

JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article:

PAUDEL R, PANTA O B, PAUDEL B, PAUDEL K, PATHAK O K, ALURKAR V M. ACUTE CORONARY SYNDROME IN ELDERLY - THE DIFFERENCE COMPARED WITH YOUNG IN INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL IN WESTERN NEPAL. *Journal of Clinical and Diagnostic Research* [serial online] 2009 February [cited: 2009 February 2]; 3:1289-1296.

Available from

http://www.jcdr.net/back_issues.asp?issn=0973-709x&year=2009&month=February&volume=3&issue=1&page=1289-1296&id=315

ORIGINAL ARTICLE

Acute Coronary Syndrome In Elderly – The Difference Compared With Young In Intensive Care Unit Of A Tertiary Hospital In Western Nepal

Paudel R*, Panta O B**, Paudel B***, Paudel K****, Pathak O K*****, Alurkar V M *****.

ABSTRACT

Introduction: Acute coronary syndrome (ACS), one of the commonest causes of intensive care unit (ICU) admission, casts a large burden of cost on the health care system, along with a huge mortality in the elderly population.

Objectives: This study determined the difference in presentation, complication, management and outcome in elderly patients with acute coronary syndrome, as compared to the young patients.

Material And Methods: Records of all patients who were diagnosed to have acute coronary syndrome, admitted to the ICU in the Manipal Teaching Hospital in the month of March 2006 to June 2007, was entered in a designated Proforma. Demographic details, clinical findings, treatment and complications were recorded. A total of 153 patients were analyzed and elderly patients (≥ 65 yrs) were compared with young patients (< 65 yrs) using SPSS-10.0 software.

Results: Elderly patients constituted 51% (78) of the study population, among which 46.2% (36) were females. 7.7% (6) elderly patients presented with atypical symptoms, among which syncope was the commonest. Young patients were more likely to be hypertensive as compared to the elderly patients (70.7% vs. 39.7%; $p < 0.001$). The median time of presentation to the hospital after chest pain was comparable in the two groups: 16 hours overall, but in cases of STEMI, elderly patients were brought to the hospital comparatively late, with a median time of 15 hours (IQ 5.5 - 72 as compared to young individuals in which median time was 7.25 hours (IQ 2.87 - 39 hours), which was statistically significant ($p = 0.000$). Non ST elevated myocardial infarction (NSTEMI) and ST elevated myocardial infarction (STEMI) were similar in distribution among the elderly and young patients. Complication was seen predominantly among the elderly, with 62.8% (49) Vs 38.7% (29); $p = 0.03$. Overall, heart failure was the commonest complication (28.2%), followed closely by arrhythmias (26.9%). Cardiogenic shock complicating STEMI resulted in high patient mortality in both the age groups. Thrombolysed patients were similar in distribution in both groups. But the success rate of thrombolysis was lower in elderly patients (50%) as compared to young patients (76.9%). Beta blockers were less commonly used in the elderly- 47.4% (34) than in young patients- 61.3% (46). A combination of aspirin and clopidogrel was also less commonly used in the elderly patients {60.3% (47) Vs 76% (57); $p = 0.03$ }. Mortality was higher in the elderly patients (24.4% Vs 10.7%; $p = 0.03$)

Conclusion: Elderly patients are more prone to complications, have less success rate for thrombolysis and have a higher mortality rate as compared to young patients of ACS.

Key Words: Acute coronary syndrome, Elderly, Nepal, Young.

* MD, Lecturer, Dept of Medicine,
Intern, *MD, Asst Professor, Dept of Medicine
****Intern, ***** MD DM (Cardiology), Professor,
Dept of Medicine, Manipal College of Medical
Sciences, Pokhara, (Nepal).
Corresponding Author
Dr. Raju Paudel
MD, Lecturer, Dept of Medicine
Manipal College of Medical Sciences
Pokhara, (Nepal).
E-mail: paudelraju@yahoo.com
Phone: +977 61 526416 Extn: 117/221

Introduction

Acute coronary syndrome (ACS), encompassing a range of disorders from unstable angina through non ST elevation to ST elevation myocardial infarction, is a leading cause of death in the world in both developed and developing countries. The South Asian countries of India, Pakistan, Bangladesh, Sri Lanka, and Nepal account for about a quarter of the world's population and contribute the highest proportion of the burden of cardiovascular diseases as compared with any other region globally[1],[2],[3]. Death claims mostly the elderly population; in US, 83 % of IHD deaths were in patients of more than 65 years of age[4]. The elderly are also at a higher risk for complication than the younger population. The elderly are a subgroup known to be at high risk, but community practice patterns continue to demonstrate that less use of cardiac medications and invasive care even among elderly individuals are likely to benefit them[4]. Despite the large and expanding elderly population presenting for ACS care, existing evidence is limited and insufficient to guide management in this subgroup, to the same degree of certainty as in younger populations[5]. Deaths related to cardiovascular disease also occur 5 to 10 years earlier in South Asian countries than they do in Western countries[6],[7]. Data from Nepal in this regard is lacking. Hence, the present study was undertaken with the following objectives:

1. To study the demographic details of the patients presenting with acute coronary syndrome
2. To compare the differences in the elderly and young patients with regards to presentation risk factors, management and the outcome among the acute coronary syndrome patients

Materials and methods

The study population consisted of 153 patients of acute coronary syndrome, admitted and managed in the intensive care unit of Manipal Teaching Hospital during March 2006 to June 2007. The study population was prospectively observed during the hospital stay and the demographic details, presentation, clinical findings, management and outcome were recorded in a preformed proforma. The standard case definition of the American Heart Association (AHA) was used for classifying patients into categories of unstable angina, Non ST Elevation Myocardial Infarction (NSTEMI) and ST Elevation Myocardial Infarction (STEMI). Successful thrombolysis was defined clinically when the patients had relief from chest pain and electrocardiographically, by the decrease in the ST segment elevation by 50 % of the presenting ECG.

The study population was divided in two groups viz. ≥ 65 yrs of age and <65 yrs of age. The two groups were compared for patient characteristics, presentation, clinical findings, course of treatment at the hospital and the evolution of complication during the admission.

Statistics

The SPSS package version 10.0 was used to carry out the statistical analysis. The categorical data was analysed using χ^2 test. Continuous data are presented in the form of mean and median.

Results

A total of 153 cases fulfilled the criteria of ACS, of which 78 (50.98%) were elderly and 75(49.02%) were young. Almost 50% of the patients in both the groups were females: 36 (46.2%) in the elderly and 35 (46.7%) in the young groups, respectively. The demographic details of the patients and risk factors are listed in [Table/Fig 1].

(Table/Fig 1) Baseline patient characteristics

Characteristics	Elderly (> 65 yrs) (N=78)	Young (< 65 yrs) (N=75)	OR	95% CI	Significance
Mean Age	73.47 ± 6.63	54.57 ± 8.58	-	-	-
Sex					
Female:	36 (46.2%)	35 (46.7%)			$\chi^2 = 0.04$, df=1, p=0.949
Male:	42 (53.8%)	40 (53.3%)			
Types of ACS			1.21		$\chi^2 = 0.34$, p=0.558
STEMI	38 (48.7%)	33(44%)			
Unstable Angina	32(41%)	34(45.3%)			
NSTEMI	8 (10%)	8(10%)			
Median time (Inter quartile range)	16 (5.25-72 hrs)	15 (5.25-72 hrs)	-	-	-
Median time of presentation in STEMI	15 (5.5-72hrs)	7.25 (2.87-39 hrs)	-	-	p= 0.000
Hypertension	31 (39.7%)	53 (70.7%)	0.28	0.14 - 0.55	$\chi^2 = 14.209$, df=1, p=0.001
Smoking (ever smoked)	58 (74.4%)	47 (62.7%)	1.73	0.87 - 3.45	$\chi^2 = 2.428$, df=1, p=0.163
Smoker (current)	35 (44.9%)	30 (40.0%)	1.22	0.64 - 2.32	$\chi^2 = 0.371$, df=1, p=0.542
Alcohol	29 (37.2%)	17 (22.7%)	2.02	0.99 - 4.10	$\chi^2 = 3.830$, df=1, p=0.50
Diabetes mellitus	15 (19.2%)	9 (12.0%)	1.77	0.72 - 4.35	$\chi^2 = 1.599$, df=1, p=0.206
Prior history of CAD	19(24.4%)	16 (21.3%)	1.187	0.56 - 2.53	$\chi^2 = 0.198$, df=1, p=0.656

Type of ACS

STEMI and unstable angina were the predominant types of ACS seen in both the groups in proportionate amounts [n=38 (48.7%)] in the elderly and [n=33 (44%)] in the young patients and [32 (41%)] in the elderly and [34 (45.3%)] in the young patients, respectively. NSTEMI was seen in only 10% of cases in both groups. There was no statistical significance in the type of ACS seen when compared between the two groups.

Onset of symptoms to presentation

The median time of presentation to the hospital after the symptoms, was 16 hours (IQ -5.25 – 72) in the elderly and 15 hours (IQ - 5.25 – 72) in the young and there was no statistical difference between the groups. However, among patients with STEMI, the median time of presentation to the hospital in young patients was 7.25 hours (IQ 2.87 – 39

hours) as compared to 15 hours (IQ 5.5 – 72 hours) in elderly patients, which was statistically significant (p=0.000).

Presenting Symptoms

Most of the individuals with ACS presented with chest pain, but those who presented with symptoms other than chest pain, like epigastric pain, sweating, breathlessness and syncope were classified as atypical presentation. Atypical presentation was more common in the elderly as compared to the young (7.7 % vs 4.2%), but this was also not statistically significant.

Risk factors

Young patients were more likely to be hypertensive as compared to the elderly patients (70.7% vs 39.7%; p <0.001). However, there was no difference between the two age groups with regards to the habit of smoking (p=0.163), presence of diabetes (p=0.206), alcohol consumption (p=0.5) and a prior history of CAD (p=0.656).

Wall involvement in STEMI

Among a total of 71 STEMI patients, involvement of inferior wall and extensive anterior wall was seen in 36.6% (n=26) and 35.2% (n=25) patients respectively, followed by anterior wall 22.5% (n= 16) and lateral wall 8.5% involvement (n=6). There was no statistical significance with regards to the wall involvement among the elderly and young populations.

Complications

Overall, more complications were observed in the elderly population as compared to the younger group 62.8% vs 38.7%; p=0.03. Common complications seen in both of these groups were heart failure, seen in 24.4% of the elderly and 17.35% of young patients, arrhythmia in 23.1% of the elderly patients vs 16% of young patients, cardiogenic shock in 14.1% of the elderly patients vs 10.7% of young patients and hypotension in 7.7% of the elderly patients vs 5.3% of young patients. There was no statistical significance in the

type of individual complications . Presentation with sudden cardiac death was observed in 3.8 % of elderly patients, whereas there was none in the young age group. The details are listed are listed in [Table/Fig 2].

(Table/Fig 2) Complications

	Elderly	young
Any Complication ^a	49 (62.8%)	29 (38.7%)
Heart Failure	19 (24.4%)	13(17.3%)
Arrhythmia	18 (23.1)	12 (16%)
Hypotension	6 (7.7%)	4 (5.3%)
Sudden cardiac death	3 (3.8)	none
Cardiogenic shock	11 (14.1%)	8 (10.7%)

^a = $\chi^2=8.93$, df=1, p=0.03

Medications

The elderly patients were less likely to be treated with B –blockers as compared to the young individuals (47.4% vs 61.3%). A combination of aspirin and clopidogrel was also less commonly used in the elderly 60.3% (47) than the young 76% (57), which was statistically significant(p= 0.03).Use of ACE inhibitors and statin was uniform in the both the groups.

Outcome

Mortality was higher in elderly 19 (24.4%) patients as compared to young patients 8(10.7%) (p value 0.026) (OR of 2.69 with 95% CI). Among those with ACS, mortality was mainly seen in 13 cases of STEMI among elderly patients and in 8 patients among young individuals .There was a high mortality rate when patients presented with cardiogenic shock and congestive heart failure. The mortality was mainly seen in patients with extensive anterior wall MI (11 out of 16), followed by inferior wall STEMI (7 out of 26).

Thrombolysis

Only 19 (33.9%) patients were thrombolysed, out of which 8 were elderly (30.8%) and 11 were young (36.7%). Four cases (50%) of thrombolysis in elderly patients were successful whereas only 9 (81.8%) cases were successful among the young.

Reasons for not giving thrombolysis

When we analyzed the reasons for not giving thrombolysis in STEMI, the main reason was late presentation of the patient, observed in 24 (38) of elderly patients and 16(33) of young individuals .The other reasons being history of stroke in 4 patients, 2 in each group, followed by the previous use of streptokinase in 3 individuals (2 in the elderly group and 1 in young age group) and non availability of streptokinase in the hospital, in 3 patients.

Discussion

In our study, we found that sex distribution in both the elderly and young patients were almost equal, with a male:female ratio of 1.14:1. The various studies done previously showed that elderly patients were more likely to be females, due to the loss of the protective action of oestrogen in these individuals [8]is trend was not seen in our study, as compared to previous studies done in south East Asia and USA. [9],[10].

Smoking (74% vs 62 %), Alcohol intake (29% vs 17%) , Diabetes mellitus(19 % vs 12 %) ,and Prior CAD were (24 % vs 21 %) seen more commonly in the elderly than in young patients, however, the younger patients were found to have hypertension (70% vs 40 %), which was statistically significant. Control of hypertension is of utmost importance, as this is one of the major risk factors, irrespective of the age group.

The main risk factors which showed consistently significant associations across all South Asian countries in both sexes, were current and former smoking, high ApoB100 /Apo-I ratio, history of hypertension and history of diabetes. Alcohol consumption did not appear to be protective in native South Asians and this may be related to a lower prevalence or differences in patterns of drinking (binge drinking in South Asians vs regular drinking in other countries). In South Asian households, prolonged cooking of vegetables is a common practice, which may destroy 90% of the folate content, leading to

an increased risk for CAD [11]. A similar inverse association between the intake of vegetables and AMI has been reported in a case-control study from India [12]. These data collectively provide the basis for public health education, aimed at substantially increasing the consumption of fruits and vegetables.

It is likely that the recent increase in CHD in South Asians is due to lifestyle changes associated with urbanization, perhaps interacting with a genetic predisposition that leads to abdominal obesity, dysglycaemia, and dyslipidaemia [13]. So, the knowledge of underlying risk factors in population subgroups will be useful for targeting the secondary preventive strategies. In this study, we did not consider the risk factors like apolipoprotein and homocysteine levels which are the important risk factors of CAD, specially in Asian countries, besides the conventional risk factors.

In our study, the atypical presentation was seen more commonly in elderly individuals as compared to the younger group, as shown by previous studies. In GRACE (Global Registry of Acute Coronary Events), the average age of patients presenting with atypical symptoms was 72.9 years, whereas the average age of patients presenting with typical symptoms was 65.8 years. In NRMI, only 40% of those aged 85 years of age, had chest pain on presentation as compared with 77% of those aged 65 years. Although chest pain remains a common symptom of ACS, elderly patients were more likely to present with dyspnoea (49%), diaphoresis (26%), nausea and vomiting (24%), and syncope (19%) as a primary complaint; hence, MI may go unrecognized[14].

Atypical presentations have been shown to result in portend, a worser prognosis (a 3-fold higher risk of in-hospital), in part, because of delays in diagnosis and treatment and less use of evidence-based medications. Because of the high prevalence of atypical features and associated worse outcomes in the elderly, a

high index of suspicion for ACS is advisable[14],[15]. A typical presentation was recorded in very less individuals in our study, seen in only 3.8 % of the elderly population and most of them presented with syncopal attack. Mortality was observed in 50% of the elderly, presenting with atypical symptoms. Future prospective studies should focus on various atypical presentations.

The median time of presentation after the symptoms started in our study, was 16 hours, and this was more in elderly individuals as compared to the younger group, which was supported by similar studies done in India and developing countries. When the data of STEMI was looked into, the median time of hospital presentation was 7.25 hours in younger individuals as compared to 15 hours in elderly individuals. It might be because the elderly mainly had atypical presentations. The time from onset of symptoms to presentation at the hospital is typically longer among patients in India, than in the West. 16-20 The time from onset of symptoms to arrival at the emergency department, for patients with acute ST elevation myocardial infarction (STEMI) ranges between 110 and 140 minutes in North America,[16],[17] while in India, it is 180–330 minutes[18], [19]. In the recently concluded CREATE registry, the median symptom-to-door time was 300 minutes for patients with STEMI (unpublished data). This delay in presentation is due to several factors, including lack of symptom awareness, longer distances travelled to reach hospital and problems of transportation [18], [19]. Only 5.4% of patients are brought to hospital in an ambulance, with the large majority using public transport (buses) and hired vehicles (taxi, auto rickshaws, etc)[18]. Of interest is the fact that consultation with the family doctor, local practitioner or local primary health centre has been found to be an important cause of delay in presenting at the hospital [18],[19],[20]. In addition, older people and women have been observed to present disproportionately late, irrespective of whether their symptoms were typical or

atypical. Since the transit time to reach hospital plays an important role in outcomes, there is a need for increasing public awareness about the symptoms, facility of ambulance services, etc.

Thrombolytic therapy was instituted in individuals who presented within 12 hours of STEMI, if there was no contraindication. Among 31 patients with STEMI who presented within 12 hours, 10 patients from the younger group (58.8%) were thrombolysed and 8 (57.1%) among the elderly individuals were thrombolysed. The reasons for not thrombolysing individuals presenting within 12 hours, were mainly stroke (n=4), prior use of streptokinase (n=3) and surgery in the recent past (n=1). Failure to reach the hospital within 12 hours is the primary reason for not instituting the thrombolytic therapy in STEMI, which was seen in 24 (38) of elderly patients and 16 (33) of the younger group. Several other studies have also shown that fewer elderly were thrombolysed, mainly due to the delay in seeking medical care.[21],[22].

Individuals in whom there was prior use of streptokinase could not be thrombolysed due to unavailability of t-PA. Though t-PA is expensive and affordability can be a problem in developing countries, availability in hospitals if ensured, can be used in needy cases.

Elderly individuals had more complications as compared to young patients, which was statistically significant (62.8% vs 38.7%) (p=0.03). The common complications observed were heart failure, cardiogenic shock, arrhythmias and sudden cardiac death. Among the arrhythmias observed, heart block was predominant, followed by atrial fibrillation, ventricular tachycardia, junctional rhythm and supraventricular tachycardia.

The mortality in the elderly was significantly higher as compared to young individuals (19 (24.4%) vs 8 (10.7%) (p=0.026). Among the elderly, 13 of 19 STEMI patients died during

the hospital stay as compared to all the 8 young STEMI patients who remained alive. Likewise, more patients presenting with cardiogenic shock (100% vs 87.5% in young) and congestive heart failure died in the hospital. Sudden cardiac death was also more common among the elderly.

Age is a powerful predictor of adverse events after ACS.23-25 After accounting for other factors, the odds for in-hospital death increase by 70% for each 10-year increase in age[23].

The use of beta blockers was less in the elderly population as compared to the young population, though it was not statistically significant (p=0.569), despite various studies recommending the optimal use of β -blockers in elderly individuals. Though in our study, the use of β -blockers was optimized, till there was a clear cut contraindication, like in patients with severe heart failure (KILLIP III and IV class), AV blocks were seen in ECG and patients of COPD with significant bronchospasms. Numerous large multicenter randomized trials have confirmed the beneficial role of oral β -blocker therapy in lowering mortality rate and recurrent coronary ischaemic events with similar or greater efficacy in older patients as compared to younger patients after acute MI [26],[27][28],[29],[30],[31] Use of combination antiplatelets, Aspirin and Clopidogrel, was less in elderly individuals as compared to the young patients (60.3% vs 76%) (p=0.03). However, the use of ACE inhibitors and statins were uniform in both the groups.

Limitations

Our study had a small sample size with observation of in-hospital mortality cases only. Follow up studies were not done subsequently after the discharge. Angiographic studies were not done in our patients, thus making our data primitive.

Conclusion

Our study was able to identify the differences in various aspects between the elderly and

young patients of ACS. The complication rate and the mortality rate were found to be higher in elderly individuals with ACS. Upgrading the existing facilities in the hospital with the use of evidence based management will be helpful to manage these patients properly and to decrease the complications and mortality in patients with ACS. The preventive strategies for modifying the conventional and unconventional risk factors through public education and awareness will go a long way in curtailing the cases of ACS, especially in developing countries. Long term prospective follow up study with angiography will be required in the future to overcome the limitations of our study.

Acknowledgements

The authors would like to acknowledge Dr. Abishek Maskey and Dr. Gaurav Shrestha, Post graduate students in Internal Medicine, for helping us in data collection.

References

- [1]. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation* 1998; 97: 596-601.
- [2]. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of diseases, part 1: general considerations, the epidemiologic transition, risk factors and impact of urbanization. *Circulation* 2001;104: 2746-53.
- [3]. Reddy KS. Cardiovascular diseases in non-Western countries. *N Engl J Med* 2004; 350: 2438- 40.
- [4]. Avezum A, Makdisse M, Spencer F, et al. GRACE Investigators. Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J*. 2005; 149:67-73.
- [5]. Alexander KP, Newby LK, Cannon CP et al. Acute coronary care in the elderly, part I: Non-ST-segment-elevation acute coronary syndromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation* 2007; 115 (19): 2549-69
- [6]. Murray CJL, Lopez AD. *Global Health Statistics, Global Burden of Disease and Injury Series*. Boston, Mass: Harvard School of Public Health; 1996.
- [7]. Murray CJL, Lopez AD. *Global Comparative Assessments in the Health Sector*. Geneva, Switzerland: World Health Organization; 1994.
- [8]. Chew S, Ng SC. Hormone replacement therapy (HRT) and ischaemic heart disease: Getting to the heart of the matter. *Singapore Med J* 2002; 43 (1):41-4.
- [9]. Kam R, Cutter J, Chew SK, Tan A, Emmanuel S, Mak KH, Chan CNS, Koh TH, Lim YL. Gender differences in outcome after an acute myocardial infarction in Singapore. *Singapore Med J* 2002; 43(5): 243-8.
- [10]. Tresch DD. Management of the older patient with acute myocardial infarction: difference in clinical presentations between older and younger patients. *J Am Geriatr Soc* 1998; 46(9):1157-62.
- [11]. Matthews JH, Wood JK. Megaloblastic anemia in vegetarian Asians. *Clin Lab Haematol*. 1984; 6:1-7.
- [12]. Rastogi T, Reddy KS, Vaz M, et al. Diet and risk of ischemic heart disease in India. *Am J Clin Nutr*. 2004; 79: 582-92.
- [13]. Joshi P, Islam S, Pais P. et al. Risk Factors for Early Myocardial Infarction in South Asians Compared With Individuals in Other Countries. *JAMA* 2007; 297 (3):286-94
- [14]. Brieger D, Eagle KA, Goodman SG, et al. GRACE Investigators. Acute coronary syndromes without chest pain, an under diagnosed and under treated high-risk group: Insights from the Global Registry of Acute Coronary Events. *Chest*. 2004; 126:461-69.
- [15]. Kanne WB, Abbott RD. Incidence and prognosis of unrecognized myocardial infarction: an update on the Framingham study. *N Engl J Med* 1984;311: 1144-47.
- [16]. Luepker RV, Raczynski JM, Osganian S, et al. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. *JAMA* 2000; 284: 60-7.
- [17]. Anand SS, Pais P, Pogue J, et al. A comparison of practice patterns for acute myocardial infarction between hospitals in Canada and India. *Indian Heart J* 1997; 49: 35-41.
- [18]. George E, Savitha D, Pais P. Pre-hospital issues in acute myocardial infarction. *J Assoc Physicians India* 2001; 49: 320-3.
- [19]. Rajagopalan RE, Chandrasekaran S, Pai M, et al. Pre-hospital delay in acute myocardial infarction in an urban Indian hospital: a prospective study. *Natl Med J India* 2001; 14: 8-12.
- [20]. Malhotra S, Gupta M, Chandra KK, et al. Prehospital delay in patients hospitalized with acute myocardial infarction in the emergency

- unit of a north Indian tertiary care hospital. *Indian Heart J* 2003; 55: 349-53.
- [21]. Boucher JM, Racine N, Thanh TH, Rahme E, Brophy J, Theroux P. Age-related differences in in-hospital mortality and the use of thrombolytic therapy for acute myocardial infarction. *Canadian Medical Association Journal* 2001; 164(9):1285-90.
- [22]. Straznicky IT, French JK, White HD, Califf RM. Fibrinolysis for acute myocardial infarction in the elderly patient: Is it effective or too dangerous? *Am J Geriatr Cardiol* 1998; 7(1): 22-7.
- [23]. GrangerCB, GoldbergRJ, DabbousO, et al. Global Registry of Acute Coronary Events Investigators. Predictors of Hospital mortality in the Global Registry of Acute Coronary Events. *Arch Intern Med.*2003; 163: 2345-53.
- [24]. EagleKA, LimMJ, DabbousOH, et al. GRACE Investigators. A validated prediction model for all forms of acute coronary syndrome:estimating the risk of6-month post discharge death in an international registry. *JAMA* 2004; 291: 2727-33.
- [25]. BoersmaE, PieperKS, SteyerbergEW, et al. Predictors of outcome In patients with acute coronary syndromes without persistent ST-segment elevation: results from an international trial of 9461 patients. *Circulation* 2000; 101:2557-67.
- [26]. Hjalmarson A, Elmfeldt D, Herlitz J, et al. Effect on mortality of metoprolol in acute myocardial infarction: a double-blind randomised trial. *Lancet.* 1981; 11: 823-27.
- [27]. A randomized trial of propranolol in patients with acute myocardial infarction, I: mortality results. *JAMA.* 1982; 247: 1707-14.
- [28]. A randomized trial of propranolol in patients with acute myocardial infarction, II: morbidity results. *JAMA.* 1983; 250: 2814-19.
- [29]. Gundersen T, Abrahmsen AM, Kjekshus J, Ronnevik PK. Timolol-related reduction in mortality and reinfarction in patients ages 65-75 years surviving acute myocardial infarction: prepared for the Norwegian Multicentre Study Group. *Circulation.* 1982; 66: 1179-84.
- [30]. Pedersen TR. Six-year follow-up of the Norwegian Multicenter Study on timolol after myocardial infarction. *N Engl J Med.* 1985; 313: 1055-58.
- [31]. Soumerai SB, McLaughlin TJ, Spiegelman D, Hertzmark E, Thibault G, Goldman L. Adverse outcomes of underuse of beta-blockers in elderly survivors of acute myocardial infarction. *JAMA.*1997; 277: 115-21.