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Original Article

Chest pain centers contribute to decrease in acute cardiac complications and better short-term prognosis for patients with AMI

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Abstract: Background: Acute myocardial infarction (AMI), especially ST elevation myocardial infarction (STEMI), not only increases risk for cardiovascular complications and mortality but also leads to decreased quality of life. Recently, the creation of Chest Pain Centers (CPCs) in China has ensured that AMI patients are diagnosed and treated in a timely fashion. This present study aimed to compare different patterns of acute cardiac complications and short-term prognosis in STEMI patients treated in the CPC. Methods: Prior to creation of the CPC, 53 STEMI patients were selected and carefully examined (January 2014-December 2014). Baseline clinical data were also included in the evaluation. After creation of the CPC, another 52 STEMI patients were enrolled (January 2015-December 2015). All patients received formal AMI treatment to ameliorate symptoms and preserve the structure and function of the heart according to AMI guidelines for China (2014-2016). Acute cardiac complications, within 7 days, for these STEMI patients were compared. The groups were also compared in terms of short-term prognosis (at 90 days) using a Kaplan-Meier estimator. Cox proportional-hazard models were further used to analyze association of the prognosis and effects of CPC after adjusting for confounding factors (diabetes, cerebral infarction, hypertension, smoking, hyperlipidemia, and renal insufficiency). Results: The first medical contact to oral medication load time (FMC2M) was significantly lower in patients after creation of the CPC compared with STEMI patients before the CPC was created ($p < 0.001$). First medical contact of patients to balloon opening time (FMC2B) was also significantly decreased in STEMI patients after creation of the CPC ($p < 0.001$). Acute cardiac complications, within 7 days, were significantly lower in these STEMI patients after creation of the CPC ($p < 0.001$). In addition, these STEMI patients also showed decreased cardiovascular events in the next 90 days after creation of the CPC. Univariate Kaplan-Meier analysis further revealed significant differences between the two groups ($p < 0.001$). Conclusions: The Chest Pain Center produced lower incidence of cardiac complications and better prognosis for STEMI patients. Effective, efficient, and timely treatment under the influence of a CPC may greatly explain the causality.

Keywords: Myocardial infarction, chest pain center, percutaneous coronary intervention

Introduction

Chest pains are the subjective feelings of sharp or dull pains, including pressure, shortness of breath, and often accompanied by anxiety or fear. Chest pains are one of the most common symptoms for an emergency activation. One cross-sectional study in Beijing showed that chest pain patients accounted for approximately 4.7% of emergency patients [1]. A total of 13,740 chest pain patients were followed up for 1 year in the British General Practitioner Study Database. Results showed that ischemic heart disease was the leading cause of death in these chest pain patients, accounting for 36% of deaths during the one-year follow up period [2]. Acute coronary syndrome is, potentially, the most serious type of chest pain. It is often life-threatening and includes unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction [3]. In addition, chest pains currently represent one of the most important causes of worldwide morbidity and mortality [4, 5]. Optimal prevention of myocardial infarction in patients with chest pain has remained a challenge due to the

Table 1. Baseline characteristics

Clinical Characteristic	Group A (n = 53)	Group B (n = 52)	t/X^2	*P*-value
Age (years)	62.8 ± 11.2	60.9 ± 11.7	0.827	0.410
Sex (male %)	33 (62.3%)	36 (69.2%)	0.565	0.452
Family history of CAD	21 (39.6%)	14 (26.9%)	1.905	0.168
Cerebral infarction	12 (22.6%)	19 (36.5%)	2.436	0.119
Smoking	10 (18.9%)	14 (26.9%)	0.966	0.326
eGFR (ml/min/1.73 m^2)	72.3 ± 20.8	69.6 ± 20.1	0.692	0.491
Hypertension	30 (56.6%)	20 (38.5%)	3.464	0.063
Diabetes mellitus	16 (30.2%)	22 (42.3%)	1.669	0.196
Lipids (mmol/L)				
LDL cholesterol (mmol/L)	3.07 ± 1.01	2.98 ± 1.12	0.397	0.083
TnI (ng/ml) TnI peak (ng/ml)	5.95 ± 0.79	5.05 ± 0.81	0.790	0.431
BNP ≥ 500 (pg/ml)	20 (37.7%)	15 (28.8%)	0.933	0.334
Medication, n (%)				
Double antiplatelet agents	53 (100%)	52 (100%)	-	-
Statins	53 (100%)	52 (100%)	-	-
Beta-blockers	49 (92.5%)	47 (90.4%)	-	0.741
IIb/IIIa inhibitors or Low molecular weight heparin	49 (92.5%)	50 (96.2%)	-	0.678
ACE inhibitors or ARBs	40 (75.5%)	46 (88.5%)	2.988	0.084
GRACE score			3.523	0.172
≤ 108	7 (13.2%)	10 (19.2%)		
109-140	4 (7.50%)	9 (17.3%)		
≥ 140	42 (79.2%)	33 (63.5%)		

Baseline Clinical Characteristics of STEMI patients. Group A, STEMI patients selected before the creation of a CPC; Group B, STEMI patients selected after the creation of a CPC. Values are mean ± SD, or n (%). ACEI: angiotensin-converting enzyme inhibitors; CAD: Coronary artery disease; BNP: B-natriuretic peptide; TnI Troponin I; eGFR: estimated glomerular filtration rate; LDL: low-density lipoprotein; ARB: angiotensin II receptor antagonists; GRACE: The Global Registry of Acute Coronary Events.

Table 2. Comparison of number of related offending vessel lesions

Group	N	Offending vessel lesions (%)				Number of vessels involved (lesions ≥ 50%)		
		LM	LAD	LCX	RA	One	Two	Three
Group A	53	7 (13.2%)	15 (28.3%)	13 (24.5%)	18 (34.0%)	23 (43.4%)	16 (30.2%)	14 (26.4%)
Group B	52	5 (936%)	20 (38.5%)	12 (23.1%)	15 (28.8%)	20 (38.5%)	20 (38.5%)	12 (23.1%)
t/x^2	-		1.351				0.798	
P Value	-		0.717				0.671	

Group A, STEMI patients selected before the creation of a CPC; Group B, STEMI patients selected after the creation of a CPC; LM, Left main coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; RA, right coronary artery.

difficulty of early recognition and timely treatment of AMI. In recent years, diagnosis and treatment of myocard-ial infarction, especially acute ST-segment Elevation Myocardial Infarction (STEMI), has progressed under the backdrop of established guidelines for AMI and influence of the creation of CPCs. This present study aimed to compare and analyze different patterns of acute cardiac complications and short-term prognoses in STEMI patients treated in the CPC.

Materials and methods

Study population

All enrolled patients were STEMI patients. All patients were admitted to the Cardiac Center of Zhongda Hospital, Affiliated with Southeast University, and received formal AMI treatment, including percutaneous coronary intervention (PCI), to ameliorate symptoms and preserve the structure and function of the heart according to

Table 3. Door-to-balloon times for each group

Group	FMC time (h)	FLAM time (h)	FMC2B time (h)
Group A	3.45 ± 0.40	4.03 ± 0.40	4.29 ± 0.38
Group B	2.40 ± 0.38	2.45 ± 0.36	2.50 ± 0.23
t/χ^2/Fisher	1.910	2.939	4.070
P Value	0.059	0.004*	< 0.001*

Group A, STEMI patients selected before the creation of a CPC; Group B, STEMI patients selected after the creation of a CPC; FMC, first medical contact time; FLAM, first oral loading of antiplatelet agents time; FMC2B, first medical contact to balloon opening time. *P ≤ 0.05 vs. the control group.

AMI guidelines for China (2014-2015). Prior to creation of a CPC, 53 STEMI patients were selected and carefully examined (Group A). In addition, 52 STEMI patients were enrolled after creation of the CPC (Group B). Clinical data in terms of comorbidities, cardiovascular or cerebrovascular disease history, smoking history, blood pressure, cholesterol, estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), drugs taken, and GRACE scores were mostly acquired from hospital medical records. This study was approved by the local Ethics Committee and performed in accordance with the Declaration of Helsinki.

Definitions of STEMI

For patients having ST elevation myocardial infarction (STEMI), at least two of the following criteria had to be met in addition to ST segment elevation in 2 or more contiguous leads (Cut-off point: ≥ 0.1 mv) [6, 7]: typical symptoms or typical signs of AMI including angina equivalents (severe substernal chest pain, chest tightness or severe precordial discomfort with cold sweat, and an impending sense of doom) and an increased level of biomarkers specific for myocardial injury, especially Troponin I (TnI ≥ 0.04 ng/mL). Subjects with any of the following exclusion criteria were not allowed: ≥ 80 years old or < 18 years old, severe liver or kidney diseases, glomerular filtration rate (GFR) of < 30 ml/(min·1.73 m^2) or Child-Turcotte-Pugh (CTP) score ≥ 6, coagulation disorders associated with significant bleeding, intake of systemic immunosuppressive agents, occurrence of other serious disorders during the study period, and life expectancy of less than 6 months.

Definitions of primary end points

Primary end points of the study included incidence of acute myocardial infarction complications in the acute phase (within 1 week) and incidence of cardiovascular events in the short-term (90-days). Myocardial infarction complications were defin-ed as follows: arrhythmia (including atrial fibrillation, ventricular tachycardia, ventricular fibrillation, ≥ II° atrioventricular block), acute left ventricle failure, aneurysm, papillary muscle dysfunction or rupture (confirmed by color Doppler), ventricular wall rupture, and subsequent sudden cardiac death. Adverse cardiovascular events were defined as heart failure, re-admission, target vessel revascularization, stent thrombosis, recurrent myocardial infarction, non-hemorrhagic stroke, and ischemic or vascular thrombosis-related deaths. All criteria were in accordance with Academic Research Consortium criteria [8, 9].

Statistical analysis

Data management and statistical analysis were performed with Statistical Package for Social Sciences software (SPSS version 19.0 for Windows, SPSS Inc.). Data are expressed as mean ± standard deviation or as median and interquartile range when necessary. Categorical variables were compared using X^2 test or Fisher's exact test. For continuous data, group comparisons were performed using an unpaired *t* test or Mann-Whitney U-test. Log-rank Mantel-Cox tests and Kaplan-Meier survival curves were used to compare event-free survival. Results were considered statistically significant if the two-sided *p*-value was ≤ 0.05.

Results

Baseline characteristics for the two groups

Clinical characteristics of STEMI patients in the two groups are summarized in **Table 1**. There were no significant differences between the groups in terms of age, sex, smoking history, diabetes mellitus, hypertension, or other chronic diseases. Risk factors in AMI patients after creation of the CPC, such as cholesterol, GRACE scores, and clinical medication, seem to have been reduced. However, there were still no significant differences revealed. The culprit vessel and number of diseased blood vessels of these STEMI patients are shown in **Table 2**.

Time of first medical contact to balloon opening in the two groups

The amount of time required to treat patients with acute myocardial infarction is expected

Table 4. Acute cardiac complications within the first 7 days

Group	Acute cardiac complications				
	Total complications	Cardiac death	Ventricular aneurysm	Acute heart failure	Arrhythmia
Group A	32	3	3	11	15
Group B	15	1	2	5	7
t/x^2/Fisher	1.55	-	-	2.522	3.490
P Value	< 0.001*	0.618	1.0	0.112	0.062

Group A, STEMI patients selected before the creation of a CPC; Group B, STEMI patients selected after the creation of a CPC; Arrhythmia (including atrial fibrillation, ventricular and supraventricular tachycardia, ventricular fibrillation, ≥ 2nd degree atrioventricular block). *P ≤ 0.05 vs. the control group.

Table 5. Cardiovascular events between the two groups

Group	Cardiovascular Events						
	Total Events	HF	Re-Admission	Target vessel revascularization	Stent Thrombosis	Re-AMI	Death
Group A	31	4	20	1	0	1	5
Group B	19	2	12	3	0	0	2
t/χ^2/Fisher	5.071	-	2.662	-	-	-	-
P Value	0.024*	0.678	0.103	0.363	-	-	0.437

Group A, STEMI patients selected before the creation of a CPC; Group B, STEMI patients selected after the creation of a CPC; HF, Heart failure; Re-AMI, Recurrence of acute myocardial infarction; Death, Non-hemorrhagic stroke, and Ischemic or vascular thrombosis-related death. *P ≤ 0.05 vs. the control group.

to be less under the establishment of chest pain center. This study found that the first medical contact time in group B (STEMI patients enrolled after creation of the CPC) was shorter than in Group A (STEMI patients enrolled before creation of the CPC), though there were no significant differences between the groups (FMC, 2.40 ± 0.38 vs. 3.45 ± 0.40, p = 0.059). However, both the first time of oral loading doses of antiplatelet agents (FLAM, 2.45 ± 0.36 vs. 4.03 ± 0.40, p = 0.004) and first medical contact to balloon opening time (FMC2B, 2.50 ± 0.23 vs. 4.29 ± 0.38, p < 0.001) were signifcantly shorter in group B than in group A (**Table 3**).

7-day incidence of acute cardiac complications

The establishment of a chest pain center is to ensure that AMI patients receive medical treatment as quickly as possible. Therefore, cardiac complications at the time of the acute phase is expected to be less than those prior to the inception of the CPC. This study defined acute myocardial infarction complications as follows: cardiac death due to papillary muscle dysfunction or the rupture of the ventricular wall as confirmed by color Doppler, ventricular aneurysm, acute heart failure, and arrhythmia (including atrial fibrillation, ventricular and supraventricular tachycardia, ventricular fibrillation, ≥ II° atrioventricular block). It was found that incidence of complications in STEMI patients was significantly lower in group B than in group A (28.8% vs. 60.4%, t = 10.55, p < 0.001). Specific complications are listed in **Table 4**.

Comparison of cardiovascular events between the two groups

Retrospective analysis of major cardiovascular events in the 90 days after an AMI (-heart failure, readmission, target vessel revascularization, stent thrombosis, recurrent myocardial infarction, non-hemorrhagic stroke, and ischemic or vascular thrombosis-related deaths) showed significant differences between the groups (36.5% vs. 58.5%, χ^2 = 5.071 p = 0.024). Incidence of adverse events in group B (19 cases) was significantly lower than in group A (31 cases), after establishment of the Chest Pain Center. There were only 2 patients that suffered from ischemic or vascular-related deaths after creation of the CPC, compared to 5 patients in group A. There were 12 patients readmitt-

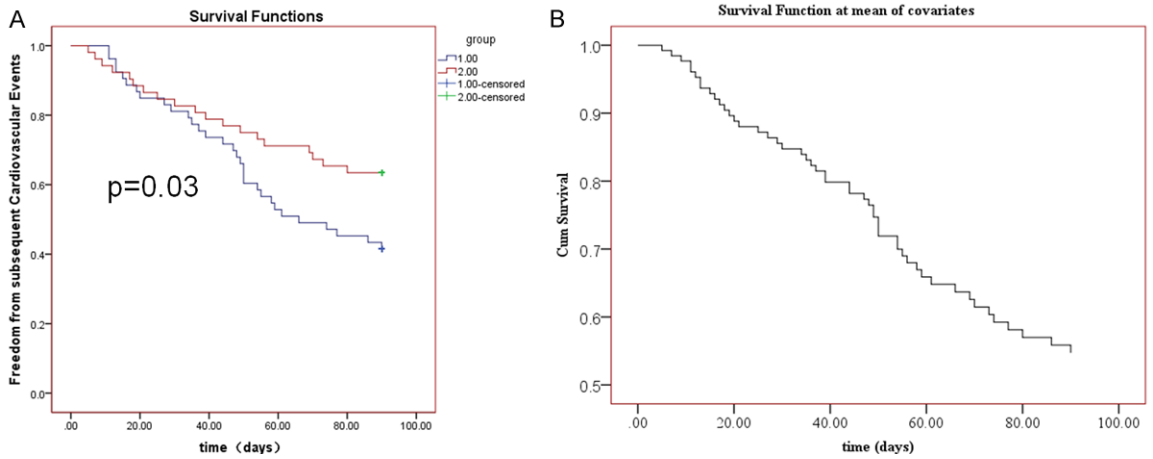

Figure 1. Univariate Kaplan-Meier and multivariate regression analysis. A. Survival functions in two groups of STEMI patients before (blue line) and after (red line) the creation of a CPC. B. Multivariate regression analysis after adjusting for confounding factors in STEMI patients.

Table 6. Multivariate regression analysis of 90-day survival functions

							95.0% CI for Exp (B)	
	B	SE	Wald	Df	Sig.	Exp (B)	Lower	Upper
Diabetes mellitus	-.117	.305	.146	1	.703	.890	.489	1.619
Cerebral infarction	-.273	.364	.561	1	.454	.761	.373	1.555
Hypertension	.647	.312	4.296	1	.038*	1.909	1.036	3.519
Smoking	.329	.331	.989	1	.320	1.389	.727	2.656
Hyperlipidemia	-.417	.321	1.690	1	.194	.659	.351	1.236
Renal insufficiency	.708	.313	5.119	1	.024*	2.031	1.099	3.752

Multivariate regression analysis of 90-day survival functions of the mean covariates after adjusting for confounding factors in STEMI patients in the equation are shown. B: Partial regression coefficient; SE: Standard error of partial regression coefficient; Wald: test of the significance between the total partial regression coefficient and zero,when v = 1, W = (B/SE)^2; Exp (B): relative risk (RR value). *P ≤ 0.05 vs. the control group.

ed for various reasons in group B compared to 20 patients in group A (**Table 5**). Statistically significant differences between the two groups were further shown in the Kaplan-Meier suvival curves (41.5% vs. 63.5%; log-rank test χ^2 = 4.24, p = 0.039) (**Figure 1A**). Multivariate regression analysis was further applied after adjusting for diabetes mellitus, cerebral infarction, hypertension, smoking, hyperlipiemia, and renal insufficiency. Results indicated that STEMI patients in group B had less adverse cardiovascular outcomes (X^2 = 20.625, p = 0.004). Survival function at the mean of covariates is shown in **Figure 1B**. Furthermore, results showed that renal insufficiency (HR: 2.031, 95% CI: 1.099-3.752, p = 0.024) and hypertension (HR: 1.909, 95% CI: 1.036-3.519, p = 0.038) were associated with occurrence of adverse cardiovasclarevents (**Table 6**).

Discussion

The leading symptom for emergency patients, chest pains can have numerous causes, including acute pericarditis, pulmonary embolism, aortic dissection, and gastroenterological disease. Chest pains might require an immediate and targeted diagnostic and therapeutic straegy [10]. Chest Pain Centers have been created to exclusively treat chest pain patients. The symptoms of chest pain may be sharp, dull, burning, aching, and stabbing or they may be a tight, squeezing, or crushing sensation. Acute myocardial infarction (heart attack) is a more severe discomfort accompanied by crushing sub-sternal pain. AMI is an acute and urgent inflammatory disease characterized by the rupture of arterial plaques and interruption of blood supply to the myocardium.

This present study demonstrated that the foundation of a Chinese Chest Pain Center significantly lowered incidence of acute cardiac complications in the first week. Furthermore, cardiac events significantly decreased in the following 3 months after creation of the Chest

Pain Center (patients in group B). These results indicate that the quick reactions of a Chest Pain Center, especially in preparation of the cardiac catheterization lab, play a very active role in the diagnosis and treatment of AMI patients, including re-canalization of acutely occluded vessels in STEMI patients.

It should be noted there are still many other possible critical factors that could have contributed to a decrease in cardiac complications and adverse cardiovascular events. This study further analyzed first medical contact time, oral dose loading time of antiplatelet agents, and balloon time in the two groups. This study is the first to show that loading of antiplatelet agents (aspirin 300 mg and ticagrelor 180 mg) was very timely in STEM patients, after creation of Chest Pain Center, in comparison to that before. Most AMI patients received a loading of antiplatelet agents only after admittance to the Emergency Department and confirmation by ECG and cardiac enzymes of AMI. It should be noted that most STEMI patients in group B received a loading dose of antiplatelet agents just after first medical contact with Emergency Medical Services (EMS) providers within the allotted 120 minutes of transport time. In addition, these patients were directly transferred to the Cardiac Catheter Lab for emergency coronary angiographies instead of being admitted to the Emergency Department. This specifically contributed to decreased door-to-balloon times. Thus, these various time-saving procedures greatly reduced the extent of cardiomyocyte deaths and myocardial necrosis.

These results also partially confirm the ideal reported by Steven M. et al. [30], stating that Chest Pain Centers aim to provide care that is safe, effective, efficient, timely, and patient-centered. Translation of these aims into clinical practice for STEMI patients ensures the timely transfer of STEMI patients to PCI-capable centers [11, 12]. According to ACC/AHA/SCAI guidelines that are focused on primary percutaneous coronary intervention for patients with STEMI [13-15], Emergency Medical Services and integrated PCI networks are critical for these patients regarding door-to-balloon times of less than 90 minutes and transport to PCI-capable centers of less than 120 minutes. In fact, there remains a great discrepancy between clinical reality and recommendations of the guidelines, particularly in developing countries [16, 17]. However, according to this present study, the Chest Pain Center contributed to reduction of this discrepancy and greatly reduced door-to-balloon times.

Diabetes mellitus, cerebral infarction, hypertension, smoking, hyperlipidemia, and renal insufficiency are all risk factors for cardiovascular disease, contributing to reverse remodeling in AMI patients [18, 19]. This study found that renal insufficiency and hypertension are associated with occurrence of adverse cardiovascular events, indicating that long-term chronic inflammatory lesions accompanied by higher oxidative stress and increased ROS plays an important adversarial role in cardiovascular events in AMI patients. However, this retrospective study had the limitations of a small sample. Prospective, multi-center, large sample studies are urgently needed. On the other hand, the construction of China's Chest Pain Center was arrived late by 2013 and the current number of CPCs is less than one hundred compared to thousands of PCI-capable centers in America [20]. Meanwhile, growth of PCI-capable centers has not been uniform in relation to prevalence of AMI or distance between PCI-capable facilities [21]. Thus, more chest pain centers are urgently needed to lower incidence of acute cardiac complications and adverse cardiac events.

Conclusions

This retrospective study found that establishment of the Chest Pain Center contributed to lower incidence of acute cardiac complications and decreased adverse cardiovascular outcomes, suggesting better prognosis for STEMI patients treated in the Chest Pain Center. In addition, this study concludes that renal insufficiency and hypertension can affect the prognosis of these STEMI patients, indicating that early, effective, efficient, and timely intervention is necessary. However, whether the current model of the Chest Pain Center can further optimize and enrich the prognosis of STEMI patients while serving as a standard therapeutic strategy for AMI should be further studied.

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Disclosure of conflict of interest

None.

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