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ASSESSMENT OF CLINICAL PROFILE OF ELDERLY PATIENTS WITH ACUTE ST-ELEVATION MYOCARDIAL INFARCTION UNDERGOING REPERFUSION THERAPY

Cardiology

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ABSTRACT

Objective The main aim of the study is to study the influence of age on the clinical outcomes in STEMI patients undergoing primary PCI or fibrinolytic therapy. Also, it assessed the angiographic profile of STEMI patients and compared the outcomes of primary PCI vs. fibrinolytic therapy in STEMI patients aged >65 years.

Methods This is a prospective observational study which analysed the clinical profile of 500 consecutive patients with STEMI undergoing primary PCI or thrombolysis at the Department of Cardiology, Government Medical College, Kottayam, Kerala, India from August 2011 to September 2012. The primary endpoint of the study is major adverse cardiovascular events (MACE) at the end of hospitalization. MACE comprises of recurrent angina, re-infarction, heart failure, arrhythmia and death. Secondary end-points comprises of safety outcomes like major bleeding and disabling stroke

Results Patients were categorized into four groups depending on the age (<55 years, 55-65 years, 66-75 years and >75 year). The incidence of triple vessel disease (TVD) and tortuous calcified coronaries were more in those aged more than 65 years.In-hospital and one-year outcomes including death, re-infarction, stroke and major bleeding were compared in different age groups. In-hospital re-infarction rate was comparable between the two groups aged <65 years and >65 years. But, there was significant difference between two groups in terms of mortality (4.30 vs. 9.80, p=0.03).There was no statistical difference in the incidence of major bleed between different age groups. In all age-groups thrombolyzed patients had a higher mortality compared to PCI (p=0.04**).**

Conclusion The clinical outcomes of acute STEMI was more adverse in patients aged more than 65 years compared to those aged less than 65 years in terms of mortality, recurrent ischemia, re-infarction and stroke irrespective of the mode of reperfusion therapy. Additionally, primary PCI was superior to fibrinolysis in reducing death, reinfarction and disabling stroke in older patients with STEMI aged more than 65 years.

KEYWORDS

Fibrinolysis, elderly patients, ST-elevation, acute myocardial infarction

Introduction

Management of elderly patients with acute myocardial infarction is a controversial issue. Elderly patients are not only contraindicated to thrombolytic therapy but also have higher incidence of hemorrhagic stroke after it. Additionally, elderly patients often present with adverse comorbid conditions and as a result have prolonged hospital stay, greater adverse ischemic and non-cardiac events, and increase early and late mortality compared to their younger counter-parts. Thus, taking into consideration these correlations, elderly patients with AMI are less often treated with reperfusion (1).

Primary coronary balloon angioplasty has been shown to be effective in high-risk patient subset, including the elderly patients. However, the impact of age on the outcomes of patients with AMI undergoing mechanical perfusion is not thoroughly evaluated, which is especially essential with the evolution of stent techniques (2). Moreover, the implantation of stent requires the use of potent antiplatelet antagonists. The routine use of these agents in elderly population pose unique challenge owing to age-related alterations in the way drugs are distributed and metabolized in the body (3).

The selection of appropriate method of reperfusion for elderly patients with AMI is one of the great enigmas of acute cure cardiology, particularly when the elderly patients constitutes about one-third of the AMI patients and more than one-half of the patients with AMI mortality. Despite of these, there have been no randomized trials focusing specifically on these high-risk patients who have been notably underrepresented in randomized trials (4, 5). Meta-analysis of large randomized trials of thrombolytic therapy have found diminished relative benefit from thrombolytic therapy but persistent absolute benefit with 1 to 3.4 lives saved per 100 patients treated (6). Two large observational studies suggest that for patients >75 years, thrombolytic therapy involves no benefit and possible harm, despite the fact that elderly thrombolytic patients actually are healthier than those managed without the reperfusion therapy (7). Given the limitations of both randomized trials and observational studies, the data are conflicted and scant. Randomized controlled trial is quite different from community practice where patients tend to be older, with a longer symptom-to-presentation interval, greater comorbidity and more relative contraindications whereas, observational studies are inherently liable to unmeasured selection bias.

Thus, the main aim of the study is to study the influence of age on the clinical outcomes in STEMI patients undergoing primary PCI or fibrinolytic therapy. Also, it assessed the angiographic profile of STEMI patients and compared the outcomes of primary PCI vs. fibrinolytic therapy in STEMI patients aged >65 years.

Methods

This is a prospective observational study which analysed the clinical profile of 500 consecutive patients with STEMI undergoing primary PCI or thrombolysis at the Department of Cardiology, Government Medical College, Kottayam, Kerala, India from August 2011 to September 2012. Data relating to complete clinical profile with emphasis on the age, angiographic features, procedural complexities and outcomes including mortality were recorded. The study was conducted according to the principles of Good Clinical Practice and the Declaration of Helsinki. Written informed consent was obtained from all the patients enrolled in the study.

Exclusion criteria

Patients who were contraindicated to fibrinolytic therapy or had previous history of STEMI or have serious medical illness like CKD, malignancy or stroke were excluded. Also, patients who refused to give informed consent were not included in the study.

Study endpoints

The primary endpoint of the study is major adverse cardiovascular events (MACE) at the end of hospitalization. MACE comprises of recurrent angina, re-infarction, heart failure, arrhythmia and death. Secondary end-points comprises of safety outcomes like major bleeding and disabling stroke.

Statistical analysis

Descriptive analysis was calculated in terms of mean and standard deviation for continuous variables and frequency with percentage for categorical variables. All data were analysed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 15

Results

Baseline demographic characteristics

Patients were categorized into four groups depending on the age (<55

years, 55-65 years, 66-75 years and >75 year). Overall, male patients dominated over the female patients. The prevalence of different risk factors and mode of reperfusion across different age groups is outlined in **table 1.**

Table 1: Baseline demographic characteristics

Characteristic		< 55 years		55 - 65 years		66 - 75 years		>75 years	
		PCI	Lysis	PCI	Lysis	PCI	Lysis	PCI	Lysis
Number , N		150	58	86	74	58	42	6	26
Males (%)		84	75	74	66	65	70	60	70
CVA (%)						1.7		3.8	
POVD (%)		0.6		2.3		5.1			
Prior CAD, (%)		1.3		3.4	5.8	6.8		16	
Prior PCI, (%)				1.1		1.7			
Diabetes, (%)		14	16.5	20.9	16	22.8	18.5	25.6	24.5
Smoking, (%)		30.4	20.5	28.6	25.7	42.8	16.9	36	24.3
Dyslipidemia, (%)		28.2	15.3	30.4	32.5	20.6	15.7	25.8	16.9
Hypertension, (%)		35.9	40.8	50.7	45.5	58.4	52.3	60.2	54.1
Window period, (min)		200	180	240	260	280	250	300	270
Killip class 3 or 4, (%)		5	9	14	20	15	10	17	18
LVEF, (%)		40	50	45	52	40	52	45	52
MI territory	AW	50	55	60	95	35	35	45	45
	IW	50	45	40	35	65	65	55	55

Angiographic and procedural characteristics

Table 2 shows comparison between two age groups (<65 years vs. >65 years) in terms of infarct-related artery in the coronary angiogram. Involvement of left anterior descending artery was more frequently observed in the age group above 65 years. Left main disease (LMCA) was seen in 33% of patients aged more than 65 years and 13% below 65 years of age. The incidence of triple vessel disease (TVD) and tortuous calcified coronaries were more in those aged more than 65 years.

Table 2: angiographic and procedural characteristics

Characteristics		< 65 years (n = 236)	>65 years (n = 64)
LAD, (%)		35	45
LCx, (%)		15	10
RCA, (%)		50	45
LMCA, (%)		13	33
No. of vessels occluded, (%)	SVD	25	17
	DVD	40	33
	TVD	35	50
Calcified vessels, (%)		15	25
Tortuous vessels, (%)		12	20
Procedure, (%)	Stenting	72	66
	POBA	22	23

Clinical outcomes

In-hospital and one-year outcomes including death, re-infarction, stroke and major bleeding were compared in different age groups **(Table 3 and table 4).**

Table 3: In-hospital outcomes across different age groups

Characteristic	< 55 years		55 - 65 years		66 - 75 years		>75 years	
	PCI (n=150)	Lysis (n=58)	PCI (n=86)	Lysis (n=74)	PCI (n=58)	Lysis (n=42)	PCI (n=6)	Lysis (n=26)
Death, n (%)	5 (3.4%)	3 (5.1%)	3 (3.4%)	5 (6.7%)	4 (6.8%)	4 (9.5%)	1 (16%)	5 (19%)
Re-infarction, n (%)	-	-	1 (1.2%)	2 (2.7%)	1 (1.7%)	1 (2.4%)	-	-
Ischemic stroke, n (%)	-	-	-	-	-	1 (2.4%)	-	-
ICH, n (%)	-	-	-	-	-	1 (2.4%)	-	-
Major bleeding, n (%)	2 (1.3%)	-	1 (2.4%)	-	1(1.7)	1 (2.4%)	-	-

Table 4: One-year outcomes across different age groups

Characteristic	66 - 75 years		>75 years	
	PCI (n=58)	Lysis (n=42)	PCI (n=6)	Lysis (n=26)
Death, n (%)	1 (1.7%)	1 (2.3%)	1 (16%)	1 (3.8%)
Re-infarction, n (%)	1 (1.7%)	2 (4.7%)	-	2 (7.6%)
Ischemic stroke, n (%)	-	1 (2.3%)	-	-
ICH, n (%)	-	-	-	1 (3.8%)
Major bleeding, n (%)	-	-	1 (16.6%)	-

In-hospital re-infarction rate was comparable between the two groups aged <65 years and >65 years. But, there was significant difference between two groups in terms of mortality (4.30 vs. 9.80, p=0.03). Stroke, both ischemic and haemorrhagic, were more in those aged more than 65 years. There was no statistical difference in the incidence of major bleed between different age groups. In all age-groups thrombolyzed patients had a higher mortality compared to PCI (p=0.04) **(Table 5).**

Table 5: Mortality rate stratified by age and modality of reperfusion (p=0.04)

Above 65 years	Above 65 years	Below 65 years	Below 65 years
PCI (n=64)	Lysis (n=68)	PCI (n=236)	Lysis (n=132)
7.8%	11.7%	3.3%	6%

At one-year follow-up, there were 3 deaths. One was due to non-cardiac cause (carcinoma lung) and another due to possible late stent thrombosis. Inferior wall STEMI with cardiac arrest was the cause of death in another patient. Four patients who were thrombolysed presented with re-infarction during follow-up period and were treated by primary PCI. There were two incidence of stroke in the thrombolyzed group. One was an ischemic stroke and other one was a hemorrhagic stroke. One PCI patient had massive upper GI bleed requiring blood transfusion in the follow-up period.

Discussion

In the present study, 300 patients who underwent primary PCI were compared with 200 patients who underwent thrombolysis. The incidence of triple vessel disease and tortuous calcified coronaries were found to be more in those aged more than 65 years. Among those who underwent primary PCI, the number of patients achieving post procedure TIMI III flow was lesser among those aged more than 65 years. Among those who underwent primary PCI, the number of patients achieving post-procedure TIMI III flow was lesser among those aged more than 65 years. Irrespective of age group, thrombolysed patients had higher in hospital mortality compared to PCI group. Strokes were more common in those aged more than 65 years. In the elder as well as the younger age groups, the thrombolyzed group had a higher mortality compared with primary PCI group.

In the Global use of Strategies to open occluded coronary arteries (GUSTO)-II B trial, the largest trial comparing angioplasty with thrombolytic therapy, 1138 patients were randomized to receive either accelerated TPA or primary angioplasty (8, 9). Although primary angioplasty resulted in better 30-day outcomes, there was no significant difference in death/MI at 6-months.While the absolute benefit of angioplasty was greater with each decade of life, the relative benefit was no greater in older than in younger patients. Although the number were small (n=90) there was no difference in mortality for

patients (27.3% with angioplasty versus 26.7 % with TPA).

Elderly patients tend to delay longer before presenting for treatment, thus reducing window of opportunity for myocardial salvage. This is particularly disadvantageous in patients treated with primary angioplasty, who already face a longer wait for reperfusion once they arrive at hospital, compared with those treated with thrombolytic therapy, which can be initiated sooner. The elderly also tend to have more severe coronary stenosis and greater impairment of thrombolysis in myocardial infarction (TIMI) grade III flow at baseline. In GUSTO-IIB for instance, TIMI grade 3 flow was present in 19% of patients aged <40 versus 6% of those aged 70 to 79.

In the controlled Abciximab and Device investigation to lower late angioplasty complications (CADILLAC)trial, 2082 patients with acute MI were randomized to balloon angioplasty, angioplasty plus abciximab, stenting alone or stenting plus abciximab. One-year mortality increased with increasing age greater than or equal to 65 years (10).

In the ADMIRAL trial, 300 patients were randomized to abciximab plus stenting or stenting alone. Age >65 years was associated with significantly better 30-day and 6-month outcomes with abciximab. Interestingly, patients aged <65 years showed no difference in outcomes consequent to adjunctive drug therapy with abciximab versus placebo. Thus, the conclusion of benefit of glycoprotein II/IIIa inhibitors in acute STEMI is strongly dependent on the elderly subgroup (11).

In the primary angioplasty in myocardial infarction (PAMI) study, which compared angioplasty with the older 3-h tissue plasminogen activator (TPA) infusion regiment, the greatest benefit was observed in patients over 65 (12). There was no significant reduction in the combined endpoints of death/MI in patients under 65 (0.8% mortality in both groups), but there was a marked reduction in the same endpoint in patients ≥65 years.

Conclusion

The clinical outcomes of acute STEMI was more adverse in patients aged more than 65 years compared to those aged less than 65 years in terms of mortality, recurrent ischemia, re-infarction and stroke irrespective of the mode of reperfusion therapy. Moreover, elderly patients had complex multivessel disease, tortuous and calcified coronary arteries. Additionally, primary PCI was superior to fibrinolysis in reducing death, reinfarction and disabling stroke in older patients with STEMI aged more than 65 years.

Study limitation

The major limitation of the study is the small patient sample size and the limited availability of the follow-up data.

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