Gender differences in treatment strategies among patients ≥80 years old with non-ST-segment elevation myocardial infarction

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Background: This study aims to investigate the gender differences in treatment strategies among non-ST-segment elevation myocardial infarction (NSTEMI) patients ≥80 years old in China.

Methods: A total of 190 consecutive NSTEMI patients ≥80 years old in Fuwai Hospital were included from 2014 to 2017. These patients were grouped by gender, and sub-grouped by conservative treatment or invasive treatment. The clinical characteristics, medical history, discharge drug used, and prognosis were collected and compared between these two treatment strategies.

Results: There were significant differences between these two treatment strategies in terms of GRACE grade, history of myocardial infarction (MI), after coronary artery bypass grafting (CABG), III grade, renal dysfunction, anemia, and use of diuretic (P<0.05). In addition, the age, creatinine and Killip class of female patients, and the death and good prognosis of male patients were found to be significantly different between these two treatment strategies (P<0.05). The multivariate logistic regression analysis revealed that the death of males was significantly associated with treatment strategies in the multivariable logistic regression analysis (P<0.05). In addition, the Kaplan-Meier survival analyses revealed that the survival rates of invasive strategy were significantly higher, when compared to that of conservative strategy in males (P=0.001) and females (P=0.015).

Conclusions: There were gender differences in treatment strategies among NSTEMI patients ≥80 years old. The difference in treatment strategies in males was more pronounced than in females, in terms of long-term survival rate.

Keywords: Non-ST-segment elevation myocardial infarction (NSTEMI); gender differences; treatment strategy; older patients

Introduction

Myocardial infarction (MI) is the leading cause of death in the United States, and a major cause of mortality around the world (1). The good news is that the mortality of MI patients has considerably decreased worldwide, and this improvement has been considered to be correlated to improved treatment strategies during the last 20 years (2,3). However, these improvements are mainly reflected in young patients and males, while females with MI continue to have

a high mortality rate and worse prognosis (4). In addition, previous studies have revealed that gender differences exist in the management of non-ST-segment elevation myocardial infarction (NSTEMI) (5,6).

Present guidelines recommend the use of an early invasive strategy for high-risk patients diagnosed with NSTEMI, regardless of age (7). Furthermore, given that 50% of MI patients have an onset age under 65 years old in the United States, the disease is not defined as "disease for the elderly". However, elderly patients usually have high adverse events after invasive treatment, and the gender-related differences in mortality were found to be associated with age in both STEMI and NSTEMI patients (8,9). Furthermore, few studies have been reported on gender differences in treatment strategies for older patients with NSTEMI, especially for patients ≥80 years old.

In the present study, a retrospectively study was performed, which included NSTEMI patients ≥80 years old in Fuwai Hospital, in order to investigate the gender difference in treatment strategies and prognosis in China. It is hoped that the present study can provide guidance for clinicians in the decision-making of treatment strategies for NSTEMI patients ≥80 years old.

Methods

The present study included 190 consecutive patients ≥80 years old, who presented with NSTEMI in Fuwai Hospital from September 2014 to August 2017. The clinical diagnosis of NSTEMI was defined as patients who had angina pectoris at rest, ST-segment depression and T wave inversion by electrocardiogram at rest, and positive cardiac markers, including creatine kinase-MB or troponin I/T associated with NSTEMI within 24 hours after initial presentation. These patients were grouped by gender, and each group was stratified by treatment strategy. The invasive strategy included emergency percutaneous coronary intervention (PCI), emergency coronary angiography, emergency balloon dilatation, selective coronary angiography, and selective PCI. The treatment strategy was determined by the clinicians. The last follow-up day was July 31, 2018.

Aspirin and clopidogrel were used for antiplatelet treatment, while statin, beta-receptor-blocking agent, angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) and diuretics were used, when needed. The patient's basic information, medical history, discharge medications and prognosis conditions were collected and compared among patients who underwent invasive and conservative strategies. The relationship between mortality and treatment strategies in male and female patients were analyzed. The survival curves of treatment strategies with different genders were separately analyzed.

Statistical analysis

SAS software was used for the data analysis in the present study. Continuous variables were presented as mean ± standard deviation (SD). Normal distribution measurement data were analyzed by the Student's t-test, while measurement data of skewness distribution were analyzed by rank-sum test. Categorical variables were analyzed by chi-square test. Logistic regression analysis was performed to compare the gender differences in mortality and treatment strategies. The survival curves of these two groups were compared by log-rank test in the Kaplan-Meier survival analysis.

Results

The clinical characteristics of patients are summarized in *Table 1*. Among the 190 NSTEMI patients ≥80 years old, 107 patients were male and 83 patients were female. In terms of basic information, there was a significant difference in age, creatinine, GRACE grade and Killip class between conservative and invasive strategies in female patients, while only GRACE grade was significantly different between these two treatment strategies in male patients (P<0.05). The medical history, including history of MI, after coronary artery bypass grafting (CABG), III grade, and renal dysfunction, was significantly different between the two treatment strategies in male patients, while the history of MI, diabetes mellitus, renal dysfunction, history of cerebral infarction, and anemia were significantly different between the two strategies in female patients (P<0.05). In addition, in terms of discharge medications, there was a significant difference in the use of diuretics between the two treatment strategies in male patients, while the use of aspirin and diuretics were significantly different between the two treatment strategies in female patients (P<0.05). In the prognostic analysis, death and good prognosis were significantly different between the conservative and invasive strategies in male patients (P<0.05), while there was no significant difference in prognosis in female patients who underwent conservative

Table 1 Comparison of clinical characteristics between invasive and conservative strategies in NSTEMI patients aged ≥80 years

Characteristics	Male (n=107)			Female (n=83)		
	Conservative (n=42)	Invasive (n=65)	P	Conservative (n=27)	Invasive (n=56)	P
Basic information						
Age, mean ± SD (years)	84.0±2.9	82.9±2.7	0.0509	83.8±3.2	82.2±2.2	0.0235
Creatinine	97.4 (81.9, 133.1)	90.5 (77.9, 110.6)	0.0524	88.6 (78.3, 143.5)	78.0 (64.5, 92.4)	0.0051
SBP, mean ± SD (mmHg)	135.6±24.1	137.9±2.8	0.6084	144.6±27.1	143.2±22.9	0.8071
DBP, mean ± SD (mmHg)	71.4±11.6	75.0±12.5	0.1323	69.0±16.9	73.8±14.4	0.1847
HR	82.5 (67.0, 91.0)	75.0 (66.0, 87.0)	0.1473	77.0 (66.0, 99.0)	73.0 (66.0, 85.5)	0.2510
GRACE grade, mean ± SD	178.7±16.5	171.7±14.9	0.0243	174.8±13.9	167.7±12.2	0.0284
Lesion branches, n (%)			–			–
1	0	1 (0.8)		0	6 (10.7)	
2	0	17 (14.1)		0	17 (30.4)	
3	0	31 (25.6)		0	3 (58.9)	
4	0	72 (59.5)		0	0	
Left main disease, n (%)	0	14 (100.0)	–	0	6 (100.0)	–
EF, n (%)			0.0945			0.1159
<50%	16 (38.1)	15 (23.1)		9 (33.3)	10 (17.9)	
≥50%	26 (61.9)	50 (76.9)		18 (66.7)	46 (82.1)	
Killip class, n (%)			0.1348			0.0325
I	21 (50.0)	47 (72.3)		11 (40.7)	41 (73.2)	
II	16 (38.1)	13 (20.0)		11 (40.7)	10 (17.9)	
III	4 (9.5)	4 (6.2)		4 (14.8)	3 (5.4)	
IV	1 (2.4)	1 (1.5)		1 (3.7)	2 (3.6)	
Medical history, n (%)						
History of MI	23 (54.8)	18 (27.7)	0.0049	13 (48.1)	10 (17.9)	0.0039
After stenting	12 (28.6)	0	0.9213	3 (11.1)	11 (19.6)	0.3308
After CABG	7 (16.7)	3 (4.6)	0.0365	3 (11.1)	1 (1.8)	0.0631
Valvular heart disease	4 (9.5)	7 (10.8)	0.8359	7 (25.9)	9 (16.1)	0.2863
Atrial fibrillation	10 (23.8)	14 (21.5)	0.7833	8 (29.6)	14 (25.0)	0.6544
III grade	4 (9.5)	0	0.0112	1 (3.7)	0	0.1474
Hypertension	33 (78.6)	50 (76.9)	0.8418	26 (96.3)	45 (80.4)	0.0531
Diabetes mellitus	19 (45.2)	29 (44.6)	0.9496	20 (74.1)	26 (46.4)	0.0176
Hyperlipidemia	41 (97.6)	60 (92.3)	0.2436	26 (96.3)	55 (98.2)	0.5935
Renal dysfunction	18 (42.9)	14 (21.5)	0.0187	10 (37.0)	4 (7.1)	0.0007
History of cerebral infarction	6 (14.3)	15 (23.1)	0.2635	11 (40.7)	4 (7.1)	0.0002
Hematencephalon	1 (2.4)	1 (1.5)	0.7534	0	0	–

Table 1 (*continued*)

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Characteristics	Male (n=107)			Female (n=83)		
	Conservative (n=42)	Invasive (n=65)	P	Conservative (n=27)	Invasive (n=56)	P
Peptic diseases	9 (21.4)	23 (35.4)	0.1236	9 (33.3)	21 (37.5)	0.7113
Gastrointestinal bleeding	2 (4.8)	4 (6.2)	0.7599	0	1 (1.8)	0.4848
Anemia	9 (21.4)	9 (13.8)	0.3059	10 (37.0)	4 (7.1)	0.0007
Peripheral arterial disease	6 (14.3)	10 (15.4)	0.8763	1 (3.7)	4 (7.1)	0.5373
Respiratory system disease	8 (19.0)	8 (12.3)	0.3398	6 (22.2)	8 (14.3)	0.3657
Discharge medications, n (%)						
Aspirin	39 (92.9)	62 (95.4)	0.5790	23 (85.2)	55 (98.2)	0.0194
Clopidogrel	39 (92.9)	59 (90.8)	0.704	23 (85.2)	51 (91.1)	0.4191
Statin	38 (90.5)	63 (96.9)	0.1569	24 (88.9)	55 (98.2)	0.0631
Beta-receptor-blocking agent	33 (78.6)	53 (81.5)	0.7059	21 (77.8)	49 (87.5)	0.2536
ACEI/ARB	21 (50.0)	32 (49.2)	0.9381	12 (44.4)	31 (55.4)	0.3513
Diuretic	21 (50.0)	14 (21.5)	0.0022	20 (74.1)	19 (33.9)	0.0006
Prognostic analysis						
Death, n (%)	19 (45.2)	11 (16.9)	0.0015	10 (37.0)	10 (17.9)	0.0556
Good prognosis, n (%)	17 (40.5)	40 (61.5)	0.033	15 (55.6)	30 (53.6)	0.8650
Complications, n (%)						
Stenocardia	1 (2.4)	2 (3.1)	0.8314	0	4 (7.1)	–
Heart failure	1 (2.4)	1 (1.5)	–	1 (3.7)	2 (3.6)	0.9759
Atrial fibrillation	0	1 (1.5)	–	0	0	–
AMI	0	0	–	0	0	–
Cerebral infarction	0	0	–	0	1 (1.8)	–
Re-hospitalization, n (%)	4 (9.5)	8 (12.3)	0.6559	1 (3.7)	10 (17.9)	0.0748
Follow-up time, mean ± SD (days)	599.0±252.6	665.4±332.4	0.2719	663.9±383.4	805.0±353.7	0.1012

P<0.05 indicates statistically significant. NSTEMI, non-ST-segment elevation myocardial infarction; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; EF, ejection fraction; MI, myocardial infarction; CABG, coronary artery bypass grafting; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AMI, acute myocardial infarction.

and invasive strategies (P>0.05).

In logistic regression analysis of death and treatment strategies in NSTEMI patients ≥80 years old, the risk ratio was 4.06 [95% confidence interval (CI): 1.67–9.86] in males and 2.71 (95% CI: 0.96–7.64) in females. After adjusting for age, the risk ratio was 3.56 (95% CI: 1.41–8.96) in males and 2.91 (95% CI: 0.98–8.64) in females. After adjusting for age, hypertension, diabetes and hyperlipemia, the risk ratio was 3.60 (95% CI: 1.42–9.16) in males and 2.98 (95% CI: 0.92–9.58) in females. After adjusting for age, hypertension, diabetes, hyperlipemia, renal insufficiency and anemia, the risk ratio were 3.08 (95% CI: 1.17–8.11) in males and 2.49 (95% CI: 0.73–8.54) in females (*Figure 1*).

In the Kaplan-Meier survival analysis of survival probability and treatment strategies in NSTEMI patients ≥80 years old, the survival probability of invasive strategy was significantly higher than that of conservative strategy in males (P=0.001) and females (P=0.015) (*Figure 2*). The survival curve of invasive strategy in males and females were similar during the follow-up, while the

Population	OR	Low 95% CI	Up 95% CI	P value
Males				
Model 1	4.06	1.67	9.86	0.0020
Model 2	3.56	1.41	8.96	0.0071
Model 3	3.60	1.42	9.16	0.0071
Model 4	3.08	1.17	8.11	0.0228
Females				
Model 1	2.71	0.96	7.64	0.0602
Model 2	2.91	0.98	8.64	0.0549
Model 3	2.98	0.92	9.58	0.0678
Model 4	2.49	0.73	8.54	0.1467
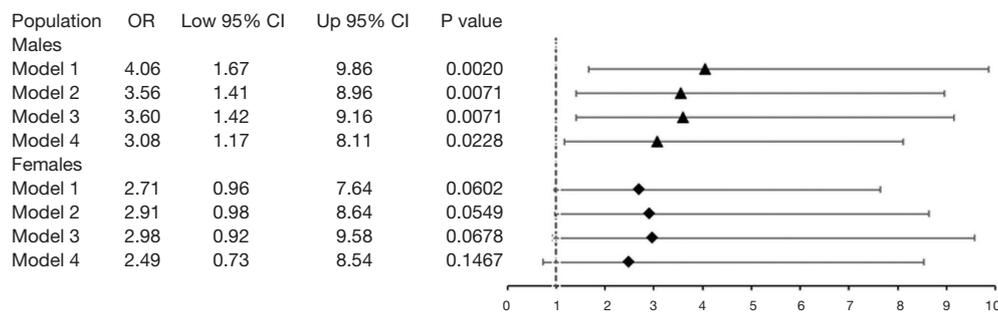
Figure 1 Logistic regression analysis of death and treatment strategies in males and females aged ≥80 years with NSTEMI. NSTEMI, non-ST-segment elevation myocardial infarction; OR, odds ratio; CI, confidence interval.
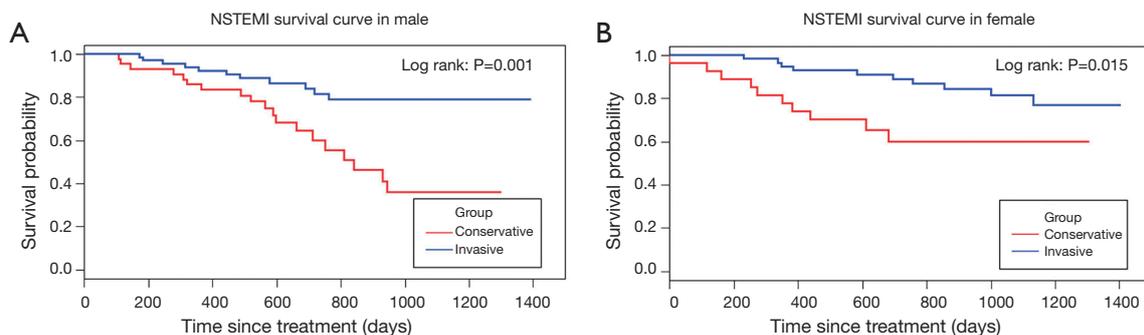

Figure 2 Kaplan-Meier survival analyses of NSTEMI patients. (A) Survival curves of males underwent invasive and conservative strategies; (B) survival curves of females underwent invasive and conservative strategies. NSTEMI, non-ST-segment elevation myocardial infarction.

lowest survival rate of conservative strategy decreased to approximately 0.35 in males, and approximately 0.6 in females. This indicates that the difference in treatment strategies in males was more pronounced than in females, in terms of long-term survival rate.

Discussion

Gender differences in treatment strategies for older patients, especially in patients over 80 years old remain unclear in China. In the present study, a retrospectively study was performed to investigate the gender difference in treatment strategies in NSTEMI patients ≥80 years old in China. The results revealed that good prognosis and death were significantly different between invasive and conservative strategies in males. Mortality was significantly correlated with treatment strategies in males in the multivariate logistic regression analysis. In addition, the survival probability of invasive strategy was significantly higher than that of conservative strategy in

males and females during the follow-up, but the difference was more obvious in males, in terms of long-term survival probability.

It is noteworthy that gender differences exist in the underlying pathogenesis, clinical course, therapeutic approach and prognosis of NSTEMI (10,11). Women with NSTEMI usually have worse baseline characteristics, when compared to men (12,13). A published study revealed that the rate of adverse events, including death and bleeding, were different by gender in NSTEMI patients with a median age of under 68 years old (14). Although women with NSTEMI had worse baseline characteristics, their outcomes were comparable with those in men (15,16). In line with previous studies (17,18), it was found that women with NSTEMI were more likely to have comorbidities than men.

Previous studies have demonstrated that NSTEMI patients who were noninvasively managed had a greater risk for long-term mortality, and the decrease in mortality was associated with the use of an invasive strategy (19-21). In addition,

the study conducted by Tegn *et al.* revealed that invasive strategy was superior for NSTEMI patients of 80 years old or older, when compared to conservative strategy (22). The present study demonstrated that NSTEMI male patients ≥80 years old, who were invasively treated, had a significantly lower death rate and better prognosis, when compared to patients conservatively treated, while these were no statistical difference for females. It was also found that the mortality of NSTEMI patients over 80 years old was significantly correlated to treatment strategies in male after adjusting for some characteristics, but not in females. This suggests that the invasive strategy is indeed superior to conservative strategy, in terms of death and prognosis in NSTEMI patients ≥80 years old, but gender difference was present.

In addition, the survival curve between invasive and conservative strategies were significantly different in both males and females ≥80 years old with NSTEMI during the follow-up period. However, the survival probability was not significantly different between these two treatment strategies in males and females during the 1-year following up. This is similar to the study conducted by Alabas *et al.*, in which survival was not evident between males and females with NSTEMI in the 6-month and 1-year following up periods (23). The survival probability of invasive strategy decreased to approximately 0.8 and 0.75 during the following up in males and females, respectively, while the survival probability of conservative strategy decreased to approximately 0.4 and 0.6 during the following up in males and females, respectively. This indicates that the benefit of invasive strategy in males ≥80 years old with NSTEMI was certain in the long-term following up. This founding was verified by a previous study conducted by Alfredsson *et al.*, in which men with NSTEMI could benefit from invasive strategy in the long-term follow-up (24). Although the difference in survival rate between invasive and conservative strategies was significant in males and females, the difference was more obvious in males in terms of long-term follow-ups. This indicates that clinicians may consider gender and clinical features when considering treatment strategies for patients ≥80 years old with NSTEMI, especially in males.

To our knowledge, the present study is the first time to investigate the gender difference in treatment strategies in NSTEMI patients ≥80 years old in China. The present study increases the confidence in a clinician's choice of treatment strategy for NSTEMI patients ≥80 years old. Given the small number of NSTEMI patients over 80 years old in China, and that the present study was performed in only one center, the sample size may be not be sufficient. Hence, further studies should be performed in multi-centers with a larger sample size.

Conclusions

Gender differences exist in invasive and conservative strategies in NSTEMI patients ≥80 years old. Death is significantly associated with treatment strategies in males, but not in females. The survival curve was significantly different between these two treatment strategies in males and females, especially in males.

Acknowledgments

Footnote

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. A written informed consent was obtained from each patient in the present study. The ethics approval for the present study was obtained from the Fuwai Hospital Health Human Research Ethics Committee.

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