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Original Article

Sex and Medium-term Outcomes of ST-Segment Elevation Myocardial Infarction in Kerala, India: A Propensity Score–Matched Analysis

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ABSTRACT

Background: Sex-based differences have been found in outcomes following ST-segment myocardial infarction (STEMI). Studies assessing sex-based differences in STEMI among Indian patients have reported conflicting results.

Methods: A prospective multicenter registry of consecutive patients with STEMI who presented to percutaneous coronary intervention (PCI)–capable hospitals in the Indian state of Kerala between June 2013

RÉSUMÉ

Contexte : Des différences entre les sexes ont été constatées dans les résultats obtenus à la suite d'un infarctus du myocarde avec élévation du segment ST (STEMI). Des études évaluant les différences entre les sexes parmi des patients indiens ayant subi un STEMI ont produit des résultats contradictoires.

Méthodologie : Un registre multicentrique et prospectif de patients consécutifs qui ont subi un STEMI et se sont présentés dans des

Women in India face an accelerated increase in ischemic heart disease–associated morbidity and mortality, compared with men.[1] This escalation parallels the burgeoning numbers of cardiometabolic risk factors affecting women in India.[1] Sex-based disparities in the outcomes of acute coronary syndromes exist across many geographic locations.[2,3] However, studies from India assessing sex-based differences in outcomes of acute coronary syndromes have produced conflicting results.[4-7] Gender inequity levels vary significantly among countries,[8] and women in India may be vulnerable to worse outcomes following acute coronary syndromes, compared with men. Compared with populations in developed countries, patients from India presenting with acute coronary syndromes tend to have much higher rates of ST-segment elevation myocardial infarction (STEMI).[9,10] We designed this study to evaluate sex-based differences in performance indicators and clinical outcomes among STEMI patients undergoing reperfusion at percutaneous coronary intervention (PCI)–capable hospitals.

Methods

We used a prospective multicentre registry of consecutive patients with STEMI who presented to PCI-capable hospitals in central and northern Kerala—an Indian state with a

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Ethics Statement: We obtained informed consent from all patients. For patients deemed too sick to provide consent, we obtained permission from a patient representative. We adhered to the **St**rengthening the **R**eporting of **Ob**servational Studies in **E**pidemiology (STROBE) guidelines for reporting results of observational studies. The study was approved by the CSI Kerala Central Ethics Committee, as well as individual hospital ethics committees, where applicable.

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and March 2017 was used to assess 1-year outcomes. The primary endpoint was a composite of major adverse cardiac events (MACE), including death, stroke, nonfatal myocardial infarction, and rehospitalization for heart failure. Outcomes of 2 sex-based propensity score–matched groups were compared.

Results: We included 3194 patients (19.4% women). Women presenting with STEMI were older, had more traditional cardiovascular risk factors, and were more likely to be classified as living in poverty. After propensity-score matching, women experienced greater incidence of MACE (20.9% vs 14.3%, $P < 0.01$), primarily driven by increased 1-year mortality (14.3% vs 8.6%, $P < 0.01$). Women were more likely to experience prehospital delays, compared with men. Although reperfusion rates were similar between the groups, men were more likely than women to undergo reperfusion within the first 12 hours of chest pain onset. Among patients undergoing primary PCI, women were more likely to have delayed PCI than were men (80.2% vs 72.9%, $P = 0.03$). Procedural characteristics were similar between groups.

Conclusions: Women in this cohort experienced higher incidence of MACE at 1 year, compared to men, primarily owing to increased mortality. Timeliness of reperfusion appears to be the primary factor impacting differences in outcomes between the 2 groups and may represent an attractive target for quality-improvement initiatives.

hôpitaux où pouvait être pratiquée une intervention coronarienne percutanée (ICP) dans l'État indien du Kerala entre juin 2013 et mars 2017 a été utilisé pour évaluer les résultats à 1 an. Le paramètre d'évaluation principal regroupait des événements cardiaques indésirables majeurs (ECIM) comprenant le décès, l'accident vasculaire cérébral, l'infarctus du myocarde non fatal et la réhospitalisation pour cause d'insuffisance cardiaque. Les résultats de deux groupes appariés selon les scores de propension en fonction du sexe ont été comparés.

Résultats : Nous avons inclus 3 194 patients (19,4 % de femmes). Les femmes qui avaient subi un STEMI étaient plus âgées, présentaient des facteurs de risque cardiovasculaire plus classiques et étaient plus susceptibles d'appartenir à la catégorie des personnes vivant dans la pauvreté. Après l'appariement selon les scores de propension, l'incidence des ECIM était plus élevée chez les femmes (20,9 % *vs* 14,3 %, $p < 0,01$), surtout en raison d'une mortalité accrue à 1 an (14,3 % *vs* 8,6 %, $p < 0,01$). Les femmes étaient plus susceptibles de subir des retards avant l'hospitalisation que les hommes. Bien que les taux de reperfusion étaient semblables dans les groupes étudiés, les hommes étaient plus susceptibles que les femmes de subir une reperfusion dans les 12 premières heures suivant l'apparition de la douleur thoracique. Parmi les patients ayant subi une ICP primaire, les femmes étaient plus susceptibles d'être touchées par un retard d'intervention que les hommes (80,2 % *vs* 72,9 %, $p = 0,03$). Les caractéristiques de l'intervention étaient similaires dans les groupes étudiés.

Conclusions : L'incidence des ECIM à 1 an au sein de cette cohorte était plus élevée chez les femmes que chez les hommes, surtout en raison d'une mortalité accrue. La rapidité de la reperfusion semble être le principal facteur ayant des répercussions sur les différences de résultats entre les deux groupes et pourrait représenter une cible intéressante dans le cadre d'initiatives d'amélioration de la qualité.

population of 33.4 million, per the 2011 census. The study was conducted from June 2013 until March 2017, across 16 PCI-capable hospitals. Patients were followed for 1 year. This study was carried out in 2 phases, with the first phase covering central Kerala, and the second phase extending to northern Kerala. Of the patients from 16 hospitals, we excluded those from 3 hospitals, as they were nonconsecutive patients. Supplemental Table S1 shows patient enrollment rates, by hospital. Baseline risk factors, patient financial status, including insurance coverage, clinical presentation details, mode of reperfusion, timeliness of reperfusion, angiographic as well as primary PCI (PPCI) procedural details, and 1-year major adverse cardiovascular events were captured. We obtained informed consent from all patients. For patients deemed too sick to provide consent, we obtained permission from a patient representative. We adhered to the **St**rengthening the **R**eporting of **Ob**servational Studies in **E**pidemiology (STROBE) guidelines for reporting results of observational studies.[11] The study was approved by the Cardiological Society of India Kerala Central Ethics Committee, as well as individual hospital ethics committees, as applicable.

Inclusion and exclusion criteria

We enrolled consecutive patients presenting with STEMI at PCI-capable hospitals. We excluded those patients who presented with STEMI > 24 hours after symptom onset, and those who did not receive reperfusion. In addition, we excluded patient who received late reperfusion therapy (after 24 hours of pain onset). Patient with STEMI who presented between 12 and 24 hours after symptom onset with no clinical or electrocardiographic evidence of ongoing ischemia as well as patients who underwent reperfusion before arrival at the enrolling hospital were also excluded.

Outcomes

The primary outcome was major adverse cardiovascular events: a composite of death, rehospitalization for heart failure, stroke, and nonfatal myocardial infarction, assessed at the 1-year follow-up. The occurrence of the primary outcome and its components for the 2 sex-based propensity score–matched groups were compared. Delayed thrombolysis was defined as first medical contact (FMC) to needle time > 30 minutes for those presenting directly to a PCI-capable center and those requiring transfer. Delayed primary PCI was defined as FMC to device time > 60 minutes for directly presenting patients and > 120 minutes for transferred patients.

Statistical analysis

We presented descriptive data in terms of frequency, along with percentage, for categorical variables. We depicted continuous variables as mean with standard deviation, or as median with interquartile range, as applicable. We compared baseline characteristics utilizing the Pearson χ^2 test and Fisher's

exact test for categorical variables, and Student's *t*-test or Mann-Whitney *U* test for continuous variables. We considered a type I error rate of < 0.05 to be statistically significant.

To obtain a comparable cohort of patients with similar baseline characteristics, we adopted the propensity score–matching technique. The propensity score was estimated with the use of a multivariable logistic regression model, with sex as the dependent variable, and the baseline characteristics shown in Table 1 as predictors. Greedy matching techniques without replacement, and a caliper width equal to 0.1, were applied to match male to female patients in a 1:1 ratio. We used the standardized difference to quantify differences in means or prevalence between the 2 groups, to evaluate the balance after propensity-score matching. After the match, incidences of the primary outcome at the 1-year follow-up were compared. We used the Cox regression model to estimate the hazard ratio of having the primary outcome at 1 year, for comparison between the 2 groups. The log-rank test and the Gray test were used for all-cause-mortality and nonfatal outcomes, respectively. Cumulative incidence of the primary outcome and its components was plotted. Quality-of-care indicators were also compared and tested for statistical significance. Statistical analysis was performed using SAS 9.4 (SAS Institute, North Carolina).

Results

Baseline characteristics

A total of 3194 patients were enrolled, including 619 (19.4%) women and 2575 (80.6%) men. Men and women differed markedly in terms of baseline characteristics, as shown in Table 1. Women presenting with STEMI were considerably older than men doing so (66.1 ± 11.8 vs 57.5 ± 11.9 years, $P < 0.001$), with a higher prevalence of hypertension (45.2% vs 32.1%, $P < 0.001$), diabetes (52% vs 38.9%, $P < 0.001$), dyslipidemia (74.5% vs 69.1%, $P = 0.013$), and prior cerebrovascular accident (4.0% vs 2.5%, $P = 0.035$). By contrast, women had a lower incidence than men of family history of premature coronary artery disease (15.7% vs 22.1%, $P < 0.001$), prior angiographically proven coronary artery disease (2.7% vs 6.6%, $P < 0.001$), prior myocardial infarction (2.9% vs 9.3%, $P < 0.001$), and prior PCI (0.3% vs 3.3%, $P < 0.001$). Women were more likely than men to present with congestive heart failure at admission (17.6% vs 12.3%, $P < 0.001$). The incidence of smoking was much lower for women, compared with that for men (0.2% vs 51.4%, $P < 0.001$). Moreover, women were more likely than men to be classified as living in poverty (41.2% vs 36.8%, $P = 0.041$).

Clinical outcomes

Propensity-score matching returned 510 matched pairs of men and women with STEMI who were treated at PCI-capable hospitals in Kerala. The 2 groups were well matched in terms of baseline characteristics (Supplemental Table S2). Women experienced significantly more major adverse cardiovascular events at 1 year than men (20.9% vs 14.3%, $P < 0.01$; Table 2). This difference was driven mainly by a difference in the 1-year mortality rates between the 2 groups (14.3% among women vs 8.6% among men, $P < 0.01$). There were no significant differences between the 2 groups in the rates of stroke, nonfatal myocardial infarction, or rehospitalization for heart failure. The trajectories of major adverse cardiovascular event rates of the 2 groups, especially mortality, continued to diverge in the initial few months following the index event. This difference was maintained throughout the study period (Figs. 1 and 2). Table 3 depicts the hazard ratio for adverse clinical outcomes at 1-year, as determined by Cox regression analysis. Figures 3 and 4 indicate the cumulative incidence of stroke and nonfatal myocardial infarction for the two groups, respectively. Figure 5 delineates the cumulative incidence of major adverse cardiovascular events across both the groups.

Table 1. Baseline characteristics of study population (before propensity-scorematching)

Baseline characteristic	Women (n = 619)	Men (n = 2575)	*P*
Age, y	66.1 ± 11.8	57.5 ± 11.9	< 0.01
Systemic hypertension	280(45.2)	826 (32.1)	< 0.01
BMI, kg/m^2	23.2 ± 3.7	23.6 ± 3.1	0.01
Diabetes mellitus	322 (52.0)	1002 (38.9)	< 0.01
Dyslipidemia	403 (74.5)	1607 (69.1)	0.01
Current smoker	1 (0.2)	1324 (51.4)	< 0.01
Family history of premature CAD	97 (15.7)	570 (22.1)	< 0.01
Known prior angiographic obstructive CAD	17 (2.7)	169 (6.6)	< 0.01
Prior MI	18 (2.9)	239 (9.3)	< 0.01
Prior CABG	3 (0.5)	32 (1.2)	0.10
Prior PCI	2 (0.3)	86 (3.3)	< 0.01
Known CKD	19 (3.1)	90 (3.5)	0.60
Prior CVA	25 (4.0)	64 (2.5)	0.03
COPD	50 (8.1)	236 (9.2)	0.40
Classified as living in poverty	255 (41.2)	947 (36.8)	0.04
Self-paid	420 (67.9)	1753 (68.1)	0.08
STEMI type			0.71
Anterior	288 (46.5)	1216 (47.2)	—
Inferior	299 (48.3)	1254 (48.7)	—
Posterior	16 (2.6)	55 (2.1)	—
Lateral wall	16 (2.6)	51 (2.0)	—
LBBB	10 (1.6)	43 (1.7)	0.92
Cardiac arrest prior to hospital arrival	21 (3.4)	104 (4.0)	0.46
CHF at admission	109 (17.6)	316 (12.3)	< 0.01

Values are mean ± standard deviation, or n (%), unless otherwise indicated.

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; LBBB, left bundle branch block; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

Table 2. 1-year outcomes

1-year outcome	Women (n = 510)	Men (n = 510)	*P*
MACE	107 (20.9)	73 (14.3)	0.003
Mortality	73 (14.3)	44 (8.6)	0.003
HF readmission	36 (7.8)	30 (6.2)	0.28
Stroke	7 (1.4)	7 (1.4)	0.92
Nonfatal MI	20 (4.1)	12 (2.4)	0.11

HF, heart failure; MACE, major adverse cardiac events; MI, myocardial infarction.

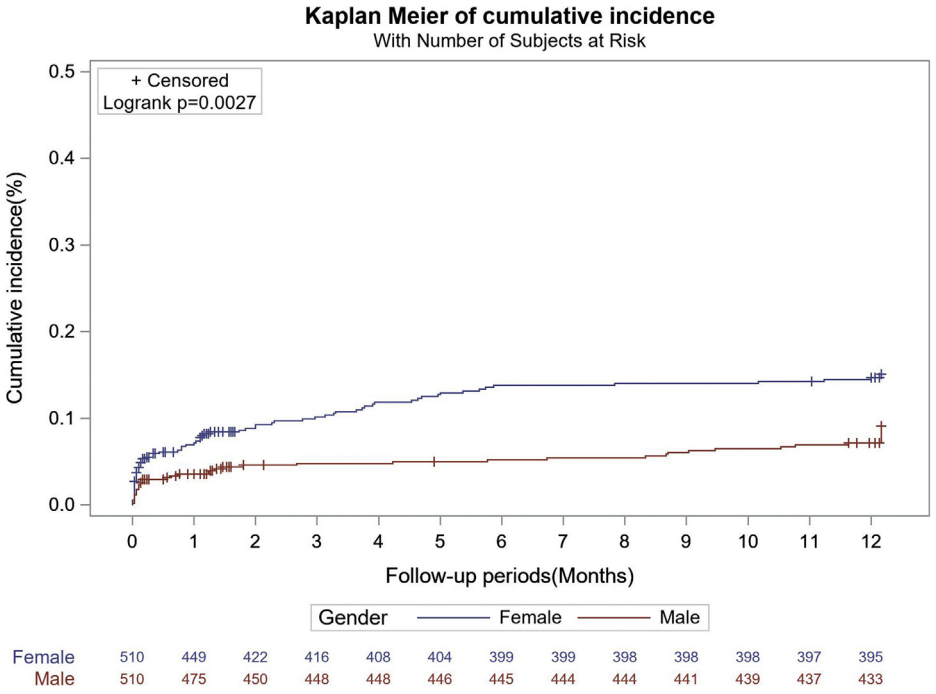

Figure 1. Kaplan Meier plot of cumulative incidence for women vs men of all-cause mortality.

STEMI performance indicators in the propensity score–matched groups

STEMI performance indicators were comparable between the 2 propensity score–matched groups, except for timeliness indicators. Table 4 describes the quality-of-care indicators across the 2 groups. Less than one third of either group presented directly to a PCI-capable hospital without seeking care at another healthcare facility. Only about half of patients arrived at the PCI-capable hospital in a ground ambulance (50.0% among women vs 46.5% among men, $P = 0.21$). Symptom-to-FMC time was delayed in women, compared with that for men (median [interquartile range] 2.0 [2.75] hours vs 1.3 [2.08] hours, $P < 0.01$). The overall rates of

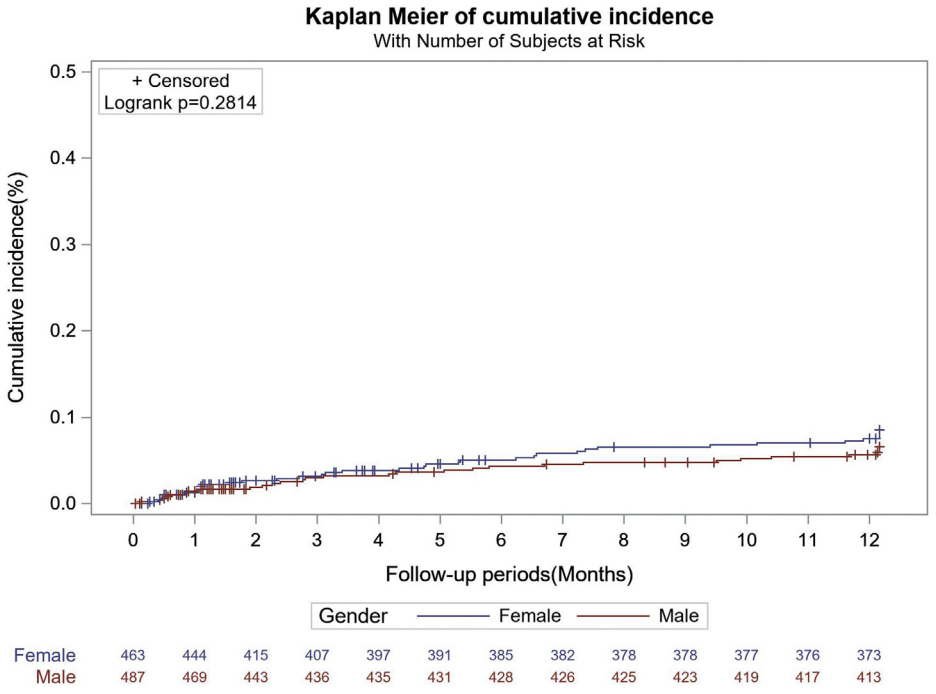

Figure 2. Kaplan Meier plot of cumulative incidence for women vs men of heart failure readmission.

Table 3. Univariable Cox regression

1-year outcome (Men used as reference)	Hazard ratio	95% CI		*P*
		Lower limit	Upper limit	
MACE	1.560	1.159	2.101	< 0.01
Mortality	1.757	1.208	2.554	< 0.01
HF readmission	1.304	0.803	2.117	0.28
Stroke	1.057	0.371	3.014	0.92
Nonfatal MI	1.790	0.875	3.661	0.11

CI, confidence interval; HF, heart failure; MACE, major adverse cardiac events; MI, myocardial infarction.

reperfusion did not differ significantly between groups, as indicated in Table 4. However, more men underwent reperfusion, either with thrombolysis or primary PCI, within the first 12 hours of chest pain onset (83.5% women vs 88.0% men, $P = 0.04$). The FMC-to-needle time was prolonged, but similar, in the 2 groups (median [interquartile range] 1.8 [2.1] hours for women vs 1.6 [1.9] hours for men, $P = 0.22$). Both groups had very low rates of timely thrombolysis (11.7% of thrombolyzed women vs 14.2% of thrombolyzed men, $P = 0.59$). Catheterization labs performed primary PCI (PPCI) within 12 hours of symptom onset in 62.9% of women and 67.3% of men. Among patients who underwent PPCI (within 12 hours), rates of timely PPCI were significantly lower for women compared with those for men (19.8% vs 27.1%, $P = 0.03$). For patients transferred from a non−PCI-capable hospital, total ischemic time was more prolonged for women, compared with that for men. This difference in total ischemic time did not achieve significance for patients presenting directly to PCI-capable facilities.

Procedural characteristics were compared between groups. For patients undergoing PPCI, within 24 hours after symptom onset, radial vascular access rates were similar between the 2 groups (51.4% for women vs 59.4% for men, $P = 0.07$). Thrombus aspiration usage rates were high, but not significantly different, in the 2 groups (40.8% for women vs 45.0% for men, $P = 0.25$). Similarly, glycoprotein 2b3a inhibitor use was also high and comparable across the 2 groups, as indicated in Table 4. The number of patients undergoing balloon angioplasty alone and the number of stents implanted per patient were similar in the 2 groups.

Aspirin prescription rates at discharge were marginally lower in women, compared with those in men (96.5% vs 98.8%, $P = 0.02$). There was no difference in the use of P2Y12 inhibitors, statins, beta-blockers, angiotensin-converting enzyme inhibitors, aldosterone receptor blockers, diuretics, or spironolactone between the 2 groups.

Discussion

This study, using a multicentre prospective registry, highlights several important aspects of STEMI care in India. First, men and women differed significantly in terms of their baseline risk profiles. Second, women presenting with STEMI were more likely than men to be classified as living in poverty. Third, women experienced longer delays to FMC, compared with those for men. Fourth, even though the overall reperfusion rates did not differ significantly between the 2 groups, the rate of timely PPCI was much lower in women than in men. Fifth, most STEMI patients were transferred from non−PCI-capable hospitals, and for such patients, women had more prolonged total ischemic time than men. Finally, long-term outcomes, especially mortality rates, differed significantly between the 2 groups, with women having much higher rates of major adverse cardiovascular events at the 1-year follow up.

Sex-based differences in STEMI care in low- and middle-income countries are key areas of STEMI quality-of-care

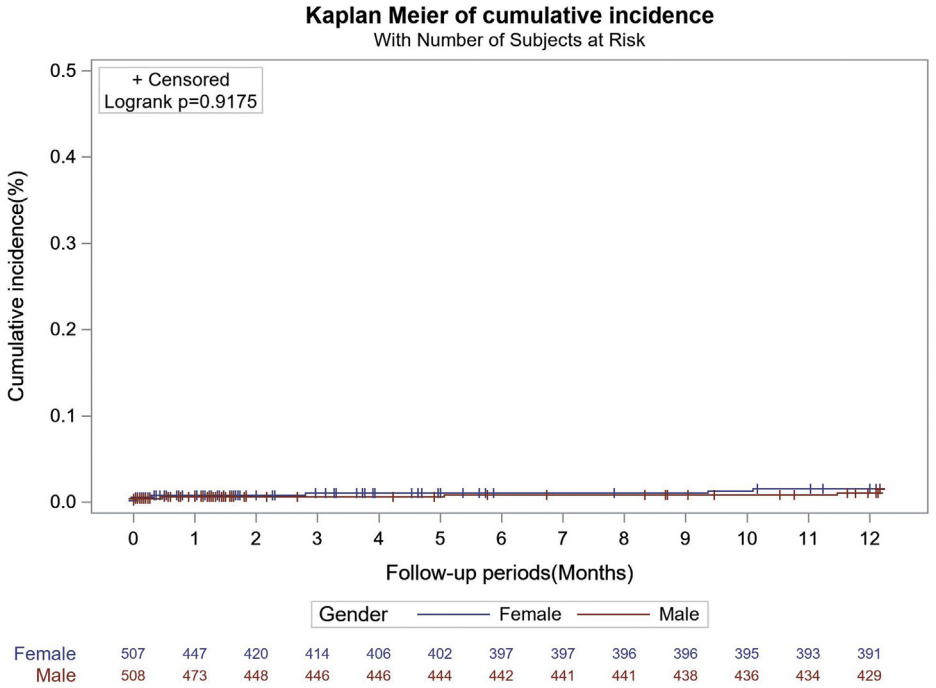

Figure 3. Kaplan Meier plot of cumulative incidence for women vs men of stroke.

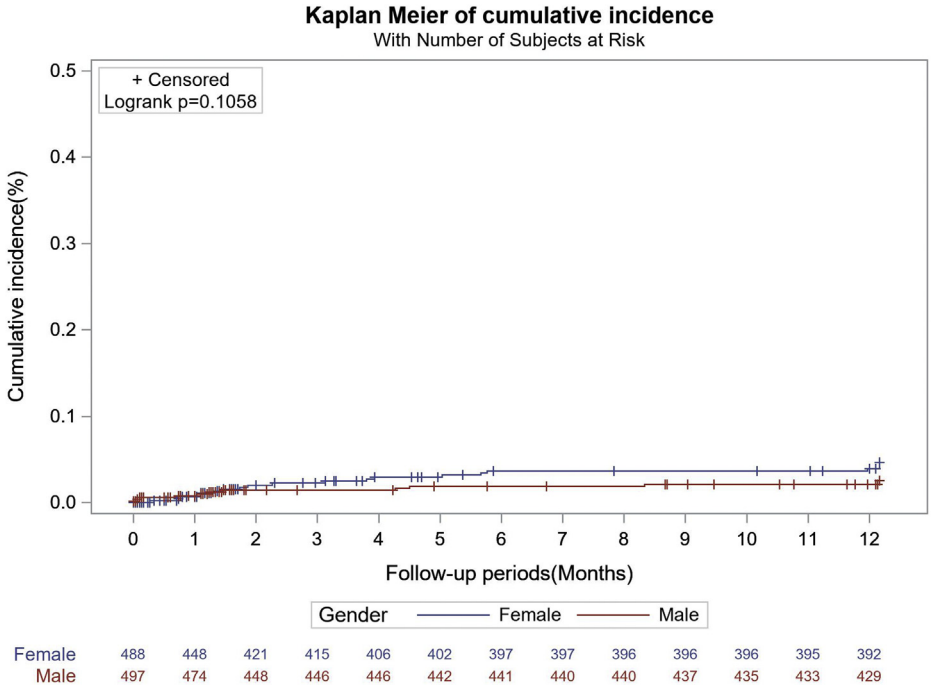

Figure 4. Kaplan Meier plot of cumulative incidence for women vs men of nonfatal myocardial infarction.

and outcome-improvement research. Moreover, addressing obstacles to improving acute coronary syndrome care in such countries is a critical step on the path to reducing the global burden of acute and chronic coronary syndromes.[12] India is projected to be the world's most populous country for most of the 21st century.[13] Strikingly, more than half a billion women live in this country. Given that Asian Indian women have a more significant burden of cardiovascular risk factors, especially at a younger age,[14] any systematic biases in the administration of timely reperfusion therapy and other guideline-directed medical therapies can profoundly and negatively affect STEMI outcomes in this population.

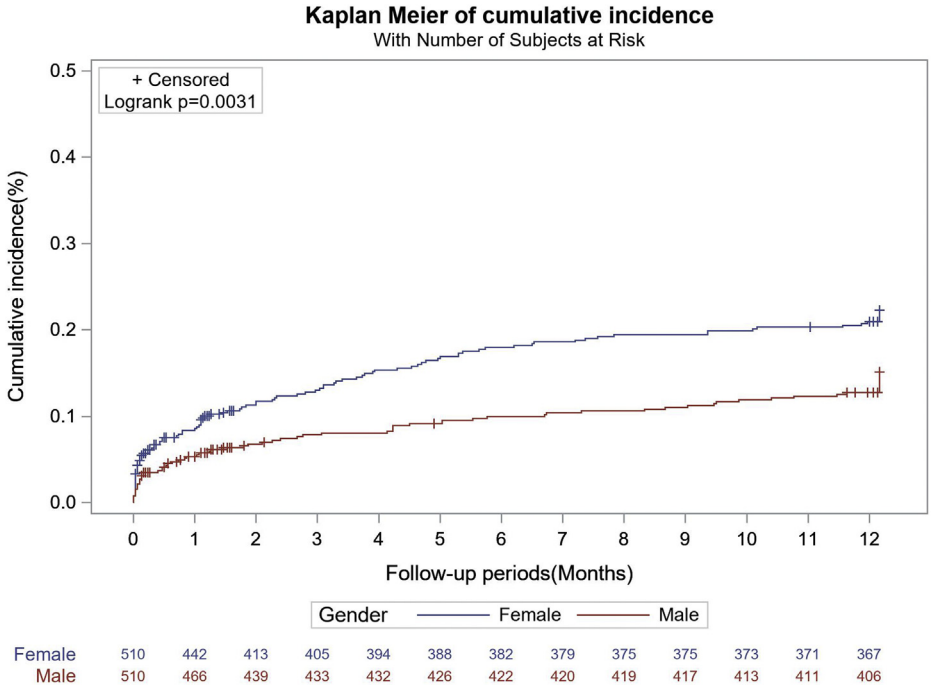

Figure 5. Kaplan Meier plot of cumulative incidence for women vs men of major adverse cardiovascular events (composite of nonfatal mycardial infarction, stroke, heart failure readmission, and mortality at 1 year).

Table 4. Quality indicators

Quality-of-care indicators	Women	Men	*P*
Arrival at PCI-capable hospital in an ambulance	255 (50.0)	237 (46.5)	0.21
Direct presentation to PCI-capable hospital	139 (27.3)	164 (32.2)	0.09
Reperfusion			0.50
Thrombolysis	105 (20.6)	106 (20.8)	—
PPCI < 12 h after symptom onset	321 (62.9)	343 (67.3)	—
PCI 12−24 h after symptom onset	37 (7.3)	26 (5.1)	—
Late STEMI PCI > 24 h after symptom onset	5 (1.0)	3 (0.6)	—
No reperfusion (includes diagnostic angiogram only, and no reperfusion)	42 (8.2)	32 (6.3)	—
Timeliness, h, median (IQR)			
Symptom to FMC	2 (2.75)	1.3 (2.08)	< 0.001
FMC to needle time (if reperfusion = thrombolysis)	1.8 (2.1)	1.6 (1.9)	0.22
FMC to balloon time (if reperfusion = PPCI at < 12 h)	2.4 (1.9)	2.3 (1.7)	0.06
Door to balloon time (if reperfusion = PPCI at < 12 h)	1.3 (0.8)	1.2 (0.7)	0.06
Timely thrombolysis	12/103 (11.7)	15/106 (14.2)	0.59
Timely PPCI	63/319 (19.8)	93/343 (27.1)	0.02
Total ischemic time, h, median (IQR)			
For directly presenting patients	3.3 (3.8)	2.9 (2.8)	0.11
For transferred-in patients	5.3 (4.4)	4.2 (3.4)	< 0.01
For patients undergoing reperfusion with PCI (at < 24 h)	(n = 358)	(n = 369)	
Radial access	184 (51.4)	219 (59.4)	0.07
Thrombus aspiration	146 (40.8)	166 (45.0)	0.25
Gp2b3a inhibitor use:			0.68
Tirofiban	292 (59.8)	301 (81.6)	—
Bivalirudin	8 (2.2)	7 (1.9)	—
Abciximab	2 (0.6)	0 (0.0)	—
Eptifibatide	12 (3.4)	14 (3.8)	—
Balloon angioplasty only	36 (10.1)	25 (6.8)	0.11
Number of stents implanted			0.09
0	36 (10.1)	21 (5.7)	—
1	281 (78.5)	292 (79.1)	—
2	38 (10.6)	53 (14.4)	—
3	3 (0.8)	3 (0.8)	—
Contrast volume	154.5 ± 59.5	157.5 ± 57.3	0.48
Ejection fraction, %	50.3 ± 11.6	50.8 ±11.3	0.28
Medications at discharge	(n = 483)*	(n = 499)*	
Aspirin	466 (96.5)	493 (98.8)	0.016
Any P2Y12 inhibitor use	477 (98.8)	498 (99.8)	0.052
Statin	479 (99.2)	497 (99.6)	0.390
Beta-blocker	298 (61.7)	313 (62.7)	0.739
ACEI	143 (29.6)	152 (30.5)	0.770
ARB	44 (9.1)	43/498 (8.6)	0.794
Diuretics	149/481 (31.0)	160/498 (32.1)	0.698
Spironolactone	99/478 (20.7)	107/496 (21.6)	0.742

Values are mean ± SD or n (%), unless otherwise indicated. Delayed thrombolysis defined as first medical contact (FMC) to needle > 30 minutes for both directly presenting and transferred-in patients. Delayed primary percutaneous coronary intervention (PPCI) defined as FMC to device > 60 minutes for directly presenting patients, and > 120 minutes for transferred-in patients. FMC to device time was missing for 2 women who underwent PPCI within 12 hours of symptom onset. Similarly, FMC to needle time was missing for 2 women who underwent thrombolysis.

ACEI, angiotensin-converting enzyme inhibitor; ARB: aldosterone receptor blocker; IQR, interquartile range; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

*With exceptions indicated.

Unraveling the sex-based disparities in the care of patients presenting with STEMI across India would help create awareness and channel resources to mitigate these differences.

Worldwide, women presenting with STEMI have worse outcomes, compared with those of men. Most of these differences can be accounted for by variations in baseline cardiovascular risk factors and differences in clinical presentation.[15-17] However, access to care, time to diagnosis, timely effective reperfusion, and the use of guideline-directed medical therapy can significantly affect STEMI outcomes. Small observational studies from Kerala suggest an absence of sex-based disparities in the in-hospital and discharge management of patients with acute coronary syndromes.[4,5] Additionally, across sexes, these studies report a convergence in the in-hospital and short-term mortality following incidence of acute coronary syndromes.[4,5] However, other studies from India suggest that women living with cardiovascular disease in rural areas, and younger women, are less likely than men to receive guideline-directed medical management.[6,7] These studies were limited by a lack of medium- to long-term follow-up data.

There are many possible explanations for the sex-based differences in long-term outcomes noticed in our study. Even though younger women have worse outcomes following STEMI and are less likely to receive revascularization than men,[18] age at presentation is unlikely to contribute to the difference in outcomes observed in our study, as we included age in the propensity-matching model. Also, the marked difference in smoking rates between the 2 groups is unlikely to

impact the long-term mortality rates of the 2 groups.[19] Delays in presentation and time to reperfusion can significantly contribute to worse outcomes in women.[20,21] Prolonged total ischemic time, especially in patients transferred in from a non−PCI-capable hospital, is likely to be a factor contributing to the sex-based differences in STEMI outcomes. Additionally, the rates of timely PPCI were lower in women. Several studies have examined the sex differences in timely reperfusion in patients with acute myocardial infarction.[20,22-25] Sex-based differences in time to reperfusion are found across multiple geographic areas.[21,26,27] Reperfusion delay is associated with higher mortality in STEMI patients.[28-32] In a Swiss STEMI population, ischemic time was longer in women, owing to patient-level delays to first medical contact.[33] Similarly, a French study of 16,733 consecutive STEMI patients showed significant patient-level delays in ischemic time.[34] Even though neither of these studies reported system-level delays, a several studies have reported such delays.[20,23,35-37] Very few studies have looked at medium- to long-term STEMI outcomes in India. A cohort study from India to analyze the timeliness of reperfusion in patients with STEMI, categorized by sex, reported a greater mortality rate in women than in men.[38] This study reported much higher prehospital delays among women, compared with those among men.[38] The findings of this study, from a different geographic area in India, are consistent with the significant delays to first medical contact identified in our cohort. Among the STEMI quality indicators disparities we could identify across the 2 groups are in prehospital delay, total ischemic time delay, timely PCI rates, and aspirin use at discharge.

This study has certain limitations. First, we acknowledge the significant difference, at baseline, across multiple measured confounders between the 2 groups of patients. Naturally, this difference raises the possibility of substantial residual confounding from unmeasured variables, even after use of propensityscore matching techniques. Unmeasured confounders may include risk factors such as frailty and sedentary lifestyle, as well as comorbidities, including connective tissue disease and valvular heart disease.[39,40] Also, unmeasured confounders, such as differences in referral and enrollment rates for cardiac rehabilitation, can affect outcomes. Second, a referral bias may have existed, from management of healthier women in non−PCI-capable hospitals with pharmaco-invasive strategy, and selective referral of sicker women to PCI-capable hospitals without initial thrombolysis. Third, given that women with STEMI were more likely to be classified as living in poverty, this factor may have impacted long-term prescription drug compliance and outcomes. We did not document prescription drug compliance on follow-up.

Fourth, we did not measure implantable cardioverter defibrillator implantation rates for primary or secondary prevention. Differences in the rates of defibrillator implantation between the 2 groups may have impacted the rate of sudden cardiac death on follow-up. The rates of sudden cardiac death and fatal myocardial re-infarction may explain differences in mortality between the 2 groups, despite their having no difference in other outcomes, including nonfatal myocardial infarction, stroke, and heart failure hospitalization. Finally, Kerala is a socioeconomically advanced part of India, and hence, the findings of this study may not be generalizable to the whole population of India.

Some of the reasons for system-level delays to reperfusion in women include presentation with atypical symptoms, and delays at the emergency-room level.[36] Emergency-room bypass with direct transfer to a catheterization lab will significantly improve the timeliness of reperfusion.[41] A qualitative study identified specific patient-level factors and poor emergency medical services infrastructure as prehospital barriers to acute syndrome care in Kerala.[42] A recent study showed that a 4-step protocol comprising emergency room−based catheterization lab activation, use of a STEMI "safe handoff" checklist, immediate transfer to the nearest available catheterization lab, and a radial-first approach to PPCI may mitigate gender-based disparities in STEMI care.[43] We recommend a similar STEMI quality-improvement initiative in this geographic area, focusing on achieving timely reperfusion in women, to improve overall STEMI care in India.

Conclusions

Women in Kerala, India, have much higher rates of major adverse cardiovascular events after STEMI, compared to men, even after adjusting for baseline risk. Notwithstanding similar rates of reperfusion between the 2 groups, this difference in outcomes appears to be driven primarily by markedly low rates of timely PPCI in women. This study identifies specific performance indicators that can be adapted for use in quality-improvement initiatives designed to improve outcomes in women presenting with STEMI.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

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