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Effect of a distal protection device on epicardial blood flow and myocardial perfusion in primary percutaneous coronary intervention

ZHOU Bin-quan[†1], TAHK Seung-Jea[2]

([1]*Department of Cardiology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310016, China*)

([2]*Department of Cardiology, School of Medicine, Ajou University, Suwon 443749, Korea*)

[†]E-mail: zhoubq@hotmail.com

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Abstract: Objective: The beneficial effect of percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI) has been well established, but there is the problem of no-reflow phenomenon which is an adverse prognostic factor in primary PCI. In the present study the effect of a distal protection device (PercuSurge GuardWire; GW) on epicardial blood flow and myocardial perfusion was evaluated. Methods and Results: Patients with AMI were randomly divided into 2 groups, the GW and the control groups. The GW group included 52 patients with AMI who underwent primary PCI with GW protection and the control group included 60 patients who underwent primary PCI without GW protection. Epicardial blood flow in the infarct-related artery (IRA) and myocardial perfusion were evaluated according to the thrombolysis in myocardial infarction (TIMI) flow grade and the myocardial blush grade (MBG). We found TIMI score of 3 was obtained significantly more frequently in the GW group (96%) than in the control group (80%). The MBG score of 3 was obtained also significantly greater in the GW group (65%) than in the control group (33%). Conclusion: Primary PCI with GW protection can significantly improve epicardial blood flow and myocardial perfusion.

Key words: Acute myocardial infarction (AMI), Distal protection device, Percutaneous coronary intervention (PCI)
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INTRODUCTION

In acute myocardial infarction (AMI), percutaneous coronary intervention (PCI) is the most successful method for recanalizing the occluded artery. However, no-reflow phenomena can occur during ballon dilation and stent implantation, which is characterized by impaired myocardial perfusion despite reopening of the epicardial coronary artery. No-reflow phenomenon occurs in 10%~20% of patients with AMI and is predictive of poor prognosis (Morishima *et al*., 1995; 2000). It is difficult to treat no-reflow phenomena. Pharmaceutical means may not be highly effective in managing this phenomenon. The best treatment of distal embolization is to prevent its occurrence. Mechanical protection with distal protection devices (PercuSurge GuardWire; GW) has been used in recent years during coronary procedures. However, its effects on epicardial blood flow and myocardial perfusion in patients with AMI have not been well studied. In this study, we report our results in using this distal protection device in primary PCI. The effects of this device on epicardial blood flow and myocardial perfusion were evaluated.

PATIENTS AND METHODS

Patient population

Consecutive patients admitted for AMI between July 2003 to Nov. 2005 were eligible for this study if they were treated with primary PCI. Inclusion criteria of AMI for this study were (1) continuous chest pain that lasted >30 min, (2) within 12 h from the onset of chest pain, (3) ST-segment elevation ≥0.1 mV in 2 or more contiguous precordial ECG leads, (4) culprit leision with diameter stenosis ≥70% and thrombolysis in myocardial infarction (TIMI) flow grade ≤2. Ex-

clusion criteria were (1) patients undergoing thrombolytic therapy before PCI, (2) use of glycoprotein IIb/IIIa inhibitors before the procedure, (3) a culprit lesion in the left main coronary artery, (4) reference vessel diameter <3.0 mm, (5) Killip IV or cardiogenic shock. Eligible patients were randomized by means of sealed envelopes to the GW group in which patients were treated by primary stenting with GW protection or the control group in which patients were treated by primary stenting without GW protection. The study protocol was approved by the ethics committee of our institution, and patients gave written informed consent for participation.

Coronary interventional procedures

Each patient was administered 300 mg oral aspirin (before PCI and then 100 mg daily) and clopidogrel (300 mg loading dose, 75 mg daily) and brought to the catheter laboratory. Use of glycoprotein IIb/IIIa inhibitors was discouraged. During the procedure, unfractionated heparin was given intravenously to achieve an ACT (activated coagulation time) of 300 s or above; cardiac catheterization was performed by the femoral approach, using a 7F sheath and catheters. In the PCI with a distal protection device, it was first attempted to cross the lesions with the 0.014″ PercuSurge GuardWire. In unsuccessful cases, a conventional coronary guide wire was placed across the lesion, followed by another attempt of the GuardWire with the conventional wire in-situ. If the IRA (infarct-related artery) was the right coronary artery, then the occlusion balloon was positioned distal to the right coronary artery prior to the bifurcation. If IRA was LAD (left anterior descending), then the occlusion balloon was placed at the distal part of mid LAD. If the IRA was LCX (left circumflex), then the occlusion balloon was placed at the midportion of LCX. The distal elastomeric occlusion balloon was then inflated to 0.5 mm above the reference vessel diameter and further inflated if necessary until occlusion of flow was observed. Finally, the optimal size of the balloon was inflated up to 1.2~1.4 times of the RLD (reference luminal diameter) of the IRA or the balloon was just changed from a spherical to an elapsed shape. Then repeated dye injection was used to make sure the distal flow was already totally occluded. The export aspiration catheter was used to remove the thrombus and debris forward and backward several times before lesion dilatation. Ballon predilation and stent implantation were performed in standard manner under distal protection. All lesions were predilated. Export catheter was advanced again to aspirate embolic debris, protection balloon was then deflated and final result was evaluated.

Assessment of coronary flow and myocardial blush grade

TIMI flow grades in the IRA and myocardial blush grade (MBG) immediately after PCI were evaluated by two experienced investigators, who were otherwise blinded to all clinical data. MBG was assessed as reported (Gibson *et al*., 2000): MBG 0 was defined as no apparent tissue-level perfusion (no ground-glass appearance of blush or opacification of the myocardium) in the distribution of the culprit artery; MBG 1 indicates presence of myocardial blush but no clearance from the microvasculature (blush or a stain was present on the next injection); MBG 2 indicates that blush clears slowly (blush is strongly persistent and diminishes minimally or not at all during 3 cardiac cycles of the washout phase); and MBG 3 indicates that blush begins to clear during washout (blush is minimally persistent after 3 cardiac cycles of washout). The duration of cine filming was required to exceed 3 cardiac cycles in the washout phase to assess washout of the myocardial blush. Care was taken not to mistake filling of the venous system, such as the great cardiac vein.

Data analysis

Continuous data expressed as mean±*SD* were compared by the Student's *t* test, and categorical data were compared by the χ^2 test between groups. A P value of <0.05 was regarded as statistically significant.

RESULTS

Patient characteristics

From July 2003 to Nov. 2005, a total of 162 AMI patients were treated with primary PCI and 125 patients who fulfilled the enrollment criteria were randomized. Nine patients refused consent and 4 patients were excluded from analysis because of protocol violation. Finally there were 52 patients in the GW

group and 60 patients in the control group analyzed (Fig.1). Table 1 shows the baseline characteristics of the patients in the present study. There were no significant differences in terms of age, gender, coronary artery disease risk factors, and left heart function between the 2 groups. Use of heparin, glyceryl trinitrate (GTN), verapamil and adenosine were similar (Table 2). No glycoprotein IIb/IIIa inhibitor was used in both groups. All coronary angioplasty procedures were successful. Table 3 shows the angiographic and procedural findings. There were no significant differences with regard to the IRA, time from onset to PCI, multivessel disease, culprit lumen diameter, or reference lumen diameter between the 2 groups.

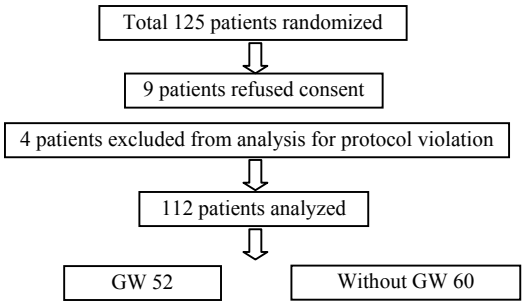

Fig.1 Enrolment flow chart of the study

Table 1 Baseline clinical characteristics of the patients

	GW group (*n*=52)	Control group (*n*=60)	*P*
Age (years)	55±14	57±15	>0.05
Male	32 (62%)	40 (67%)	>0.05
Anterior MI (%)	28 (54%)	36 (60%)	>0.05
Hypertension	19 (37%)	21 (35%)	>0.05
Diabetes mellitus	12 (23%)	13 (22%)	>0.05
Smoking	35 (67%)	36 (60%)	>0.05
Total cholesterol (mg/dl)	180±35	192±37	>0.05
Triglyceride (mg/dl)	138±100	135±92	>0.05
LDL-chlesterol (mg/dl)	112±35	124±36	>0.05
HDL-cholesterol (mg/dl)	42±11	40±8	>0.05
LVEF (%)	53±10	50±9	>0.05

Plus-minus values are means±*SE*. LDL: Low density lipoprotein; HDL: High density lipoprotein; LVEF: Left ventricular ejection fraction

Table 2 Adjunctive drug therapy

	GW group (*n*=52)	Control group (*n*=60)	*P*
Heparin dose (IU)	7840±898	7600±502	>0.05
GTN use	94%	95%	>0.05
Verapamil use	9.6%	9.3%	>0.05
Adenosine use	31%	30%	>0.05

Plus-minus values are means±*SE*

Table 3 Angiographic and procedural findings

	GW group (*n*=52)	Control group (*n*=60)	*P*
Time from onset to PCI (min)	310±145	315±176	>0.05
Pre-stent			
Minimal lumen diameter (mm)	0.19±0.26	0.20±0.41	>0.05
Diameter stenosis (%)	95±8	94±12	>0.05
Stent diameter (mm)	3.3±0.5	3.2±0.4	>0.05
Reference diameter (mm)	3.4±0.4	3.3±0.5	>0.05
IRA studied			>0.05
LAD	28 (54%)	29 (48%)	
LCX	5 (10%)	6 (10%)	
RCA	19 (36%)	25 (42%)	

Plus-minus values are means±*SE*

Epicardial blood flow and myocardial perfusion

However, the final TIMI 3 flow and the myocardial blush grades of the IRA were significantly higher in group 1 than in group 2. TIMI 3 flow was achieved in all but two patients, one developed no-reflow phenomena, one achieved final TIMI 2 flow from an initial TIMI 0 flow (Table 4). There was no procedure-related major adverse clinical event (MACE) during hospitalization. There were no device-related complications such as perforation or elastomeric balloon-induced local dissection.

Table 4 Post-stent angiographic TIMI score and TBG

	GW group (*n*=52)	Control group (*n*=60)	*P*
TIMI flow			<0.05
TIMI 0/1	1	4	
TIMI 2	1	8	
TIMI 3	50 (96%)	48 (80%)	
MBG			<0.05
MBG 0/1	3	18	
MBG 2	15	22	
MBG 3	34 (65%)	20 (33%)	

DISCUSSION

Microembolization during angioplasty has been a well-recognized phenomenon in daily practice. The benefit of primary PCI is limited by a 5% to 20% incidence of no-reflow. Although the cause of

no-reflow phenomenon has not been clarified, microvascular obstruction is frequently implicated as the underlying cause. This may be due to microvascular plugging, spasm or edema, or due to platelet aggregation (Topol and Yadav, 2000). It is difficult to treat no-reflow phenomena. Drugs such as adenosine, nitrates, verapamil may help in relieving microvascular spasm. When particulate debris from atherosclerotic lesions passes into distal capillary beds, pharmaceutical means may not be effective in clearing such debris. Adjunctive distal protection will likely prove beneficial. Mechanical devices have recently emerged as an attractive tool to prevent both embolization in the microvasculature and no-reflow. The occlusive ballon type distal protection device (PercuSurge GuardWire; GW) has been shown to be able to reduce major adverse events during percutaneous intervention of saphenous vein grafts when compared with stenting over a conventional angioplasty guide wire (Baim *et al*., 2002). In the present study, our results indicate that the PercuSurge GuardWire system is safe and feasible in patients with AMI, and is better at restoring epicardial coronary flow. The final TIMI flow grade after primary PCI was significantly higher in the GW group than in the control group. TIMI 3 flow was achieved in most patients (96%).

The mechanism of the GW device for preventing no-reflow phenomenon is to prevent the distal embolization during PCI. There were still 2 cases with TIMI 0/1, which suggested myocardial or/and microvascular damage had already developed at the time of reperfusion. This device could not prevent all no-reflow phenomenon completely.

The aim of PCI in AMI is the reperfusion of involved myocardium as well as restoration of the epicardial coronary flow. The MBG after PCI is a simple and reliable parameter of myocardial perfusion, and is a predictor of long-term prognosis (van't Hof *et al*., 1998; Stone *et al*., 2002; Haager *et al*., 2003). In our study, the MBG score was significantly higher in the GW group than in the control group, which suggested that successful prevention of distal embolization with this device would translate into higher rates of successful myocardial reperfusion. Primary PCI with GW protection can achieve better myocardial perfusion than conventional treatment.

Our study has some limitations. It was a relatively small study. However, we believe it can still evaluate to some degree the effects of the GW device in primary PCI. The present findings may not apply to patients with culprit vessel diameters <3.0 mm or after thrombolytic therapy.

In our study, none of the patients received glycoprotein IIb/IIIa receptor blockade during the procedure, which might affect microvascular integrity and clinical prognosis and therefore we could evaluate the effect of the distal protection device more clearly. But use of glycoprotein IIb/IIIa inhibition has been contemporary management of patients with AMI. It is possible that in the presence of glycoprotein IIb/IIIa inhibition, the results of this study may not be reproduced.

The long-term effects of the distal protection device are still in controversy. The enhanced myocardial efficacy and recovery by aspiration of liberated debris (EMERALD) trial failed to show the effectiveness of the distal protection device in patients with AMI (Stone *et al*., 2005). They showed that the use of the distal protection device was not associated with reduced infarct size or improved clinical outcomes. However, there are some differences in the characteristics of enrolled patients between their report and our study. One is that we included patients who were within 12 h of the onset of AMI, whereas the EMERALD trial included those within 6 h of the onset of AMI. Nakamura *et al*.(2004) reported the benefit of distal protection during PCI for anterior MI patients within 24 h of the onset of AMI. Furthermore, in the EMERALD trial, 83% of enrolled patients received glycoprotein IIb/IIIa inhibitor periprocedurally. Using glycoprotein IIb/IIIa receptor blockade might have reduced the chances of additional improvement through distal protection in the EMERALD trial.

Mizote *et al*.(2005) revealed that distal protection reduced microcirculation damage and left ventricular dysfunction in patients with AMI who had ruptured plaque. Yoon *et al*.(2006) also found that distal protection may effectively preserve the microvascular integrity of the myocardium during primary PCI in AMI patients. So, it requires further randomized and large-scale studies to see if successful prevention of distal embolization with this device would translate into better long-term clinical outcomes, when compared with traditional unprotected angioplasty.

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