

Original Article:

Gender Differences in the Clinical and Angiographic Profile in STEMI Patients Undergoing Primary Angioplasty

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ABSTRACT

Background

Cardiovascular disease is the major cause of death in women and is still under-recognized and undertreated. Cardiovascular disease develops 7 to 10 years later in women than in men. There are major differences in the prevalence of various risk factors such as diabetes mellitus, hypertension, family history of CAD, dyslipidemia, obesity and cigarette smoking. The presenting symptoms also differ as women are more likely to present with atypical chest pain, neck pain, nausea, fatigue and dyspnea. Characteristics of coronary lesion also vary widely amongst women. This often leads to a higher mortality after the first episode of myocardial infarction and a greater incidence of complications among women necessitating a gender specific approach to primary and secondary prevention

Objective

To study the gender specific difference in risk factors, clinical features, complications and angiographic patterns of coronary artery involvement in patients with STEMI undergoing primary angioplasty.

Methodology

Consecutive 113 male and 111 female patients admitted with STEMI in ICCU and who underwent primary angioplasty were studied. Detailed history and clinical examination were done after taking informed consent. The risk factors which were studied include hypertension, diabetes mellitus, smoking, dyslipidemia and family history of premature coronary artery disease. ECG and Echocardiography were taken at diagnosis and whenever patient's condition demanded. Invasive Coronary angiography was done in patients as a part of primary percutaneous coronary angioplasty and SYNTAX score was calculated. Data were coded and entered in Microsoft Excel and analyzed using IBM SPSS software.

Results

Consecutive 113 male patients and 111 female patients were studied. Mean age in the male group was 55.08 ± 10.21 years and in female group was 59.21 ± 10.24 ($p < 0.003$) years. Higher prevalence of diabetes (60.3% vs 46.9%) and dyslipidemia (40.54% vs 31.8%) in females and higher prevalence of hypertension in male group (36.2% vs 32.7%) were observed. Smoking history was present in 61% of male patients. On admission most of the patients were in Cedar Sinai class I. Among male patients mean window period was 4.86 ± 1.93 hours and in female patients 6.92 ± 3.12 hours. Fifty-nine male patients and fifty female patients had Anterior wall myocardial infarction. Most of the patients underwent PCI through Radial route. Diabetic females tend to have more multi vessel disease. The mean SYNTAX score in male patients was 16.52 ± 6.59 and in female patients was 17.51 ± 5.87 . High SYNTAX score correlated with worse in-hospital outcome. Compared to men, women received stents with lower diameters (2.48 ± 0.87 mm vs 2.68 ± 0.96 mm). Most of the patients underwent PTCA using second generation DES. Post infarction angina (24% vs 14%) and cardiac failure (21% vs 14%) were more frequent in female group. In hospital mortality in female group was 7% and in male group was 3.5%.

Conclusion

In our study female patients with STEMI presented at later age and the mean age difference was 4 years. There were major differences in risk factors as higher prevalence of diabetes and dyslipidemia observed in female group and high prevalence of hypertension in male group. More number of male patients had family history of coronary artery disease and previous history of coronary artery disease. Smoking and alcoholism were seen solely in male group. Female patients had significant prehospital delay. SYNTAX score well correlated with the in-hospital outcome in both groups. More number of female patients had post infarction angina and cardiac failure. In hospital mortality was more in female patients

Key words

Gender difference; STEMI; Primary PCI, SYNTAX score; Cardiac failure

INTRODUCTION

Coronary Artery Disease (CAD) for long has been called “men’s disease”¹. Cardiovascular disease remains the leading cause of mortality in women. There are both biologic and sociocultural differences in cardiovascular disease and its outcomes among males and females. There are major differences in the prevalence of various risk factors such as diabetes mellitus, hypertension, family history of CAD, dyslipidemia, obesity and cigarette smoking in females. The presenting symptoms also differ as women are more likely to present with atypical symptoms.

Women have varied presentation of coronary artery disease from single vessel disease to multi vessel disease. Characteristics of coronary lesion also vary widely amongst women. This often leads to a higher mortality after the first episode of myocardial infarction and a greater incidence of complications among women necessitating a gender specific approach to primary and secondary prevention

AIM

To study the gender specific difference in risk factors, clinical features, complications and angiographic patterns of coronary artery involvement in patients with STEMI undergoing primary angioplasty.

MATERIALS AND METHODS

This was a prospective analytical study conducted over a period of 12 months.

Study population

Patients admitted in ICCU of Cardiology Department, Government Medical College, Kottayam, Kerala with a diagnosis of ST elevation myocardial infarction and undergoing primary angioplasty.

Sample size

The sample size was estimated using the formula for calculation of comparing proportions:

$$\text{Sample size } N, = (Z\alpha + Z\beta)^2 [P_1(1 - P_1) + P_2(1 - P_2)] / (P_1 - P_2)^2$$

$P_1 = 28$ and $p_2 = 46$ from previous study¹; applying to above equation, sample size estimated was 108 and corrected to 110. Consecutive 113 male and 111 female patients were included in the study.

Inclusion criteria

1. Consecutive patients of STEMI, defined by Symptoms of ischemia, Electrocardiogram changes indicative of new ischemia with at least two contiguous leads with ST-segment elevation ≥ 2.5 mm in men < 40 years, > 2 mm in men > 40 years, or ≥ 1.5 mm in women in leads V2–V3 and/or > 1 mm in the other leads or development of pathological Q waves and imaging evidence of infarction undergoing primary angioplasty.
2. Age group of ≥ 18 years.

Exclusion criteria

1. Congenital heart disease
2. Cardiomyopathy
3. Valvular heart disease
4. Myocarditis
5. Acute myocardial infarction secondary to aortic dissection
6. Patients not willing for PCI
7. Patients with absent cardiac biomarker elevation

Methodology

Myocardial infarction was diagnosed according to Fourth Universal Definition of Myocardial Infarction (2018).

Definition of Myocardial Infarction

The term ‘Acute Myocardial Infarction’ should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for Myocardial Infarction:

Criteria for acute myocardial Infarction.

Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:

- Symptoms of ischemia.
- New or presumed new significant ST-segment–T wave (ST–T) changes or New left bundle branch block (LBBB).
- Development of pathological Q waves in the ECG.
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- Identification of an intracoronary thrombus by angiography or autopsy.
- Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.

Percutaneous coronary intervention (PCI) related Myocardial Infarction is arbitrarily defined by elevation of cTn values ($>5 \times 99$ th percentile URL) in patients with normal baseline values (≤ 99 th percentile URL) or a rise of cTn values $>20\%$ if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischemia or (ii) new ischemic ECG changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.

After admission, detailed history and systematic examination were done. The risk factors which were studied include hypertension, diabetes mellitus, smoking, dyslipidemia and family history of premature coronary artery disease. ECG and Echocardiography were done after admission and whenever patient's condition demanded. Invasive Coronary angiography was done in patients as a part of primary percutaneous coronary angioplasty and SYNTAX score was calculated. Patients were managed according to the standards of our institution in evidence-based manner. Patients were followed up at hospital till discharge

Data management and statistical analysis.

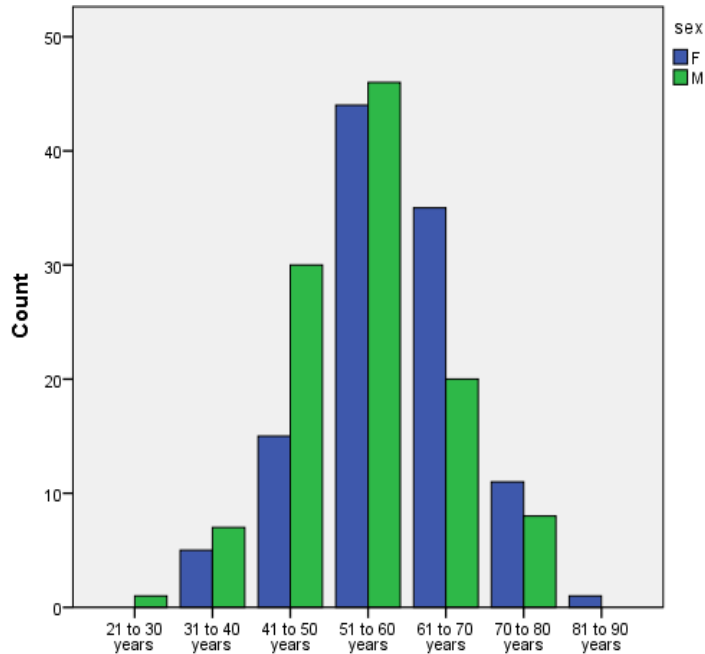
Data were coded and entered in Microsoft Excel and analyzed using IBM SPSS software Qualitative data was analyzed using percentage and proportion. Quantitative data analyzed using mean and standard deviation (for normally distributed data), median and interquartile range (for not-normally distributed data). Differences between groups was compared with Student's t-test for parametric continuous variables. Chi-square test was applied for estimating the occurrence of categorical variables. A p value < 0.05 is used as threshold for significance.

RESULTS

We have compared the gender differences in the clinical characteristics, coronary angiographic features, and in hospital outcome in patients with STEMI undergoing primary angioplasty

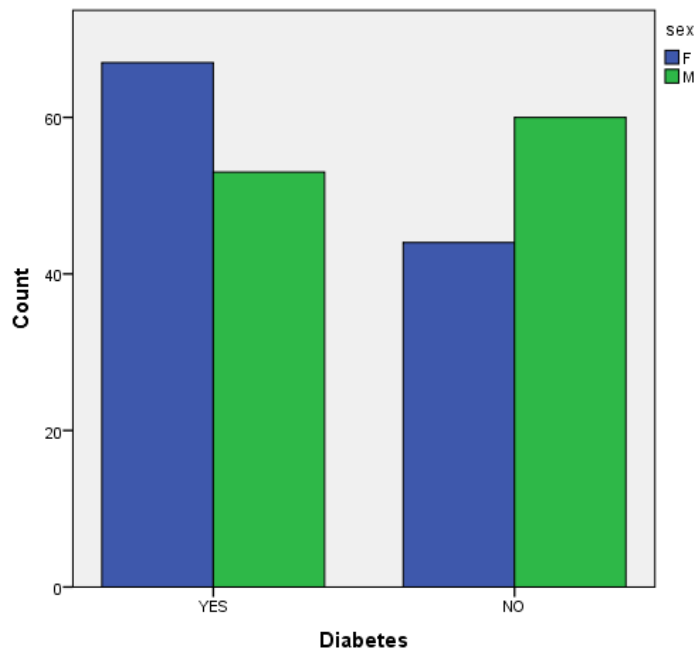
Consecutive 113 male and 111 female patients presenting with STEMI who underwent primary angioplasty were studied.

Mean age in the male group was 55.08 ± 10.2 years and in female group was 59.21 ± 10.2 years ($p = 0.003$)



Risk factors.

Out of 113 male patients, 53(46.9%) had history of diabetes. Among 111 female patients 67(60.3%) were having diabetes ($p = 0.03$).



37 female patients had history of hypertension (32.7%) and 41 male patients were having history of hypertension (36.2%) ($p = 0.30$).

45 female patients had history of dyslipidemia ((40.54%) and 36 male patients had dyslipidemia (31.8%) ($p = 0.20$).

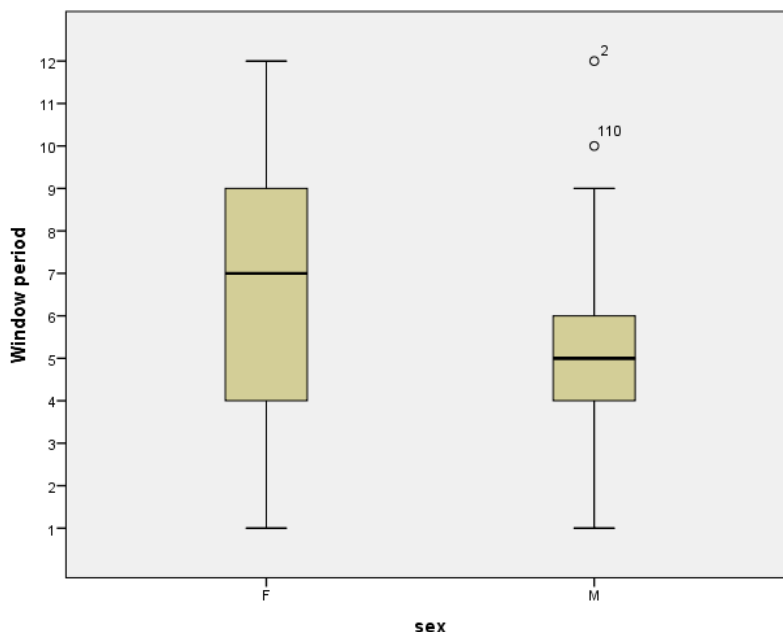
10 female patients (9%) and 16 male patients (14%) had family history of coronary artery disease ($p = 0.10$).

Smoking and alcohol use were solely seen in male group. 69 male patients had history of smoking (61%) 38 male patients had history of alcoholism (33%). 4 female patients and 2 male patients had history of ischemic stroke in the past. 5 female patients and 1 male patient had history of hypothyroidism.

Clinical presentation.

Window period.

Among male patients, mean window period was 4.86±1.93 hours and in female patients 6.92± 3.12 hours (p value 0.001)



Cedar Sinai (CS) class at the time of admission:

Table No. 1- Cedar Sinai (CS) Class at the time of admission.

CS Class	Female	Male
CS I	73 (63%)	75 (66%)
CS II	8 (7%)	12(10%)
CS III	22 (19%)	16 (14%)
CS IV	8 (7%)	10 (8%)

Territory of STEMI:

Table No.2- Territory of STEMI

Territory involved	MALE	FEMALE
AWMI	59	50
IWMI	12	17
IW+RV MI	16	22
IW+PW MI	18	17
IW+LW MI	1	0
IW+PW+RV MI	5	3
IW+PW+LW MI	2	2

59 male patients and 50 female patients had anterior wall myocardial infarction. 12 male patients and 17 female patients with inferior wall myocardial infarction underwent

primary angioplasty. 16 male patients and 22 female patients had inferior with right ventricular infarction. Inferior with posterior myocardial infarction was seen in 18 male and 17 female patients. One male patient had inferolateral myocardial infarction. 5 male patients and 3 female patients had infero-posterior with right ventricular myocardial infarction. 2 male and 2 female patients had infero-posterolateral myocardial infarction.

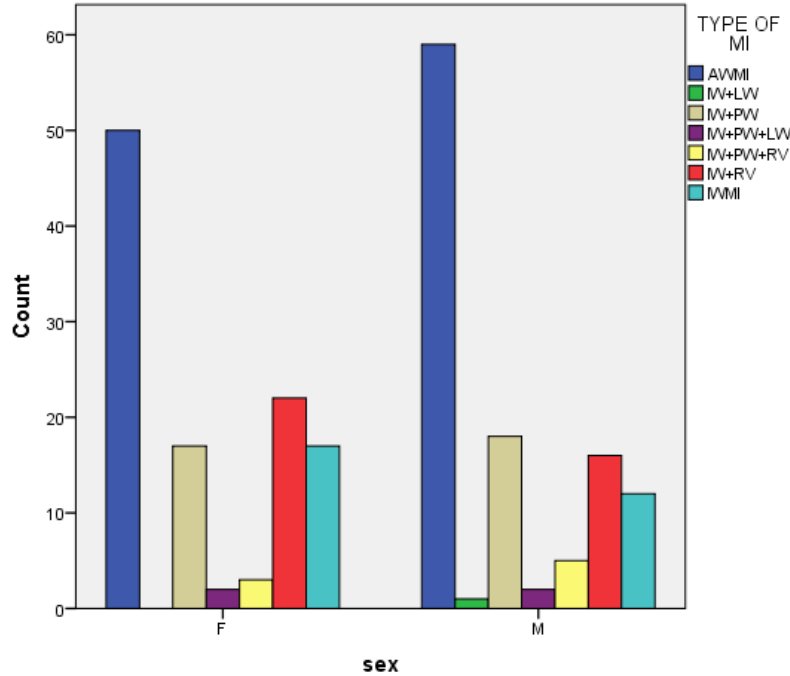


Table No.3- Territory of STEMI

Territory involved	Male	Female
Anterior	59	50
Inferior related	54	61

Arrhythmia on admission

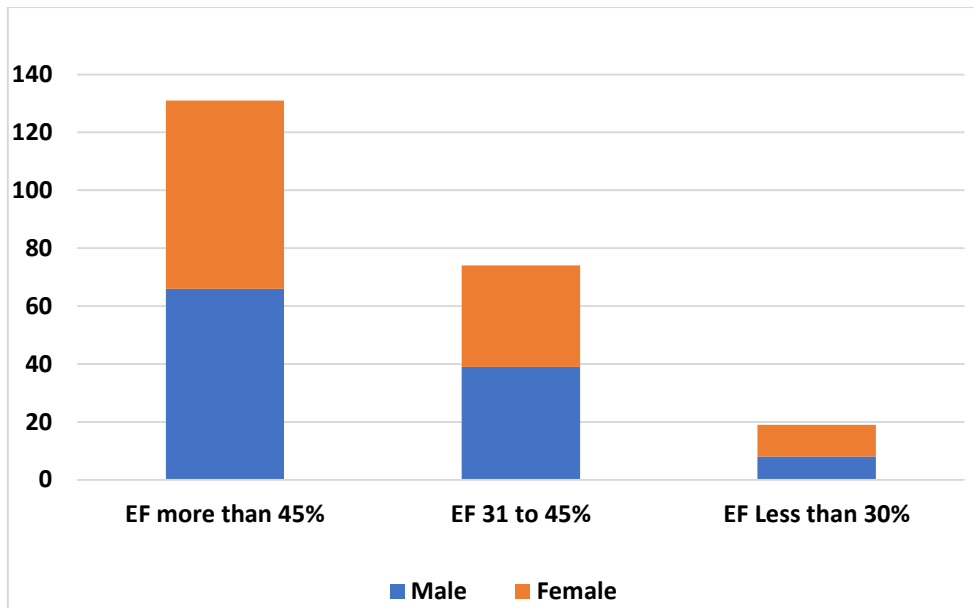
9 female patients and 4 male patients had atrial fibrillation. 16 female patients and 17 male patients had AV blocks. 6 male patients and 2 female patients had ventricular tachycardia, 2 female patients and 2 male patients had ventricular fibrillation. 3 male patients and 6 female patients had RBBB

LV function

Mean ejection fraction among female patients was 46.62 +/- 9.19 and in male patients was 46.96 +/- 8.62 percentage

Table No.4- LV function

Ejection fraction	Male	Female
Less than 30%	8	11
31 to 45%	39	35
More than 45%	66	65



Vascular Access for coronary angiogram and angioplasty.

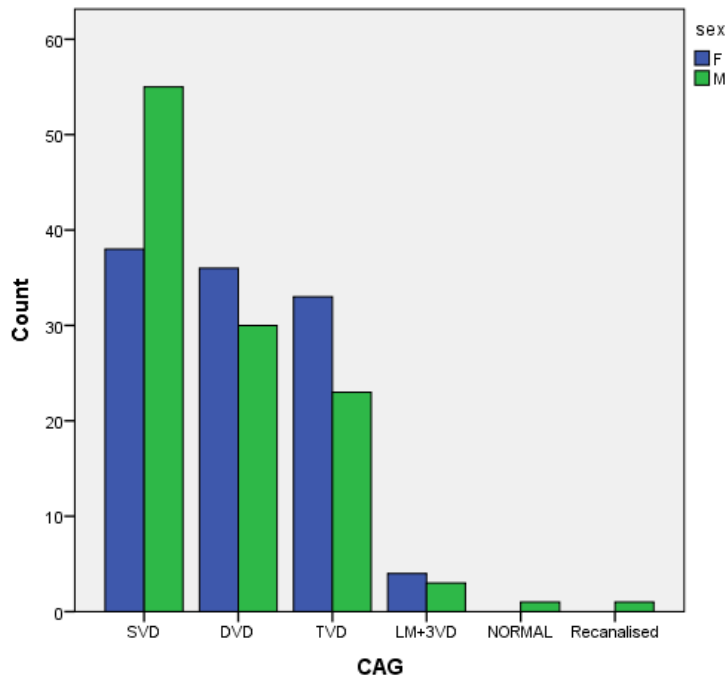
Radial approach was the default strategy for intervention. 22 female patients and 14 male patients underwent the procedure through femoral access (p = 0.09) due to technical difficulties for radial approach.

Angiographic profile

55 male patients and 38 female patients had single vessel disease. 30 male patients and 36 female patients had double vessel disease. 23 male patients and 33 female patients had three vessel disease. Left main + three vessel disease was the finding in 3 male and 4 female patients. One male patient had normal coronaries and one male patient had recanalized vessel.

Table No. 5- Angiographic profile

Angiographic profile	Male	Female
Single Vessel Disease (SVD)	55	38
Double Vessel Disease (DVD)	30	36
Tripple vessel disease (TVD)	23	33
Left main with TVD	3	4
Normal/ recanalized vessel	2	0



In female patients, 3 out of 4 patients (75%) with left main disease, 24 out of 33 three vessel disease patients (73%) and 24 out of 36 patients (67%) with double vessel disease had diabetes mellitus.

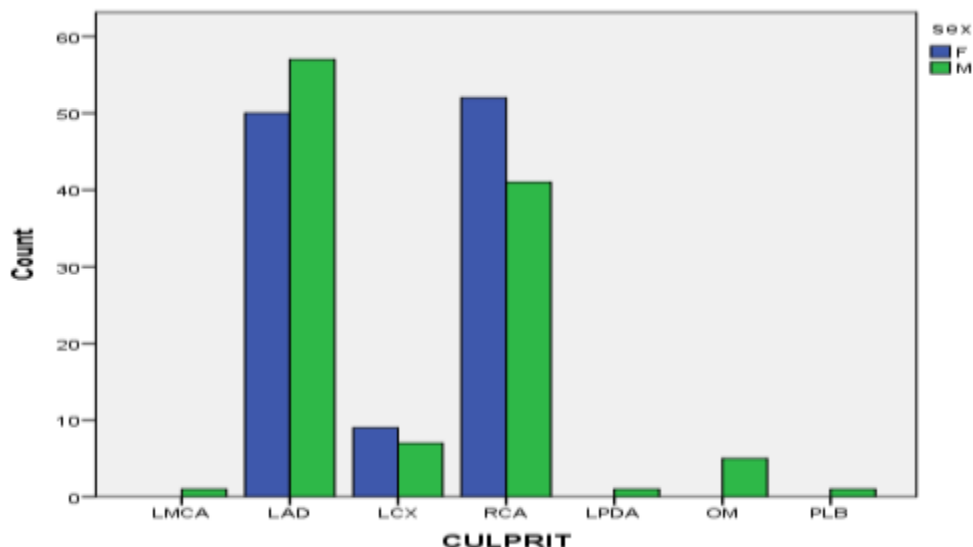
In male patients, 3 left main disease patients, 12 out of 23 three vessel disease patients (52%) and 16 out of 30 double vessel disease patients (53%) had diabetes mellitus.

In both sexes diabetic patients prone for having multivessel disease and was statistically significant in female group (p= 0.039)

Culprit Vessel.

In male group 55 patients had left anterior descending artery (LAD), 7 patients had left circumflex (LCx), 42 patients had right coronary artery (RCA), one patient had left main coronary artery (LMCA), one patient had left posterior descending artery (LPDA) and 5 patients had obtuse marginal (OM) as the culprit artery.

In female group 50 patients had LAD, 9 patients had LCx and 52 patients had RCA as the culprit vessel.



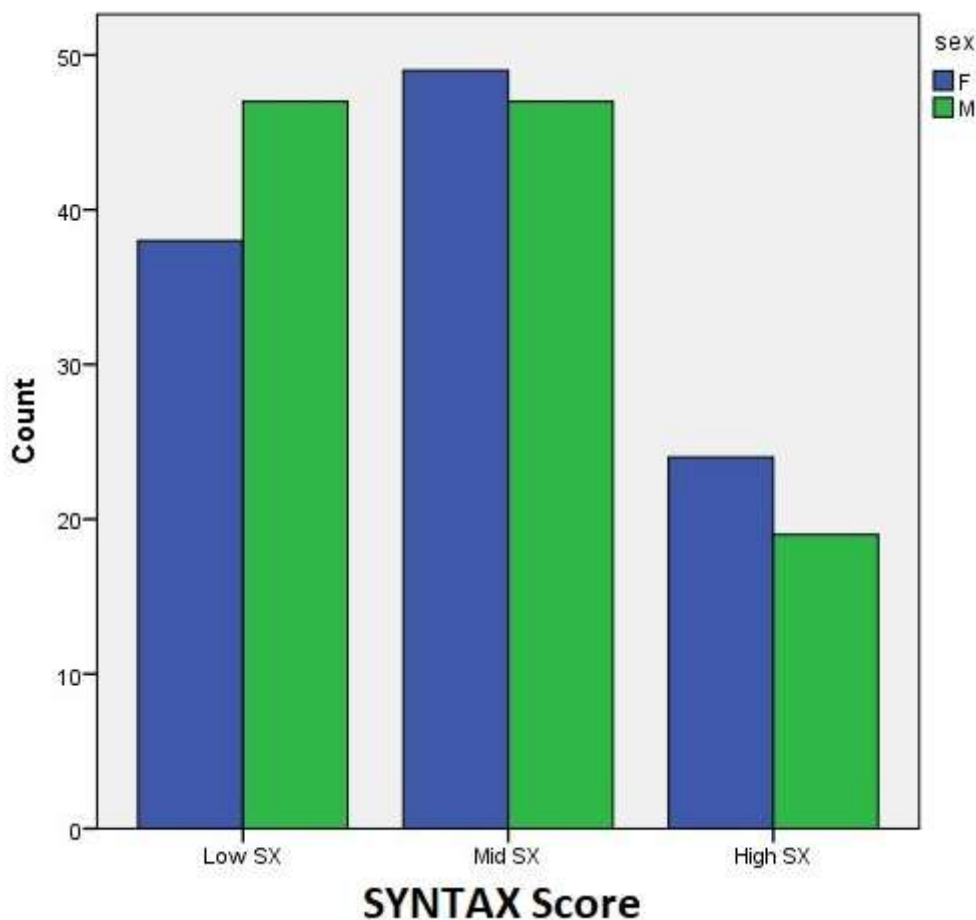
SYNTAX score

In female group mean SYNTAX score was 17.51+5.87 and in male group mean SYNTAX score was 16.52+6.59.

Patients were categorized according to SYNTAX score as Low SYNTAX score (Low SX = score less than 16) Mid SYNTAX score (Mid SX =score 16-22) and High SYNTAX score (High SX =score more than 22) according to previous study².

Table No.6- SYNTAX score

SYNTAX	Male	Female
Low SX	47 (41%)	38(34%)
Mid SX	47 (41%)	40(36%)
High SX	19 (16%)	24(21%)

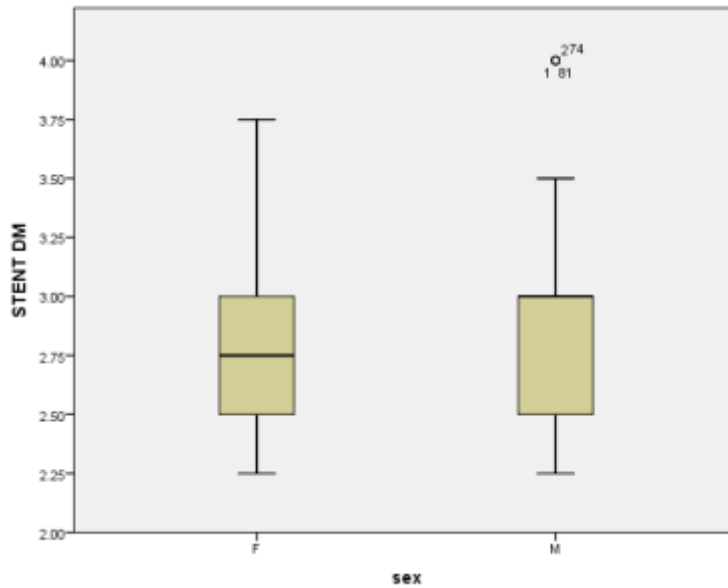


Procedure

101 female patients and 101 male patients underwent primary PTCA with stenting. 10 male patients and 10 female patients underwent primary PTCA with Balloon angioplasty (POBA) alone, 4 female patient and 3 male patients had undergone thrombus aspiration during procedure in view of heavy thrombus

Stent size

Mean stent diameter in female group was 2.48 +/- 0.87mm and in male group was 2.68 +/- 0.96mm (p value 0.038)



Mean stent length in female group was 27.69 ± 13.41 mm and in male group was 26.28 ± 12.5 mm

Major Adverse Cardiac Events (MACE) during hospitalization:

Post infarction angina.

24 female patients and 16 male patients experienced post infarction angina ($p = 0.09$). 21 female patients and 16 male patients experienced symptoms of heart failure ($p = 0.20$)

Acute kidney injury.

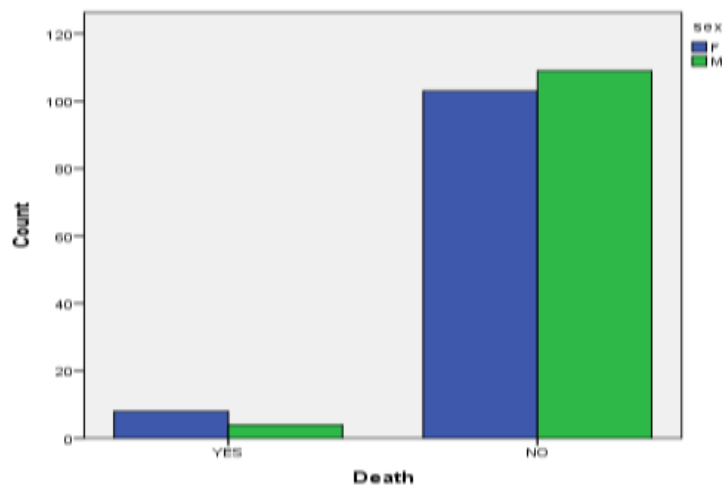
10 female patients and 8 male patients developed acute kidney injury following primary angioplasty

Other complications:

3 female patients had acute stent thrombosis. One female patient had coronary artery perforation during intervention. One female patient had ventricular septal rupture

In-hospital Mortality.

Mortality in female group was 8 and in male group was 4 ($p = 0.17$)

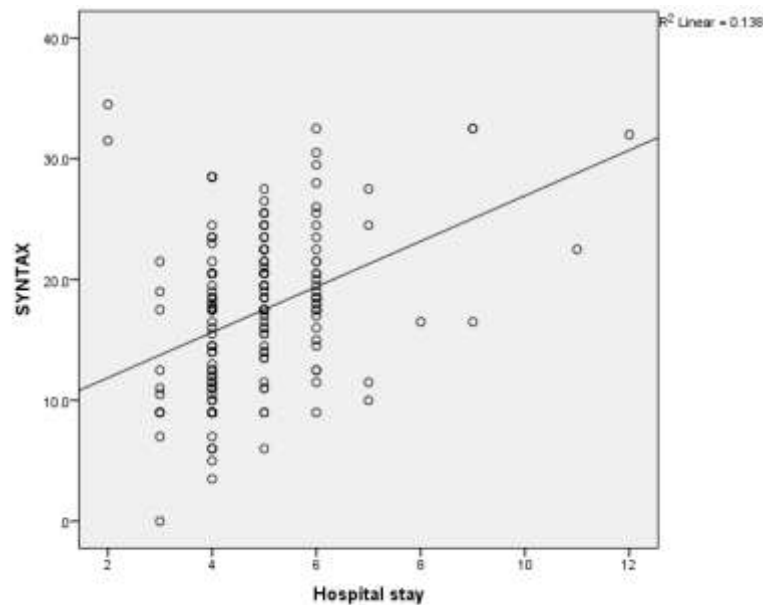


Duration of hospital stay.

Mean hospital stay in female group was 4.97 ± 1.19 days and in male group was 4.50 ± 1.23 days (p value 0.04)

SYNTAX score and Hospital stay.

SYNTAX score is having a positive correlation with hospital stay duration($r=0.76$).

**SYNTAX score and in hospital mortality.**

In-hospital mortality in male group was 4 out of 113 patients (3.5%). One mortality in low SYNTAX score group and 3 in high SYNTAX score group (p value 0.001).

In-hospital mortality in female group was 8 (7.2%). One mortality in mid SYNTAX group and 7 mortality in high SYNTAX group (p value <0.0001).

In both male and female group high SYNTAX score was associated with higher in-hospital mortality.

DISCUSSION

We have compared the clinical characteristics, coronary angiographic profile and in hospital outcome in male and female patients presented with acute STEMI undergoing primary angioplasty. Consecutive 113 male patients and 111 female patients were studied

Age

In this study, mean age in the male group was 55.08 ± 10.21 years and in female group was 59.21 ± 10.24 (p 0.003) years. Data from Kerala ACS registry shows mean age of STEMI presentation being 60 ± 12 years³ and women were approximately 5 years older than men at presentation⁴. CREATE registry shows mean age of STEMI presentation being 57.5 ± 12.1 ⁵.

Diabetes mellitus

Out of 113 male patients 53 (46.9%) had history of diabetes: Among 111 female patients 67(60.3%) patients had diabetes (p =0.03). In their study, Menghe Zhou et al⁶ showed a high prevalence of diabetes in female patients with ACS (45% vs 35%). Edyta Radomska in their study⁷ also found a higher prevalence of diabetes mellitus in female population (28% vs 16%).

Hypertension

In our study 37 female patients (32.7%) and 41 male patients (36.2%) had history of hypertension. In GUSTO 1 trial prevalence of history of previous hypertension in ACS was 38.1%^{8,9}.

Dyslipidemia

Our study shows a high prevalence of dyslipidemia in female group (40.54% vs 31.8%) but was not statistically significant. India Migration Study(rural) showed high prevalence of dyslipidemia among female (27.8% vs 21%)^{10,11}. But in another study Sawant et al showed higher prevalence of dyslipidemia among male (38.7% vs 23.3%) in south Indian population¹¹.

Clinical presentation.**Window period**

Our study shows, among male patients mean window period was 4.86 ± 1.93 hours and in female patients 6.92 ± 3.12 hours (p value 0.001). Previous studies also observed a delay in medical care among female patients¹².

Arterial territory of STEMI.

Our study showed a higher number of anterior wall myocardial infarction in both male and female group. There are discrepancies between published studies. Some studies showed a higher incidence of anterior wall myocardial infarction¹³. Higher incidence of inferior wall myocardial infarction is also reported¹⁴.

Angiographic profile

In our study Left main + three vessel disease was the finding in 3 male and 4 female patients. 55 male patients and 38 female patients had single vessel disease. 30 male patients and 36 female patients had double vessel disease. 23 male patients and 33 female patients had three vessel disease. One male patient had normal coronary and one male patient had recanalized vessel. Results were comparable to previous studies. Similar to previous study our study also showed that diabetic patients are prone to have multivessel disease¹⁵.

SYNTAX score

In female group mean SYNTAX score was 17.51 ± 5.87 and in male group mean SYNTAX score was 16.52 ± 6.59

Originally, the SYNTAX score was introduced to predict clinical outcomes in stable patients with 3-vessel and/or left main disease undergoing percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), based on data from the SYNTAX trial. Later on, the SYNTAX score was applied to a variety of patient populations with diverse clinical presentations including those with acute coronary syndromes (ACS) undergoing primary PCI. Previous study shows an average SYNTAX score around 15.93 in patients undergoing primary PCI¹⁶.

Similar to previous studies, in both male and female patients, high SYNTAX score was associated with increased mortality. Studies have proven that in patients undergoing PPCI for acute STEMI, quantification of the presence, severity, and complexity of coronary vessel disease by the SYNTAX score is a useful tool in determining short-term and long-term outcome independently of any other clinical and angiographic and procedural characteristics¹⁷.

Stent dimensions.

Mean stent diameter in female group was 2.48 ± 0.87 mm and in male group was 2.68 ± 0.96 (p value 0.038). Mean stent length in female group was 27.69 ± 13.41 and in male group was 26.28 ± 12.5 . Similar to other study Compared to men, women received stents with lower diameters¹⁸.

In-hospital complications.

In our study 24 female patients and 16 male patients experienced post infarction angina. Studies have shown that female were prone for post infarction angina.¹⁹. In our study 21 female patients and 16 male patients experienced symptoms of heart failure. Previous studies showed higher incidence of post myocardial infarction cardiac failure among female²⁰.

In this study 10 female patients and 8 male patients developed acute kidney injury following primary angioplasty. Other studies found that incidence of AKI in myocardial infarction can be up to 16%²¹.

In our study 3 female patients had acute stent thrombosis. One female patient had coronary artery perforation during intervention. One female patient had ventricular septal rupture. Although Women are at higher risk than men for post-procedural complications after PCI, regardless of age, studies could not establish any gender difference in occurrence of stent thrombosis²².

Mortality in female group was 7.2% and in male group was 3.5%. In hospital STEMI mortality in post primary angioplasty were 3 -5% among various studies²³. Female having higher in hospital and short-term mortality²⁴. Multiple factors contribute to this sex difference, including older age at presentation, increased cardiovascular risk profile, differences in reperfusion time and therapy, and differences in STEMI pathophysiology in women.

Conclusions.

Gender differences in the clinical, angiographic profile and in hospital outcome in patients with STEMI undergoing primary angioplasty were studied

Following findings were noted

- Female patients with STEMI presented at later age than males and the mean age difference was 4 years ($p = 0.003$)
- Higher prevalence of diabetes seen in female group which was statistically significant ($p = 0.03$)
- Female patients had significant prehospital delay compared to male patients ($p = 0.001$)
- The mean stent diameter was significantly lower in female patients compared to males ($p = 0.038$)
- Mean hospital stay was significantly longer in female patients compared with male patients ($p = 0.04$)
- Coronary angiogram revealed single vessel disease as the most common pattern in both groups. But a greater number of female patients had left main and multivessel disease. In both groups diabetic and hypertensive patients tend to have multivessel disease
- Female patients had higher mean SYNTAX score
- In hospital events including post infarction angina, cardiac failure, acute kidney injury and overall mortality were more observed in female patients.

Limitations of the study.

There may be a selection bias by excluding patients who were managed medically by thrombolytic therapy. Being a single center study, the present observations may not reflect the trend in the community. There is no follow-up of the patients beyond the in-hospital phase.

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