Original Article
Long-term effects of direct percutaneous coronary intervention on left ventricular remodeling in elderly patients with acute myocardial infarction

Xingyi Yang, Shumei Li, Changwen Qu, Qian Zhang

Department of Medical Care for Cadres, The Branch of Shanghai First People's Hospital, Shanghai 200081, China

Abstract: Objective: This study aims to investigate the long-term effects of direct percutaneous coronary intervention (PCI) on left ventricular remodeling in elderly patients with acute myocardial infarction (AMI). Methods: A total of 101 patients with AMI were included into the study. Direct PCI was completed within 12 hours from onset. Subjects in the non-PCI group received conventional conservative treatment of drugs. Patients were followed up for 0.5-8 years, in which cardiac function (NYHA grade) were evaluated and ultrasonic cardiogram detected. Results: All 101 patients completed the follow-up. Among these patients, two female patients who did not receive PCI died during the follow-up, one patient died of sudden cardiac death, and another patient died of severe pneumonia. Compared with the non-PCI group, cardiac function (NYHA) grade, (P = 0.015) was significant lower and left ventricular end-systolic and -diastolic volume decreased in the direct PCI group (end-systolic volume: P = 0.0019; end-diastolic volume: P = 0.0012). However, left ventricular ejection fraction (LVEF, P = 0.0308) increased in the direct PCI group. In addition, there was a significant decline in the ventricular wall motion index (WMI, P = 0.0195) in the direct PCI group. Furthermore, patients revealed a significantly larger E/A value (P = 0.0002), shorter E wave deceleration time (P = 0.0003) and smaller left ventricular mass index (LVMI) (P = 0.0001) in the direct PCI group. Moreover, compared with the non PCI group, left ventricular long axis diameter (P = 0.0246) and short axis diameter (P = 0.0001) significantly decreased and the spherical index (SI) (P = 0.0092) increased in patients in the direct PCI group. Conclusions: Direct PCI treatment improves chronic ventricular remodeling in elderly patients with AMI, and contributes to long-term improvement in cardiac function.

Keywords: Acute myocardial infarction, ventricular remodeling, percutaneous, coronary artery, intervention therapy

Introduction

With the acceleration of the population aging process, the numbers of patients with acute myocardial infarction (AMI), who are 80 years old and older, have continuously increased. The number of patients who are 75 years old and older accounts for more than one third of patients with AMI. The incidence of heart failure after AMI increases with age. Hence, patients who are 65 years old and below account for only 11.7%, while patients who are 84 years old and older account for 44.6% [1]. In addition, the occurrence of heart failure is related to progressive ventricular remodeling after AMI [2, 3]. In order to reduce the incidence of heart failure after AMI, ventricular remodeling

after AMI should be intervened in the early stage. Among these intervention measures, the beneficial effects of drugs have been proven. The number of necrotic myocardial is a decisive factor among factors influencing ventricular remodeling. Direct percutaneous coronary intervention (PCI) can quickly open infarct-related arteries, improve myocardial ischemia, saving the ischemic myocardium, and thereby improving ventricular remodeling. This has been confirmed in patients aged ≤80 years old [4]. For AMI patients aged ≥80 years old, the number of patients who timely chose direct PCI remains relatively few due to the lack of evidence for evidence-based practice and concerns from clinicians about renal dysfunction in AMI patients, bleeding complications, and so on. Hence, can

direct PCI save the infarcted myocardium without necrosis in elderly patients with AMI, and improve ventricular remodeling after myocardial infarction?

Ventricular remodeling after AMI is divided into two phases: acute phase and chronic phase. The acute phase occurs mainly during a few hours to 1-2 weeks after infarction. The chronic phase occurs 1-2 weeks after infarction, and may last for a long time or even a lifetime [5, 6]. We selected elderly patients with AMI in this study, and we hope to provide reference for the treatment in elderly patients with AMI in the acute phase through follow-up of chronic left ventricular remodeling after direct PCI.

Objects and methods

Objects

A total of 101 AMI inpatients (58 male patients and 43 female patients) aged 80-89 years old, with an average age of 83.03 ± 3.15 years old, were included into the study. AMI was confirmed by clinical manifestations, electrocardiogram (ECG) and markers of myocardial necrosis. Patients were excluded for any of the following reasons: (1) patients with old myocardial infarctions; (2) patients with bundle branch block or implanted with a pacemaker; (3) patients with severe valvular disease or hypertrophiccardiomyopathy diagnosed by echocardiography; (4) patients with severe liver and kidney dysfunction; (5) patients with non-anterior and non-inferior wall myocardial infarction.

Methods

Conventional treatment: Serum myocardial enzyme and troponin were given to all patients, and patients were dynamically observed after administration. Dynamic ECG changes were recorded. Low molecular weight heparin, aspirin (an antiplatelet drug), angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB), β-receptor blockers, statins and nitrate esters were routinely given.

Coronary angiography and PCI treatment: Patients enrolled into the study received coronary angiography and PCI treatment within 12 hours after AMI. In coronary angiography, two or more than two projection positions were taken to determine the diseased vessels and lesion

sites. The antegrade flow of infarct-related arteries was scored with reference to the definitions of perfusion in the TIMI trial [7]. Grades 0-1 were defined as no perfusion or penetration without perfusion. After coronary angiography, considering angiography results and the family's wishes, PCI was carried out; and conventional coronary angioplasty was adopted. Patients were routinely administered with 100-300 mg of aspirin, 300 mg of clopidogrel and 100 U/kg of heparin through the sheath. After balloon pre-dilatation, coronary stents were placed in the infarct-related arteries. Standards of successful PCI: The angiography that was immediately performed after surgery effectively opened the vascular lesions (grades 2-3, according to the definitions of perfusion in the TIMI trial), and did not result in any significant residual stenosis or serious complications in surgery. After surgery, patients were given 100 mg of aspirin and 75 mg of clopidogrel for at least 12-18 months.

Follow-up and echocardiographic examinations: Patients were followed up through the clinic or telephone. Symptoms, signs and the New York Heart Association (NYHA) functional class were recorded. Echocardiographic follow-up was performed by a fixed staff. A two-dimensional color Doppler echocardiography (HP55-00) was operated with a 2.5-3.5 MHz probe by a fixed professional technician. The recorded and collected ultrasound image data were used for playback and analysis. Peak E, peak A and E wave deceleration time were detected.

Left ventricular ejection fraction (LVEF): through left ventricular end-diastolic and end-systolic endocardial volumes of the recorded apical four-chamber view, the single plane area-length method was used to calculate the left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV).

LVEF = [(LVEDV-LVESV)/LVEDV]%

Sphericity index (SI) [8]: The parasternal left ventricular long-axis view was recorded, and the distance between the apical and midpoint of the mitral annulus was measured as the left ventricular long-axis diameter. The short-axis view of the papillary muscle was recorded, and the distance between the left ventricular wall through the papillary muscle was measured as the left ventricular short-axis diameter. SI = left

Table 1. General circumstance of the two groups

	PCI group	Non-PCI group	P values
Cases	39	60	
Males	23 (58.97%)	35 (58.33%)	5.02
Ages (years)	83.41 ± 3.17	83.70 ± 3.25	0.33
Mass index (kg/m²)	37.97 ± 3.37	37.00 ± 2.98	0.07
Time from onset to PCI (hours)	9.26 ± 1.89	----------	
Time from onset to follow-up (Years)	2.63 ± 2.58	2.30 ± 1.57	0.24
NYHA functional class	1.85 ± 0.71	2.15 ± 0.61	0.015*
Positions of acute myocardium infarction			
Anterior wall (%)	31 (79.49%)	49 (81.67%)	7.88
Inferior wall (%)	8 (20.51%)	10 (16.67%)	3.84
Concomitant diseases			
High blood pressure (%)	33 (84.62%)	50 (83.33%)	6.63
Diabetes (%)	20 (51.28%)	29 (48.33%)	7.88
Concomitant medications			
Aspirin (%)	37 (94.87%)	55 (91.67%)	3.84
Clopidogrel (%)	23 (58.97%)	21 (35.00%)	0.25
β-receptor blockers (%)	32 (82.05%)	50 (83.33%)	0.95
Statins (%)	38 (97.43%)	59 (98.33%)	0.75
ACEI/ARB (%)	31 (79.49%)	55 (91.67%)	0.18
Nitrate esters (%)	32 (82.05%)	48 (80.00%)	0.99
Diuretics (%)	4 (10.25%)	7 (11.67%)	0.95
Results of coronary angiography			
Single-vessel disease (%)	10 (25.64%)	---	
Two-vessel disease (%)	13 (33.33%)	---	
Three-vessel disease (%)	16 (41.03%)	---	

ACEI/ARB: angiotensin-converting enzyme inhibitors/angiotensin II receptor antagonist, NYHA: New York Heart Association, *$P<0.05$.

ness (LVPWT) were measured. Based on a previous study [9], LVMI was calculated. LVM=0.8{1.04[(LVD+IVST+LVPWT)3-LVD3]}+0.6, LVMI = LVM/body surface area (BSA).

Statistical methods

All data analysis was conducted using SPSS version 17.0. Measurement data were presented as $\bar{x}$ ± standard deviation (SD), and *t*-test and chi-square test were used. A *P*-value <0.05 was considered statistically significant.

Results

General circumstances (Table 1)

A total of 101 patients (58 male patients and 43 female patients) were included into the study and were followed up for 0.5-8 years. During the follow-up, two female patients who were not treated with PCI died: one patient died of sudden cardiac death, and the other patient died of severe pneumonia. Ninety-nine patients completed the follow-up. Among these patients, 39 patients chose to receive direct PCI treatment. Among these 39 patients, 23 patients were male (58.97%); and these patients had an average age of 83.41 ± 3.17 years old and an average body mass index of 37.97 ± 3.37 kg/m². The average time from onset to PCI was 9.26 ± 1.89 hours, and the average time from onset to follow-up was 2.63 ± 2.58 years. Sixty patients did not choose to receive direct PCI treatment. Among these 60 patients, 35 patients were male (58.33%); and these patients had an average age of 83.70 ± 3.25 years old and a body mass index of 37.00 ± 2.98 kg/m². The average time from onset to follow-up was 2.30 ± 1.57 years. Apart from the significantly lower NYHA functional class (1.85 ± 0.71 *vs*. 2.15 ± 0.61, *P* = 0.015), the PCI group was not significant different from the

ventricular long-axis diameter/left ventricular short-axis diameter.

Ventricular wall motion index (WMI): Horizontal sections of the mitral valve, papillary muscle and the apex were recorded. A 20-segment model was used to conduct the semi-quantitative analysis of wall motion abnormalities: 0 point for movement enhancement, 1 point for normal movement, 2 points for weakened movement, 3 points for no movement, 4 points contradictory movement, and 5 points for ventricular aneurysm. WMI = Total points of the ventricular wall motion/20.

Left ventricular mass index (LVMI): The parasternal left ventricular long-axis view was recorded. Left ventricular end-diastolic diameter (LVD), interventricular septum thickness (IVST), and left ventricular posterior wall thick-

Table 2. Ultrasound follow-up of patients in both groups

	PCI group	Non-PCI group	*P*-values
Left ventricular end-systolic volume (ml)	37.31 ± 22.02	50.00 ± 18.22	0.0019**
Left ventricular end-diastolic volume (ml)	66.03 ± 29.07	83.75 ± 24.03	0.0012**
LVEF (%)	0.45 ± 0.12	0.41 ± 0.10	0.0308*
Left ventricular			
Long-axis diameter (mm)	68.15 ± 11.18	72.85 ± 7.64	0.0246*
Left ventricular			
Short-axis diameter (mm)	39.69 ± 6.25	44.50 ± 2.62	0.0001**
SI	1.75 ± 0.29	1.64 ± 0.12	0.0092**
WMI	1.17 ± 0.32	1.31 ± 0.32	0.0195*
IVST (cm)	1.03 ± 0.04	1.02 ± 0.05	0.0921
LVPWT (cm)	1.00 ± 0.09	1.00 ± 0.07	0.4705
LVD (cm)	4.90 ± 0.38	5.13 ± 0.34	0.0017**
LVMI (g/m^2)	112.53 ± 10.21	121.00 ± 10.96	0.0001**
Peak E (cm/s)	67.48 ± 9.00	57.63 ± 16.13	0.0001**
Peak A (cm/s)	78.68 ± 19.81	86.58 ± 11.47	0.0140*
E/A	0.93 ± 0.36	0.69 ± 0.26	0.0002**
E wave deceleration time (s)	173.89 ± 57.47	218.50 ± 66.70	0.0003**

LVEF: Left ventricular ejection fraction. SI: Sphericity index. WMI: Ventricular wall motion index. IVST: Interventricular septum thickness. LVPWT: Left ventricular posterior wall thickness. LVD: Left ventricular end-diastolic diameter. LVMI: Left ventricular mass index. *$P<0.05$, **$P<0.01$.

non-PCI group in the aspects of gender, age, body mass index and follow-up time, as well as AMI site, comorbidities and concomitant medications (*P*>0.05). Coronary angiography results revealed that 10 patients (25.64%) had single-vessel disease, 13 patients (33.33%) had 2-vessel disease, and 16 patients (41.03%) had 3-vessel disease in the direct PCI group.

Ultrasound follow-up of the two groups of patients (Table 2)

Compared with the non-PCI group, the direct PCI group revealed decreased LVESV and LVEDV (LVESV: 37.31 ± 22.02 ml *vs.* 50.00 ± 18.22 ml, *P* = 0.0019; LVEDV: 66.03 ± 29.07 ml *vs.* 83.75 ± 24.03 ml, *P* = 0.0012), but a greater LVEF (0.45 ± 0.12 *vs.* 0.41 ± 0.10, *P* = 0.0308) and small WMI (1.17 ± 0.32 *vs.* 1.31 ± 0.32, *P* = 0.0195). In addition, the direct PCI group revealed a shorter left ventricular long-axis diameter and short-axis diameter (left ventricular long-axis diameter: 68.15 ± 11.18 mm *vs.* 72.85 ± 7.64 mm, *P* = 0.0246; left ventricular short-axis diameter: 39.69 ± 6.25 mm *vs.* 44.50 ± 2.62 mm, *P* = 0.0001). Meanwhile, in the direct PCI group, SI was greater (1.75 ± 0.29 *vs.* 1.64 ± 0.12, *P* = 0.0092), E/A was larger (0.93 ± 0.36 ratio of 0.69 ± 0.26, *P* =

0.0002), E wave deceleration time was shorter (173.89 ± 57.47 seconds *vs.* 218.50 ± 66.70 seconds, *P* = 0.0003), and LVMI was smaller (112.53 ± 10.21 g/m^2 *vs.* 121.00 ± 10.96 g/m^2, *P* = 0.0001).

Discussion

As the population aging process accelerates, the incidence of heart failure after AMI increases with age. The number of patients aged 84 years and older has reached up to 44.6% of the overall number of patients with heart failure after AMI [1]. In addition, the occurrence of heart failure has been associated to progressive ventricular remodeling after AMI [2, 3]. In order to fundamentally improve the prognosis of heart failure after AMI, infarct-related arteries should be opened as soon as possible after myocardial infarction, and the myocardial should be saved as much as possible, intervening ventricular remodeling.

Methods to open infarct-related arteries in the early period of AMI treatment include venous thrombolysis, direct PCI and coronary artery bypass graft surgery (CABG). Intravenous thrombolysis is relatively contraindicated for elderly patients (≥80 years old) [4], and CABG is

also an impractical option. There is no age limit for direct PCI. However, treatment options for direct PCI are relatively few due to the lack of evidence of evidence-based practice, concerns from clinicians about renal dysfunction in AMI patients, bleeding complications and other complications, the attitude of the patient's relatives, and other factors. Therefore, can direct PCI improve ventricular remodeling after myocardial infarction and improve the prognosis of these patients?

A three-year study [10] conducted in Japan on elderly patients (≥80 years old) with AMI (low-risk) who received primary percutaneous transluminal coronary angioplasty (PTCA) and conservative medical therapy revealed that these two treatment strategies have no significant differences in their effects on left ventricular remodeling and the combined end-point of cardiovascular complications. However, a comparative study in Italy on patients aged 65 years and older and patients aged under 65 years found that when PCI was performed inpatients with acute anterior myocardial infarction, clinical benefits of left ventricular remodeling gained by patients aged 65 years and older were not different from patients aged under 65 years [11]. Both of these studies have shortcomings. Although the study in Japan lasted for three years, it only focused on PTCA and did not involve stent implantation, which is currently common in China. This may underestimate the beneficial effects of interventional therapy on post-MI remodeling. The observation time of the study in Italy was only 90 days, which was very short. As a result, the benefits of PCI for elderly patients, especially long-term benefits, may be overestimated. Unfortunately, there is no domestic research data.

Elderly AMI patient populations (≥80 years old) were chosen for this study. During the 0.5-8 years of follow-up after AMI, ultrasonography in patients receiving direct PCI therapy and those receiving drug therapy alone revealed that in the aspect of systolic function, patients who received direct PCI therapy had higher LVEF. This resulted in better systolic function, lower WMI, and fewer abnormal contraction segments. At the same time, the improvement in diastolic function in elderly patients with AMI caused by direct PCI was significant: direct PCI reduced LVMI and E wave deceleration time in elderly patients with AMI, and induced the E/A

ratio to be closer to normal. Improvement in systolic and diastolic functions increased the SI of the entire ventricle, and alleviated changes in sphericity. Therefore, direct PCI treatment lowered the NYHA functional class in elderly AMI patients, and made patients feel better about themselves.

Ventricular remodeling after AMI was divided into two phases: acute phase and chronic phase. The acute phase occurs mainly during a few hours to 1-2 weeks after infarction. Due to changes in ventricular load conditions caused by the decreased number of viable myocardial cells, the activation of the neuroendocrine system may cause early infarct expansion, elongation and the slide of cardiomyocytes, ventricular wall thinning, reactive hypertrophy in the non-infarcted area, and other changes. These changes in ventricular remodeling were related with collagen dissolution, which lasts for two weeks after infarction at the molecular level. The chronic phase occurs 1-2 weeks after infarction, and probably lasts a long time or even a lifetime. Its main manifestations are gradual stop of infarct expansion accompanied by interstitial fibrosis caused by collagen proliferation, the stretching of shrinking segments, and the post-AMI progressive enlargement of the entire ventricle. In addition, ventricular shape becomes spherical, and an ultimately irreversible heart dysfunction is caused [5, 6].

Our observation results confirmed that direct PCI can improve chronic left ventricular remodeling after AMI, which is directly related to the timely opening of infarct-related arteries, the salvage of more dying myocardium, and the improvement of blood supply of the ischemic myocardium by direct PCI. The increase in the number of viable myocardial cells in the acute phase can alleviate ventricular load conditions in the acute phase and reduce neuroendocrine activation, weakening remodeling activities such as early infarct expansion, the elongation and slide of cardiomyocytes, ventricular wall thinning, and reactive hypertrophy in the non-infarcted area. Similarly, alleviation of ventricular remodeling in the acute phase improves post-infarction continued collagen dissolution at the molecular level. This also alleviates interstitial fibrosis caused by collagen proliferation in the chronic phase and reduces the weight of the ventricular myocardium, giving the corresponding protection to ventricular diastolic

function [5-6], and reducing changes in sphericity, as well as the occurrence of heart failure.

There is still a lack of evidence of large-scale evidence-based practice at home and abroad concerning how to choose interventional treatments and whether interventional therapy has advantages in the treatment of elderly patients with AMI (≥80 years old). Our study provides a useful reference for AMI patients who are ≥80 years old, because our study would help determine whether or not direct PCI treatment in the early period of AMI treatment can improve ventricular remodeling, thereby improving cardiac function in patients. However, due to the limited number of specimens in this study, a large-sample study is expected to further confirm our results.

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Disclosure of conflict of interest

None.

Address correspondence to: Xingyi Yang, Department of Medical Care for Cadres, The Branch of Shanghai First People's Hospital, Shanghai 200081, China. Tel: +86 021-56663031-1603; Fax: +86 021-65420854; E-mail: xingyiy1@sina.com

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