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Original Article

Do patients with non-ST-elevation myocardial infarction without chest pain suffer a poor prognosis?

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ABSTRACT

Objective: Previous studies have discussed acute myocardial infarction (AMI) patients without chest pain, but have not focused on non-ST-elevation myocardial infarction (NSTEMI).**Materials and methods:** This 1-year study investigated whether chest pain presence relates to demographics, risk factors, and outcomes in NSTEMI patients. We retrospectively reviewed 194 patients, 73 without chest pain vs. 121 with chest pain, and compared the differences between clinical presentations, risk factors, medical management, and outcomes of these two groups.**Results:** Compared to patients with chest pain, patients without chest pain were significantly older, had lower SBP, higher HR, more cerebrovascular disease, less ischemic heart disease, higher delay to ED (emergency department) visit, lower ED medication prescriptions, lower percutaneous cardiac intervention, and higher in-hospital and one-year mortality rate. In a multivariate logistic regression, the adjusted odds ratios (OR) of patients without chest pain were 4.38 for the elderly, 0.99 for every 1 mmHg increase in SBP, 1.02 for every beat/min HR increase, 0.37 for those with ischemic heart disease, and 5.09 for those with cerebrovascular disease. The adjusted OR of in-hospital mortality were 3.09 for patients without chest pain, 0.32 for those with hypertension, 0.32 for smokers, 3.98 for those with shock, and 0.16 for those with percutaneous cardiac intervention. Finally, the only significantly adjusted OR of one-year mortality was 5.37 for patients without chest pain.**Conclusion:** NSTEMI patients without chest pain were significantly older, had lower SBP, more tachycardia, more cerebrovascular disease, but less ischemic heart disease. They also experienced higher in-hospital and one-year mortality rates.© 2019 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Acute myocardial infarction (AMI) both with ST elevation (STEMI) and without ST elevation (NSTEMI) is a true emergency condition in emergency departments (EDs). The classic symptom is chest pain, however, previous reports have shown that atypical

presentations without chest pain are commonly seen in the elderly, female patients, and those with diabetes [1–7]. In the Framingham study, more than 25 percent of AMI patients were discovered only during routine biennial electrocardiographic examinations. Almost half of these cases were truly asymptomatic, and the reminders had atypical symptoms [8]. Dorsch et al. and Canto et al. reported that about 20.2–33% of AMI patients did not have chest pain upon presentation to the hospital, and these patients were older, more often women, more likely to have a history of heart failure, and associated with increased mortality [1,5]. Among AMI patients, NSTEMI patients represent a larger proportion than STEMI patients

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[9–11], have more atypical presentations [12], and experience higher post-discharge mortality rates [9–11].

To our knowledge, previous studies have discussed AMI patient presentations without chest pain and were not only focused on NSTEMI [1,2,5,7,13–15]. A question remains of whether NSTEMI patients without chest pain share the same risk factors, management approaches, and outcomes. We undertook this study to investigate NSTEMI patients without chest pain in terms of demographics, clinical presentations, risk factors, medical management, and outcomes at a medical center hospital in Northern Taiwan. The goal is to describe the characteristics, management, and outcomes of these patients in an ED and to provide information to emergency physicians and staff.

Materials and methods

This study was approved by our Hospital Institutional Review Board and entails a retrospective review of 194 NSTEMI patients who visited the hospital's ED from January 1 to December 31, 2008, a calendar year. All patients were treated at our hospital, a 2060-bed medical center in Northern Taiwan. Every emergency physician, staff member, and nurse was fully qualified through the Advanced Cardiac Life Support (ACLS) 2005 guideline training course [16]. We excluded patients younger than 18 years old and divided the enrolled patients into two groups: a non-chest-pain group and a chest-pain group. The exclusion criteria consisted of patients who were younger than 18, had out-of-hospital cardiac arrest, were pregnant, had been admitted through the outpatient department, whose onset of AMI occurred during hospitalization, and had been transferred from another hospital.

According to the American Heart Association guidelines [16], NSTEMI is defined as ischemic ST-segment depression < 0.5 mm (0.05 mV) or dynamic T-wave inversion with pain or discomfort in combination with elevated cardiac markers (Troponin I/CK-MB). In contrast, STEMI is defined as ST-segment elevation > 1 mm (0.1 mV) in two or more contiguous precordial leads, two or more adjacent limb leads, or a presumed new left bundle branch block (LBBB), in combination with subsequent elevation of cardiac markers (Troponin I/CK-MB). Cardiac biomarkers should be measured during the initial evaluation of the patient and followed at least once 4–6 h following the procedure because they are insensitive during this period. However, reperfusion therapy for patients with STEMI should not be delayed pending the results of these tests [17]. Shock was defined as systolic blood pressure < 90 mmHg.

The symptoms of the chest-pain patients were defined as chest pain, chest tightness, or any chest discomfort. Other symptoms that might be considered as non-chest-pain include shortness of breath; nausea, vomiting, or dizziness; syncope or collapse; fatigue or diaphoresis; and abdominal pain. Patient information was collected from emergency medical service data, medical charts, and reports after admission. The main variables included age, gender, vital signs, presenting symptoms, risk factors, intervals between the time of having initial symptoms and visiting the emergency department, intervals between the time of visiting the emergency department and ascertaining diagnoses, heart-attack locations, medical treatment, cardiac intervention, survival after discharge from the hospital, survival around one year, and length of stay at the hospital. All records were reviewed and rechecked by two physicians.

Statistical analysis was conducted using SPSS software version 12.0. Chi-squared tests and Fisher's exact tests were performed for categorical variables, while independent-sample t-tests were used for continuous variables. Multivariate logistic regression model analyses were performed to identify potential predictive factors for

non-chest-pain patients and for mortality among NSTEMI patients. A p value < 0.05 was the criterion for statistical significance.

Results

We reviewed 540 AMI cases that resulted in discharge or death after a diagnosis of AMI (ICD code 410), of which only 194 patients with NSTEMI met the defined criteria. There were 73 patients (37%) with no chest pain and 121 patients with chest pain. Table 1 shows the demographics, risk factors, medical management, and outcomes. Compared with chest-pain patients, the non-chest-pain patients were an average of 9 years older (mean age 73.6 vs. 64.1, $p < 0.001$), and they had significantly lower systolic BP (mean pressure 129 mmHg vs. 142 mmHg, $p = 0.016$), higher heart rate (106 beats/min vs. 91 beats/min, $p = 0.001$), a significantly higher proportion of elderly individuals (76.7% vs. 50.4%, $p < 0.001$), more prevalence of cerebrovascular disease (31.5% vs. 7.4%, $p < 0.001$), less ischemic heart disease (34.2% vs. 49.6%, $p = 0.037$), higher interval from onset to ED visit with an average of 8 h delay (19.22 ± 26.44 vs. 11.33 ± 19.37 h, $p = 0.033$), fewer prescriptions for aspirin (46.6% vs. 80.2%, $p < 0.001$), clopidogrel (42.5% vs. 64.5%, $p = 0.003$), heparinization (17.8% vs. 45.5%, $p < 0.001$), nitroglycerin (35.6% vs. 77.7%, $p < 0.001$), and morphine (6.8% vs. 33.9%, $p < 0.001$), lower in-hospital PCI (34.2% vs. 77.7%, $p < 0.001$), higher in-hospital mortality rate (30.1% vs. 7.4%, $p < 0.001$), and one-year mortality rate (38.4% vs. 13.2%, $p < 0.001$). There were no significant differences between the two groups in gender, DBP, RR, shock, maximum cardiac enzyme rise, DM, HTN, smoking, hyperlipidemia, CHF, previous MI, arrival at diagnosis, place of onset, or hospital stay.

Table 2 shows the main presenting symptom of non-chest-pain patients. The most common presentation was shortness of breath (49.3%), followed by nausea, vomiting, or dizziness; syncope or collapse; fatigue or diaphoresis; and abdominal pain. Table 3 shows the results of multivariate logistic regression analysis of non-chest-pain presentation. The adjusted odds ratios of non-chest-pain presentation were 4.38 (95% confidence interval (CI), 1.91 to 10.05) for elderly patients, 0.99 (95% CI, 0.98 to 0.99) for every one mmHg increase in systolic BP, 1.02 (95% CI, 1.01 to 1.03) for every one beat/min in heart rate, 0.37 (95% CI, 0.17 to 0.80) for those with ischemic heart disease history, and 5.09 (95% CI, 1.93 to 13.40) for those with cerebrovascular disease history.

Fig. 1 shows the multivariate logistic regression analysis results of mortality. The adjusted odds ratios of in-hospital mortality were 3.09 (95% CI, 1.13 to 8.50, $p = 0.028$) for non-chest-pain patients, 0.32 (95% CI, 0.12 to 0.85, $p = 0.022$) for those with hypertension, 0.32 (95% CI, 0.11 to 0.94, $p = 0.039$) for smokers, 3.98 (95% CI, 1.42 to 11.15, $p = 0.009$) for those with shock, and 0.16 (95% CI, 0.06 to 0.48, $p = 0.001$) for those with PCI. Finally, the only significant adjusted odds ratio of one-year mortality was 5.37 (95% CI, 2.31 to 12.48, $p < 0.001$) for non-chest-pain patients.

Discussion

To the best of our knowledge, this is the first study to compare clinical presentation, management, and outcomes between NSTEMI patients with and without chest pain. We found that more than one-third of the NSTEMI patients did not have chest pain upon presentation to the ED, and the most common symptom was shortness of breath. NSTEMI was not an indication for primary PCI or thrombolytic therapy and was not as likely as STEMI to be a timely emergency disease [17]. However, early recognition of this disease and advanced care could still be important for decreasing mortality in the ED [11]. In addition, the proportion of NSTEMI patients increased among AMI patients, but the mortality rate of

Table 1

Comparison of demographics, presentations, treatment, and outcomes between NSTEMI patients with and without chest pain in the emergency department.

	With chest pain (n = 121)	Without chest pain (n = 73)	p
Age (y)	64.11 ± 14.78	73.64 ± 15.58	<0.001***
Elderly	61 (50.4)	56 (76.7)	<0.001***
Female	41 (33.9)	33 (45.2)	0.116
Systolic BP	142.15 ± 34.78	129.09 ± 36.02	0.016*
Diastolic BP	77.31 ± 21.31	70.06 ± 33	0.070
Heart rate	90.74 ± 26.94	105.94 ± 30.74	0.001**
Respiratory rate	20.6 ± 9.19	20.55 ± 4.53	0.968
Shock	20 (16.5)	16 (21.9)	0.350
Peak CK	946.61 ± 1225.91	1313.29 ± 2424.27	0.232
Risk factors			
Diabetes mellitus	45 (37.2)	33 (45.2)	0.270
Hypertension	83 (68.6)	48 (65.8)	0.682
Smoking	54 (44.6)	23 (31.5)	0.070
Ischemic heart disease	60 (49.6)	25 (34.2)	0.037*
Hyperlipidemia	59 (48.8)	26 (35.6)	0.074
Cerebrovascular disease	9 (7.4)	23 (31.5)	<0.001***
Congestive heart failure	53 (43.8)	34 (46.6)	0.707
Previous AMI	22 (18.2)	10 (13.7)	0.415
Interval from			
Onset to ED visit (hours)	11.33 ± 19.37	19.22 ± 26.44	0.033*
Arrival to diagnosis (hours)	6.74 ± 16.70	9.46 ± 31.84	0.444
Place of onset			
NSTEMI at home	38 (31.4)	30 (41.1)	0.171
Medication at ED			
Aspirin	97 (80.2)	34 (46.6)	<0.001***
Clopidogrel	78 (64.5)	31 (42.5)	0.003**
Heparinization	55 (45.5)	13 (17.8)	<0.001***
Nitroglycerin	94 (77.7)	26 (35.6)	<0.001***
Morphine	41 (33.9)	5 (6.8)	<0.001***
PCI			
PCI in hospitalization	94 (77.7)	25 (34.2)	<0.001***
Outcomes			
Hospital stay (day)	14.06 ± 30.53	19.48 ± 25.28	0.204
In-hospital mortality	9 (7.4)	22 (30.1)	<0.001***
One-year mortality	16 (13.2)	28 (38.4)	<0.001***

Data are presented as n (%) or mean ± SD.

NSTEMI = non-ST-elevation myocardial infarction; STEMI = ST-elevation myocardial infarction; AMI = acute myocardial infarction; ED = emergency department;

PCI = percutaneous coronary intervention.

*P < 0.05; **P < 0.01; ***P < 0.001.

NSTEMI patients was higher than in STEMI patients [9,11,18]. Focusing on NSTEMI patients is thus more important than STEMI patients.

Dorsch et al. and Canto et al. reported that about 20.2–33% of AMI patients did not have chest pain upon presentation and were older, more often women, more likely to have a history of heart failure, and had association with increased mortality [1,5]. In our study of NSTEMI patients, about 37.6% had no chest pain and were significantly older, had more cardiovascular disease, less ischemic heart disease, and higher mortality. There were insignificantly higher rates of female gender, diabetes mellitus, and heart failure. In addition, patients without chest pain were likely to have tachycardia, but patients with chest pain were likely to have higher systolic BP at ED presentation, as Dorsch et al. reported [1].

In AMI patients, chest pain is the most common presentation, but is not necessarily present in all patients [6,8,13,14]. Among non-chest-pain patients in our study, shortness of breath (49.3%) was the most common presentation, as in previous studies [1,6], followed by other symptoms, including nausea, vomiting, or dizziness; fatigue or diaphoresis; syncope or collapse; and abdominal pain. The pathophysiological mechanism for this presentation remains unexplained. We found that patients without chest pain were significantly older, had a higher incidence of prior stroke, and a lower incidence of ischemic heart disease. The elderly population has a somewhat reduced pain perception and is more likely to have diabetes-associated autonomic nerve dysfunction [19,20]. Prior stroke also might influence chest pain sensation during NSTEMI attacks [1].

Table 2

Main symptoms of NSTEMI patients without chest pain in the emergency department.

Presentations	Without chest pain (n = 73)
Shortness of breath	36 (49.3)
Nausea/vomiting/dizziness	12 (16.4)
Syncope/collapse	12 (16.4)
Fatigue/diaphoresis	8 (11)
Abdominal pain	5 (6.8)

Data are presented as n (%).

NSTEMI = non-ST-elevation myocardial infarction.

Table 3

Adjusted odds ratios (95% CI) for non-chest-pain presentation of NSTEMI patients.

Variable	Adjusted odds ratio		
	OR	95% C.I.	p
Age (elderly:adult)	4.38	1.91–10.05	p < 0.001
Systolic BP	0.99	0.98–0.99	0.007
Heart rate	1.02	1.01–1.03	0.002
Ischemic heart disease (yes:no)	0.37	0.17–0.80	0.011
Cerebrovascular disease (yes:no)	5.09	1.93–13.40	0.001

NSTEMI = non-ST-elevation myocardial infarction.

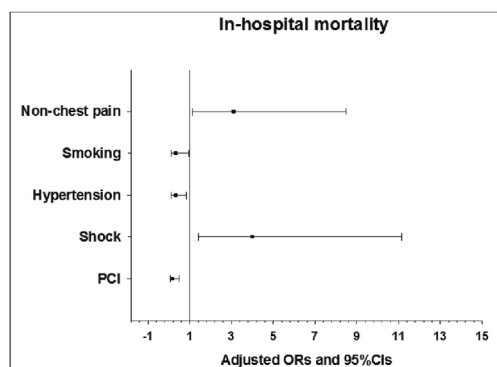


Fig. 1. Adjusted odds ratios (95% CI) for In-hospital mortality in NSTEMI patients. PCI = percutaneous coronary intervention; NSTEMI = non-ST-elevation myocardial infarction.

It is an interesting discovery that patients without chest pain had a significantly lower incidence of ischemic heart disease [14] and insignificantly lower incidence of smoking [14] and hyperlipidemia. Patients with these factors might be more conscious about chest pain, and ED staff caring for these patients might pay more attention to chest pain complaints. However, in our triage training, questions about chest pain must be asked, which might reduce the risk of the confounding factor. Female gender, diabetes mellitus, and heart failure were considered to be associated without chest pain presentation in AMI patients [1,5,21] but the results were insignificant in our study, which could be related to the small sample size.

Knowing the distribution of risk factors for non-chest-pain patients may help in developing preventive strategies. First, we should be concerned about non-chest-pain NSTEMI in the elderly, those with tachycardia, prior stroke, those without prior ischemic heart disease, and smokers. Shortness of breath and other atypical symptoms like nausea/vomiting/dizziness, syncope/collapse, fatigue/diaphoresis, and even abdominal pain should be considered as triggers of NSTEMI attacks. Although the non-chest-pain patients were insignificantly less likely to have a history of previous AMI, over 80% of the patients in both groups suffered from new onset of AMI, as in previous studies [6,22]. Health education for awareness about NSTEMI is important for the general population.

As Canto et al. and Uretsky et al. reported, MI patients without chest pain tended to have delayed presentation to the hospital [5,14]. The presentation of non-chest-pain NSTEMI patients to the ED was significantly delayed on average by more than 7 h from the onset of symptoms, and diagnosis was also insignificantly delayed on average by more than 2 h from ED arrival. Furthermore, non-chest-pain patients in the ED were less likely to receive standard therapies that are known to improve outcomes, such as aspirin, clopidogrel, heparine, enoxaparine, nitroglycerin, and morphine [17]. Also, these non-chest-pain patients were less likely to receive percutaneous cardiac intervention (PCI) after hospitalization and had an average of 5 days longer hospital stay than chest-pain patients.

Patients with no chest pain had 4 times higher in-hospital mortality and more than 2 times higher one-year mortality. A delay in sending non-chest-pain patients to the ED was noted in our study, which may be due to their older age and higher likelihood of having age-related cognitive impairment and social constraints [23,24]. In addition, the non-chest-pain patients seemed more likely to have an NSTEMI attack at home (41.1%) and delayed diagnoses in the ED. In dealing with these patients, an emergency doctor should always keep these considerations in mind. Although

previous reports have shown benefits of anti-platelet therapy and heparin therapy [5,17,25], our study found that the non-chest-pain patients were less likely to have used these therapies than other patients. Concerns about non-chest-pain patients were their higher age, risks of peptic ulcer, major bleeding, and comorbidity, which may impede emergency physicians in properly providing these therapies [23,26].

Although coronary angiography and PCI are the standard procedures for AMI [17,27], our study indicated that non-chest-pain patients underwent these procedures significantly less often during hospitalization. This invasive therapy is recommended for NSTEMI patients [27,28] and also benefits elderly patients, although there are more bleeding complications than in conservative treatment [29]. Reasons for lower rates of coronary angiography in non-chest-pain patients might need further investigation. Socioeconomic factors and national health insurance payments might be the causes.

We found significantly higher in-hospital mortality rates and longer hospital stays among non-chest-pain patients compared to previous studies [1,5,14,15]. Higher age, female gender, shock, hypertension, smoking, less prescription of standard medication, less PCI, and non-chest-pain presentation might all contribute to high in-hospital mortality rate. However, after adjustment for all factors, non-chest-pain and shock were significant predictors for in-hospital mortality, while hypertension, smoking, and PCI were negative predictors. No chest pain was the only one predictor for one-year mortality. As Dorsch et al. and Canto et al. report, a lack of chest pain was more strongly associated with mortality [1,5]. Canto et al. also found that smokers had lower rates of in-hospital mortality [5]. In addition, we found that PCI was also an important predictor for improvement of hospital mortality, as in a previous report [11].

Limitations

There were a number of limitations that are worth noting. First, this was a retrospective study with a relatively small sample size that was conducted in a single medical center in the capital of Taiwan. However, all staff were qualified, provided standard therapy to the NSTEMI patients, and provided detailed medical records. Second, the socioeconomic status of patients was not recorded, which might have influenced decision-making in regard to PCI due to some kind of cardiac stent not being covered by the national health insurance, as Alter et al. reported [30]. A prospective, regional, or national study should be undertaken to better represent the general population.

Conclusion

Compared to NSTEMI patients with chest pain, non-chest-pain patients had significantly higher rates of tachycardia, a larger proportion of the elderly, and cerebrovascular disease history, but a lower proportion of ischemic heart disease history. In addition, nearly half presented shortness of breath and experienced higher in-hospital and one-year mortality rates, especially shock upon ED arrival, and they were more likely not to receive PCI during hospitalization. We need to pay more attention to these patients and to make aggressive diagnoses and management approaches in order to improve their outcomes.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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