**Effect of Distal Protection Device on the Microvascular Integrity during Primary Stenting in Acute Myocardial Infarction: Distal Protection Device in Acute Myocardial Infarction**

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**ABSTRACT**

**Background and Objectives** : Phasic coronary flow velocity patterns and microvascular integrities are known to be prognostic factors in acute myocardial infarction (AMI). The use of a distal protection device during primary percutaneous coronary intervention (PCI) may preserve the microvascular integrity of the myocardium by preventing distal embolization of thrombotic materials. This study assessed the effects of such a device on microvascular integrity preservation through Doppler studies of the coronary flow velocities in AMI patients treated with primary PCI. **Subjects and Methods** : A total of fifty-eight consecutive patients (mean age 54±15, 46 males) with ST segment-elevated AMI, who had undergone primary PCI within 24 hours after onset, were enrolled in the study. The subjects were divided into two groups: 30 patients with the PurcuSurge GuardWire Temporary Occlusion and Aspiration System and 28 without. The TIMI flows and TMP grades (TIMI myocardial perfusion grade) were evaluated. The coronary flow velocities were measured after PCI with a Doppler wire at the baseline, and also after intracoronary adenosine (24–48 μg) induced hyperemia. The coronary flow velocity reserve (CFR), diastolic deceleration time (DDT) and microvascular resistance index (MVRI) were calculated. **Results** : Between the two groups, no significant differences were found in the angiographic characteristics and CFR. In patients with a distal protection device, however, the post-PCI TMP grades were more favorable (TMP 0/1: 13.3%, TMP 2: 23.3%, TMP 3: 63.4% vs. TMP 0/1: 35.7%, TMP 2: 35.7%, TMP 3: 28.6%, p=0.023), with TMP grade 3 being most common (63.4% vs. 28.6%, p=0.010). These patients also exhibited lower bMVRI and hMVRI levels (4.33±2.22 vs. 5.55±2.36 mmHg·m⁻¹·sec⁻¹ vs. p=0.047) and 2.39±1.40 vs. 3.14±1.36 mmHg/cm⁻¹·sec⁻¹ (p=0.045), respectively, and longer bDDT and hDDT (679±273 vs. 519±289 msec (p=0.035) and 761±256 vs. 618±272 msec (p=0.044), respectively). **Conclusions** : Distal protection with the Purcu-Surge GuardWire system may effectively preserve the microvascular integrity of the myocardium during primary PCI in AMI patients. (Korean Circulation J 2005;35:106-114)

**KEY WORDS** : Myocardial infarction : Microvascular integrity.

**Introduction**

Acute myocardial infarction (AMI) is commonly related with thrombotic occlusion following a plaque rupture. Accordingly, early relief of the occluded coronary artery and restoration of the coronary flow to the jeopardized myocardium have been demonstrated to decrease mortality and adverse outcomes.1-3 Primary percutaneous coronary intervention (PCI), with stent deployment, in AMI cases has been widely performed for restoring the coronary flow to the jeopardized myocardium, a more effective procedure than balloon angioplasty, decreasing the target vessel revascularization and restenosis rate.4-6 However, as the distal embolization of ruptured atherosclerotic plaque debris or thrombus is common during primary PCI with catheter-based interventions, stent deployment may also endow a greater chance of distal embolization than balloon angioplasty.4 Evidence that an obstruction of the distal microvasculature in the downstream bed of the infarct related artery (IRA) is caused by distal embolization of thrombotic materials and platelets during intervention has accumulated. These are critical pathophysiological events of myocardial infarction,7-8 which is subsequently related with slow-flow or no-reflow phenomenon and with additional injury to the microvasculature of the myocardium and poor
clinical outcomes. Recanalization and restoration of the epicardial coronary artery will not always guarantee reperfusion at the microvasculature of the myocardium. Therefore, reperfusion of the myocardial tissue level by preserving the microvasculature is crucial, as is opening of the epicardial coronary artery during primary PCI. It has been suggested that a distal embolization protection device may be a feasible, safe and effective tool in preserving the microvasculature of the myocardium due to prevention of distal embolization of thrombotic debris during primary PCI in AMI. The coronary angiographic TIMI myocardial perfusion (TMP) grade and phasic coronary flow velocity patterns, as assessed by intracoronary Doppler wire after primary PCI, both of which represent the myocardial reperfusion status and microvascular integrity of the IRA, were related to functional improvement of the left ventricle and prognosis of the patient. Herein, the effectiveness of the PurcuSurge GuardWire system in preserving the microvascular integrity of the myocardium during primary PCI was evaluated in AMI patients by assessing the TMP grades and phasic coronary flow velocity patterns of the IRA following primary PCI with stenting.

Subjects and Methods

Patient population

A total of fifty-eight patients (mean age: 54 ± 15 years; 46 male, 12 female) with first acute ST-segment elevated myocardial infarction, who had experienced primary PCI within 24 hours of symptom onset, were enrolled in this study. The diagnosis of AMI was based on characteristic chest pains that had persisted in excess of 30 minutes, significant ST segment elevation (>1 mm at limb lead and ≥2 mm at precordial lead) in ≥2 contiguous ECG leads, and an elevation of the myocardial band of creatine phosphokinase (CK-MB) ≥ 3 times of the upper normal limit. The exclusion criteria included the followings: 1) previous myocardial infarction, 2) cardiogenic shock, 3) previous history of coronary intervention or coronary artery bypass graft, 4) left main disease and 5) patients with significant tachy-arrhythmia or atrio-ventricular block, rendering an intracoronary Doppler study inappropriate. The study population was divided into two groups: 30 patients (group A) with the PurcuSurge GuardWire Temporary Occlusion and Aspiration System (Medtronic AVE, Santa Rosa, CA) and 28 patients (group B) without such protection during primary PCI.

Procedure

On admission, all patients were pretreated with chewable aspirin (300 mg) and clopidogrel (300–600 mg). An intravenous infusion of heparin was started (1000 U/hr) after a 5000 U intravenous bolus injection, and additional heparin administered to attain a minimum 300 seconds of activated clotting time during the procedure. After a 7 Fr guiding catheter was engaged to the IRA, via the femoral artery, a 0.014-inch GuardWire was advanced directly (or, in cases where the GuardWire could not directly pass the culprit lesion, with the use of a steerable coronary angioplasty guidewire for backup). The occlusion balloon of the GuardWire was positioned distal to the culprit lesion. Following actuation of the MicroSeal adapter, the distal occlusion balloon of the GuardWire was inflated using an EZ-flator with diluted contrast media (1/3 contrast media and 2/3 heparinized normal saline). The balloon size was adjusted according to the distal reference vessel size. In some patients, for the evaluation of the distal vessel diameter and side branches, a small amount of contrast was injected through the guiding catheter before inflation of the distal occlusion balloon of GuardWire. When protection of the distal circulation had been achieved through the system, the MicroSeal Adapter was removed, leaving the distal occlusion balloon in an inflated state. Subsequent to stent deployment, a 5 Fr mononit aspiration catheter (Export A. Aspiration Catheter) was loaded over the proximal end of the GuardWire, with several aspirations performed using the plunger of aspiration syringe. At the end of the procedure, angiography was performed to document the final TIMI flow grade and TMP grade.

Measurement of coronary flow velocity parameters and assessment of phasic coronary flow velocity patterns with intracoronary Doppler guide wire

After stenting and aspiration of the embolized materials, 100–300 μg nitroglycerin was administered into the coronary artery, and a 0.014-inch Doppler guide wire (FloWire™, Cardiometrics, Mountain View, CA, USA) introduced just distal to the culprit lesion. Maximal hyperemia was induced by a bolus of intracoronary adenosine administration (24 μg for the right coronary artery, 48 μg for the left coronary artery). The coronary flow velocity reserve (CFR) was defined as the ratio of the hyperemic averaged peak velocity (APV) to the baseline APV. The microvascular resistance index (MVRI) was calculated from the mean aortic blood pressure divided by the averaged peak velocity at the base-
line and during hyperemia, respectively. In three consecutive cardiac cycles at the baseline and during hyperemia, the deceleration time of the diastolic flow velocity (DDT) were measured and averaged for their mean values (Fig. 1).

**Statistical analysis**

Data are expressed as percentages for discrete variables and as the mean ± standard deviation for continuous variables. The continuous variables of the clinical, angiographic and intracoronary Doppler flow data were compared by the means between the two groups using the Student t-test. The categorical variables of the clinical characteristics, angiographic TIMI and TMP grades, were compared by χ² analysis or the Fisher exact test. A p of <0.05 was considered to indicate statistical significance.

**Results**

**Clinical characteristics**

The study population consisted of 58 consecutive patients, 46 men and 12 women, with a mean age of 54 ± 15 years. The clinical and laboratory data of both groups are summarized in Table 1. Of the 58 patients, 38, 17 and 3 had anterior, inferior and 3 lateral wall infarctions, respectively. All patients underwent echocardiography on admission or immediately after primary PCI. The mean ejection fraction was 52.5 ± 10.3%. The mean time elapsed from symptom onset to reperfusion with primary PCI was 392 ± 228 minutes. There were no significant differences in the clinical characteristics between the two groups, with the exception of the peak cardiac enzymes. The peak CK-MB was lower in group A than in group B patients (256 ± 165 vs. 379 ± 166 μg/mL, p = 0.011). No patient received glycoprotein IIb/IIIa inhibitors before or during PCI.

**Angiographic data**

Table 2 and 3 summarize the angiographic data obtained before and after primary PCI. Before and after the primary PCI with stenting, the mean of minimal lumen diameter (MLD), diameter of stenosis (DS) and reference vessel diameter (RVD) were insignificant between the two groups. Also, there was no significant difference in the respective TIMI flow grades before intervention (p=0.699) (Table 3).
After the primary PCI, the TIMI flow grades were more improved in patients with the distal protection device (group A) compared to those without (group B) (93.4% had TIMI grade 3, 3.3% grade 2 and 3.3% grades 0 or 1 in group A vs. 75.0, 25.0 and 0.0%, respectively, in group B, \(p=0.040\)) (Table 3). A significant difference was found in the respective TMP grades between the two groups after the primary PCI (63.4% had TMP grade 3, 23.3% grade 2 and 13.3% grades 0 or 1 in group A vs. 28.6, 35.7 and 35.7%, respectively, in group B, \(p=0.023\)) (Table 3) (Fig. 2A). Further, TMP grade 3 was more common in group A (63.4 vs. 28.6%, \(p=0.010\)). In 49 patients who achieved TIMI 3 flow after stenting, TMP grade 3 was also more common in group A (67.9 vs. 38.1%, \(p=0.048\)) (Fig. 2B).

Coronary flow velocity parameters and phasic coronary flow velocity patterns

The heart rate and baseline mean aortic blood pressure were no different between the two groups. The hyperemetic mean aortic pressure was lower in Group A than in Group B (74 ± 12 vs. 83 ± 17 mmHg, \(p=0.026\)). After the primary PCI, the bAPV and hAPV were higher in group A (21.6 ± 9.6 vs. 17.2 ± 7.0 cm/sec, \(p=0.050\); and 38.4 ± 16.8 vs. 29.9 ± 11.0 cm/sec, \(p=0.027\), respectively), and the bMVRI and hMVRI were lower in group A (4.33 ± 2.22 vs. 5.55 ± 2.36 mmHg · cm⁻¹ · sec, \(p=0.045\); and 2.40 ± 1.40 vs. 3.14 ± 1.37 mmHg · cm⁻¹ · sec, \(p=0.045\), respectively). However, the CFR was no different between the two groups (1.87 ± 0.66 vs. 1.84 ± 0.61, \(p=0.867\)). Early systolic reversal flow was documented in 1 patient with the distal protection device, compared with 2 without. The bDDT and hDDT were significantly longer in group A (679 ± 274 vs. 520 ± 289 msec, \(p=0.035\); and 761 ± 256 vs. 618 ± 272 msec, \(p=0.044\), respectively) (Table 4) (Fig. 3).

The comparative phasic coronary flow velocity patterns in cases with and without the distal protection device are illustrated in Fig. 4A, B, respectively.

Discussion

The aim of AMI treatment is the early and sustained reperfusion of the myocardium at risk. As such, primary PCI is widely performed for the restoration of the coronary flow and reperfusion to the jeopardized myocardium. Recently, primary PCI with stent deployment in AMI has been regarded as the optimal therapeutic regimen for the reperfusion of IRA, with lowering of the target vessel revascularization...
and rate of restenosis during the first 30 days and long-term follow-ups.\cite{4,6} However, primary angioplasty with stent deployment has shown no more improvement to the TIMI flow grade than primary balloon angioplasty. This might be explained by the higher likelihood of distal embolization of thrombotic materials during intervention with stent deployment.\cite{10-12} During primary PCI with either a stent or balloon, the slow-flow or no-reflow phenomenon occurred about 5–30% of AMI patients.\cite{10-12} The no-reflow phenomenon, which represents a severely damaged microvascular integrity of the myocardium, contributes to poor left ventricular functional improvement and negative clinical prognosis of AMI patients.\cite{10-12} Although the precise mechanisms of the no-reflow phenomenon have not been fully clarified, increasing evidence suggests the phenomenon might be related with embolization of athero and/or thrombotic debris, plugging with platelets and inflammatory cells, endothelial and myocardial edema, and the shedding of vasoactive proteins from the plaque.\cite{21-23} Angiographic evidence of distal embolization during primary PCI occurs in approximately 15% of cases, which is associated with a more extensive myocardial damage and poorer prognosis than when not seen.\cite{9} A distal protection device might be expected to protect the microvascular integrity of the myocardium by preventing embolization of thrombotic materials during primary PCI in AMI patients. Recently, thrombosuction before the actual angioplasty, with an export aspiration catheter, in primary PCI has achieved excellent angiographic results, with all target vessels achieving TIMI grade 3 flow.\cite{10} TIMI grade 3 flow is generally regarded as a successful reperfusion after PCI in AMI,\cite{26} which results in more desirable left ventricular functional outcomes compared to TIMI grade 0–2 flows.\cite{25,26}

In our study, no difference in the pre-PCI TIMI grades were shown between the two groups; however, the post-PCI TIMI grades significantly improved in patients with the distal protection device (group A) than in those without (group B). TIMI grade 3 flow was significantly more common in group A. These results showed that the use of the distal protection device was more desirable in restoring the epicardial coronary blood flow in AMI patients during primary PCI. However, the TIMI grade 3 flow had inhomogeneous hemodynamic characteristics, with a wide range of coronary flow velocity values, and some patients had less optimal reperfusion at the myocardial tissue level, which may be related to the different clinical outcomes.\cite{9,18}

Gibson et al\cite{17} developed the TMP grading system, a simple semiquantitative classification scheme, which can be used to characterize the filling and clearance of myocardial perfusion from an angiogram. The TMP grading system, using coronary angiography in the catheterization laboratory, facilitates the detection of microvascular obstruction as a cause of impaired myocardial perfusion, and implicated distal embolization as the most likely explanation for microvascular plugging. They reported that the TMP grading system provides independent risk stratification after thrombolitics in AMI. TMP 0/1 grades showed a three-fold increase in the 30-day mortality rates compared to TMP 3 grade, and even among patients with TIMI grade 3 flow, TMP 0/1 grade correlated with a seven-fold increase in the mortality rates compared to TMP 3 grade.

Huang et al\cite{14} reported that a distal protection device with a temporary occlusion system might be feasible, safe and effective during primary angioplasty in AMI. They reported that all patients with such a device had procedural success and exhibited positive results with respect to TMP grades (86.7% of patients achieved TMP grade 3), with none developing an angiographic no-reflow phenomenon. Yip et al\cite{16} reported the PurcuSurge device during primary PCI to be superior to adjunctive tirofiban therapy in terms of the epi-
cardiac flow, TMP grades and 30-day clinical outcomes. In our study, the post-PCI TMP grades were more favorable in group A than B. TMP grade 3 was also more common in group A and in 49 selected patients with TIMI grade 3 flow after primary PCI, TMP grade 3 was also more common in group A. These results suggested that a distal protection device is more effective in the recovery of reperfusion at the myocardial tissue level, which may be effective in preserving the microvascular integrity of the myocardium during primary PCI.

The CFR and phasic coronary flow velocity patterns are known to be prognostic factors for left ventricular functional improvement and for the clinical prognosis in AMI.\(^{19,20,27,28}\) We directly evaluated the microvascular function by assessing the coronary flow velocity and coronary flow velocity patterns using an intracoronary Doppler wire after primary PCI. In severely damaged myocardium, with diffuse obstruction of the microvasculature due to cell necrosis or multiple microvascular emboli, the distal coronary pressure increased and the coronary flow velocity rapidly decreased as a result of the increased microvascular resistance. Therefore, the increased microvascular resistance after relief of the epicardial stenosis with stenting may be related with severely damaged myocardium and microvascular dysfunction.\(^{12}\) In group A, the bAPV and hAPV were significantly higher and the bMVRI and hMVRI significantly lower than in group B. The higher APV and lower MVRI strongly suggested that patients with the distal protection device, compared to those without, had less damage, with preserved microvascular circulation of the infarct-related myocardium, due to the pre-

![Graphs showing comparison of coronary flow velocity, MVRI, and DDT between patients with and without a distal protection device.](image-url)
vention of distal embolization during primary PCI.

The CFR, as assessed immediately after the primary PCI, and within 24 hours of myocardial infarction onset, showed no difference in the left ventricular wall motion between the recovered and non-recovered groups, so was not considered to be an indicator of viable myocardium and left ventricular functional improvements in AMI patients. Hori et al. reported that the changes in the coronary blood flow after acute embolization were related to the extent of embolization. In a resting state, the coronary blood flow is maintained or even enhanced due to the hyperemia of non-occluded vessels. As the particulate burden begins to overwhelm the compensatory mechanisms, the coronary flow decreases almost linearly as embolization increases. However, in an adenosine-induced hyperemic state, according to the increased embolization, the hyperemic coronary flow progressively decreases, without a transient increase of the blood flow. In our study, the CFR showed no difference between the two groups. However, in group A, the bAPV was significantly higher, which may have been related to the compensatory hyperemic response due to the relatively small amount of distal embolization in patients with the distal protection device than in those without. Therefore, the CFR in this study might have been underestimated after primary PCI in the patients with the device.

In AMI patients with severe extensive damaged myocardium, the myocardial blood pool should be considerably decreased and the microvascular resistance increased. These facts may impact on the coronary flow velocity patterns. In these patients, coronary blood flows rapidly fill the residual intramyocardial blood pool during the diastolic phase, but soon rapidly decrease thereafter. As such, in patients with severe extensive damaged myocardium, the coronary flow velocity showed rapid deceleration of the diastolic flow. During the systolic phase, the coronary flow resulted in an early systolic retrograde flow or a decreased systolic flow. Thus,
an early systolic retrograde flow or a decreased systolic flow velocity, with rapid deceleration of the diastolic flow velocity, may be representative of severe damage to the microvascular integrity of infarct-related myocardium. In the study by Kawamoto et al., a systolic averaged peak flow velocity (SAPV) less than 6.5 cm/sec and a DDT less than 600 msec, assessed just after primary PCI, were related with poor recovery of the left ventricular function. Akasaka et al. also reported that unfavorable coronary flow velocity patterns, such as decreased DDT and SAPV or early systolic reversal flow, in TIMI 2 grade after primary PCI, were related to severe damage of the myocardium and poor functional recovery of the left ventricle.

Our study showed that patients with the distal protection device exhibited more favorable coronary flow velocity patterns. The bDDT and hDDT were significantly longer in patients with the device. These results indicate a preserved microvascular pool and less damage of the myocardium in patients with the device. Therefore, the PurcuSurge GuardWire® Temporary Occlusion and Aspiration System may be effective in preserving the microvascular integrity due to prevention of atherothrombotic microembolization or large particular embolization during primary PCI in AMI patients.

**Limitation**

This study was limited in several respects. First, it was not randomized in nature, with only a relatively small number of patients assessed. However, there were no significant clinical and angiographic characteristic differences between the two groups. Despite the small study population, statistically significant differences in the TIMI grade, TMP grade, MVRI and phasic coronary flow patterns were also observed between the two groups. These results may strongly suggest the effectiveness of the distal protection device in the preservation of myocardial integrity during primary PCI in AMI patients. Second, the coronary flow velocity and coronary flow velocity patterns might be affected, not only the microvascular integrity, but the infarct location and other hemodynamic factors also. In this study, the infarct locations between the two groups were no different. Also, there was no significant difference in the hemodynamic factors, with the exception of the hyperemic mean aortic pressure. However, the hyperemic mean aortic pressure was higher in patients without the distal protection device. Further studies will be required to evaluate the follow-up results for the left ventricular function and clinical outcomes.

**Conclusion**

This study is the first to show the effectiveness of the PurcuSurge GuardWire system as a distal protection device for preserving the microvascular integrity according to the coronary flow reserve, microvascular resistance indexes and phasic coronary flow velocity patterns using an intracoronary Doppler wire. The distal protection device is feasible and effective in the preservation of the microvascular integrity during primary PCI in AMI patients.

**REFERENCES**


