

Sex differences in presentation, management, and outcomes in chinese patients presenting to an emergency department with chest pain

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Abstract

Purpose: To assess sex difference among Chinese patients with chest pain in emergency department (ED).

Methods: All patients with non-traumatic chest pain presenting to the chest pain center (CPC) in a tertiary center in Shenzhen, China from January 1st, 2018, to September 30th, 2019 were included. Patient demographics, presenting condition, treatment and outcome were retrieved from the electronic medical record at CPC.

Results: 6603 patients (44.1% female) were included. The commonest location where patient developed chest pain was home, and more commonly in women (90.08%) than men (85.06%) ($P<0.001$). Distribution of chest pain type was significantly different between genders ($P<0.001$). Time from chest pain symptom onset to CPC presentation was similar between men and women ($P=0.28$), so was time from CPC presentation to receipt of medical care ($P=0.95$) and time from CPC presentation to first ECG evaluation ($P=0.93$). However, men were found to have longer time from CPC presentation to hospital discharge ($P<0.001$). The distribution of clinical diagnosis was significantly different between sexes ($P<0.001$), men received significantly more medical treatment than women. Older age ($P<0.001$), female gender ($P=0.007$), higher respiratory rate ($P=0.035$), faster heart rate ($P<0.001$), longer time from symptom onset to CPC presentation ($P=0.04$), longer time from CPC presentation to receipt of medical care ($P=0.04$) and positive cTnI/cTnT ($P<0.001$) were related to a higher risk of hospital admission.

Conclusions: Significant sex difference existed among Chinese patients in ED with chest pain, which should be considered in contemporary ED management to bridge the gender gaps in future clinical practice.

Introduction

Chest pain is the commonest chief complaints in emergency departments (ED). It is associated with a number of critical conditions, including the coronary artery disease [1,2]. Previous reports have confirmed gender disparities in patient with acute coronary syndromes (ACS), showing that less women than men were given evidence-based therapies and admitted for further evaluation and treatment [3-6]. It is also reported that women had higher mortality rate after ACS or myocardial infarction than men, adjusted for risk factors [7-9]. Given that most patients with acute chest pain attends ED, the management in ED is accounted heavily for prognosis. Previous reports with respect to sex differences in chest pain are based on admitted patients. The evidence based on ED patients is limited [4,10,11].

ED in China have witnessed the change of the epidemiology of medical emergencies in men and women, which is believed to be related to lifestyle changes, along with the economic growth in the past few decades [12]. It is timely to examine the gender disparities among ED patients with chest pain to improve our assessment and management. To the best of our knowledge, the gender gaps for ED patients with chest pain in China has never been reported before and is thus of great value and in urgent need.

The purpose of this study was to evaluate difference in the clinical presentation, diagnosis, management and outcome in patients with chest pain presenting to ED in China.

Materials and Methods

Study design and population

This is a retrospective cohort study. From January 1, 2018, through September 30, 2019, consecutive women, and men older than 18 years presenting to the Chest Pain Centre (CPC) of a tertiary centre in Shenzhen, China with non-traumatic chest pain or symptoms suggestive of Acute Myocardial Infarction with an onset or peak within the last 12 hours were recruited. Times from the onset and peak of acute chest pain were recorded on a dedicated form for all patients. Ethics approval for the study was obtained from HKU-SZH Ethics Review Board. The study observed the tenets of the Declaration of Helsinki.

Shenzhen, adjacent to Hong Kong, is a 40-year-old city in southern China with a population of greater than 12 million. The catchment area of the CPC covers a population of 1.5 million. The annual census of the CPC is approximately 170,000.

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Routine clinical assessment

All patients were assessed by triage nurse and then emergency physician after their arrival, for medical history, physical examination, 12-lead ECG and cardiac monitoring, pulse oximetry, standard blood test and chest radiography. Levels of troponin tests were measured by Point-of-care testing system at the presentation and serially subsequently as it is necessary. Timing of the assessments and treatment of patients were captured by EMR.

Chest pain characteristics, treatment, and clinical outcomes

Medical evaluation in CPC includes onset and symptomatology, physical findings, ECG, and other investigations were recorded. Information on treatment and patient disposition were captured by EMR.

Symptomatology includes chest pain location, pain quality, radiation, onset, duration, dynamics of pain, aggregating and relieving factors. Pain severity was quantified with using pain score ranging from 0 for no pain to 10 for worst pain. Chest pain characteristics were all recorded by emergency physicians blinded to the 12-lead ECG and troponin I levels. Administration of antihypertensives and anti-lipid agents were documented. Clinical outcomes for all patients were recorded in the EMR, including hospital discharge, hospital admission, transfers, death and unknown.

Adjudicated final diagnosis

Preliminary diagnosis was determined by the emergency physicians into the following subgroups in the EMR: non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI), unstable angina (UA), pulmonary embolism (PE), non-acute coronary syndrome cardiac chest pain (non-ACS CCP), non-cardiac chest pain (NCCP), aortic dissection and cause undetermined. The final diagnoses for patients with Acute coronary syndrome (NSTEMI, STEMI and UA) were determined by cardiologists.

Statistical analysis

Statistical analysis was performed using STATA (Version 14.0; Stata Corp, College Station, Texas, USA). Data of the included patients were extracted from the EMR and used for analysis. Age was divided into the following four subgroups: <50 years (y), 50-59 y, 60-69 y, and ≥ 70 y. Data of vital signs and CPC time measures were expressed as mean \pm standard deviation (SD). Four CPC time measures were performed, including time from symptom onset to CPC presentation, time from CPC presentation to receipt of medical care, time from CPC presentation to first ECG evaluation, and time from CPC presentation to hospital discharge. These four-time measures were calculated as the time of later timepoint minus the previous time point, and expressed as median (25% percentile, 75% percentile) given the skewed distribution. The cTnI value was dichotomized into the negative and positive group based on a cut-off value of 50 ng/ml. Group t-test and Chi square test were used to compare the baseline patient characteristic of between men and women. The clinical presentation, medical treatment and clinical outcomes were also compared between men and women. Subgroup analysis in the above comparison were done for patients with pulmonary embolism/ aortic dissection and acute coronary syndrome. Logistic regression analysis was used to assess the associations of potential risk factors with hospitalization among the study participants. A p-values of less than 0.05 was considered statistically significant.

Results

A total of 6603 patients were included in the final analysis, of whom 2914 (44.1%) were female. Details of the demographics and vital signs of the study participants is shown in Table 1. Mean age of the patients was 48.2 ± 18.6 years, and women were significantly older than men (49.8 ± 19.5 vs. 46.9 ± 17.8 ; $P < 0.001$). There was no significant difference in RR or pulse between men and women, while men tended to have higher blood pressure than women ($P < 0.001$ for both SBP and DBP). Faster HR was also observed in women participants ($P = 0.0012$).

Table 2 summarises the presenting characters of these patients. The majority of patients had chest pain onset at home (5763/6603) rather than outside, and this ratio was significantly higher in women than men ($P < 0.001$). Regarding type of chest pain, intermittent chest pain was most commonly seen in both men (51.3%) and women (54.7%), followed by chest pain relieved at CPC presentation and continuous chest pain. Distribution of chest pain type was also significantly different between sexes. Time from chest pain symptom onset to CPC presentation ("Onset-to-door" time) was similar between men and women (median: 490 vs. 445 minutes, $P = 0.28$), so was time from CPC presentation to receipt of medical care ("Door-to-triage/doctor" time) (median: 8 vs. 8 minutes, $P = 0.95$) and time from CPC presentation to first ECG evaluation (median: 12 vs. 12, $P = 0.93$). However, men were found to have longer time from CPC presentation to hospital discharge (Length of stay in? CPC) (median: 62 vs. 60 minutes, $P < 0.001$). Analysis of the cTnI/cTnT showed no significant gender difference in the percentage of positive test results (38.0% vs. 39.1%, $P = 0.35$).

As to the clinical diagnosis, the commonest two were non-ACS CCP and NCCP in both men and women. The distribution of diagnosis was significantly different between sexes, with women more likely to have non-ACS CCP and less likely to have ACS ($P < 0.001$) (Table 3). The administration of medical treatment was different between men and women, with men received significantly more 24-hours intensive statin ($p = 0.007$), β -receptor blocking agent ($P < 0.001$) and ACET/ARB treatment ($P = 0.003$) than women. The majority of patients were discharged from the hospital after treatment (61.3% for men, 68.7% for women), others were admitted to the hospital for further treatment, transferred to other hospital or died. The distribution of clinical outcome was also significantly different between men and women ($P < 0.001$).

Considering patients with ACS, women was significantly older ($P < 0.001$), had higher RR ($P = 0.003$), lower DBP ($P = 0.01$), but no significant difference with men in pulse, SBP, HR, as well as all four CPC time measures. In addition, women received less medical treatment than men ($P = 0.001$ for ACEI/ARB, $P = 0.003$ for statin). Logistic regression showed that older age ($P < 0.001$), female gender ($P = 0.007$), higher RR ($P = 0.035$), faster HR ($P < 0.001$), longer time from symptom onset to CPC presentation ($P = 0.04$), longer time from CPC presentation to receipt of medical care ($P = 0.04$) and positive cTnI/cTnT ($P < 0.001$) were related to a higher risk of hospitalization as a clinical outcome (Table 4).

Discussion

In the current study, we reported significant sex difference in the clinical presentation, management, and outcomes in ED patients with chest pain in China. Most previous studies regarding this issue were based on Caucasian populations [10-14], and to the best of our knowledge, no data from China had been reported. Our findings could help fill this gap and provide useful information for future clinical guidelines.

Table 1. Characteristics of patients with chest pain admitted to CPC by gender.

Characteristics*	Number	Total (N=6603)	Men (N=3689)	Women (N=2914)	P value
Age, years	6603	48.2±18.6	46.9±17.8	49.8±19.5	<0.001
Age group, number (%)					<0.001
<50 years	3538	33.7±9.87	34.1±9.78	33.1±9.97	
50-59 years	1087	54.5±2.77	54.4±2.78	54.5±2.76	
60-69 years	1034	64.2±2.79	64.2±2.81	64.2±2.76	
≥70 years	932	78.2±5.87	77.8±5.88	78.5±5.85	
Respiratory rate, bpm	6417	19.2±2.30	19.2±2.28	19.3±2.32	0.65
Pulse, bpm	2129	84.1±30.9	83.9±31.8	84.5±29.7	0.66
SBP, mmHg	6390	131.8±38.1	133.2±42.3	130.0±31.9	<0.001
DBP, mmHg	6390	79.6±18.7	81.3±22.1	77.5±12.7	<0.001
Heart rate, bpm	6437	84.4±21.0	83.6±19.8	85.3±22.3	0.0012

*Data are expressed as mean± standard deviation unless otherwise indicated.
Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; Bpm: Beat Per Minute.

Table 2. Clinical presentation, treatment and outcomes for patients with chest pain presented to CPC by gender.

Characteristics	Number	Men	Women	P value
Chest pain onset location, number (%)				<0.001
At home	5763	3138(85.1%)	2625(90.1%)	
Outside home	840	551(14.9%)	289(9.9%)	
Presenting pain character, number (%)				<0.001
Continuous	886	561(15.2%)	325(11.2%)	
Intermittent	3489	1894(51.3%)	1595(54.7%)	
Relieved	1490	826(22.4%)	664(22.8%)	
Missing	738	408(11.1%)	330(11.3%)	
Onset to door time, minutes*	6477	490(115, 2004)	445(115, 2169)	0.28
Door to triage/doctor time, minutes*	6064	8(4,15)	8(5,15)	0.95
Triage/Doctor to ECG time, minutes*	6446	12(8,19)	12(8,20)	0.93
Length of stay in CPC, minutes*	6242	62(25, 133)	60(25, 114)	<0.001
cTnI/cTnT, number (%)				0.35
Positive	2539	1400(38.0%)	1139(39.1%)	
Negative	4064	2289(62.0%)	1775(60.9%)	
Diagnosis, number (%)				<0.001
NSTEMI	164	135(3.7%)	29(1.0%)	
STEMI	190	162(4.4%)	28(1.0%)	
UA	190	131(3.6%)	59(2.0%)	
PE	17	12(0.3%)	5(0.2%)	
non-ACS CCP	2516	1314(35.6%)	1202(41.3%)	
NCCP	3274	1771(48.0%)	1503(51.6%)	
Aortic dissection	20	18(0.5%)	2(0.1%)	
Cause unknown	226	141(3.8%)	85(2.9%)	
Medical treatment, number (%)				<0.001
β-receptor blocking agent	343	279(81.3%)	64(18.7%)	<0.001
ACEI/ARB	439	356(81.1%)	83(18.9%)	0.003
Statin	403	328(81.4%)	75(18.6%)	0.007
Clinical outcome, number (%)				<0.001
Hospital discharge	4261	2260(61.3%)	2001(68.7%)	
Hospital admission	1069	590(16.0%)	479(16.4%)	
Transfers	5	4(0.1%)	1(0.03%)	
Death	19	16(0.4%)	3(0.1%)	
Unknown	1249	819(22.2%)	430(14.8%)	

*Data expressed as median (25th percentile, 75th percentile)
Abbreviations: CPC: Chest Pain Center; NSTEMI: Non-ST-Segment Elevation Myocardial Infarction; STEMI, ST-Segment Elevation Myocardial Infarction; UA: Unstable Angina; PE: Pulmonary Embolism; Non-ACS CCP: Non-Acute Coronary Syndrome Cardiac Chest Pain; NCCP: Non-Cardiac Chest Pain; ACEI: Angiotensin Converting Enzyme Inhibitor; ARB: Angiotensin II Receptor Antagonists.

Women who presented to the ED with chest pain were significantly older than men in our study. Earlier retirement age and longer life expectancy might be part of the reason. This finding is consistent with previous studies, which had also attributed the observed differences in management, complications, and outcomes to the older average age of female patients [3,8,15]. We also found that women had lower blood

pressure, faster heart rate, and more likely to have intermittent chest pain than men, which could be partly due to that woman are reported to have a greater burden of comorbidity and thus more likely to bear symptoms, especially these mild symptoms, than men [16,17]. In our study, chest pain occurred at home for the majority of patients for both men and women, and the most common type at ED presentation

Table 3. Clinical characteristics and management of patients with acute coronary syndrome.

characteristics	Men	Women	P value
Age, years	58.6±13.0	67.3±12.8	<0.001
Respiratory rate, bmp	19.0±2.8	19.9±6.1	0.03
Pulse, bmp	81.0±60.5	74.3±14.4	0.43
SBP, mmHg	142.3±75.5	136.2±22.6	0.39
DBP mmHg	84.6±28.6	77.8±12.7	0.01
Heart rate, bmp	79.1±18.2	79.1±19.0	0.99
Time from symptom onset to CPC presentation, minutes*	556(102,3270)	750(120,4331)	0.60
Time from CPC presentation to receipt of medical care, minutes*	10(5,23)	10(4,30)	0.99
Time from CPC presentation to first ECG evaluation, minutes*	13(7,31)	15(7,41)	0.64
Time from CPC presentation to hospital discharge, minutes*	8945(5865, 12791)	10099(5186, 14567)	0.24
cTnI/cTnT, number (%)			0.76
Positive	158(36.9%)	41(35.3%)	
Negative	270(63.1%)	75(64.7%)	
Medical treatment, number (%)			
β-receptor blocking agent	271(81.6%)	61(18.4%)	0.07
ACEI/ARB	353(81.2%)	82(18.9%)	0.001
Statin	322(81.6%)	73(18.4%)	0.003

* Data expressed as median (25th percentile, 75th percentile)

Abbreviations: CPC: Chest Pain Center; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; Bpm: Beat Per Minute; ACEI: Angiotensin Converting Enzyme Inhibitor; ARB: Angiotensin II Receptor Antagonists.

Table 4. Association between gender and hospitalization for patient with chest pain who present to the chest pain center.

Variable	Odds ratio (95% CI)	P value
Age, years	1.05(1.04 to 1.05)	<0.001
Female gender	0.81(0.70 to 0.95)	0.007
Hypertension, yes	1.07 (0.92 to 1.25)	0.38
Respiratory rate	1.03(1.00 to 1.07)	0.035
Heart rate	1.01(1.01 to 1.02)	<0.001
Time from symptom onset to CPC presentation, minutes	1.01(1.00 to 1.02)	0.04
Time from CPC presentation to receipt of medical care, minutes	1.00(0.98 to 1.00)	0.04
cTnI/cTnT, positive	1.33(1.15 to 1.55)	<0.001

Abbreviations: CPC: Chest Pain Center; CI: Confidence Interval.

was intermittent chest pain, followed by chest pain relieved at ED presentation and continuous chest pain. These findings may offer novel information for the clinical practice and further studies are needed for validation.

When evaluating a patient with acute chest pain at ED, clinicians make diagnostic and treatment decisions based on readily available information from the clinical assessment and investigation [18]. Studies regarding sex difference for patients with coronary heart disease generally reported that women were more likely to have delayed hospital presentation [3,19,20]. Other studies, mainly in developed countries, had also reported longer delays for women from symptom onset to ED presentation, to first electrocardiogram (ECG) as well as other diagnostic examinations [21-23]. However, in current study, no significant difference was observed between sexes regarding the duration from onset to presentation and the time for each care process. This discrepancy is possibly attributed to health system differences. Patient with chest pain who presents to the study hospital will be received by an ED nurse for brief inquiry on patient information and medical history, then the nurse will triage the patient to the chest pain center for more detailed assessment and ECG examination. Subsequently, patients will be evaluated by doctors at the chest pain center to decide if further assessments is needed before making a final diagnosis and clinical decision. Patient will be admitted to the hospital, if necessary, decided by the doctor. This health system workflow in the study hospital is standardized and easy to follow. Other possible explanations include

that the gender inequality on health awareness and resources between sexes is smaller in China. More studies are needed to validate and better understanding of potential mechanisms.

Increasing evidence demonstrated that women are less likely to receive timely diagnosis and treated less aggressively than men in ambulatory care, [10,11,24] which has been proposed an association with the higher rates of mortality in women with ACS [4]. Such observation is also confirmed in the current study in which women received less medical treatment than men for all medications concerned, including β-receptor blocking agent, ACEI/ARB and statin. In addition, women were found a protective factor for hospital admission, and women also had shorter length of stay, suggesting that women were less likely to be admitted to the inpatient unit for further treatment. For our patients with ACS, women received less medical treatment, which is consistent with the finding from the whole study population and other previous studies [15,25].

Our study adds to the evidence that more efforts should be taken to address the inequality in medical treatment between sexes in ED management in both developing and developed countries. Women were known lower in cTnI level, and sex difference in the cTnI level had been suggested as one explanation for the lower rate of medical treatment in women [26-28]. However, in our study, no significant difference in the positive rate of cTnI level among both overall or the patients with ACS. This was supported by another study which reported

that the lower rate of myocardial infarction diagnosis in women was not related to the level of cTnI [27]. A positive cTnI level was significantly related to a higher risk of hospital admission in our study, which was of no surprise. In addition, older age, male gender, faster respiratory rate, longer time from symptom onset to ED presentation, and longer time from ED presentation to receipt of medical care were all found to be significant risk factors for hospital admission.

Our study reported, for the first time, the sexual difference in clinical presentation, management, and outcomes among ED patients with chest pain in China. We found that women tend to have milder symptoms, less likely to received medical treatment and less likely to be admitted to the hospital. Results of the subgroup analysis in ACS patients further validated these findings. Other strengths of this study included a large population size and the availability of multiple ED time measures. Several limitations of this study need to be noted. Firstly, this study is not population-based, thus the study findings could not be applied directly to other study settings. Secondly, data on the lifestyle factors, including smoking and alcohol drinking, was not available. Lastly, data on several important medical treatments (e.g., Vasodilators) and clinical examinations (e.g., Coronary angiogram) was not available in our study, thus our multivariable analysis may not have fully adjusted for all confounders. Future studies are needed to further include these factors.

Conclusion

This study found no significant delay in ED presentation or treatment in women with chest pain compared with their male counterparts in China, but women were still more likely to be treated conservatively. Greater awareness and more efforts should be paid to help eliminate this gender gap in current guidelines and management practices.

Disclosure

The study protocol and this study received ethics approval from the HKU-SZH Ethics Review Board. The study observed the tenets of the Declaration of Helsinki, and all study participants provided informed consent. This is not a clinical trial, and no animal studies was involved. All authors declared no conflict of interests.

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