated with AMI in the Department of Medical Cardiology, Indira Gandhi Institute of Cardiology, Patna, Bihar, India. Cases from the cohort of patients with in-hospital AMI identified and compared with controls. The study duration was one year.

Inclusion Criteria:

Patients in the case group included patients with in-hospital AMI who were aged 50 years or older at the time of the event and admitted to the hospital.

The control group included patients aged 50 years or older who were admitted to a medical bed section with a diagnosis other than ischemic heart disease (*ICD-9* diagnosis codes 410-414) and did not receive a diagnosis of AMI at any time during their hospitalization.

Exclusion Criteria:

Patients with AMI onset within 24 hours of admission were excluded to ensure cases represented AMIs that truly occurred in-hospital and patients who were transferred to another care facility.

A total of 500 patients who fulfilled the inclusion criteria were included in the study. Study participants were randomly allocated to two groups: cases (n=250) & control (n=250) groups respectively.

All the data were tabulated and entered in Microsoft Excel Sheet. Statistical analysis was carried out using SPSS version 21.

Results:

Table 1. Case patients had a mean (SD) age of 65.5 (11.0) years and control individuals had a mean (SD) age of 65.5 (11.0) years. Compared with controls, in-hospital AMI cases were significantly more likely to occur in intensive care unit settings (25.2% vs. 8.4%) and to have a history of atherosclerotic disease (i.e., myocardial infarction, percutaneous

coronary intervention, coronary artery bypass graft, cerebrovascular disease, or peripheral vascular disease). Coronary

disease risk factors of hypertension, hyperlipidemia, and diabetes were also more common in patients with AMI.

Table 1. Patient characteristics on admission and in-hospital variables prior to event for acute myocardial infarction cases and controls

Characteristics	Total	%	Cases	%	Controls	%	p-value
	N=500		N=250		N=250		
Age, mean (SD), y	65.5	11.0	65.7	11.0	65.7	11.0	0.80
Married	425	85.0	218	87.2	207	82.8	0.05
Co morbidities and risk factors							
Hypertension	156	31.2	110	44.0	46	18.4	0.05
Hyperlipidemia	149	29.8	119	47.6	30	12.0	0.05
Tobacco use	199	39.8	138	55.2	61	24.4	0.001
Coronary artery disease	138	27.6	91	36.4	47	18.8	0.001
Prior myocardial infarction	54	10.8	31	12.4	23	9.2	0.05
Prior percutaneous coronary intervention	71	14.2	38	15.2	33	13.2	0.05
Prior coronary artery bypass graft	75	15.0	44	17.6	31	12.4	0.05
Heart failure	91	18.2	49	19.6	42	16.8	0.67
Cerebrovascular disease	77	15.4	51	20.4	26	10.4	0.001
Peripheral vascular disease	55	11.0	39	15.6	16	6.4	0.001
Atrial fibrillation	82	16.4	44	17.6	38	15.2	0.70
Diabetes	141	28.2	77	30.8	64	25.6	0.68
Body mass index							
Underweight (<18.5)	63	12.6	39	15.6	44	17.6	0.66
Normal (18.5 to <25)	217	43.4	104	41.6	113	45.2	
Overweight (25 to <30)	130	26.0	70	28.0	60	24.0	
Obese (≥ 30)	90	18.0	50	20.0	40	16.0	
Heart rate, beats/min							
Low (<60)	84	16.8	32	12.8	52	20.8	0.01
Normal (60-100)	297	59.4	158	63.2	139	55.6	
High (>100)	119	23.8	70	28.0	49	19.6	
Systolic blood pressure, mm Hg							
Low (<90)	35	7.0	20	8.0	15	6.0	0.51
Normal (90-120)	271	54.2	143	57.2	128	51.2	
Borderline (121-139)	101	20.2	51	20.4	50	20.0	
High (>139)	93	18.6	44	17.6	49	19.6	

Table 2: The calculated exposure odds ratio approximates the disease odds ratio when AMI is sufficiently rare. From the final model, variables associated with an increased risk of in-

hospital AMI included being married, a history of coronary artery disease, prior myocardial infarction, peripheral vascular disease, elevated heart rate.

Table 2. Independent risk factors associated with in-hospital acute myocardial infarction

Variables	Odds ratio (95% CI)	p-value
Married	1.5 (1.5-2.6)	0.001
History of anemia	0.6 (0.5-0.9)	0.001
Coronary artery disease	1.6 (1.5-2.9)	0.001
Depression	0.8 (0.6-0.10)	0.47
Prior myocardial infarction	2.4 (1.5-3.6)	0.001
Peripheral vascular disease	2.4 (1.6-3.6)	0.001
Heart rate, beats/min		
Low vs. normal	0.6 (0.5-0.6)	0.001

Discussion:

There are controversial data on whether consanguineous marriages lead to a higher incidence of congenital and acquired diseases in the offspring. Our study reports a relation between parental consanguinity and early myocardial infarction, independent of family history of cardiovascular disease. It is reasonable to speculate that consanguinity increases the likelihood of inheriting genetic factors—identified as well as unidentified—leading to premature ischemic heart disease. [19-20]

Patients surviving AMI have a higher risk of re-infarction and cardiovascular mortality compared with stable coronary artery disease patients. [20-21] Dutta et al. [22] demonstrated that in Apoe^{-/-} mice, after coronary artery ligation, the size of aortic plaques increased and vulnerable lesion morphology was induced with higher inflammatory cell content and protease activity, fuelled by persistently increased myeloid cell flux to atherosclerotic sites activated by heightened sympathetic nervous system activity. Recent studies [23-24] also demonstrated in humans that F-FDG uptake increased in infarcted myocardium and it was correlated with uptake of remote myocardium, spleen and bone marrow. Besides, a correlation was found

between spleen uptake and carotid artery uptake.

Several studies attempting to explain these findings demonstrated that AMI patients have multiple vulnerable plaques that can lead to future cardiovascular events [26-28]. However, AMI itself clearly accelerates atherosclerosis by infarct-triggering burst of systemic inflammation aimed at repair of injured heart.

Risk factors associated with an increased risk of in-hospital AMI included a history of atherosclerotic disease and cardiovascular risk factors in addition to markers of physiological stress. While contemporary studies suggest the mortality for AMI that begins outside the hospital is approximately 13% at 30 days [29] and 25% at 1 year. [30]

The occurrence of major cardiovascular events following discharge is unobservable at discharge and associated with unknown factors after discharge. Such characteristics present a challenge for predictive model development based on conventional regression methods. Latent class analysis is increasingly being used in outcomes research [31-36] and can stratify patients into subgroups based on their risk factors at discharge when outcome information is absent in a training sample. [37]

Conclusion:

From case - control design, factors associated with an increased risk of in-hospital AMI included history of atherosclerosis, traditional atherosclerotic risk factors, and markers of physiological stress. Additional research to define risk reduction and optimal treatment strategies of in-hospital AMI are needed to address this common and high-risk condition.

References:

- Peterson ED, Shah BR, Parsons L, et al. Trends in quality of care for patients with acutemyocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. *Am Heart J.* 2008;156(6):1045-1055.
- Yeh RW, Sidney S, ChandraM, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acutemyocardial infarction. *N Engl J Med.* 2010;362(23):2155-2165.
- Maynard C, Lowy E, Rumsfeld J, et al. The prevalence and outcomes of in-hospital acutemyocardial infarction in the Department of Veterans Affairs health system. *Arch Intern Med.* 2006;166(13):1410-1416.
- Erne P, Bertel O, Urban P, Pedrazzini G, Luscher TF, Radovanovic D; AMIS Plus Investigators. Inpatient versus outpatient onsets of acutemyocardial infarction. *Eur J Intern Med.* 2015;26(6):414-419.
- Dai X, Bumgarner J, Spangler A, Meredith D, Smith SC, Stouffer GA. Acute ST-elevation myocardial infarction in patients hospitalized for noncardiac conditions. *J Am Heart Assoc.* 2013;2(2):e000004.
- Kaul P, Federspiel JJ, Dai X, et al. Association of inpatient vs outpatient onset of ST-elevation myocardial infarction with treatment and clinical outcomes. *JAMA.* 2014;312(19):1999-2007.
- Garberich RF, Traverse JH, Claussen MT, et al. ST-elevation myocardial infarction diagnosed after hospital admission. *Circulation.* 2014; 129(11): 1225-1232.
- Richmond T, Holoshitz N, Haryani A, Purim-Shem-Tov Y, Sharma G, Schaar GL. Adverse outcomes in hospitalized patients who develop ST-elevation myocardial infarction. *Crit Pathw Cardiol.* 2014;13(2):62-65.
- Levine GN, Dai X, Henry TD, et al; In-Hospital STEMI Quality Improvement Project. In-hospital ST-segment elevation myocardial infarction: improving diagnosis, triage, and treatment. *JAMA Cardiol.* 2018;3(6):527-531.
- Zahn R, Schiele R, Seidl K, et al; Maximal Individual The Rapy in Acute Myocardial Infarction (MITRA) Study Group. Acutemyocardial infarction occurring in versus out of the hospital: patient characteristics and clinical outcome. *J Am Coll Cardiol.* 2000;35(7):1820-1826.
- Zmyslinski RW, Lackland DT, Keil JE, Higgins JE. Increased fatality and difficult diagnosis of in-hospital acute myocardial infarction: comparison to lower mortality and more easily recognized pre-hospital infarction. *Am Heart J.* 1981;101(5):586-592.
- Liao J, O'Donnell MJ, Silver FL, et al; Investigators of the Registry of the Canadian Stroke Network. In-hospital myocardial infarction following acute ischaemic stroke: an observational study. *Eur J Neurol.* 2009;16(9): 1035-1040.
- L'Abbate A, Carpeggiani C, Testa R, Michelassi C, Biagini A, Severi S. In-hospital myocardial infarction. Pre-infarction features and their correlation with short-term prognosis.
- Tu JV, Austin PC, Walld R, Roos L, Agras J, McDonald KM. Development and validation of the Ontario acute myocardial infarction mortality prediction rules. *J Am Coll Cardiol.* 2001;37(4):992-997.
- Smolderen KG, Buchanan DM, Gosch K, et al. Depression treatment and 1-

- year mortality following acute myocardial infarction: insights from the TRIUMPH registry (Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status). *Circulation*. 2017;135(18):1681-1689.
16. Plakht Y, Shiyovich A, Gilutz H. Predictors of long-term (10-year) mortality postmyocardial infarction: age-related differences. Soroka Acute Myocardial Infarction (SAMI) Project. *J Cardiol*. 2015;65(3):216-223.
 17. Ketchum ES, Dickstein K, Kjekshus J, et al. The Seattle Post Myocardial Infarction Model (SPIM): prediction of mortality after acutemyocardial infarction with left ventricular dysfunction. *Eur Heart J Acute Cardiovasc Care*. 2014;3(1):46-55.
 18. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation* 1998;97:596-601.
 19. Ulusoy M, Tuncbilek E. Consanguineous marriage in Turkey and its effects on infant mortality. *Nufusbil Derg* 1987;9:7-26.
 20. Modell B, Darr A. Science and society: genetic counselling and customary consanguineous marriage. *Nat Rev Genet* 2002;3:225-9.
 21. Goldstein JA, Demetriou D, Grines CL, Pica M, Shoukfeh M, O'Neill WW. Multiple complex coronary plaques in patients with acute myocardial infarction. *The New England journal of medicine*. 2000; 343 (13):915-22.
 22. Milonas C, Jernberg T, Lindbäck J, Agewall S, Wallentin L, Stenestrand U. Effect of Angiotensin-converting enzyme inhibition on one-year mortality and frequency of repeat acute myocardial infarction in patients with acute myocardial infarction. *The American journal of cardiology*. 2010; 105(9):1229-34.
 23. Dutta P, Courties G, Wei Y, Leuschner F, Gorbato R, Robbins CS, et al. Myocardial infarction accelerates atherosclerosis. *Nature*. 2012; 487(7407):325-9.
 24. Kim EJ, Kim S, Kang DO, Seo HS. Metabolic activity of the spleen and bone marrow in patients with acute myocardial infarction evaluated by 18f-fluorodeoxyglucose positron emission tomographic imaging. *Circulation Cardiovascular imaging*. 2014; 7(3):454-60.
 25. Wollenweber T, Roentgen P, Schäfer A, Schatka I, Zwadlo C, Brunkhorst T, et al. Characterizing the inflammatory tissue response to acute myocardial infarction by clinical multimodality noninvasive imaging. *Circulation Cardiovascular imaging*. 2014; 7(5):811-8.
 26. Rioufol G, Finet G, Ginon I, André-Fouët X, Rossi R, Vialle E, et al. Multiple atherosclerotic plaque rupture in acute coronary syndrome: a three-vessel intravascular ultrasound study. *Circulation*. 2002; 106 (7):804-8.
 27. Asakura M, Ueda Y, Yamaguchi O, Adachi T, Hirayama A, Hori M, et al. Extensive development of vulnerable plaques as a pan-coronary process in patients with myocardial infarction: an angioscopic study. *Journal of the American College of Cardiology*. 2001; 37(5):1284-8.
 28. 29. Hong MK, Mintz GS, Lee CW, Kim YH, Lee SW, Song JM, et al. Comparison of coronary plaque rupture between stable angina and acute myocardial infarction: a three-vessel intravascular ultrasound study in 235 patients. *Circulation*. 2004; 110(8):928-33.
 29. Wadhera RK, Joynt Maddox KE, Wang Y, Shen C, Bhatt DL, Yeh RW. Association between 30-day episode payments and acutemyocardial infarction outcomes among Medicare beneficiaries. *Circ Cardiovasc Qual Outcomes*. 2018;11(3):e004397.
 30. Spatz ES, Beckman AL, Wang Y, Desai NR, Krumholz HM. Geographic

- variation in trends and disparities in acute myocardial infarction hospitalization and mortality by income levels, 1999-2013. *JAMA Cardiol.* 2016;1(3):255-265.
31. Kim M, Wall MM, Li G. Applying latent class analysis to risk stratification for perioperative mortality in patients undergoing intraabdominal general surgery. *Anesth Analg.* 2016;123(1):193-205.
 32. Mohammed, Ebtehag Mustafa. Explanatory Factor analysis to determining the risk factors of cardiovascular disease: A hospital-based case-control study. *Journal of Medical Research and Health Sciences*, 2020;3(8).
 33. Miller CR, Sabagh G, Dingman HF. Latent class analysis and differential mortality. *J AmStat Assoc.* 1962;57(298):430-438.
 34. Crow SJ, Swanson SA, Peterson CB, Crosby RD, Wonderlich SA, Mitchell JE. Latent class analysis of eating disorders: relationship to mortality. *J Abnorm Psychol.* 2012;121(1):225-231.
 35. Leigh L, Hudson IL, Byles JE. Sleeping difficulty, disease and mortality in older women: a latent class analysis and distal survival analysis. *J Sleep Res.* 2015;24(6):648-657.
 36. Evenson KR, Herring AH, Wen F. Accelerometry-assessed latent class patterns of physical activity and sedentary behavior with mortality. *Am J Prev Med.* 2017;52(2):135-143.
 37. Ferrat E, Audureau E, Paillaud E, et al; ELCAPA Study Group. Four distinct health profiles in older patients with cancer: latent class analysis of the prospective ELCAPA cohort. *J Gerontol A BiolSci Med Sci.* 2016;71(12): 1653-1660.