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Sex Differences in Clinical Profiles and Quality of Care Among Patients With ST-Segment Elevation Myocardial Infarction From 2001 to 2011: Insights From the China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE)-Retrospective Study

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ORIGINAL RESEARCH

Sex Differences in Clinical Profiles and Quality of Care Among Patients With ST-Segment Elevation Myocardial Infarction From 2001 to 2011: Insights From the China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE)-Retrospective Study

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***Background*—**China is experiencing a marked increase in ST-segment elevation myocardial infarction hospitalizations, with 30% occurring among women and higher risk of in-hospital death in relatively younger age groups (<70). Yet, little is known about sex differences in ST-segment elevation myocardial infarction presentation and management.

***Methods and Results*—**In a nationally representative sample of patients with ST-segment elevation myocardial infarction admitted to 162 Chinese hospitals in 2001, 2006, and 2011, we examined sex differences in hospitalization rates, clinical profiles, and quality of care. Among 11 986 patients, the proportion of women was unchanged between 2001 and 2011. The estimated national rates of hospital admission per 100 000 people increased from 4.6 in 2001 to 18.0 in 2011 among men (3.9-fold increase) and from 1.9 to 8.0 among women (4.2-fold increase) (P_{trend}<0.0001). The median age of women increased from 68 years in 2001 to 72 years in 2011 (P_{trend}<0.001); however, there was no age change in men (63 years in 2011) (P_{trend}=0.48). After accounting for age, women had a higher frequency of comorbidities. Although there were significant sex differences in the time interval of >12 hours between symptom onset and admission time in 2001, since 2006 delays in presentation were comparable between women and men. Fewer women without contraindications received evidence-based therapies than men, including reperfusion (57.5% versus 44.2%), early aspirin (88.8% versus 85.9%), and clopidogrel (56.9% versus 52.5%, P<0.001 for all) and the differences were largely unchanged over time.

***Conclusions*—**Women experienced a higher increase in hospitalization rates for ST-segment elevation myocardial infarction in China between 2001 and 2011 and were less likely to receive evidence-based therapies, especially reperfusion. In addition to efforts to improve quality of care generally, understanding the reasons for this sex disparity and addressing these differences in care should be a priority.

***Clinical Trial Registration*—**URL: https://www.clinicaltrials.gov. Unique identifier: NCT01624883. **(*J Am Heart Assoc*. 2016;5: e002157 doi: 10.1161/JAHA.115.002157)**

Key Words: acute myocardial infarction • epidemiology • health policy • quality of care • sex

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Accompanying Appendix S1, which lists the members of the China PEACE-Retrospective AMI Study Site Investigators by Hospital and China PEACE Study Consultants, Tables S1 through S3, Figure S1, and Data S1 are available at http://jaha.ahajournals.org/content/5/2/e003012/suppl/DC1

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As part of China's epidemiologic transition to higher rates of noncommunicable diseases, women, like men, are experiencing a rapid increase in the incidence of acute myocardial infarction (AMI) and AMI-related mortality,[1] as seen in other low- and middle-income countries.[2] In addition, the China Patient-centered Evaluative Assessment of Cardiac Events (PEACE) study demonstrated sex differences in mortality with women at higher risk of death in younger age groups.[3] Yet, much less is known about whether sex differences in clinical profiles and care quality differ between men and women and, if so, whether these differences are explained by age, and how they change over time.

Understanding sex differences in the clinical presentation and quality of care for high-impact conditions like AMI is instrumental to the prioritization of resources for quality improvement programs. A recognition of sex differences in the treatment of myocardial infarction in the late 1990s and early 2000s[4–6] in the United States led to national campaigns[7] and female-specific guidelines.[8–10] Subsequently, sex gaps in care have narrowed over time.[5,11] Previous studies in China demonstrate similar sex differences in treatment of comorbidities and outcomes.[3,12–14] However, these studies were generally limited to single sites or centers located predominantly in urban areas and examined single points in time, warranting a national perspective on sex differences in clinical presentation and quality of care in China.[12,13] Moreover, given that women are older than men at the time of an AMI,[3,15] it remains unknown whether these differences could be explained by age or how sex-based differences have changed over the last decade during improved access and healthcare quality in China.[16]

To provide insights into differences in patient characteristics and quality of care over time between men and women, we analyzed data from the China PEACE Retrospective AMI Study,[17] which included a random nationally representative sample of patients with AMI from 63 urban and 99 rural hospitals across China in 2001, 2006, and 2011. We have previously shown women in the younger age group had higher in-hospital mortality. In this study, our primary aim is to investigate sex differences in the presenting characteristics and quality of care of patients with ST-segment elevation myocardial infarction (STEMI), whether these differences could be accounted for by age, and to examine temporal trends.

Methods

Study Design

The objectives, scope, and purpose of the China PEACE Retrospective AMI Study have been described previously.[17] In brief, using 2-stage random sampling, a nationally representative sample of patients admitted with AMI in 2001, 2006, and 2011 was obtained. We stratified the hospitals into 5 economic–geographical regions (eastern rural, central rural, western rural, eastern urban, and central–western urban) since hospital volumes and clinical capacities differ between urban and rural areas and between the 3 official economic–geographical regions (eastern, central, and western) of China. We used systematic random sampling procedures to select patients with AMI from the local hospital database of each sampled hospital in each study year. We used version 9 (410.xx) and version 10 (I21.xx; when available) ICD codes to screen for possible cases of AMI. These cases were then further confirmed by clinical record assessment. Detailed clinical data were then collected by data abstraction to identify those cases that represented initial AMI episodes according to the definition in the 2010 China National Guideline for STEMI.[18] The central ethics committee at the National Center for Cardiovascular Diseases approved the study. All collaborating hospitals either accepted central ethics approval or obtained local approval by internal ethics committees. Because of the nature of the retrospective study, the requirement of informed consent was waived.

Study Sample

Only patients with a definite discharge diagnosis of STEMI (with or without prior cardiovascular disease) were eligible for inclusion in this study. The diagnosis of STEMI was determined by the combination of clinical discharge diagnosis terms and ECG results. The type of AMI was validated by review of ECG from randomly selected records by a cardiologist not involved in data abstraction, and there was a 94.7% concordance in the selected cases (Table S1). We excluded all patients whose STEMI occurred during the course of the hospitalization and those who were transferred in, transferred out, and were discharged alive in the first 24 hours of admission (Figure S1).

Data Collection and Measures

We collected data by central abstraction of medical charts with use of standardized data definitions, including patient characteristics (age, cardiovascular risk factors, clinical characteristics on presentation, and treatments) and hospital-level characteristics (acuity level, teaching status, percutaneous coronary intervention [PCI] capability). We compared time from symptom onset to admission between men and women, which included both prehospital delay and time from arrival to admission. Admission was used to track the time of presentation because we lacked information about time to

presentation at the hospital. We evaluated the use of treatments recommended by the 2010 National Guideline for STEMI,[18] which are consistent with 2007 U.S. guidelines.[19] Rates of utilization were assessed only in patients considered to be ideal for the treatment, defined as patients without accepted contraindications. Criteria identifying ideal candidates for guideline-concordant therapies are detailed in Data S1. For the calculation of rates of diagnostic catheterization and PCI, we restricted our study group to patients admitted to facilities capable of performing PCI.

Statistical Analysis

To estimate nationally representative rates of hospitals admission in men and women for each study year, we applied weights proportional to the inverse sampling fraction of hospitals within each stratum and the sampling fraction of patients within each hospital, to account for differences in the sampling fraction for each period. Patient characteristics and treatments were compared between women and men, both overall and across the 3 study years (2001, 2006, and 2011). Categorical and continuous variables were summarized by percentages and medians (interquartile range), respectively, and compared using the χ^2 tests and Student t tests, respectively. To examine trends across the different study periods for each sex, we used the Mann–Kendall test for continuous variables and the Cochran–Armitage test for categorical variables. We investigated the association between sex and the prevalence of cardiovascular risk factors, adjusted for age in logistic regression models. To examine the association between sex and treatment received, we also adjusted for age and other baseline characteristics as listed in Table 1 using multivariable logistic models. We included the 2-way interaction term sex×year in the regression model to assess whether sex differences in presenting characteristics and treatment varied by study year. All statistical analyses were performed using SAS software (version 9.2, SAS Institute, Cary, NC).

Results

Study Sample

We sampled 18 631 cases, from which 18 110 (97.2%) had available records. We excluded 6645 cases that did not meet inclusion criteria, resulting in a study sample of 11, 986 patients with STEMI (Figure S1). There were 1364, 2541, and 4507 men (representing 29 094, 65 370, and 120 991 male patients nationally in weighted estimates) and 569, 1040, and 1965 women (representing 12 134, 27 098, and 53 585 female patients nationally in weighted estimates) in 2001, 2006, and 2011, respectively. Hospital admissions for STEMI per 100 000 people increased 4.2-fold in men (4.6 in 2001, 10.0 in 2006, and 18.0 in 2011) and 3.9-fold in women (1.9 in 2001, 4.1 in 2006, and 8.0 in 2011).

Patients Characteristics

From 2001 to 2011, the median age of patients increased from 68 to 72 years in women ($P_{trend}<0.001$) but remained stable in men (63 years in 2011) ($P_{trend}=0.48$). The proportions of men and women aged ≥80 years old significantly increased over time (Figure 1). The prevalence of cardiovascular risk factors increased over time for both women and men. Women had a higher prevalence of hypertension, diabetes mellitus, and coronary heart disease in each time period ($P<0.001$ for all comparisons) (Table 1). Similar findings were also found in the age-adjusted results (Figure 2). In addition, sex differences in the prevalence of hypertension increased from 2001 to 2011, with women having a higher prevalence. However, sex differences in the prevalence of diabetes remained stable. Although there was no significant sex difference in those with a low-density lipoprotein cholesterol >130 mg/dL in 2001, this risk factor was more prevalent in women in later time periods (Figure 2). Women were hospitalized less often in tertiary care hospitals and hospitals with the capacity to perform PCI.

Women were consistently were more likely to have systolic blood pressure over 140 mm Hg and heart rate over 100 bpm. Comparing 2001, 2006, and 2011, sex differences in heart rate >100 bpm increased, yet differences in the presence of systolic blood pressure measurements did not change. Although there were significant sex differences in the time interval of >12 hours between symptom onset and admission time in 2001, since 2006 delays in presentation were comparable between women and men (Figure 3). The age-adjusted results showed that there was no sex difference in chest discomfort in 2001 and 2006, but not 2011.

Treatment Among Ideal Candidates

The proportion of ideal patients for aspirin, clopidogrel, β-blocker, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker, and statin treatments remained unchanged over time in both sex groups (Table S2). Although the proportion of women ideal for reperfusion therapy increased significantly over the last decade (from 35.7% in 2001 to 43.0% in 2011, $P_{trend}=0.001$), they remained less likely than men (48.2%) to be ideal patients for reperfusion therapy in 2011.

Overall, differences in treatment were consistently observed over the study period. The absolute differences between men and women receiving fibrinolytic therapy,

Table 1. Patient Characteristics According to Sex and Study Year

Characteristic	Men, %*			*P* for Trends	Women, %*			*P* for Trends
	2001 (n=1364)	2006 (n=2541)	2011 (n=4507)		2001 (n=569)	2006 (n=1040)	2011 (n=1965)	
Demographic								
Age, y†	63 (53, 70)	64 (54, 73)	63 (53, 73)	0.476	68 (62, 74)	71 (65, 76)	72 (64, 78)	<0.0001
Cardiovascular risk factors								
Hypertension	38.8	45.9	47.3	<0.0001	47.8	53.4	60.6	<0.0001
Diabetes	11	15.4	18.3	<0.0001	21.1	25.8	26.9	0.010
Current smoker	38.7	41.3	48	<0.0001	6	9	11.9	<0.0001
Medical history								
Coronary heart disease	22.6	19.1	20.5	0.355	26.2	22.2	21.8	0.054
Myocardial infarction	10.3	9.7	11.6	0.058	9.5	8.8	9.3	0.970
PCI	0.4	0.9	2.7	<0.0001	0.9	0.9	1.5	0.138
Stroke	9.2	10.3	11.5	0.010	10	11.7	13.9	0.070
Symptom onset to admission, hour								
<6	42.2	40.9	41.3	0.467	30.9	34.1	36.9	0.003
6 to 12 hours	8.9	9.6	10.5	0.027	10.7	12.5	11.3	0.921
>12 hours	48.9	49.5	48.1	0.430	58.3	53.4	51.7	0.008
Clinical characteristics								
Chest discomfort	93.1	93.2	93.4	0.652	91.2	89.7	89.3	0.219
Cardiogenic shock	3.4	5.5	6	0.0005	6.2	7.6	7.9	0.205
Cardiac arrest	0.9	1.3	1.5	0.078	0.7	0.8	1.1	0.335
Acute stroke	0.7	1.5	1	0.930	1.1	2.6	1.1	0.318
Heart rate ≥100 bpm†	15.7	14.8	11.6	<0.0001	20.2	22.0	18.4	0.098
SBP ≥140 mm Hg†	31.3	31.4	32.6	0.256	37.3	39.3	39.7	0.326
LDL-C level								
<130	35.2	55.8	67.6	<0.0001	25.8	50.1	59.3	<0.0001
≥130	11.7	15.4	18.2	<0.0001	12.8	18.5	22.4	<0.0001
Unrecorded	53.2	28.7	14.2	<0.0001	61.3	31.4	18.3	<0.0001
eGFR, mL/min per 1.73 m^{2}†	75.5 (60.0, 94.6)	77.9 (61.7, 97.9)	88.1 (68.9, 109.8)	<0.0001	63.7 (49.1, 81.9)	66.4 (48.2, 84.2)	76.1 (55.7, 100.1)	<0.0001
Hospital characteristics								
Teaching hospital	85	80.6	80.1	0.0001	83.5	79.7	77.8	0.003
PCI-capable hospital	32.8	55.1	72.9	<0.0001	34.3	52.6	69	<0.0001
Hospital with CCU	81.1	76.3	79.4	0.952	78.6	77.4	78.6	0.791
Economic–geographic region								
Central	19.5	21	23.2	<0.0001	16.9	17.9	22	<0.0001
Eastern	65.7	58.4	54.7	<0.0001	71.5	63.3	59.3	<0.0001
Western	14.8	20.6	22.1	<0.0001	11.6	18.8	18.7	<0.0001
Urban/rural								
Urban	63.9	60.6	63.4	0.586	64	60.9	57.9	0.006
Rural	36.1	39.4	36.6		36	39.1	42.1	

CCU indicates cardiac care unit; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; PCI, percutaneous coronary intervention; SBP, systolic blood pressure.

*Unless otherwise indicated.

†Continuous variables displayed as median values with interquartile range.

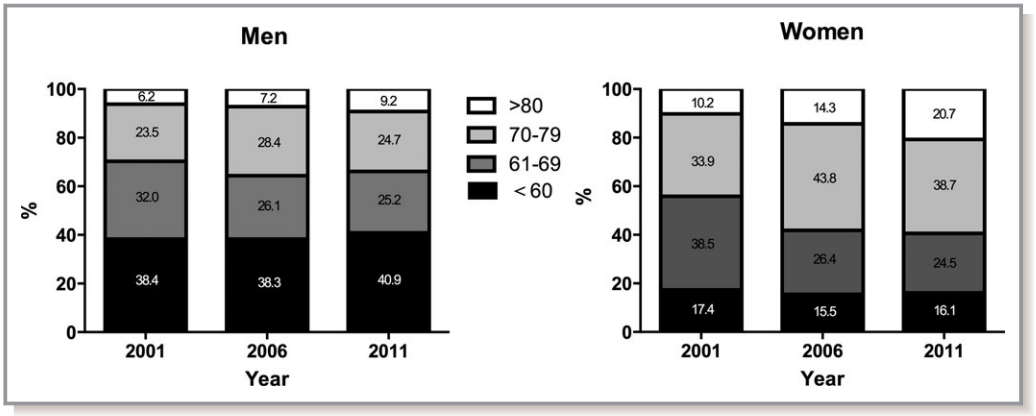

Figure 1. Age distribution of the study sample according to sex and year.

primary PCI, or any reperfusion therapy were 6.7%, 5.5%, and 13.2% in 2011, respectively. In addition, any coronary angiography and nonprimary PCI were performed less commonly during initial AMI hospitalization in women in all time periods. Fewer women received aspirin or clopidogrel within 24 hours of admission (Table 2). After adjusting for age and other baseline characteristics, women without contraindications to treatment were significantly less likely to receive reperfusion therapy, coronary angiography, and nonprimary PCI in all time periods (Table S3). No significant sex differences were observed in the administration of other examined medications, including β-blocker, angiotensin-converting enzyme inhibitor/ angiotensin II receptor blocker, and statin. Between 2001 and 2011, sex differences in treatment persisted, and in some cases widened. In particular, sex differences in the utilization of primary PCI increased (Figure 4).

Discussion

In this large, national study in China of hospitalization for STEMI, we found marked sex differences in clinical profiles and quality of care. Women, who experienced a slightly higher increase (4.2-fold versus 3.9-fold) in STEMI over the study period, were older, had greater comorbidities, and were less likely to be ideal patients for many evidence-based therapies. Among ideal patients, women were significantly less likely to receive a revascularization strategy (including fibrinolysis or cardiac catheterization with or without PCI), even after accounting for differences in clinical profiles. These sex-based differences in patient characteristics and hospital care did not change significantly over the past decade, underscoring the need to specifically address these findings with quality improvement efforts.

We had previously shown in the China PEACE study that the risk of mortality was age dependent and most pronounced among younger women (<70 years of age) with STEMI, even

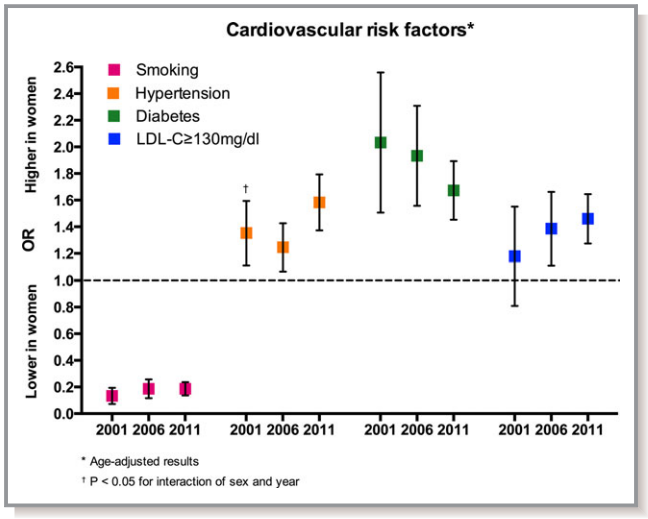

Figure 2. Temporal trends of age-adjusted results in sex differences in cardiovascular risk factors. LDL-C indicates low-density lipoprotein cholesterol; OR, odds ratio.

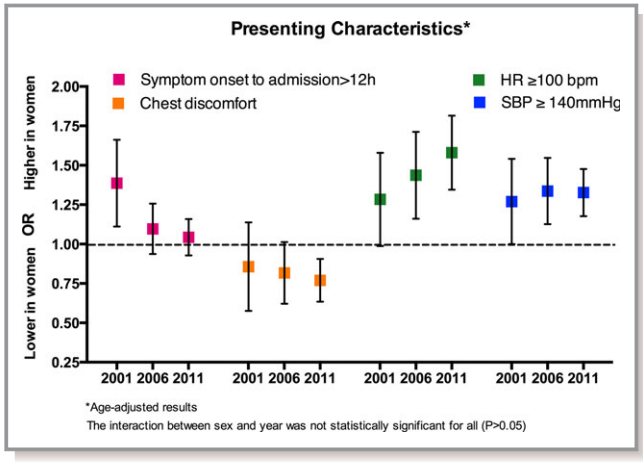

Figure 3. Temporal trends of age-adjusted results in sex differences in presenting characteristics. HR indicates heart rate; OR, odds ratio; SBP, systolic blood pressure.

Table 2. In-Hospital Treatments Among Ideal Patients According to Sex and Year

Characteristic	Overall, N (%)			Men, %				Women, %			
	Men	Women	*P* Value	2001	2006	2011	*P* for Trends	2001	2006	2011	*P* for Trends
Acute medication											
Aspirin ≤24 hours*	7023 (88.8)	2765 (85.9)	<0.0001	81.1	87.7	91.8	<0.0001	78.0	85.0	88.8	<0.0001
Clopidogrel ≤24 hours*	4454 (56.9)	1679 (52.5)	<0.0001	1.4	44.3	80	<0.0001	0.8	36.5	75.5	<0.0001
β-Blockers ≤24 hours*	2371 (56.8)	770 (52.6)	0.005	47.8	62.7	56.1	0.095	46.4	54.8	53.1	0.202
ACE-inhibitor/ARB*,†	5073 (65.8)	1994 (63.8)	0.044	60.8	69.6	65.2	0.214	59.2	66.7	63.6	0.332
Statin*,†	6180 (76.5)	2476 (75.1)	0.117	30.3	75.0	91.5	<0.0001	27.8	72.6	90.4	<0.0001
Reperfusion therapy†											
With reperfusion	2289 (57.5)	646 (44.2)	<0.0001	56.3	58.0	57.6	0.702	47.3	42.2	44.4	0.758
Primary PCI	757 (19.0)	203 (13.9)	<0.0001	8.7	15.1	24.2	<0.0001	8.4	8.9	17.7	<0.0001
Fibrinolytic therapy	1535 (38.6)	443 (30.3)	<0.0001	47.7	43.0	33.5	<0.0001	38.9	33.3	26.8	0.0002
Procedure‡											
Nonprimary PCI	1117 (21.8)	299 (14.3)	<0.0001	9.6	19.4	24.4	<0.0001	5.6	10.2	17.1	<0.0001
Cardiac catheterization	2414 (47.0)	669 (31.9)	<0.0001	34.2	41.7	51.1	<0.0001	26.2	25.0	35.5	<0.0001

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; PCI, percutaneous coronary intervention.
*Only among patients without contraindications for the treatment.
†During hospitalization.
‡Only among patients admitted into a hospital capable of PCI.

after accounting for differences in clinical presentation and treatments.[3] However, we had not investigated temporal trends in sex differences as they relate to patient characteristics and receipt of evidence-based therapies in STEMI. We found that even after adjusting for age, with the exception of smoking, a predominantly male activity in China,[20] risk factors including greater age, diabetes, hypertension, and dyslipidemia were more common in women presenting with STEMI. These are consistent with prior national and international studies.[21,22]

The clinical presentation of women differed from men. Indeed, half of the women in our study presented outside the time window for reperfusion therapy, which is consistent over the last decade. However, we did observe a decrease in the delay to admission among women, and sex differences in the time interval of >12 hours between symptom onset and admission time disappeared since 2006, which might partly be due to improved healthcare accessibility for women in China.[23]

While the quality of care improved for both men and women, significant sex gaps exist and have not improved over time. Significantly fewer women received a reperfusion strategy, even when they presented promptly for treatment.

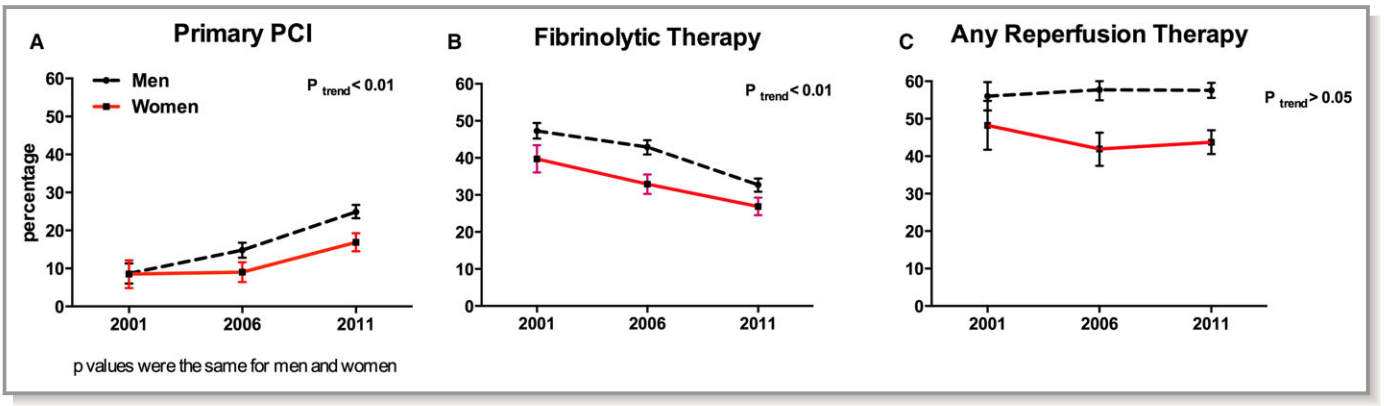

Figure 4. Temporal trends of sex differences in reperfusion therapy among ideal candidates. A, Primary PCI. B, Fibrinolytic therapy. C, Any reperfusion. PCI indicates percutaneous coronary intervention.

Additionally, among patients deemed to be ideal candidates, women were less likely than men to receive aspirin and clopidogrel. Sex differences in treatment response have not been supported by the literature; rather, prior studies indicate that both women and men derive similar reductions in morbidity and mortality with the prescriptions of aspirin, clopidogrel, and with invasive cardiac procedures,[4] and guidelines do not recommend differential use of these therapies based upon sex. The disparities in care identified in this study require full-scale investigation into clinical decision-making and targeted efforts to diminish such disparities.

The rising burden of modifiable cardiovascular risk factors among women will require local and national efforts to advance primary and secondary prevention strategies; such efforts may need to directly target women at high risk of heart attack. The marked underutilization of coronary catheterization and reperfusion therapy should prompt quality improvement efforts to ensure that the evidence-based management of STEMI is rigorously applied in patients of both sexes.[24] In the interim, large-scale educational initiatives targeting women should be implemented in both pre-hospital and in-hospital settings to increase women's and their health providers' awareness of cardiovascular disease and recognition of symptoms of AMI,[25]which has been proven to be effective in the Go Red for Women campaign, which was initiated in the United States.[25] Ultimately, dispelling myths (or old assumptions) and improving awareness is difficult and will require innovative, multipronged efforts.

Limitations

The results of our study should be interpreted with consideration of several limitations. First, residual confounding of measured or unmeasured variables might affect the observed results. However, we accounted for traditional clinical factors common among risk models predicting early mortality. Second, given that relatively few patients underwent a cardiac catheterization, we were not able to adjust our analysis to account for the severity and extent of coronary artery diseases that might contribute to the sex differences in mortality.[26] However, these data are not typically included in risk-adjusted models, and it is not clear that anatomy would affect in-hospital mortality differently in men and women.

Conclusions

In a large, nationally representative observational study in China, women hospitalized with STEMI were older, had greater delays in care seeking, more comorbidities, and worse disease severity than men. Moreover, women were less likely to be candidates for, and less likely to receive, evidence-based therapies as compared with men. These disparities have changed little over the past decade despite large-scale efforts to increase access and quality. These findings underscore the need for improved systems to ensure the prompt diagnosis and use of evidence-based treatments for women with STEMI, particularly with respect to reperfusion therapies.

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Disclosures

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