Journal of Geriatric Cardiology (2016) 13: 521−527

Perspective · **Open Access** ·

Percutaneous coronary intervention for acute myocardial infarction with mitral regurgitation

Yan TU, Qing-Chun ZENG, Ying HUANG, Jian-Yong LI

Department of Cardiology, Nanfang Hospital, Southern Medical University, Gunaghzou, China

Abstract

Ischemic mitral regurgitation (IMR) is a common complication of acute myocardial infarction (AMI). Current evidences suggest that revascularization of the culprit vessels with percutaneous coronary artery intervention (PCI) or coronary artery bypass grafting can be beneficial for relieving IMR. A 2.5-year follow-up data of a 61-year-old male patient with ST-segment elevation AMI complicated with IMR showed that mitral regurgitation area increased five days after PCI, and decreased to lower steady level three months after PCI. This finding suggest that three months after PCI might be a suitable time point for evaluating the possibility of IMR recovery and the necessity of surgical intervention of the mitral valve for AMI patient.

J Geriatr Cardiol 2016; 13: 521−527. doi:10.11909/j.issn.1671-5411.2016.06.010

Keywords: Acute myocardial infarction; Follow-up; Mitral regurgitation

1 Introduction

Ischemic mitral regurgitation (IMR) is a result of stenosis or occlusion of one or more coronary arteries, which causes myocardial ischemia and hence mitral valve dysfunction. IMR, characterized by blood reflux into the left atrium during the systole, may lead to structural and functional changes, or remodeling, of the left ventricle to cause heart failure, and even death in severe cases.[1−3] In the 2014 AHA/ACC guideline for the management of patients with valvular heart disease, severe IMR complicated by heart failure is defined as the indication for surgical mitral valve repair.[4] Current evidence suggests that revascularization procedures including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) are of benefits to lessen IMR,[5−8] but in patients with acute myocardial infarction (AMI), consensus has not been reached on the interval allowed for meliorative IMR to occur after a PCI procedure and on the time window for post-PCI mitral valve surgeries.[9] We proposed new approaches to IMR management after PCI based on the latest literature pertaining to IMR, and the diagnosis, treatment and follow-up of a 61-year-old male patient with ST-segment elevation AMI complicated with IMR.

2 Methods

All echocardiographic examinations were carried out using Acuson Sequoza 512 echocardiograph (Siemens, USA) by an experienced professor. Color flow recording of a mitral regurgitation (MR) jet was obtained from a zoomed view in four-Chamber view, and the luminal volumes of ventricles and atria were determined in Echocardiography long axis.[10]

Electrocardiography was examined by an experienced doctor using MAC5500 (General Electric Company). Standard 12-lead or 18-lead ECGs were carried out before and after PCI.[11]

Coronary angiography was performed using a special dye under a Siemens angiography X-ray system by experienced doctors. Standard positions were applied to show the blood flow in the coronary arteries.

A rest ^{99m}Tc-MIBI SPECT examination was performed to evaluate the myocardial blood perfusion in the patient at two months after AMI onset using Discovery VG-8 (General Electric Company). short axis (SA) rest (apical to basal), vertical long-axis (VLA) rest (septal to lateral) and horizontal long-axis (HLA) rest (inferior to anterior) were applied to demonstrate the myocardial blood perfusion from different directions.

Correspondence to: Jian-Yong LI, MD, PhD, & Qing-Chun ZENG, MD, PhD, Department of Cardiology, Nanfang Hospital, Southern Medical University, 1838 North Gunaghzou Ave, Guangzhou, 510515, China. E-mails: liysmn@126.com (LI JY) & qingchunzeng@smu.edu.cn (ZENG QC)

Telephone: +86-62787090 **Fax:** +86-61360416

Received: November 7, 2015 **Revised:** January 26, 2016

Accepted: March 15, 2016 **Published online:** June 28, 2016

3 Diagnosis and treatment

A 61-year-old male patient was admitted into the emergency room for complaint of chest tightness for four days with exacerbation for 4 h in July, 2012. The patient, who smoked heavily for 30 years (20–40 cigarettes per day), reported a history of hypertension for 30 years with good blood pressure control by taking amlodipine and metoprolol on an regular basis. The patient was conscious upon admission with a blood pressure of 106/72 mmHg and a respiration rate of 25 per minute; moist rales could be heard in the bilateral lower lungs and the heart rate was 63 beats/min without precordial or cardiac murmurs. ECG indicated sinus rhythm, third-degree atrioventricular block, and apparent ST-segment elevation in II, III and avF (Figure 1). Echocardiography revealed slight enlargement of the left atrium, reduced motion in the inferior left ventricular wall, and middle mitral incompetence, with mitral regurgitation area (MRA) of 6.78 cm^2 and ejection fraction (EF) of 59% (Table 1). Emergency coronary angiography was performed after the implantation of a temporary pacemaker, and the angiographic image showed a normal left main stem and complete occlusion in the middle of the left anterior descending branch (LAD) with three orders of collateral circulation established distal to the occlusion; the middle segments of both the left circumflex coronary artery (LCX) and the right coronary artery (RCA) were occluded (Figure 2, A, C, E). A Xience V 3.0/33 mm and a 3.5/33 mm stents were then implanted in the middle and the proximal segments of the RCA, respectively, and a Xience V 2.75/28 mm stent was placed in the middle segment of the LCX (Figure 2, B & D). Thrombolysis in myocardial infarction (TIMI) grade III blood flow was achieved in the RCA and LCX after stenting. The procedures were completed smoothly in spite of third degree atrioventricular block during the operation. Postoperative ECG showed sinus rhythm, advanced atrioventricular block, and acute left ventricular inferior wall infarction. The postoperative diagnosis suggested: coronary artery disease; 3-vessel coronary artery stenosis; acute ST-segment elevation infarction in the left ventricular inferior; third degree atrioventricular block; Killip class III of heart function.

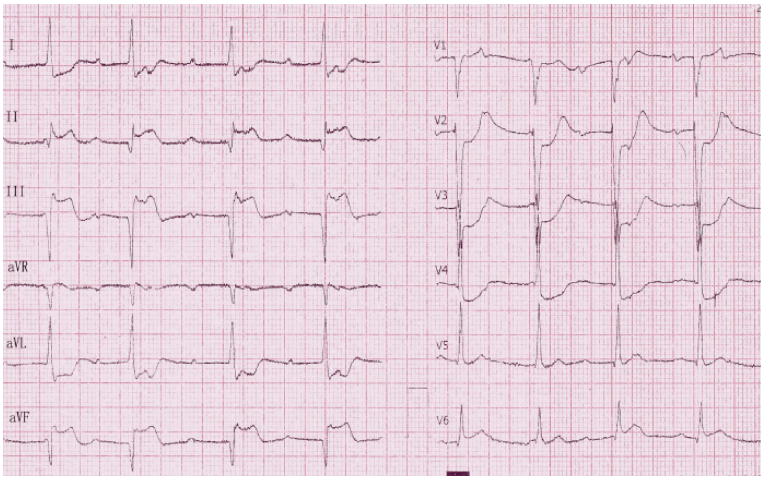

Figure 1. ECG showed Sinus rhythm, third-degree AVB, elevating ST-segments of II, III and avF leads. AVB: atrioventricular block.

Table 1. Echocardiography, BNP and cTnI during hospitalization and follow-up.

Time after PCI	Admission	5 days	1 month	3 months	1 yrs	2.5 yrs
LA, mm	38	41	40	36	38	37
LVIDd, mm	42	50	53	51	51	48
LVIDs, mm	27	33	45	40	40	35
MRA, cm^2	6.78	12.25	11.21	4.11	4.14	3.63
RA, mm	42	38	41	30	34	34
RV, mm	40	35	35	28	28	26
EF, %	59	62	64	59	54	56
BNP, pg/mL	4136	2280	2601	1479	1247	410
cTnI, ng/mL	>55	11.519	0.021	0.024	0.022	-

BNP: NT-pro-brain natriuretic peptide; cTnI: cardiac troponin I; EF: ejection fraction; LA: left atrial; LVIDd: left ventricular internal dimension diastole; LVIDs: left ventricular internal dimension systole; MRA: mitral regurgitation area; RA: right atrial; RV: right ventricle.

Oral aspirin, clopidogrel, and atorvastatin calcium were administered with subcutaneous injection of fondaparinux sodium after the operation. On day 2 and 3 after PCI, the patient experienced two episodes of acute left heart failure after onset of chest tightness, which was managed with furosemide, morphine, and sodium nitroprusside. As echocardiography showed EF > 50% and no increase of MRA (Table 1), we suspected that heart failure might have been resulted from insufficient blood supply of the left ventricular anterior wall due to LAD occlusion. Considering the importance of LAD revascularization in preventing pulmonary edema, we scheduled the stenting procedure of the LAD three weeks after the initial PCI when the troponin level showed an obvious reduction. Three stents, namely Xience V 2.5/28 mm, 2.75/33 mm, and 3.0/18 mm, were implanted successively in the distal to middle segments of the LAD (Figure 2F). The patient recovered uneventfully and was discharged one week later.

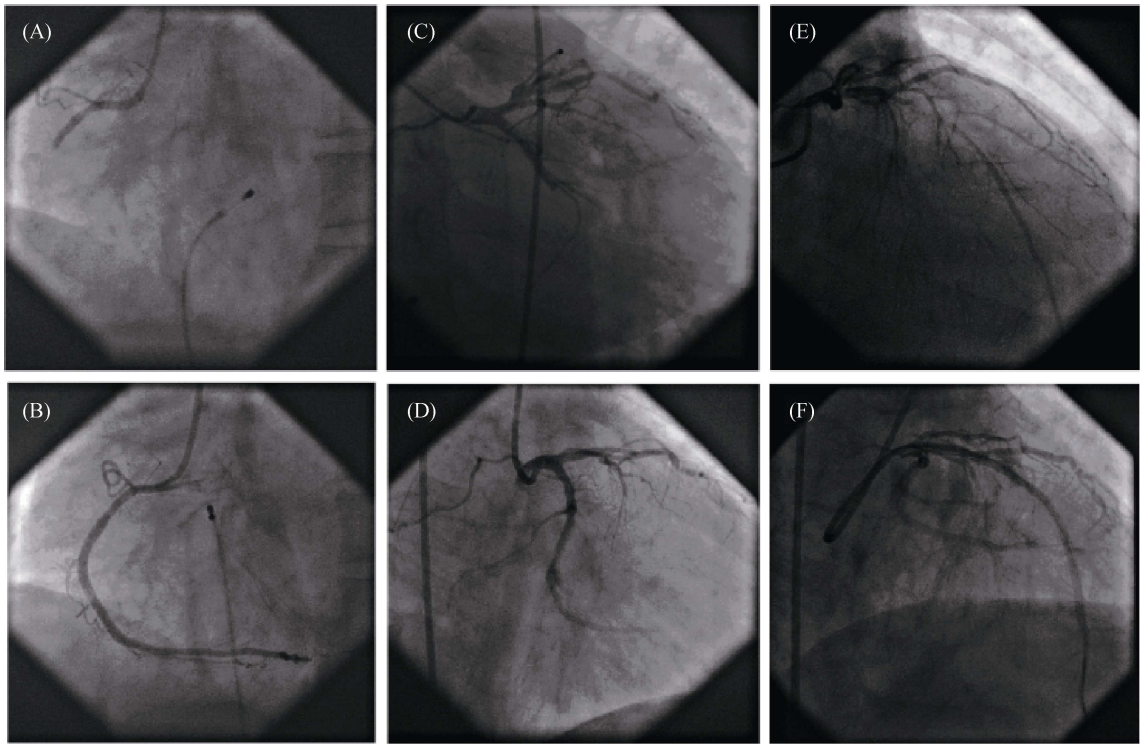

Figure 2. Angiography demonstrating severe three-vessel coronary artery disease. (A): Angiography of the right coronary artery demonstrating a totally occluded circumflex artery; (B): Xience V 3.0/33 mm, 3.5/33 mm stent were implanted in the middle and the proximal segments of the RCA; (C): the middle segment of LCX was occluded; (D): a Xience V 2.75/28 mm stent was placed in the middle segment of the LCX; (E): the middle of LAD totally occluded with three orders of collateral circulation established distal to the occlusion; (F): Xience V 2.5/28 mm, 2.75/33 mm, and 3.0/18 mm stents were implanted in the distal to middle segments of the LAD three weeks later. LAD: left anterior descending branch; LCX: left circumflex coronary artery; RCA: right coronary artery.

4 Follow-up

The patient was discharged with the prescription of oral aspirin (100 mg, once daily), clopidogrel (75 mg, once daily), atorvastatin calcium (20 mg, once daily), perindopril (4 mg, once daily), metoprolol (12.5 mg, twice daily), frusemide (20 mg, once daily), and spironolactone (20 mg, once daily). The patient was able to walk but still experienced paroxysmal apnea and tachypnea. At two months after AMI onset, the patient underwent an examination with rest ^{99m}Tc-MIBI SPECT of the myocardial blood perfusion, which revealed extensive absence image in the posterior and posterolateral walls of the left ventricle and cardiac lumen enlargement of the left ventricle (Figure 3), suggesting deficiency of the cardiac function. Three months after AMI onset, the symptom of apnea was alleviated but the patient still reported occasional episodes of tachypnea; echocardiography displayed a significant improvement of MR, MRA of 4.11 cm^2, and laboratory tests reported obviously decreased serum level of Pro-NT-brain natriuretic peptide (Pro-NT-BNP). One year after the operation, the patient displayed significant improvements of the symptoms without episodes of paroxysmal dyspnea, and echocardiographic findings and serum BNP level were all improved. The last

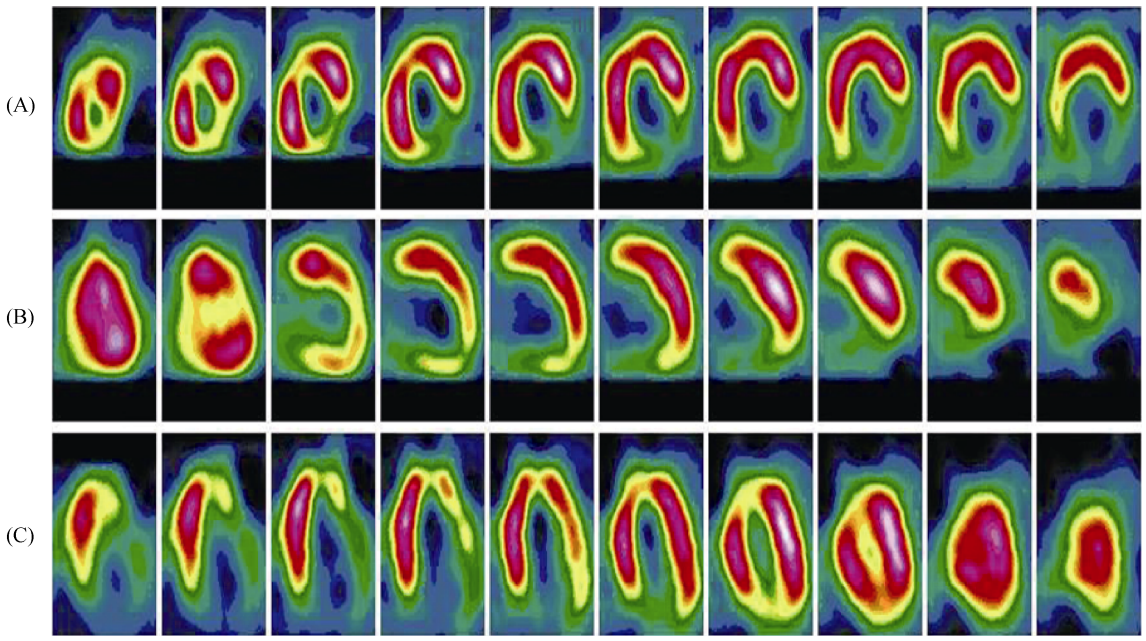

Figure 3. The examination of the myocardial blood perfusion with rest ^{99m}Tc-MIBI SPECT. SPECT demonstrated extensive absence image in the posterior and posterolateral walls of the left ventricle and cardiac lumen enlargement of the left ventricle. (A): SA rest (apical to basal); (B): VLA rest (septal to lateral); (C): HLA rest (inferior to anterior). HLA: horizontal long-axis; SA: short axis; VLA: vertical long-axis.

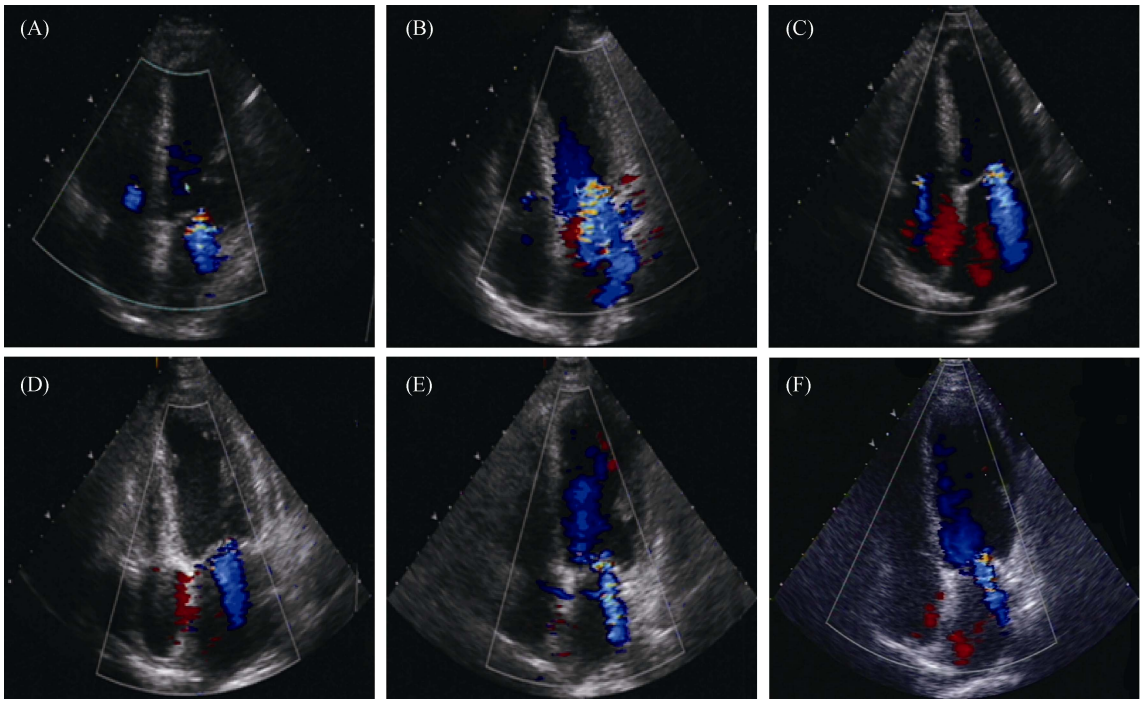

Figure 4. Echocardiographic four-chamber view with color Doppler. (A): Moderate mitral regurgitation before PCI; (B & C): severe mitral regurgitation in five days, one month after first PCI; (D & E): moderate mitral regurgitation three months, one year after first PCI; (F): mild mitral regurgitation 2.5 years after first PCI.

follow-up was January of this year (2.5 years after PCI), the patient had not complain of dyspnea and chest tightness with MRA reduced to 3.63 cm^2 and Pro-NT-BNP further decreased to 410 pg/mL (Table 1 and Figure 4). The patient was capable of taking the stairs to the third floor and handling normal daily activities.

5 Discussion

It is estimated that 1/5 of the IMR cases were resulted from myocardial infarction, and half of the IMR cases are complicated by concurrent congestive heart failure. With an incidence reaching 40% following AMI and a 5-year mortality rate up to 62%, IMR has become an independent risk factor affecting the prognosis of AMI.[12–16]

Many factors contribute to the occurrence of IMR, including post-infarct left ventricular remodeling, papillary muscle displacement (to cause imbalanced drag and full forces of the mitral valve), contractile dysfunction of the left ventricle, structural changes of the valvular ring, and ventricular electro-mechanical dys-synchrony.[17,18] Of these factors, left ventricular remodeling is thought to be the most important mechanism responsible for IMR.[19,20] The entire or local remodeling of the left ventricle results in luminal distortion and enlargement, which causes displacement of the papillary muscle attachment to pull the mitral valve towards the cardiac apex. The reduced contractility of the left ventricle following AMI further contribute to the incompetence of the mitral valve, leading thus to IMR. The location of myocardial infarct also affects the probability and severity of IMR: an infarction in the inferior wall of the in the left ventricle, which causes the posterior papillary muscles to move non-symmetrically, is more likely to cause IMR than an infarction in the anterior wall.[15]

Current interventions of IMR include conservative therapy with medications, open surgery (mitral valve replacement or repair), and percutaneous interventional therapies (percutaneous mitral annuloplasty and percutaneous edge-to-edge mitral valve repair). PCI and CABG have been shown to modify the incidence and improve the prognosis of IMR following AMI. Chua, *et al*.[16] retrospectively analyzed 318 patients with primary AMI and found that the incidence of MR was 9.9% in patients undergoing PCI, significantly lower than that in patients receiving only medications (24.5%). To assess the impact of PCI and CABG on the prognosis of IMR, Trichon, *et al*.[21] compared the outcomes of 2757 patients with moderate to severe IMR who received treatments with medical therapy, PCI, CABG, and CABG + mitral valve surgery, and average follow-up for 3.2 years. The results analysis indicated that the patients in PCI, CABG, and CABG + mitral valve surgery groups, compared with those in medical therapy group, had significantly lowered risk of death by 30% (HR = 0.69, P = 0.0001), 42% (HR = 0.58, P = 0.0001), and 42% (HR = 0.58, P = 0.0001), respectively. Nevertheless, CABG with mitral valve surgery did not reduce the risk of death compared with CABG alone.

The 2014 AHA/ACC guidelines for valvular heart disease recommend that mitral valve surgery (replacement or repair) be performed during CABG in patients with severe IMR, but the guideline based on level C evidences.[4] Currently the clinical evidence to support mitral valve surgery along with CABG remains insufficient and the long-term outcomes of mitral valve surgery are still unclear. Reports of the outcomes over 10 years after CABG with mitral valve surgery have not been available, though observations after one year were reported. According to the Randomized Ischemic Mitral Evaluation (RIME) report published in 2012,[22] for patients with moderate IMR, CABG plus mitral annuloplasty, in comparison with CABG alone, could significantly improve the peak oxygen consumption, left ventricular end-systolic volume index, MR volume, and BNP level at one year after the operation. These results demonstrate that CABG plus mitral annuloplasty can significantly improve left ventricular remodeling and reduce MR and serum BNP level. The mortality rates at 30 days and one year after the operation, however, showed no significant difference between the two groups.

Mitral valve replacement and mitral valve repair are the two major options for surgical interventional of IMR, but the question how these two approaches affect the patient survival and prognosis remains unanswered. Acker, *et al*.[23] conducted a clinical trial of mitral valve repair and chordal-sparing replacement in 251 patients with severe IMR, and they found that at one year after the operation, the two groups showed no significant difference in left ventricular end-systolic volume index or in the mortality rate, suggesting that concurrent mitral valve surgery in CABG does not affect left ventricular remodeling or survival in CAD patients with severe mitral incompetence. But the patients with mitral valve repair had a significantly higher MR recurrence rate than those with mitral valve replacement at one year after the operation (32.6% *vs*. 2.3%, $P < 0.01$). So far, the indications of IMR for surgical interventions are still controversial, mostly due to the high recurrence rate of MR following mitral valve repair and insufficient evidence for their value in promoting long-term patient survival. Nevertheless, the time window for the surgical intervention for IMR in AMI patient is still controversial. A serial animal studies reported by Beeri R's group demonstrated that repair of IMR at 90 days after AMI had no beneficial effect on LV volume or contractility in the AMI sheep model.[24,25] However, the results of basic research based on the data about animal may vary while setting in a clinical context.

In our case, the patient had AMI complicated by moderate IMR. Emergency PCI was performed to relieve stenosis of the RCA and LCX. The symptom of chest tightness was

relieved after PCI, and the patient showed gradual recovery of cardiac function with lowered serum BNP level. But the MRA increased to maximal 12.25 cm^2 five days after the emergency PCI, which might result from myocardial ischemia-reperfusion injury and left ventricular enlargement and remodeling (Table 1 and Figure 3B). Anatomically, the papillary muscles are supplied by both the left and the right coronary arteries, and revascularization of these arteries with two PCI procedures can be beneficial for functional recovery of the papillary muscles. But as full recovery from ventricular remodeling is impossible within 1 month after AMI onset, the patient still had a MRA as high as 11.21 cm^2 upon discharge. According to the diagnostic criteria of the American Society of Echocardiography,[26] MR is graded, based on the MR color flow jet area or effective regurgitant orifice area (EROA) in 2D echocardiography, into mild (MRA < 4 cm^2, or EROA < 0.20 cm^2), moderate (MRA of 4–10 cm^2, or EROA 0.20–0.39 cm^2), and severe (MRA > 10 cm^2, or EROA ≥ 0.40 cm^2) conditions. Whether mitral valve replacement or repair should be performed or leaving the patient with medical therapy was a challenging clinical decision. But considering the improvements of the clinical symptoms of the patient, we chose to continue the medical therapy and closely observed the patient's condition to evaluate the necessity of surgical intervention. At three months after AMI onset, the patient exhibited obviously reduced MRA (4.11 cm^2) and BNP level (1479 pg/mL), with also significantly alleviated symptoms. Contemporary SPECT showed myocardial necrosis in the posterior and posterolateral walls of the left ventricle and some myocardial viability in the inferior wall. Although completed three vessels revascularization, the long-term chronic occlusion in the middle and the proximal segments of LCX leads to myocardial necrosis of the left ventricular in the posterior and posterolateral walls. After three months, MRA could not become normal because of its incomplete recovery of blood supply for the cardiac myocyte. Echocardiographic examination at one year after AMI onset showed stable echocardiographic parameters of MRA (4.14 cm^2) and serum BNP level (1247 pg/mL), and MRA further reduced to 3.63 cm^2 and serum BNP to 410 pg/mL at 2.5 years follow-up after PCI (Table 1). The patient had resumed basically his activity of daily life.

In conclusion, PCI can promote the long-term recovery of IMR, but in the short term, PCI may exacerbate IMR due to factors such as myocardial ischemia-reperfusion injury, left ventricular remodeling, and decreased left ventricular functionality. Our patient recovered from IMR with PCI and adequate medical therapy three months after AMI. Consensus has not been reached currently on the time window for surgical intervention of the mitral valve in patients with severe IMR following AMI, but this case indicates that three months after PCI might be a suitable time point for evaluating the possibility of IMR recovery, hence the decision on surgical intervention of the mitral valve might be good to make at three months after PCI in AMI patients.

Acknowledgement

This project were supported by the President's Grant of Nanfang Hospital (2014H002), the General Education Reform Project of Innovation to Enhance University in Guangdong Province 2015, Natural Science Foundation of Guangdong Province (2015A030310441), and National Natural Science Foundation of China (81570352).

References

1 Hammersting C, Schueler R, Welz A, *et al*. Ischemic mitral regurgitation: pathomechanisms and current therapeutic options. *Internist* (*Berl*) 2013; 54: 39–40.
2 Elmistekawy E, Mesana T, Chan V. Ischemic mitral regurgitation: current trends and treatment. *Curr Opin Cardiol* 2013; 28: 661–665.
3 Agricola E, Ielasi A, Oppizzi M, *et al*. Long-term prognosis of medically treated patients with functional mitral regurgitation and left ventricular dysfunction. *Eur J Heart Fail* 2009; 1: 581–587.
4 Nishimura RA, Otto CM, Bonow RO, *et al*. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014; 63: 2438–2488.
5 Yousefzai R, Bajaj N, Krishnaswamy A, *et al*. Outcomes of patients with ischemic mitral regurgitation undergoing percutaneous coronary intervention. *Am J Cardiol*; 2014; 114: 1011–1017.
6 Booher AM, Chetcuti SJ, Bach DS. The impact of percutaneous coronary intervention on ischemic mitral regurgitation. *J Heart Valve Dis* 2012; 21: 564–569.
7 Poh KK, Lee GK, Lee LC, *et al*. Reperfusion therapies reduce ischemic mitral regurgitation following inferoposterior ST-segment elevation myocardial infarction. *Coron Artery Di* 2012; 23: 555–559.
8 Kang DH, Sun BJ, Kim DH, *et al*. Percutaneous versus surgical revascularization in patients with ischemic mitral regurgitation. *Circulation* 2011; 124: S156–S162.
9 Valuckiene Z, Budrys P, Jurkevicius R. Predicting ischemic mitral regurgitation in patients with acute ST-elevation myocardial infarction: does time to reperfusion really matter and what is the role of collateral circulation? *Int J Cardiol* 2016; 203: 667–671.
10 Grayburn PA, She L, Roberts BJ, *et al*. Comparison of trans-

esophageal and transthoracic echocardiographic measurements of mechanism and severity of mitral regurgitation in ischemic cardiomyopathy (from the Surgical Treatment of Ischemic Heart Failure Trial). *Am J Cardiol* 2015; 116: 913–918.
11 Pourmand A, Tanski M, Davis S, *et al*. Educational technology improves ECG interpretation of acute myocardial infarction among medical students and emergency medicine residents. *West J Emerg Med* 2015; 16: 133–137.
12 Aronson D, Goldsher N, Zukermann R, *et al*. Ishemic mitral regurgitation and risk of heart failure after myocardial infarction. *Arch Intern Med* 2006; 166: 2362–2368.
13 Perez de Isla L, Zamorano J, Quezada M, *et al*. Prognostic significance of functional mitral regurgitation after a first non-ST-segment elevation acute coronary syndrome. *Eur Heart J* 2006; 27: 2655–2660.
14 Borger MA, Alam A, Murphy PM, *et al*. Chronic ischemic mitral regurgitation: repair, replace or rethink? *Ann Thorac Surg* 2006; 81: 1153–1161.
15 Huang WL, Fu Q. Development in mechanisms of ischemic mitral regurgitation. *Chin Med J (Engl)* 2013; 126: 1766–1770.
16 Chau S, Hung J, Chung SY, *et al*. Primary percutaneous coronary intervention lowers the incidence of ischemic mitral regurgitation in patients with acute ST-elevated myocardial infarction. *Circ J* 2010; 74: 2386–2392.
17 Ge L, Wu Y, Soleimani M, *et al*. Moderate ischemic mitral regurgitation after posterolateral myocardial infarction in sheep alters left ventricular shear but not normal strain in the infarct and infarct borderzone. *Ann Thorac Surg* 2016; 101: 1691–1699.
18 Levine RA, Hagége AA, Judge DP, *et al*. Mitral valve disease--morphology and mechanisms. *Nat Rev Cardiol* 2015; 12: 689–710.
19 Szymanski C, Bel A, Cohen I, Touchot B, *et al*. Comprehensive annular and subvalvular repair of chronic ischemic mitral regurgitation improves long-term results with the least ventricular remodeling. *Circulation* 2012; 126: 2720–2727.
20 Soleimani M, Khazalpour M, Cheng G, *et al*. Moderate mitral regurgitation accelerates left ventricular remodeling after posterolateral myocardial infarction. *Ann Thorac Surg* 2011; 92: 1614–1620.
21 Trichon BH, Glower DD, Shaw LK, *et al*. Survival after coronary revascularization, with and without mitral valve surgery, in patients with ischemic mitral regurgitation. *Circulation* 2003; 108 Suppl 1: II103–II110.
22 Chan KMJ, Punjabi PP, Flather M, *et al*. Coronary artery bypass surgery with or without mitral valve annuloplasty in moderate functional ischemic mitral regurgitation: final results of the Randomized Ischemic Mitral Evaluation (RIME) trial. *Circulation* 2012; 126: 2502–2510.
23 Acker MA, Parides MK, Perrault LP, *et al*. Mitral-valve repair versus replacement for severe ischemic mitral regurgitation. *N Engl J Med* 2014; 370: 23–32.
24 Beeri R, Yosefy C, Guerrero JL, *et al*. Early repair of moderate ischemic mitral regurgitation reverses left ventricular remodeling: a functional and molecular study. *Circulation* 2007; 116 (11 Suppl): I288–I293.
25 Beaudoin J, Levine RA, Guerrero JL, *et al*. Late repair of ischemic mitral regurgitation does not prevent left ventricular remodeling: importance of timing for beneficial repair. *Circulation* 2013; 128(11 Suppl 1): S248–S252.
26 Zoghbi WA, Enriquez-Sarano M, Foster E, *et al*. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr* 2003; 16: 777–802.