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ORIGINAL ARTICLE

The Gender Spectrum of In-hospital Survival Post Primary Percutaneous Coronary Intervention for ST Elevation Myocardial Infarction: Exploring Age-driven Trends

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Abstract

Background: **The study was aimed to evaluate gender difference and age & gender specific interaction of in-hospital outcomes of patients with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).**

Methods: **This was a prospective cohort study of 1748 patients with STEMI undergoing primary PCI. The study was dichotomised according to gender to evaluate the difference in the outcome. The study was further stratified based on an age cut-off of 75 years to examine the age-specific gender relationship in survival outcomes. Independent variables for in-hospital mortality were analysed through logistic regression.**

Results: **There were 314 (17.96%) females with an average age of 60.80 years and 1434 (82.03%) males with an average age of 54.87 years. The prevalence of diabetes (24.8% vs. 13.2%) and hypertension (33.1% vs. 12.9%) was significantly higher in female patients compared to male patients, whereas the significantly higher number of male patients were smokers. On multivariate analysis, odds of female gender OR = 3.54 (1.37−9.17), killip class >2 OR = 3.05 (1.97−4.71) and baseline creatinine OR = 2.27 (1.22−4.23) were found as significant predictors of in-hospital mortality. The crude odds ratio of 2.35 (1.49−3.72) and adjusted OR of 2.05 (1.27−3.30) for female mortality was significant among patients aged <75-years. While patients with ≥75-years of age, the mortality difference was insignificant.**

Conclusion: **Although the incidence of STEMI was higher in male compared to female patients, female patients had two-fold higher in-hospital mortality than male. Female gender was an independent predictor for in-hospital mortality in patients <75-years of age.**

Keywords: Primary percutaneous coronary intervention, ST elevation myocardial infarction, Coronary artery disease, Gender, Acute coronary syndrome

1. Introduction

STEMI is characterized as occlusion in coronary arteries causing transmural MI which results in myocardial infarction and necrosis. Early diagnosis and timely treatment in acute STEMI could reduce the morbidity and mortality. The outcome difference based on gender in patients with acute STEMI is still controversial. Female STEMI patients usually present with higher mean age than their counterparts and therefore with multi-vessel disease and are at higher risk [1−3]. The diagnosis and

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prognosis in female patients have been poor and neglected mostly compared to male [4]. The fundamental mechanisms behind mortality in women patients remain unclear. Earlier published literatures have found the different clinical and outcome characteristics between gender and higher frequency of cardiac risk factors and mortality identified in female population than male [5,6]. Numerous studies have reported that compared to male patients, female patients with STEMI undergoing PAMI had higher mortality, the difference might be attributable to different cardiovascular risk factors. The age specific difference between gender have been seen mostly in younger and young adult patients however the difference between elderly patients had no specific mortality difference between both gender [7,8].

The present study was aimed to find 1) the difference in clinical risk factors and in-hospital outcome between gender 2) age specific (>75 years) difference between gender on in-hospital outcome in STEMI patients undergoing primary PCI.

Abbreviation:

ACS	Acute coronary syndrome
AWMI	Anterior wall myocardial infarction
CI	Confidence interval
DVD	Double vessel disease
IWMI	Inferior wall myocardial infarction
LAD	Left anterior descending
LCX	Left circumference
LMCA	Left main coronary artery
LV	Left ventricle
LVEF	Left ventricular ejection fraction
LWMI	Lateral wall myocardial infarction
MACE	Major adverse cardiovascular events
MI	Myocardial infarction
OR	Odds ratio
PAMI	Percutaneous angioplasty myocardial infarction
PCI	percutaneous coronary intervention
RCA	Right coronary artery disease
Re-MI	Re-Myocardial infarction
RVMI	Right ventricular myocardial infarction
STEMI	ST elevation myocardial infarction
SVD	Single vessel disease
TIMI	Thrombolysis in myocardial infarction
TVD	Triple vessel disease

2. Methods

2.1. Study design and setting

The present study was a prospective observational study carried out at our tertiary cardiac care hospital from January 2018 to June 2020. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki and was reviewed and cleared by the Ethics Committee of the institute (UNMICRC/CARDIO/2014/48). The informed written consent was obtained from all patients.

2.2. Patient population

Patients who were admitted for STEMI undergoing primary PCI were included in the study. Patients were included if they underwent primary angioplasty for STEMI within 12 h from symptom onset. Patients with suspected aortic dissection, history of bleeding, recent major surgery and history of cerebrovascular events were excluded from the study.

Demographic data, clinical data, procedural data and in-hospital complications and mortality data were collected on predesigned clinical record form. Multi vessel disease was considered if blockage present in at least two major branches of coronary arteries with more than 50 % stenosis. In-hospital complications were recorded for each patient till discharge. Patients were dichotomised according to gender and additionally to check the association of gender and age patients were divided into <75-year and ≥75-year age [9].

2.3. Definition

The primary angioplasty was defined according to the guideline ACC/AHA/SCAI 2005 [10]. The ST-elevation acute myocardial infarction was defined as the presence of chest pain lasting >20 min and of significant ST-segment elevation (>0.1 mV in two adjacent leads if leads I-III, aVF, aVL, V4–V6, and ≥0.2 mV in leads V1–V3), as recorded in the first ECG obtained. TIMI major bleeding was defined as intracerebral bleeding, bleeding requiring surgical intervention, bleeding requiring transfusion or loss of more than 5 g% haemoglobin [1].

The primary endpoint of the study was in-hospital mortality. The secondary endpoint was a composite of major adverse cardiac events together with in-hospital death, cerebro-vascular stroke, heart failure, re-myocardial infarction.

2.4. Statistical analysis

We compared baseline characteristics, lab parameters and in-hospital outcome between gender. Binary data variables were expressed as number percentage and compared using chi square analysis. Continuous data variables were represented as mean ± SD and compared using independent sample t-test. We used logistic regression model to

assess the effect of independent variables on in-hospital mortality. The odds ratio with 95% confidence interval was considered. The variables with P value P < 0.20 in univariate model were included in multivariate regression model for mortality. Mortality among different age decile was plotted using bar diagram. Additional crude odds ratio and adjusted odds ratio (for age, diabetes and hypertension) were analysed for mortality between gender among age group (<75 years and ≥75 years). Variables which presented comorbidities were entered into model for adjusted analysis and male patients were taken as reference. Survival plot analysis in both groups (<75 years and ≥75 years). were performed using Kaplan Meier method and comparison between both groups were analysed using Log Rank test (Mantel–Cox). A test was considered statistically significance based on the probability value P < 0.05. All statistical analysis was performed using SPSS version 26.

3. Results

Baseline characteristics of the population have been shown in Table 1. Female presented at significantly higher age with STEMI than male. Diabetes (24.8% vs. 13.2%) and hypertension (33.1% vs. 12.9%) were significantly higher in female patients whereas higher number of male patients were smoker 56 (3.9%) compared to female patients. Number of female patients with Killip class >2, lower LVEF (38.57 ± 10.54 vs. 40.22 ± 11.52) and multi vessel disease were significantly higher compared to men. On presentation, Troponin I was found significantly higher in female group while significantly higher value of creatinine was found in male patients. Inferior wall myocardial infarction (IWMI) was found significantly higher in female patients. The time from symptoms onset to admission and door to balloon time were significantly higher in female patients compared to male patients.

Table 2 presents the number of coronary arteries with blockage and type of vessel involved. The prevalence of multi-vessel disease was higher in female patients compared to male patients. Higher number of right coronary artery (RCA) blockage was found in female patients.

Table 3 presents in-hospital major cardiac events. Mortality was found two fold higher in female (9.9%) patients compared to male (4.9%) patients. The total MACE was found significantly higher in female gender (11.78% vs. 6.62%). While the individual cardiac events such as TIMI major bleeding, cardiogenic shock, stroke, heart failure and Re-Myocardial infarction were found similarly distributed between both genders.

Table 1. Baseline characteristics of the study population.

Variables	Total (=1748)	Female (N = 314)	Male (N = 1434)	P value
Age (years)	55.94 ± 11.76	60.80 ± 10.98	54.87 ± 11.67	<0.0001
Diabetes	268 (15.33%)	78 (24.8%)	190 (13.2%)	<0.0001
Hypertension	289 (16.53%)	104 (33.1%)	185 (12.9%)	<0.0001
Smoker	59 (3.37%)	03 (0.95%)	56 (3.9%)	0.01
Past history of ACS	73 (4.18%)	08 (2.5%)	65 (4.5%)	0.15
Systolic blood pressure (mm/Hg)	127.58 ± 20.33	129.71 ± 22.48	126.67 ± 19.75	0.02
Diastolic blood pressure (mm/Hg)	74.69 ± 14.56	74.28 ± 15.14	74.71 ± 14.05	0.63
Heart rate	85.50 ± 17.10	85.13 ± 16.69	85.54 ± 17.14	0.70
Killip class >2	504 (28.83%)	106 (33.75%)	398 (27.75%)	0.04
Tachyarrhythmias	47 (2.69%)	07 (2.23%)	40 (2.79%)	0.71
Bradyarrhythmias	126 (7.21%)	30 (9.55%)	96 (6.69%)	0.09
LV ejection fraction	39.99 ± 10.72	38.57 ± 10.54	40.22 ± 11.52	0.02
Lab variables				
Haemoglobin	13.3 ± 2.16	11.52 ± 1.86	13.72 ± 2.01	<0.0001
Creatinine	1.05 ± 0.46	0.94 ± 0.37	1.07 ± 0.47	<0.0001
Troponin I	12497.50 ± 22672.26	14885.38 ± 33988.52	11972.55 ± 19294.16	0.04
Location of infarct on ECG				
AWMI	832 (47.60%)	150 (47.45%%)	682 (47.49%)	0.7814
IWMI	611 (34.95%)	125 (39.81%)	486 (33.89%)	0.05
IWMI + RVMI	70 (4%)	09 (3.18%)	61 (4.18%)	0.5098
PWMI	172 (9.84%)	23 (7.32%)	149 (10.39%)	0.1218
LWMI	65 (3.72%)	7 (2.23%)	58 (4.04%)	0.1691
Time from symptoms onset to admission (hours)	8.61 ± 4.08	8.09 ± 3.56	7.95 ± 4.1	<0.0001
Door to balloon time (minutes)	50.62 ± 6.33	55.10 ± 5.60	46.15 ± 7.05	<0.0001

(ACS; Acute coronary syndrome, AWMI; Anterior wall myocardial infarction, IWMI; Inferior wall myocardial infarction, LV; Left ventricle, LWMI; Lateral wall myocardial infarction, PWMI; Posterior wall myocardial infarction, RVMI; Right ventricular myocardial infarction).

Table 2. Comparison of coronary artery lesion between both groups.

Variables	Total (=1748)	Female (N = 314)	Male (N = 1434)	P value
No. of Vessels blocked				
SVD	764 (43.71%)	105 (31.8%)	659 (45.95%)	0.0001
DVD	583 (33.35%)	121 (36.9%)	462 (32.22%)	0.04
TVD	401 (22.94%)	88 (28%)	313 (21.83%)	0.02
Type of vessel blocked				
Left main coronary artery (LMCA)	210 (12.01%)	38 (12.1%)	172 (12%)	0.9659
Left anterior descending (LAD)	1475 (84.38%)	269 (85.7%)	1206 (84.1%)	0.5435
Left circumference (LCX)	926 (52.97%)	179 (57%)	747 (52.1%)	0.1291
Right coronary artery disease (RCA)	1071 (61.27%)	214 (68.2%)	857 (59.8%)	0.01

(DVD; Double vessel disease, LAD; Left anterior descending LCX; Left circumference, LMCA; Left main coronary artery, RCA; Right coronary artery disease,SVD; Single vessel disease TVD; Triple vessel disease).

Table 3. Comparison of in-hospital outcome between both groups.

Variables	Total (=1748)	Female (N = 314)	Male (N = 1434)	P value
TIMI major bleeding	36 (2.06%)	7 (2.23%)	29 (2.02%)	0.3388
Cardiogenic shock	40 (2.29%)	07 (2.2%)	33 (2.3%)	0.8957
Heart failure	27 (1.54%)	06 (1.91%)	21 (1.64%)	0.7426
Re-Myocardial infarction	02 (0.11%)	00	02 (0.14%)	0.7953
Cerebro-vascular stroke	02 (0.11%)	00	02 (0.14%)	0.7953
Mortality	101 (5.78%)	31 (9.9%)	70 (4.9%)	<0.0001
MACE (Stoke + HF + Re-MI + Mortality)	132 (7.55%)	37 (11.78%)	95 (6.62%)	0.003

(HF; Heart failure, MACE; Major adverse cardiovascular events Re-MI; Re-Myocardial infarction, TIMI; Thrombolysis in myocardial infarction).

On Univariate regression analysis; age, Female gender, diabetes, Killip class >2, Troponin I and creatinine had significantly higher odds of mortality. However, on multi variate regression analysis; female gender (OR = 3.54), Killip class >2 (OR = 3.05) and creatinine (OR = 2.27) had higher odds ratio for mortality shown in Table 4.

Table 5 presents in-hospital Mortality and Odds Ratios for mortality among gender according to different age groups. Higher number of mortality was found in female patients (9.24%) than male (4.39%) amongst <75-year age group whereas the difference remained insignificant between gender in ≥75-years of age. In patients with <75-year age crude odds ratio (OR) of female for mortality was OR = 2.35 (1.49–3.72) significantly higher whereas the OR was little decreased when female gender was adjusted for comorbidities OR = 2.05 (1.27–3.30) but remained significant predictor for in-hospital mortality. While odds of female mortality were insignificant for in patients with ≥75-year of age.

Figure 1 presents in-hospital mortality according to different age group between gender. We found gender based mortality difference when grouped age in different age decile in male and female. Mortality was significantly higher in female patients with <55, 55–65 and 65–75 years age whereas ≥75 years age mortality was found similar between both gender.

Kaplan Meire curve shown in Fig. 2 shows mortality cum survival. Female had significantly (chi square value = 12.47 with log rank P value < 0.0001) higher mortality compared to male patients with <75 years age (fig-2A). while the similar rate of mortality (chi square = 0.557 with P = 0.456) was found between both gender among ≥75 years age (fig-2B).

Table 4. Predictors of mortality.

	Univariate regression			Multi variate regression		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.04	1.02–1.06	<0.0001	1.01	0.97–1.06	0.53
Female	2.13	1.37–3.32	0.001	3.54	1.37–9.17	0.01
Diabetes	2.13	1.34–3.37	0.001	1.21	0.43–3.40	0.71
Hypertension	1.18	0.71–1.98	0.53			
Smoking	1.26	0.45–3.57	0.66			
Killip class>2	6.24	1.97–19.75	0.002	3.05	1.97–4.71	<0.0001
Troponin I	1.001	1–1.002	0.005	1.001	0.99–1.003	0.45
Creatinine	4.15	2.95–5.85	0.0001	2.27	1.22–4.23	0.01

Table 5. In-Hospital Mortality and Odds Ratios for mortality among gender according to different age groups.

	Female (N = 314)	Male (N = 1434)	P value
In-hospital mortality			
Age <75-year	29 (9.24%)	63 (4.39%)	0.001
Age≥75-year	02 (0.64%)	07 (0.49%)	0.92
Odds ratio (OR) in age <75 years			
Unadjusted OR (95%) CI	2.35 (1.49–3.72)	1.00	<0.0001
Adjusted for age OR (95%) CI	2.06 (1.29–3.30)	1.00	0.02
Adjusted for comorbidities OR (95%) CI	2.31 (1.45–3.69)	1.00	<0.0001
Adjusted for age and comorbidities OR (95%) CI	2.05 (1.27–3.30)	1.00	0.003
Odds ratio (OR) in age >75 years			
Unadjusted OR (95%) CI	0.58 (0.11–2.99)	1.00	0.517
Adjusted for age OR (95%) CI	0.53 (0.10–2.76)	1.00	0.45
Adjusted for comorbidities OR (95%) CI	0.58 (0.11–2.99)	1.00	0.518
Adjusted for age and comorbidities OR (95%) CI	1.11 (0.93–1.31)	1.00	0.25

(CI; Cardiac index, OR; Odds ratio).

4. Discussion

The main findings of the current study were 1) The female population presented with poor cardiac profile and mean age on presentation was around 6 years older compared to male patients. 2) In-hospital mortality was significantly higher in female patients. On multi variate regression analysis we found female patients had 3-fold higher risk of death compared to male gender. 3) In age stratified analysis between gender, among patients with <75 years age, female population presented significantly higher odds for death compared to male study population. Although, patients with ≥75 years of age there was no significant association of death determined between gender.

A multi centric observational study included data from two German myocardial infarction registries and showed significant higher incidence of diabetes and hypertension in female patients [1]. The Brazilian study reported women with STEMI had significantly higher prevalence of diabetes [7]. In recently published sex stratified analysis of STEMI patients reported female patients presented with higher hypertensive and diabetic profile [3]. We found similar risk factors distribution between gender with poorer cardiac profile among female patients. The NORIN-STEMI registry with prospective cohort of STEMI patients revealed, female patients presenting with STEMI were older, had a higher burden of traditional risk factors [11]. In line with previous study, and current study analysis showed higher risk profile of female population undergoing PAMI. The possible reason behind poor cardiac risk profile among female patients probably due to female patients present at significantly advanced age compared to male counterparts and delayed presentation. Delayed healthcare presentation by female in developing countries may be attributed to sociocultural norms, economic

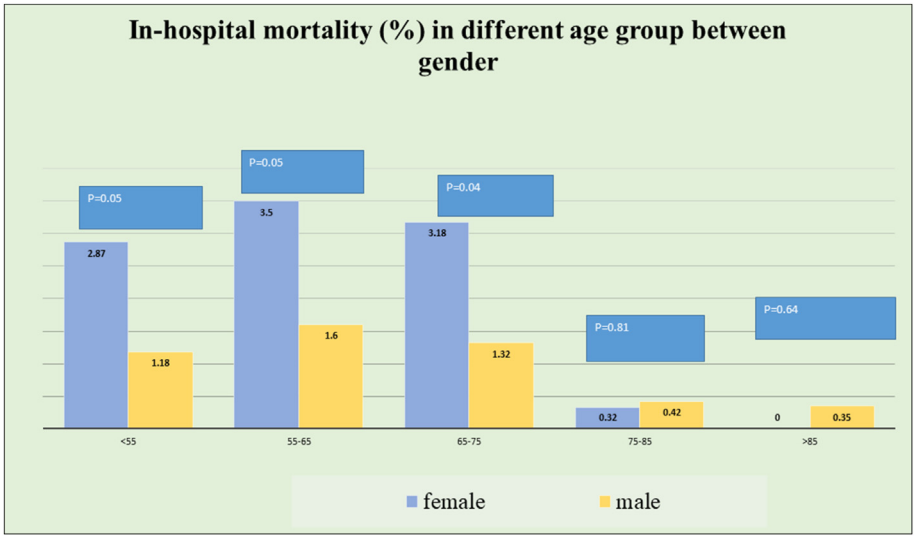

Fig. 1. In-hospital mortality (%) in different age group between gender.

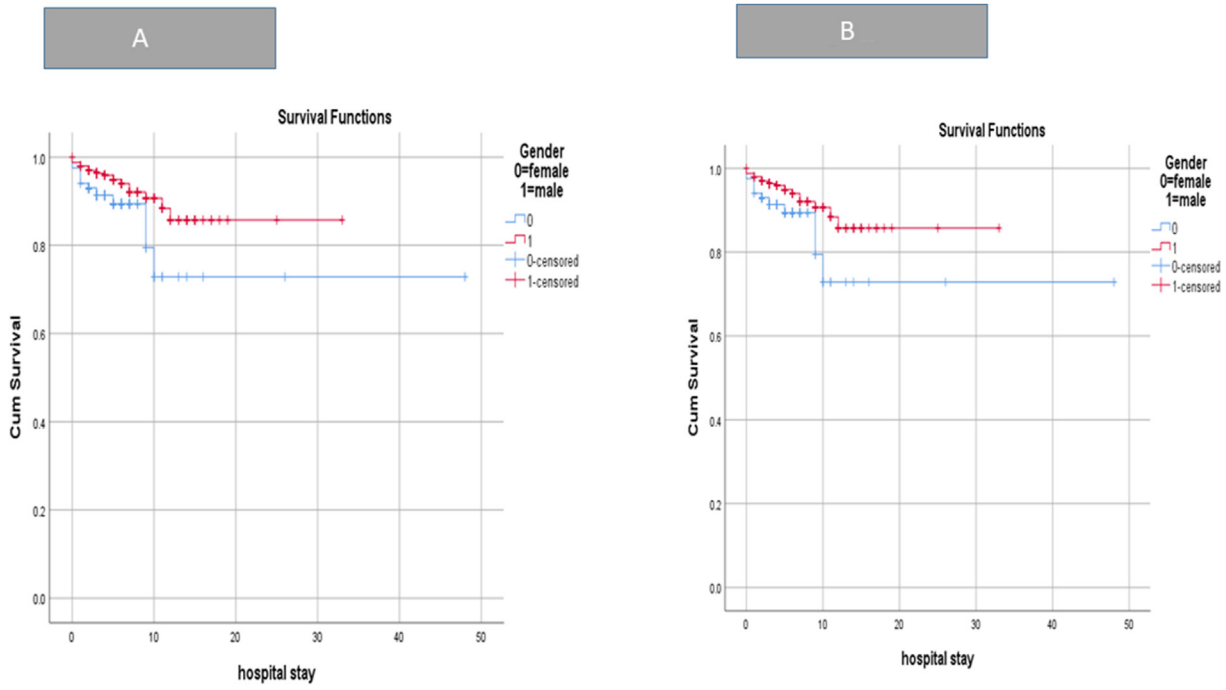

Fig. 2. Gender wise Kaplan Meire curve in patients with 2A) < 75 years age 2B) ≥75 years age.

contraints, limited awareness, gender bias and stigma. It has been reported that early identification of symptoms such as chest pain or discomfort improve patients outcome.

The CADILLAC study found significantly higher in-hospital and follow up death after primary PCI in female patients and reported female gender remains an independent predictor for adverse outcome [4]. Previous study on PAMI patients included patients from 3 randomized trials, demonstrated from unadjusted analysis that women had a significantly higher risk for mortality and other cardiac complications than men both at short term and long term, even after adjusting for confounder factors, female sex remained associated with an increased risk for mortality than male [12]. In Kermanshah STEMI Registry reported higher in-hospital mortality in women [13]. In A comprehensive meta-analysis included 48 STEMI studies and reported short term mortality remains higher in women than men [14]. In current analysis we identified similar higher incidence of in-hospital mortality in female compared to male. The risk of being a female had 3 fold higher odds than male for in-hospital mortality. In multivariate analysis for in-hospital mortality showed female gender, Killip class >2 and higher creatinine were associated with significantly higher odds of mortality.

Shi Tai et al. reported study on gender difference in acute coronary syndrome in elderly (≥75 years) age and revealed no gender specific difference was associated with in-hospital mortality among elderly patients with age ≥75years [15]. In female population of Shi Tai et al. [15] data higher incidence of hypertension and diabetes were identified. Study by Otten et al. [16]. on gender difference in STEMI stratified by age (≥65 years), reported that women with <65 age had worse survival compared to male of similar age groups. The age group stratification in that study was different compared to our study. Berger et al. [17]. study on gender–age interaction in early mortality following primary angioplasty revealed that in-hospital mortality was significantly higher in female patients with <75 years age compared to male and concluded female gender (<75 years) remains as an independent predictor of in-hospital mortality, however they found insignificant results in age >75 years between gender among same age group. Our study results are in consistent with other study that in female patients (<75 years age) had higher incidence of in-hospital mortality and found female as an independent predictor after adjusting for comorbidities compared to same age group male patients. While female patients with ≥75 years age, the difference in mortality and odds were remained insignificant in unadjusted and adjusted for comorbidity analysis. In present study in patients with <75 year age female patients presented 2.35 fold higher risk of mortality compared to male in unadjusted analysis even after adjustment the risk was reduced little however it remained as a significant predictor for mortality. The possible

reason behind difference in mortality with <75-year female might be due to delay in presentation and treatment of early atherosclerosis leading to significant myocardial infarction in these women. Another reason for higher mortality in female could be attributed to an elevated incidence of risk factors such diabetes and hypertension as well as higher prevalence of multi-vessel disease compared to male gender.

It has been reported that early identification of symptoms such as chest pain or discomfort can improve patients outcome. Patients with absence of symptoms on arrival are likely to die twice as compared to patients with symptoms [2]. Previous review article on presentation symptoms of women with ACS reported that the absence of symptoms in ACS patients were marked higher in female population than their counterparts [18]. Despite the awareness and more advanced techniques available now a days severity of disease in female has not been changed over a time. Several potential factors, including differences in cardiovascular risk profiles, hormonal influences, variation in the presentation of coronary artery disease and delay in seeking medical attention may play a role in this outcome discrepancy. It is imperative that health care provider and policy makers prioritize strategies aimed at reducing these disparities. Improved awareness, early intervention, personalized treatment plans and continued efforts to close gender related gaps in cardiovascular care can play a pivotal role in mitigating the elevated mortality rates observed among the female STEMI patients undergoing PAMI. Additionally, ongoing research should delve deeper into the intricacies of this issue to better inform clinical practice and ultimately improve outcomes for all patients.

5. Limitations

The present study was single centre observational study with no randomized comparison. Even though we conducted adjustments for potential confounding factors, it is possible that undetected variables still exist that could impact the association between gender and outcomes. Since this study lacked a long term follow up, we cannot ascertain whether the survival rate trends identified among women and men in this research would persist beyond hospital discharge.

6. Conclusion

Observation of higher mortality rates in female compared to males under 75 years of age following primary percutaneous coronary intervention (PCI) is clinically significant and concerning. This gender based disparity in post-PAMI outcomes highlights the need for a comprehensive exploration of the underlying factors contributing to this difference.

Author contribution

Conception and design of Study: IP, PV, KN, KK. Literature review: VS, SJ, DJ, SD, SNB. Acquisition of data: IP, PV. Analysis and interpretation of data: IP, PV, KN. Research investigation and analysis: IP, PV, KN. Data collection: IP, PV. Drafting of manuscript: IP. Revising and editing the manuscript critically for important intellectual contents: PV. Data preparation and presentation: IP, PV, KN. Supervision of the research: IP, PV, KN, KK. Research coordination and management: VS, SJ, DJ, SD, SNB.

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Key message

Understanding gender disparities in post primary percutaneous intervention outcomes is crucial for optimizing patient care. In-hospital mortality in patients who underwent PCI for STEMI is twice as high in female patients under the age of 75 years. However, for patients aged older than 75 years, there is no mortality difference between male and female.

Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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