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Original Article

Outcomes in ST Elevation Myocardial Infarction; a comparison of a tertiary care center in Pakistan with European centers

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Abstract

Objectives: To evaluate the clinical characteristics and in hospital outcome data of patients presenting to the Aga Khan University Hospital with ST elevation Myocardial Infarction (STEMI) and its comparison with data from patients enrolled in the European Heart registry for the same duration.

Methods: Data on 296 patients with STEMI was prospectively collected from 1st January 2010, till 31st December 2010 from the cardiology section at the Aga Khan University Hospital. European data was collected on 7485 patients retrieved from the Eurobservational Research programme Acute Coronary Syndrome Registry 2010 for the same duration.

Results: A total of 296 patients were enrolled from AKUH and 7485 from European centers for the year 2010. Majority of patients in both groups were male. Pakistani patients were more likely to be younger and diabetic ($p<0.05$) with higher frequency of prior myocardial infarction and angina ($p<0.05$). They were less likely to be smokers and previously diagnosed as dyslipidemic. Most patients presented to hospital with chest pain, median time between symptom onset and hospital arrival was 3.8 (2.0-8.5) hours. One third of European patients received a thrombolytic agent compared with less than 5% of AKU/Pakistani patients. Almost 90% of AKU/Pakistani patients underwent primary percutaneous intervention. Approximately 5.8% of our patients were not candidates for any reperfusion therapy vs. 4.8% of European patients.

On coronary angiogram, the majority of patients had single or two vessel Coronary Artery Disease. We had a higher frequency of high risk lesions, 97.86 vs. 84.14 %($p=0.002$).Our patients had more drug eluting stents 42.5% vs. 25.9 %($p=0.01$) implanted, due to more diabetics and smaller vessel size. We also had a similar proportion of patients undergoing coronary artery bypass graft. Frequency of complications was similar for both cohorts. Median hospital stay in our patients was shorter, survival at hospital discharge being similar between both groups ($P=0.42$)

Conclusions: The patients presenting to Aga Khan University Hospital with STEMI were younger and more likely to be diabetic. They had a higher frequency of prior Myocardial Infarction and angina. They underwent revascularization with primary percutaneous intervention more often and usually for more complex lesions requiring greater use of drug eluting stents. Survival at discharge was similar compared to European Centers.

Keywords: ST elevation MI, Primary angioplasty, Thrombolysis (JPMA 61: 1215; 2011).

Introduction

An atherosclerotic plaque with a large lipid core, thin fibrous cap and evidence of inflammation may result in fissuring of the plaque. Plaque rupture and resultant platelet activation and thrombosis leads to epicardial artery occlusion, accounting for the majority of ST segment elevation myocardial infarction (STEMI). Distal embolisation of thrombus compounds the problem. In patients without obstructive coronary artery disease (CAD) the reasons for STEMI are coronary artery dissection, embolisation and vasospasm. This may occur in 5-10% of cases.[1-4] Restoration of coronary blood flow to the infarct related artery is the guiding principle of treatment of STEMI. Rapid availability of reperfusion therapy, whether pharmacological (fibrinolytic therapy) or catheter based intervention, primary percutaneous intervention (PCI) limits infarct size and improves survival.[5] The Global Registry of Acute Coronary Events (GRACE) suggested that up to 40% of patients with STEMI do not receive reperfusion therapy.[6] When facilities for primary PCI are available; it has been proven superior to fibrinolysis in respect to improved survival, recurrent myocardial infarction and stroke.[7-13]

Administration of thrombolytic therapy within the first hour is associated with greatest benefit with regards to mortality. Collective data from several large trials revealed a 22% short term mortality reduction when patients underwent PCI as compared with fibrinolysis.[14] White and colleagues suggested that increasing the numbers of patients treated with reperfusion therapy would save an estimated 270 lives per 10 000 STEMI patients. Reducing time to fibrinolysis or changing to a PCI strategy from lysis would save an estimated 154 lives / 10 000 STEMI patients.[1] STEMI is the component of the acute coronary syndrome with highest in hospital mortality. As physicians in the developing world, with limited

resources our challenge is to evaluate our own population presenting with this illness .We need to compare their clinical characteristics, management and outcomes with those from other communities. This is how we will assess our own practices and identify areas where improvement is necessary.

The objective was to evaluate the clinical characteristics and in hospital outcomes of patients presenting to the Aga Khan University Hospital with ST elevation MI and compare them with data from patients enrolled in the European Heart registry[33] for the same time period.

Patients and Methods

This is a cross sectional observational study with data on 296 patients with STEMI prospectively collected from 1st January 2010, till 31st December 2010 at the Aga Khan University Hospital .All patients admitted to the coronary care unit with the primary diagnosis of ST Elevation Myocardial Infarction, either from emergency room or within the hospital were enrolled after informed consent. The inclusion criteria was adults presenting with STEMI to the Aga Khan University hospital. STEMI was defined as clinical presentation with chest pain $\geq$ 20 minutes and ST elevation of more than 1mm in at least 2 contiguous leads or new onset left bundle branch block on 12 lead ECG. The exclusion criteria was patients were excluded if they had STEMI as a complication of PCI or CABG.

European data was retrieved from 7485 patients enrolled with the Euro Observational Research programme Acute Coronary Syndrome Registry 2010 during the same period.[33]

SPSS© (version 19) was used for data analysis. Results were reported as mean ± standard deviation for quantitative variables and frequency (percentage) for qualitative variables. Median and inter-quartile range was calculated for non-symmetric variable like age. Student's t test was used to compare means of quantitative variables and Chi square (or Fisher's exact) test for categorical variables. All P values were 2 sided and values <0.05 were considered significant.

Results

Mean age of our patients was less than that of the European patients. Majority of patients in both series were male (p=0.003). The patient population presenting to Aga Khan University Hospital with STEMI was younger and more likely to be diabetic. They had a higher proportion of prior myocardial infarction and angina (p<0.005).There was a statistically insignificant trend towards a larger number of prior interventions, both PCI and CABG. We had a lower proportion of both current and former smokers as well as persons with dyslipidaemia compared with the Europeans (Table-1).

Two thirds of patients in both groups were not on any medical therapy prior to this hospitalization. Most patients presented to hospital with chest pain (Table-2), fewer presented with dyspnoea, syncope, arrhythmias and cardiac arrest (or aborted sudden cardiac death).

Symptom onset to hospital arrival occurred in a median 3.8 (2.0-8.5) hours in our patients compared with 3.0(1.7-6.5) hours in the European patients.

The majority of patients in both groups were characterized as being in Killip class 1 on presentation, since they had no evidence of heart failure or cardiogenic shock on arrival.

About a third of European patients, but only around 5% of our patients received thrombolysis (Table-3). Our patients had a higher proportion undergoing primary

Table-1: Baseline Data.

Risk factors	European registry n=7485 (%)	AKUH n=296 (%)	P value
Age Median (IQR)*	59.7(50.1-71.8)	57.8 (50.1-66.6)	P=0.88
Age >75 years %	1496 (19.6)	34(11.5)	p<0.005
Male	5887 (78.7)	238 (80.4)	P=0.003
Female	1598 (12.3)	58 (19.6)	
Diabetes Mellitus	1759 (23.7)	102 (34.4)	p<0.001
Hypertension	3633 (49.1)	153 (51.7)	p=0.38
Dyslipidemia	2538 (36.8)	69 (21.7)	P=0.013
Family History of premature CAD	1815 (25.6)	72 (24.3)	p=0.62
Current smoker	3268(44.3)	70 (23.6)	p<0.001
Prior MI/angina	2185 (29.4)	126 (42.6)	p<0.001
Prior history of CHF	336 (4.5)	3(1)	P=0.17
Prior History of PCI	514 (6.9)	29 (9.8)	P=0.44
Prior History of CABG	108 (1.4)	10 (3.4)	P=0.31
Chronic Kidney disease	212 (2.8)	7 (2.4)	P=0.65
Prior use of ASA	1378 (25)	74 (18.6)	P=0.30

IQR =interquartile range ,p value calculated by Mann Whitney U test. P<0.05-Significant.
CAD: Coronary Artery Disease. MI: Myocardial Infarction. CHF: Congestive Heart Failure. PCI: Primary Percutaneous Intervention. CABG: Coronary Artery Bypass Graft.

percutaneous intervention (PCI) as the preferred reperfusion strategy (88.4 vs. 52.3%).

Around 5.4 % (4.8% for Europeans) patients were treated medically and did not receive reperfusion therapy, mostly due to late arrival and completed infarcts.

On coronary angiogram, the majority of patients had single or two vessel CAD (Figure).

Table-2: Clinical presentation.

Presenting complaints	European registry n=7485 (%)	AKUH n=296 (%)	P value
Chest pain	6870 (91.8)	262 (88.5)	0.04
Dyspnea	187 (2.5)	14(4.7)	0.01
Syncope	116 (1.6)	4(1.4)	0.73
Cardiac arrest	155(2.1)	3 (1)	0.19

Table-3: Reperfusion Strategy.

Reperfusion strategy	European registry n=7485 (%)	AKUH n=296 (%)	P value
No reperfusion received	360 (4.8)	16(5.4)	p=0.63
Thrombolytic	2493 (33.3)	14 (4.7)	p<0.005
PCI strategy:			
Primary	3408 (52.3)	236 (88.4)	p<0.005
Facilitated	180(2.4)	3(1.1)	
Rescue	546(7.3)	1(0.4)	
CABG	299 (4)	18(6)	P=0.08

Table-4: Left Ventricular function post STEMI.

Pre-discharge LV function	European registry n=7485 (%)	AKUH n=296	P value
EF Preserved (>50%)	2957(40.6)	123(48.6)	0.28
EF Mildly reduced (41-50%)	3378(25.4)	65(25.7)	
EF Moderately reduced (31-40%)	2077(16.1)	36(14.2	
EF Severely reduced (<30%)	1047(7.8)	19(7.5)	

EF: Ejection Fraction. LV function not assessed in 10% European patietns and 4% Pakistani patients.

Table-5: Complications of Myocardial Infarction.

Complications	European registry n=7485 (%)	AKUH n=296	P value
Congestive heart failure	1257(16.8)	47(13.9)	0.57
Cardiogenic shock	483(6.5)	3(1)	0.12
Mitral regurgitation	87(1.2)	3(1)	1.0
Stroke	65(0.9)	1(0.3)	1.0
Major bleeding episode	95(1.3)	3(1)	1.0

Table-6: in hospital survival post STEMI.

Survival	European registry n=7485 (%)	AKUH n=296	P value
Alive	6970(93.1)	272(91.9)	0.42
Dead	514(6.9)	24(8.1)	

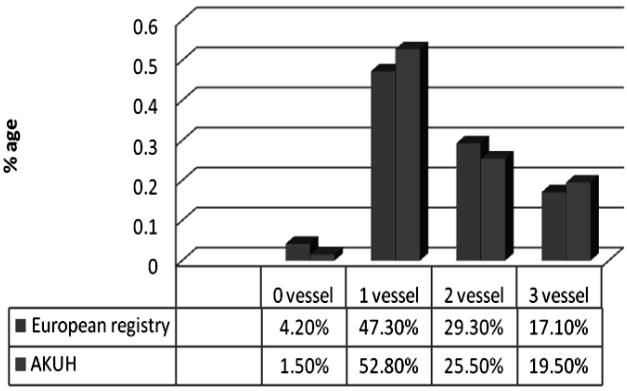

Figure: Number of coronary arteries involved in patients with STEMI.

About a fifth of patients in both groups had 3 vessel CAD. Less than 1% percent patients in both groups had the left main coronary artery as the culprit vessel.

Angiographically, our patients had a higher proportion of high risk lesions 97.86 vs. 84.14 %(p=0.002).Our patients had more drug eluting stents implanted 42.5% vs. 25.9% (p=0.01), due to more diabetics, smaller vessel size and complex coronary anatomy. Procedural success, defined as achievement of TIMI III flow in the infarct related artery, was 98.1%. Rates of referral for CABG were similar in both groups (8.9% vs. 6.08%).

The majority of patients in this study had preserved left ventricular function assessed on echo prior to hospital discharge (Table-4), reflecting timely management and indicative of myocardial salvage in these patients. Despite comparatively delayed presentation, only 21.7% of our patients had an ejection fraction below 40%.

Clinically significant complications from myocardial infarction were infrequent, with no statistically significant difference in both groups (Table-5).A major bleeding episode was defined as overt clinical bleeding with a drop in haemoglobin of >0.5g/litre (or a drop in haematocrit by 15%).

Medical therapy received was similar in both groups, with no significant differences in anti-platelets agents, beta blockers, ACE inhibitors/ angiotension receptor blockers or statins between both groups (p values NS for all)

Median hospital stay in our series was shorter, 4.0 (3.5-6.0) days as compared with 7.0 (5.0-10). Survival at hospital discharge was also similar between both groups, 91.9% for the AKUH cohort vs. 93.1% (P =0.42) for European patients.

Discussion

This study was done to evaluate the clinical profile of

patients presenting with STEMI at a tertiary care center in Pakistan. Our patients had a mean age of 58 similar to those reported by other centers from the same part of the world, which is consistently younger than patients presenting with STEMI from the west.[15-22]

Numerous previous series have reported a male preponderance in patients presenting with STEMI. Women are known to have advanced age, increased co-morbidity and increased short term mortality than men with STEMI. They are also more likely to have symptoms labeled as "atypical" .They are liable to receive less aggressive therapy and be subject to delays, even if socio cultural and financial factors are not considered.[24,25] Female representation ranges from 18.2-35% in the literature, which is similar to our experience.[12,23]

Diabetes was present in around a third of our patients, which is similar to data from India, reported by Xavier et al.[12] Jafary et al, from the same center found prevalence of diabetes to be 41.7% and 32.1% in patients with STEMI undergoing fibrinolysis and primary PCI respectively.[26,27]

Our population had prior history of a myocardial infarction or angina in just less than half the patients which was more than the Europeans (29.4%). In the registry from India a previous MI was reported in 11.8% and a prior episode of CHF was mentioned in less than 1% patients.[12] Some of these differences can be attributed to a referral center bias, because of which patients with prior cardiac events ,co morbidities and generally older age may be advised admission to a multidisciplinary tertiary care center, even if they are initially diagnosed to have STEMI at another local hospital.

The Pakistani cohort presented to a tertiary care center in Karachi, that is JCIA certified and has a cardiac catheterization laboratory with 24 hour coronary angiography and PCI facilities.

Median presenting time since the onset of symptoms was 3.8 hours ranging from 2 to 8.5 hours. This was longer than the European patients, whose mean arrival time was 3 hours .In the Indian series 58.8% of patients presented later than 4 hours after symptom onset.[12] Jafary et al from the same center had reported a mean 4.5 hour delay between symptoms and hospital arrival for patients undergoing primary PCI and 90 minutes for those undergoing thrombolysis.[26,27]

Reasons for delay in presentation by the patient may include lack of awareness as to the significance of symptoms, lack of transport facilities, financial difficulties, and even inaccurate initial diagnosis. In a society where majority of patients do not have access to health insurance, there may be a combination of reasons. Similar to our findings, Xavier et al had reported government or insurance payment in 12.8% of patients with STEMI in India.[12]

About a fifth of our patients had a left ventricular function less than 40% who may be candidates for an implantable cardioverter-defibrillator or cardiac resynchronization therapy later on.

Pooled data from 23 randomized trials analyzed by Keely et al suggested a mortality benefit with primary PCI.[9] Timmer et al had reported that primary PCI was associated with decreased mortality in both diabetic and non diabetic patients, but with greater benefit in the diabetics.[13]

A significant majority of our patients underwent Primary PCI compared to the European patients. The registry data from India revealed that 58.5% of patients underwent thrombolysis and 8% had undergone a primary PCI.

One of the main reasons why primary PCI was considered to be a superior strategy by the attending cardiologists at our center was the fact that the available fibrinolytic agent was streptokinase, which is not fibrin specific and has a lower rate of achieving TIMI III flow,[28,29] however it costs approximately $68 per patient. Alteplase, a superior fibrinolytic, though available, costs approximately similar to that of a primary PCI, $2408 vs. $2500 for PCI (currently the US dollar stands at 85.9 Pakistani Rupees). Other reasons for preferring an interventional strategy were that the 24 hour availability of the cardiac catheterization laboratory guaranteed that the estimated door to needle time would be minimized. Being a multidisciplinary hospital, many of the patients presenting to the AKUH were likely to be older and have more co-morbidities. For the reasons mentioned above they were more likely to have contraindications to thrombolysis such as a prior history of intracranial pathology, (especially stroke) recent surgery, trauma, malignancy and be advised anticoagulation for other indications.

Navarese et al had found that the reduction of mortality in STEMI was associated with earlier presentation and when the patients were treated at high volume PCI centers (defined as >65 primary PCIs per year. For later presentation a higher number of procedures (>145/year) is required to provide a survival benefit.[30] Our center therefore qualified as a high volume PCI center and this may have factored into the decision of the primary cardiologists to favour an interventional strategy.

Procedural success for primary PCI in this study was 98.1%, similar to that reported by Jafary et al from the same center (97.1%) in a 5 year review.[27] Similar rates have been quoted by Farman et al (98.2%) and Shaikh et al (97%), from public and private sector hospitals in Karachi.[31,32]

Mortality in our series was comparable to that of the European registry data 8.1 vs 6.9%, and similar to figures from India which reported mortality from STEMI to be 8.6%.[9]

Conclusions

The patient population presenting to Aga Khan University Hospital with STEMI was younger and more likely to be diabetic. They had a higher proportion of both prior coronary artery related events, as well as interventions. They underwent revascularization with primary PCI more often and for more complex lesions requiring greater use of DES. Complications and survival at discharge were similar compared to European Centers.

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