Interventional Treatment for Very Young Adults With Acute Myocardial Infarction
Clinical Manifestations and Outcome

Jun SHIRAISHI,1 MD, Hirokazu SHIRAISHI,2 MD, Hironori HAYASHI,3 MD, Takahisa SAWADA,4 MD, Tetsuya TATSUMI,4 MD, Akihiro AZUMA,4 MD, and Hiroaki MATSUBARA,4 MD

SUMMARY

Direct percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) is now established as a standard therapy for older patients. However, experience with PCI in very young adults with AMI has been limited. In this report we retrospectively evaluated the effectiveness of PCI for very young adults with AMI and estimated their clinical characteristics and outcome. Of the 502 patients with AMI, 5 were 35 years old or younger (1.0%) during a period of 4 years (2000-2004). We assessed the utility of PCI in these five consecutive patients under the age of 35 presenting with a first AMI. Five AMI patients, ranging in age from 20 to 34 years (median, 27 ± 5 years) underwent direct PCI for the culprit lesions. The lesions targeted for PCI were located in the left anterior descending artery in 3 patients and in the right coronary artery in 2 patients. One patient had a past history of Kawasaki disease (KD). In all of the patients, PCI were angiographically effective at the acute phase without complication. In hospital course, a subacute stent thrombosis occurred in one patient. Follow-up angiograms performed 6 months after the procedure revealed no restenosis, but identified a new coronary aneurysm in one patient with a past history of KD and a regressed giant coronary aneurysm probably due to atypical KD in another patient, which were confirmed by intravascular ultrasound. There was one death ascribed to heart failure 8 months after the initial PCI. The findings of this report suggest that PCI for very young adults with AMI can be safe and effective in the short-term. (Int Heart J 2005; 46: 1-12)

Key words: Percutaneous coronary intervention, Kawasaki disease, Coronary aneurysm, Intravascular ultrasound

ACUTE myocardial infarction (AMI) is rare in young adults. Previous studies have estimated that young patients less than 45 years old make up between 2% and 10% of all AMIs.1 The etiology of their AMI varies but is usually not due to
atherosclerotic plaque rupture except for the AMI with familial hyperlipidemia. Besides smoking, nonclassical risk factors such as vasospastic tendencies, thrombophilic conditions, and a past history of Kawasaki disease (KD) have also been proposed as the cause of AMI in young patients.1-4) The majority of previous studies on AMI in “young” adults have studied patients less than 40 to 50 years of age.1,3) In contrast, few reports have focused on the “very young” before the age of 35.5,6)

Direct percutaneous coronary intervention (PCI) is now widely accepted as a therapeutic strategy for older patients with AMI. Early, complete revascularization can salvage myocardium at risk and improve survival. However, on the basis of the difference in etiology of AMI, there is a possibility that the clinical effectiveness of PCI for very young adults with AMI might be different from that for older patients. In this report, we therefore retrospectively evaluated the effectiveness of PCI for very young adults with AMI and estimated their clinical characteristics and outcome.

METHODS

Patients: Five of 502 patients admitted to university-affiliated community hospitals due to AMI were aged 35 or younger (1.0%) between January 2000 and January 2004. The study population comprised these 5 consecutive patients with a first AMI under the age of 35 in this period. All were male with a mean age of 27 ± 5 (range 20 to 34) and underwent direct PCI for the culprit lesions. The diagnosis of AMI was made according to the following 3 criteria: (1) characteristic clinical history, (2) serial changes on the ECG suggesting infarction (Q-waves) or injury (ST-segment elevations), and (3) transient increase in cardiac enzymes. Clinical characteristics of the patients are summarized in the Table.

Procedure: Prior to emergency coronary angiography, the patients received intravenous heparin administration (5000 U, bolus) and oral premedication including aspirin (100 mg/day) and cilostazol (100 mg/day) if possible. A 6F sheath was inserted percutaneously into the radial artery in 4 patients and into the femoral artery in 1 patient. A 5F catheter was advanced through the sheath to the ostium of the right coronary artery (RCA) or left coronary artery (LCA) using the Judkins technique. After intracoronary injection of isosorbide dinitrate, cineangiography of the RCA and LCA was performed by manual injection. In case 1 and case 5, an intraaortic balloon pumping (IABP) catheter was inserted percutaneously into the femoral artery before angiography.

PCI was performed after the culprit lesions were ascertained by coronary angiography. After additional heparin administration (5000 U, bolus), a 6F coronary guiding catheter was engaged into the target vessel and then direct PCI was
performed. In case 3, a 5F temporary pacing catheter was inserted percutaneously through the right femoral vein into the right ventricle during PCI. For each procedure, interventional success at the acute phase was defined as an obstruction or a stenosis of the infarct-related vessel having been reduced to < 50% stenosis with thrombolysis in myocardial infarction (TIMI) 3 flow just after PCI. A follow-up angiography was performed for all patients 6 months after the initial angiography. Restenosis was defined as coronary stenosis of > 50% observed by angiography.

**RESULTS OF CORONARY INTERVENTION**

**Case 1**: A 20-year-old-male was admitted to our hospital with continuous chest pain and palpitations for eight hours after vomiting due to excess alcohol consumption. He had no obvious past history of cardiovascular disease. On arrival, he had clinical signs of cardiogenic shock such as a pale face and a cold sweat. Under the support of IABP, emergency coronary angiography indicated the presence of total occlusion in the proximal left anterior descending coronary artery
(LAD) (Figure 1A) but no abnormalities in the RCA or left circumflex artery (LCx). This was followed by a direct PCI to the proximal LAD occlusion. After several dilations using a balloon catheter (3.5/20 mm at 6 and 8 atm for 60 seconds), TIMI 3 flow was obtained. However, a massive thrombus in the proximal LAD and slit-like residual stenosis in the mid LAD were observed. An attempt at stent implantation failed because the stent delivery system could not pass through the slit-like stenosis. Afterwards, we injected 6,000,000 units of alteplase into the left coronary artery through the guiding catheter. The thrombus and the 25% residual slit-like stenosis still remained (Figure 1B).

Figure 1. Case 1. Panel A: right anterior caudal view of left coronary angiography before direct percutaneous coronary intervention (PCI). Left anterior descending coronary artery (LAD) was totally occluded in the proximal segment. Panel B: left coronary angiography immediately after direct PCI. This image showed a thrombus in the proximal LAD and a slit-like stenosis in the mid LAD. Panel C: one-month follow-up left coronary angiography and intravascular ultrasound (IVUS) image of the culprit lesion. Coronary angiography showed no thrombus, restenosis, or aneurysm. The IVUS image at the culprit lesion (white arrowhead) showed a large coronary aneurysm with a markedly thickened intimal layer. The lumen was oval and the intimal layer was asymmetrically thickened with heterogeneous echo intensity. Panel D: six-month follow-up left coronary angiography showed no restenosis. From J Invas Cardiol 2001;13:69-72. Copyright HMP Communications. Reprinted with permission.
Case 2: A 26-year-old male was admitted to our hospital with continuous chest pain for three hours after swimming. He had a past history of KD at three years of age. Emergency coronary angiography indicated total occlusion in the proximal portion of the LAD (Figure 2A). No other abnormalities were found in the RCA or LCx. This was followed by a direct PCI to the proximal LAD occlusion. After two dilations using a balloon catheter (3.0/20 mm at 8 and 12 atm for 60 seconds), TIMI 3 flow and an optimal angiographic result were obtained (Figure 2B).

Case 3: A 29-year-old male was admitted to our hospital with continuous chest pain for five hours under alcohol intoxication. Emergency coronary angiography indicated total occlusion in the mid RCA (Figure 3A) but no abnormalities in the...
LAD or LCx. This was followed by direct PCI to the mid RCA occlusion. Several aspirations using a percutaneous thrombectomy catheter and additional dilations using a balloon catheter (3.0/20 mm at 8 and 14 atm for 30 seconds) resulted in successful dilatation with 25% residual stenosis and TIMI 3 flow (Figure 3B).

Case 4: A 34-year-old-male was admitted to our hospital with continuous chest pain for two hours after swimming and drinking heavily. Emergency coronary angiography indicated total occlusion in the proximal RCA (Figure 4A) but no abnormalities in the LAD or LCx. This was followed by direct PCI to the proximal RCA occlusion. Injection of 480,000 units of urokinase into the RCA through the guiding catheter and additional dilations using a balloon catheter (3.0/20 mm at 8 atm for 30 seconds and 4.0/20 mm at 7 atm for 30 seconds) resulted in successful dilatation with 25% residual stenosis and TIMI 3 flow (Figure 4B).
Case 5: A 27-year-old-male was transferred to our hospital with cardiopulmonary arrest. He had been taking excessive doses of common cold drugs containing ephedrine and caffeine over the preceding ten years. On arrival, his electrocardiogram showed ventricular fibrillation and defibrillation counter shock was performed. After the return of spontaneous circulation with the support of intubation, ventilation, and IABP, emergent coronary angiography indicated a severe stenosis with thrombus in the proximal LAD and TIMI 2 flow (Figure 5A) but no abnormalities in the RCA or LCx. This was followed by direct PCI to the proximal LAD stenosis. Direct implantation of a stent (4.0/18 mm at 9 atm for 60 seconds) at the culprit lesion provoked plaque shift to a distal site. Subsequent implantation of an additional stent (4.0/9 mm at 9 atm for 60 seconds) at the distal site of the prior stent resulted in successful dilatation and TIMI 3 flow (Figure 5B).
Acute results of PCI, in-hospital course, IVUS findings, and follow-up: In all of the patients at the acute phase, the percentage diameter stenosis in the culprit lesions with effective PCI decreased and the TIMI grade improved. The in-hospital course was uneventful for all 5 patients except case 5. In case 5, a subacute stent thrombosis occurred 5 days after the procedure (Figure 5C) and repeat angioplasty was able to restore the coronary flow. One-month repeat coronary angiography and IVUS were performed in case 1 and case 2 because follow-up transthoracic echocardiography showed a coronary aneurysm at the culprit lesion in the proximal LAD in both cases. On one-month follow-up angiography, a new aneurysm appeared at the site of PCI in case 2 (Figure 2C), while no aneurysm was observed in case 1 (Figure 1C). However, in case 1, IVUS revealed a regressed large coronary aneurysm in the proximal LAD that had a lumen diameter of $5 \times 4$ mm and a vessel diameter of $12 \times 10$ mm (Figure 1C). The coronary aneurysm had a huge vessel area, and the intimal layer was markedly and
asymmetrically thickened with heterogeneous echo intensity (Figure 1C). The lumen size in the large aneurysm was similar to that of the proximal LAD near the aneurysm. Superficial calcification existed near the outlet of the aneurysm presenting the slit-like stenosis. In case 2, IVUS showed a coronary aneurysm in the proximal LAD which had a lumen diameter of $8 \times 5$ mm and a vessel diameter of $9 \times 6$ mm (Figure 2C). The coronary aneurysm had calcification on the intimal surface, and an extensive intimal-medial deep tear (Figure 2C). On 6-month follow-up angiography, no patient had developed restenosis at the coronary artery where the procedure had been performed (Figure 1D, 2D, 3C, 4C, 5D). The neo-aneurysm remained unchanged in case 2 (Figure 2D). The patients were followed-up 8 months to 4 years after the procedure. They have had no symptoms or events that suggest the presence of myocardial ischemia. There was one death due to heart failure 8 months after the onset of AMI (case 5). The patient in case 5 lacked an understanding of how serious his heart disease was and decided not to take his oral medication regularly after leaving our hospital.

**Complications:** No procedure-related complications such as slow flow, no reflow, distal embolism, or coronary artery rupture occurred during PCI. However, subacute stent thrombosis occurred 5 days after the initial PCI in case 5, and neo-aneurysm appeared on follow-up angiography in case 2.

**DISCUSSION**

The present report suggests that direct PCI for very young adults with AMI can be safe and effective in the short-term. Direct PCI has been the mainstay of revascularization strategy for AMI. However, experience in very young adults under the age of 35 has been limited. Moreover, direct PCI for AMI due to KD in young patients is extremely rare. Previous studies concerning young patients with stable angina, unstable angina, and AMI showed that the balloon angioplasty in younger populations has a high immediate success rate with relatively few complications. In contrast, with respect to the long-term outcome of PCI, young patients with angina have a high need for repeat revascularisation and many of them suffer an AMI in the follow-up period, while young patients with AMI have a low restenosis rate. However, it is unclear how many KD patients were involved in the population of patients with AMI in these reports.

The mechanisms of coronary artery occlusion in KD remain uncertain. Acute occlusion of coronary aneurysms may be due to massive thrombus formation, occurring primarily during the acute or subacute phase of KD. Another potential mechanism of coronary artery occlusion in long-term KD is marked progression of intimal thickening in aneurysm walls, often associated with calcification. Percutaneous transluminal coronary recanalization and intravenous
coronary thrombolysis have been used to treat AMI in patients with KD. A previous study has found that balloon angioplasty is not an effective means of revascularization in patients with coronary arterial stenosis due to KD because the lesions are stiff and often associated with calcification. Moreover, as in our case 2, coronary aneurysms newly develop at sites of balloon dilatation in some patients. Stent implantation is also not always useful for the treatment of the coronary stenotic lesions of KD because it is often difficult to deliver the stent into the severe stenotic and stiff lesions that have developed over a long period as a sequela of KD. Recent studies suggest that percutaneous transluminal coronary rotational ablation (PTCRA) may be the most suitable catheter intervention for the treatment of coronary arteries with severe stenosis and calcification occurring as long-term sequelae of KD.

The clinical effectiveness of direct PCI for coronary artery occlusion due to KD remains uncertain. Although in our two patients with KD, TIMI-3 flow could be restored by direct PCI, one of them had a new coronary aneurysm at the intervention site despite an excellent acute response to PCI. The results of IVUS suggest that not only intimal-medial dissection caused by balloon angioplasty with relatively high pressure but also lesion stiffness associated with severe superficial calcification might cause the new aneurysm. Taken together, in the case of AMI due to KD with severe calcified lesions, it might be an appropriate strategy to do aspiration and subsequent balloon angioplasty with relatively low pressure to minimize vessel wall damage and obtain TIMI 3 flow in the acute phase, and to perform PTCRA to obtain an optimal angiographic result in the chronic phase. During PCI for patients with KD, IVUS also contributes to an exact evaluation of the coronary artery and a decision concerning the interventional procedure of choice.

Case 1 had no history or signs of KD. However, the wall structure of the LAD on IVUS closely resembled that associated with KD. Previous studies have demonstrated that patients with coronary aneurysms who do not fulfill the diagnostic criteria of KD might have had antecedent atypical KD. Therefore, we speculate that he had preceding atypical KD and that thrombus formation at the regressed giant coronary aneurysm resulted in AMI. When examining young adults with coronary artery disease, cardiologists should obtain a detailed history and include atypical KD in the differential diagnosis, even if the past history provides no evidence of KD. We therefore cannot completely exclude the possibility that atypical KD might have contributed to the pathogenesis of AMI in cases 3, 4, and 5, because we did not perform detailed examinations of the vessel wall structures by IVUS in these cases.

The abuse of a drug, such as cocaine, amphetamine, ephedrine, or caffeine, has been implicated as one of the triggers for coronary spasm leading to
Therefore, we cannot rule out the possibility that ephedrine and caffeine in the cold remedy played a crucial role in the pathogenesis of AMI in case 5. In addition, both smoking and alcohol have also been shown to provoke coronary artery spasm.25,26) Some recent reports have shown that most younger AMI patients were heavy smokers.5,6) In the current report, all patients were young male smokers and 3 of 5 patients suffered an AMI after drinking alcohol. Coronary vasoconstriction itself may damage the endothelium, thereby increasing platelet adhesion and thrombus formation.

Despite successful reperfusion therapy leading to a reduced early mortality rate and improved prognosis in patients with AMI, postinfarction heart failure resulting from ventricular remodeling remains unresolved. Recent studies have demonstrated that intracoronary infusion of circulating blood- or bone marrow-derived progenitor cells might exert beneficial effects on postinfarction remodeling processes in patients with AMI.27,28) In the treatment of young patients with broad AMI, in particular, direct PCI combined with regenerative medicine might become a standard therapy in the near future.

In conclusion, the present findings suggest that direct PCI for very young adults with AMI can be safe and effective in the short-term. However, the long-term efficacy of direct PCI for very young adults with AMI is uncertain and more long-term follow-up is needed. Moreover, the very small sample size of our report is a major limitation and a larger study should be performed to confirm our findings.

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REFERENCES


