

Effectiveness of Distal Protection With the GuardWire Plus™ During Primary Angioplasty for Acute Myocardial Infarction

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Abstract

Objectives. To evaluate the effectiveness of distal protection with the GuardWire Plus™ during primary angioplasty in patients with acute myocardial infarction.

Methods. Thirty-eight consecutive patients undergoing stent implantation with distal protection using the GuardWire Plus (DP-group) were compared with a matched control group undergoing conventional stent implantation after balloon angioplasty without distal protection (NDP-group). Microvascular circulation after revascularization was assessed by Thrombolysis in Myocardial Infarction (TIMI) flow grade, myocardial blush grade (MBG), serum creatine kinase peak release, and ST resolution. Left ventricular ejection fraction was measured by echocardiography at discharge. Follow-up quantitative coronary angiography and left ventriculography were performed 6 months after percutaneous coronary intervention. Quantitative coronary angiography data, restenosis rate, target lesion revascularization rate and follow-up left ventricular ejection fraction were also compared between the two groups.

Results. No significant differences were observed in baseline clinical and angiographic characteristics between the two groups. The TIMI flow grade (DP-group 81.6% vs NDP-group 57.9%) and MBG 3 (57.9% vs 30.6%) were significantly greater in the DP-group respectively ($p < 0.05$). Post procedural ST-segment resolution $\geq 50\%$ was found in a significantly higher percentage of patients in the DP-group (68.4% vs 42.1%, $p < 0.05$). Left ventricular ejection fraction at discharge was significantly greater in the DP-group ($55.5 \pm 8.5\%$ vs $45.7 \pm 11.1\%$, $p < 0.05$). However, 6 months after the percutaneous coronary intervention, no significant difference was observed between the two groups. Restenosis rate and target lesion revascularization rate were similar in the two groups.

Conclusions. Distal protection with the GuardWire Plus improved the microvascular circulation as assessed by TIMI flow grade, MBG, and ST resolution. Furthermore, left ventricular ejection fraction at discharge was improved.

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Key Words

■ Revascularization ■ Coronary microcirculation ■ Angioplasty
■ Myocardial infarction, treatment ■ Stent

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INTRODUCTION

Primary angioplasty including stent implantation is an important option for the treatment of patients with acute myocardial infarction¹ and is associated with a higher reperfusion rate than pharmacological therapy². However, primary angioplasty including stent implantation carries the risk of mobilizing thrombus and plaque components, causing distal embolization. Distal embolization may lead to distal vessel occlusion and obstructions in the microvascular system, resulting in impaired myocardial reperfusion³⁻⁵. Therefore, the clinical benefit of primary angioplasty is reduced⁶⁻¹¹. Recently, a mechanical device has become available to prevent distal embolism, but whether it is effective in improving myocardial reperfusion after primary angioplasty is unknown.

This study evaluated the microvascular circulation in the infarct area and left ventricular function after primary percutaneous coronary intervention (PCI) using distal protection with the GuardWire PlusTM in patients with acute myocardial infarction.

SUBJECTS AND METHODS

Patient population

Thirty-eight consecutive patients in this study underwent stent implantation with distal protection of the GuardWire Plus (DP-group) from December 1, 2002 to November 30, 2003. The inclusion criteria were as follows: presentation within 12 hr from symptom onset, chest pain lasting > 30 min and resistant to nitrates, ≥ 0.2 mV ST-segment elevation in at least 2 contiguous leads on a 12-lead electrocardiogram (ECG), and an infarct-related native artery with a reference lumen diameter > 3.0 mm.

Primary percutaneous coronary intervention with distal protection

At the beginning of the procedure, a conventional guide wire was advanced across the target lesion. An aspiration catheter was advanced over the guide wire and the lesion was aspirated. Next, the GuardWire Plus was passed across the target lesion, the occlusion balloon was inflated, and stent implantation was performed in the standard fashion. After stent implantation, an aspiration catheter was advanced and the lesion aspirated proximal to the occlusion balloon. Finally, the occlusion balloon was deflated. During the PCI, heparin sodium was administered to maintain the activated clotting

time at 200 - 250 sec. Immediately after stent implantation, all patients received aspirin (100 mg/day) and ticlopidine (200 mg/day).

Method comparison

To compare markers of effective reperfusion in the DP-group, a case-matched control group of 38 patients undergoing primary PCI without distal protection (NDP-group) was selected from January 1, 1999 to November 30, 2002 in our database. Matching was performed through an automatic query on the database, blinded to procedural and clinical outcomes. The matching parameters in order of sequential selection were as follows: infarct-related artery, pre-PCI Thrombolysis in Myocardial Infarction (TIMI) flow grade, sex, age ± 5 years, and time to revascularization ± 2 hr.

Angiographic analysis

TIMI flow grade and myocardial blush grade (MBG) were graded on angiograms made immediately after the primary coronary angioplasty by two experienced investigators. TIMI flow grade was assessed as previously described^{12,13}. MBG was defined¹⁴ as follows: 0, no myocardial blush or contrast density; 1, minimal myocardial blush or contrast density; 2, moderate myocardial blush or contrast density but less than that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery; and 3, normal myocardial blush or contrast density comparable with that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery.

When myocardial blush persisted (staining), this phenomenon suggested leakage of the contrast medium into the extravascular space, and was graded 0. The single view that best isolated the myocardial infarct zone was chosen from multiple orthogonal projections, most commonly the right anterior oblique projection with cranial angulation for the left anterior descending artery, the right anterior oblique projection with caudal angulation for the left circumflex artery, and the left anterior oblique projection for the right coronary artery distribution.

All angiograms were obtained with a 7F guiding catheter using the standard approach after 2.5 mg intracoronary isosorbide dinitrate had been given immediately after the primary angioplasty. Quantitative coronary angiography was performed before and immediately after primary coronary

Table 1 Study population

	DP-group (n = 38)	NDP-group (n = 38)	p value
Male/female	28/10	28/10	NS
Age(yr, mean \pm SD)	62 \pm 12	64 \pm 10	NS
Hypertension(%)	55.2	57.8	NS
Diabetes mellitus(%)	26.3	25.7	NS
Hyperlipidemia(%)	40.6	40.0	NS
Current smoking(%)	50.0	47.1	NS
Previous myocardial infarction(%)	0	0	NS
Time from onset to revascularization(hr)	4.9	5.2	NS

DP = distal protection ; NDP = non-distal protection.

angioplasty using a quantitative coronary angiography analysis system(GE Medical Systems). Six months later, follow-up quantitative coronary angiography was performed and the binary angiographic restenosis rate and target lesion revascularization rate were calculated.

Electrocardiographic analysis

ECGs were done on admission, and immediately after the primary coronary angioplasty. Twelve-lead ECG was assessed just before revascularization and immediately after the primary coronary angioplasty. ST segment score was calculated as the sum of ST segment elevation > 0.1 mV for leads $V_1 - V_6$ and aVL in the case of anterior infarction and for leads V_1, V_4F, V_5 and V_6 in the case of inferior infarction. In the case of true posterior infarction, reciprocal ST-segment depressions in V_1 and $V_2 > 0.1$ mV were also included. The two ECGs were compared, and ST-segment elevation was defined as improved if regression $\geq 50\%$ was observed.

Enzymatic infarct size

Serial measurement of serum creatine kinase was possible in all patients, and the maximum level was used as an enzymatic marker of the infarct size. Samples were obtained at 4-hour intervals after the primary angioplasty procedure.

Assessment of left ventricular function

The left ventricular ejection fraction was measured by echocardiography using Simpson's rule in all patients at discharge. Six months later, follow-up left ventriculography was performed in all patients and left ventricular ejection fraction was

calculated with center-line wall motion analysis using a left ventriculogram analysis system(GE Medical Systems).

Statistical analysis

Differences in clinical characteristics between the groups were examined by ANOVA for parametric data. Differences in allelic frequencies among the groups were analyzed using the χ^2 test. A probability of less than 0.05 was taken to be significant.

RESULTS

Study population and baseline characteristics

The clinical and angiographic details of the enrolled patients are summarized in **Tables 1, 2**. There was no difference in baseline characteristics between the two groups. Median age, male sex, coronary risk factors, extent of coronary artery disease, and infarct-related vessel were similar in both groups. Angiographic evidence of TIMI flow grade 0 before the procedure was observed in the majority of patients, with no significant difference between the two groups.

Primary angioplasty

All patients in both groups received one or more stents. Stent length and number of implanted stent per patient were similar in both groups. There was no significant difference in quantitative coronary angiographic data immediately after primary angioplasty(**Table 3**).

TIMI flow grade and MBG analysis

TIMI flow grade 3 was achieved immediately after primary coronary angioplasty in 31 patients (81.6%) of the DP-group, and in 22 patients

Table 2 Baseline lesion characteristics

	DP-group (n = 38)	NDP-group (n = 38)	p value
Target vessel(TIMI flow grade 0/1/2/3)			
Left descending coronary artery	17(12/1/4/0)	17(12/1/4/0)	NS
Left circumflex coronary artery	1(1/0/0/0)	1(1/0/0/0)	NS
Right coronary artery	20(12/1/5/2)	20(12/1/5/2)	NS
Reference diameter(mm, mean \pm SD)	3.02 \pm 0.76	3.12 \pm 0.55	NS
TIMI flow grade(Pre PCI)			
0	25	25	NS
1	2	2	NS
2	9	9	NS
3	2	2	NS

TIMI = Thrombolysis in Myocardial Infarction; PCI = percutaneous coronary intervention. Other abbreviations as in Table 1.

Table 3 Angiographic data immediately after percutaneous coronary intervention

	DP-group (n = 38)	NDP-group (n = 38)	p value
Post reference diameter(mm)	3.41 \pm 0.77	3.21 \pm 0.44	NS
Post minimum lumen diameter(mm)	3.07 \pm 0.59	2.81 \pm 0.81	NS
Post diameter stenosis(%)	11.0 \pm 10.6	14.3 \pm 22.5	NS
Acute gain(mm)	2.75 \pm 0.97	2.63 \pm 0.80	NS
TIMI flow grade			
0	0	2(5.3)	NS
1	0	1(2.6)	NS
2	7(18.4)	13(34.2)	NS
3	31(81.6)	22(57.9)	< 0.05
Myocardial blush grade			
0	0	3(7.9)	NS
1	1(2.6)	17(44.7)	< 0.05
2	15(39.5)	7(18.4)	< 0.05
3	22(57.9)	11(30.6)	< 0.05

Continuous values are mean \pm SD.() %.

Post = immediately after primary coronary angioplasty. Other abbreviations as in Tables 1, 2.

(57.9%) of the NDP-group. MBG 3 was achieved in 22 patients(57.9%) in the DP-group, and in 11 patients(30.6%) of the NDP-group. Both parameters showed significantly greater improvement in the DP-group($p < 0.05$; **Table 3**).

In-hospital outcome

Post procedural ST-segment resolution $\geq 50\%$ achieved in 26 patients(68.4%) of the DP-group, and in 16 patients(42.1%) of the NDP-group($p < 0.05$). The creatine kinase peak release was not significantly different between the two groups. Left

ventricular ejection fraction at discharge was significantly greater in the DP-group(55.5 \pm 8.5% vs 45.7 \pm 11.1%, $p < 0.05$; **Table 4**).

Follow-up angiography and ventricular function

Follow-up angiography was performed 148 \pm 83 days after the procedure. The restenosis rate, target lesion revascularization rate, and left ventricular ejection fraction were similar in the two groups (**Table 4**).

Table 4 In-hospital outcome and follow-up result

	DP-group (n = 38)	NDP-group (n = 38)	p value
ST-segment resolution $\geq 50\%$	26 (68.4%)	16 (42.1%)	< 0.05
Maximum creatine kinase(IU/l)	3,053 \pm 2,638	3,831 \pm 2,213	NS
Left ventricular ejection fraction at discharge(%)	55.5 \pm 8.5	45.7 \pm 11.1	< 0.05
Left ventricular ejection fraction at follow-up(%)	54.7 \pm 11.1	54.5 \pm 13.4	NS
Restenosis rate(%)*	28.6	31.6	NS
Target lesion revascularization rate(%)	13.2	15.7	NS

*More than 50% stenosis by quantitative coronary angiography.
Abbreviations as in Table 1.

DISCUSSION

Thrombus is the most important factor to consider in the course of acute myocardial infarction¹⁵⁻¹⁹), but other complications also occur during primary coronary angioplasty such as distal embolization and no reflow phenomenon. The present study investigated the effectiveness of distal protection with the GuardWire Plus as an adjunct to stenting during primary angioplasty. In patients with acute myocardial infarction, rapid restoration of epicardial flow has been recognized as an important predictor of clinical and angiographic outcome²⁰). Moreover, the MBG after reperfusion therapy as seen on the coronary angiogram can be used to describe the effectiveness of myocardial reperfusion and is an independent predictor of long-term mortality¹⁴). In addition, previous studies have shown that normal myocardial perfusion as assessed by the MBG is a more powerful predictor of survival than attaining TIMI flow grade 3, and that improvement of myocardial blush after PCI correlates with long-term mortality^{14,21,22}). Therefore, we used TIMI flow grade and blush grade as markers of microvascular circulation status after revascularization.

In the present study, TIMI flow grade 3 and MBG-3 were achieved significantly more often in the DP-group. However, visual assessment of myocardial blush remains subjective, and a more quantitative approach such as using coronary flow reserve²³) and myocardial contrast echocardiography²⁴) is presently being developed. These are clinically useful methods to evaluate microvascular circulation, but cannot be performed routinely. However, it is noteworthy that the tissue perfusion status assessed by contrast echocardiography is

closely associated with ST segment elevation²⁵) after revascularization as well as with the TIMI flow grade.

Several studies have examined the implication of a persistently elevated ST-segment as a marker of impaired microvascular reperfusion for prognosis after acute myocardial infarction^{26,27}). Therefore, we also examined ST-resolution. In patients with acute myocardial infarction, post procedural ST-segment resolution $\geq 50\%$ is associated with greater myocardial salvage and better clinical outcome^{26,28,29}). In this study, ST-segment resolution $\geq 50\%$ was observed in a significantly higher percentage of patients in the DP-group, and left ventricular ejection fraction at discharge was significantly greater in the DP-group. However, no benefit in follow-up left ventricular ejection fraction was demonstrated. It is possible that distal protection reduces myocardial stunning. As long-term mortality could not be investigated, we used surrogate markers known to be associated with improved ventricular function and mortality.

MBG 3 was achieved significantly more often in the DP-group, and post procedural ST-segment resolution $\geq 50\%$ was lower in a significantly higher percentage of patients in the DP-group. Thus, there is a possibility that the distal protection with the GuardWire Plus as an adjunct to stenting during primary angioplasty improves microvascular circulation in the infarct area. Recently, studies involving a small number of patients have reported that a distal protection device reduces the incidence of the no reflow phenomenon and improves late outcome in patients with acute myocardial infarction. These findings were confirmed convincingly in the present study. A larger study on distal protection devices for acute myocardial infarction patients

should be conducted.

Study limitation

The present study represents a single-center experience with a limited number of nonrandomized patients designed as a retrospective case-matched study. The strategy for revascularization, especially the use of the GuardWire Plus, was based on the physician's decision. Therefore, this study was limited to thrombus-containing lesions in relatively large coronary arteries and did not include the entire acute myocardial infarction population.

In this study, the TIMI flow grade and MBG, ST-segment score and left ventricular ejection fraction were used as indicators of the coronary microvascular circulation status. However, these indicators are not directly relevant to the microvascular circulation status. The indicators directly relevant to the microvascular circulation state, such as direct measurement of the coronary flow reserve and assessment of myocardial perfusion, which can be

defined by contrast echocardiography or myocardial perfusion single-photon emission computed tomography, were not performed routinely. In addition, left ventricular ejection fraction was calculated by different modalities at discharge and follow up for clinical reasons. Moreover, pathological analysis of the aspirated debris was not performed. Finally, the small size of the sample is a major limitation and a larger study should be performed to confirm our findings.

CONCLUSIONS

Our data demonstrate that distal protection with the GuardWire Plus as an adjunct to stenting during primary angioplasty for acute myocardial infarction improves microvascular circulation as assessed by MBG, and ST resolution. These findings suggest that distal protection with the GuardWire Plus before stent implantation may minimize myocardial ischemic insult presumably by reducing the derangement of the coronary microvascular circulation.

要 約

急性心筋梗塞に対する GuardWire Plus™ を用いた末梢保護下の冠動脈形成術の有効性

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目 的: 急性心筋梗塞症例に対して GuardWire Plus™ を用いた末梢保護下のステント留置と、従来のバルーン拡張後でのステント留置とを比較検討する。

方 法: 対象は、当院で GuardWire Plus を用いて末梢保護下にステントを留置し、遠隔期造影が行われた急性心筋梗塞連続 38 例(末梢保護群)と末梢保護群に患者背景、病変背景の一致した非末梢保護下にステント留置を行った過去の症例を当院データベースから抽出した 38 例(非末梢保護群)を対照とした。2 群間において、経皮的冠動脈インターベンション終了時の Thrombolysis in Myocardial Infarction(TIMI) grade 3 獲得率および、myocardial blush grade(MBG) 3 獲得率、ST-resolution、血清クレアチンキナーゼ最高値、退院時、遠隔期の左室駆出率、急性期、遠隔期定量的冠動脈造影データについて比較検討した。

結 果: 末梢保護群と非末梢保護群間の患者背景に差は認められなかった。TIMI grade 3 獲得率(81.6% vs 57.9%)、MBG 3 獲得率(57.9% vs 30.6%)はともに末梢保護群において有意に高率であった(ともに $p < 0.05$)。ST-segment resolution $\geq 50\%$ は末梢保護群において有意に高率であった(68.4% vs 42.1%, $p < 0.05$)。クレアチンキナーゼ最高値は 2 群間に差は認められなかった。退院時の左室駆出率は末梢保護群において有意に高値であった($55.5 \pm 8.5\%$ vs $45.7 \pm 11.1\%$, $p < 0.05$)が、遠隔期の左室駆出率は 2 群間に差は認められなかった。

結 論: 急性心筋梗塞に対する GuardWire Plus を用いた末梢保護下のステント留置は、非末梢保護下のステント留置と比較して、TIMI grade、MBG、ST-resolution により評価された冠微小循環と

退院時の左室駆出率が良好であった。

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