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Benefits of stenting with PercuSurge GuardWire Plus™ System for myocardial salvage in acute myocardial infarction patients as observed from myocardial SPECT

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Subjects were 56 patients with successful reperfusion from percutaneous coronary intervention performed for acute myocardial infarction, and patients were divided into the stenting with PercuSurge GuardWire Plus™ system group or PS group (17 patients) and the conventional stenting group or CS group (39 patients) for a comparative study. We calculated for total defect score (TDS) of perfusion SPECT (^{201}Tl or ^{99m}Tc-MIBI) and ^{123}I-BMIPP dual isotope imaging at rest. The difference between TDS of perfusion SPECT and ^{123}I-BMIPP was classified a mismatch. Results of myocardial SPECT showed the mismatch in TDS was significantly higher in the PS group ($p < 0.05$). The rate of change in left ventricular end diastolic volume from the acute to chronic phase was significantly lower in the PS group ($p < 0.05$). Myocardial SPECT showed PS group to have better results for myocardial salvage than CS group, as well as contributing to inhibition of left ventricular remodeling.

KEY WORDS: embolic protection device, no-reflow, myocardial SPECT, acute myocardial infarction

I. Introduction

Percutaneous coronary intervention (PCI) has in recent years become the treatment of first choice for revascularization in acute myocardial infarction (AMI). Its widespread use has led to substantial improvement of AMI patient prognoses. Occurrence of no-reflow phenomenon, however, is known to accompany the PCI procedure, posing a major issue for myocardial salvage in patients with AMI.[1)] One mechanism of the no-reflow phenomenon is distal coronary embolization by thrombus or plaque.[2)] Embolic protection devices have been developed to prevent this. The PercuSurge GuardWire Plus™ system (PercuSurge) (Medtronic Co., Ltd.), in which a balloon occludes distal flow and thrombus and plaque are aspirated by a thrombectomy catheter during the PCI procedure, has been introduced for use in Japan. A small study has already reported achievement of better results in reperfusion assessed by myocardial blush grade when PCI for AMI was performed with PercuSurge compared to conventional PCI with stenting after plain old balloon angioplasty (POBA).[3)]

However, there are few reports of studies on the benefits of PercuSurge for myocardial reperfusion using assessments by myocardial single photon emission tomography (SPECT).

In the present study, we used myocardial SPECT assessments to compare the benefits of stenting with PercuSurge with that of stent placement following POBA for myocardial salvage in patients with AMI.

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II. Subjects and Methods

1. Subjects

Of first acute ST-segment elevation myocardial infarction 148 patients who underwent PCI at our institution from January 2002 to January 2004 within 12 hours of onset to achieve thrombosis in myocardial infarction (TIMI) grade 3 flow[4)] (excluding patients with left main lesions, complicated by cardiogenic shock, or undergoing treatment by a thrombectomy device alone), 56 patients meeting the following 5 criteria were the subjects of this study.

(1) Were able to undergo myocardial SPECT examination within 14 days following the PCI procedure. (2) Target vessel in the left anterior descending or right coronary artery. (3) TIMI flow grade of 0 or 1 in coronary angiograms prior to the procedure. (4) Collateral circulation of Rentrop classification[5)] grade 0 or 1 in coronary angiograms prior to the procedure. (5) Reference vessel diameter of 3 mm or more. The patients were classified into two groups, the PercuSurge or PS group (17 patients, 17 lesions) undergoing stent placement while using PercuSurge from January 2003 to January 2004, and the conventional stenting or CS group (39 patients, 39 lesions) undergoing conventional stent implantation after POBA from January 2002 to January 2003, for a retrospective study comparing clinical outcomes.

2. Diagnosis of AMI and PCI strategy

Diagnosis of AMI was defined as chest pains lasting for

30 minutes or more, ST-segment elevation on the electrocardiogram, and elevation of myocardial enzymes.

For coronary angioplasty, a 6 Fr or 7 Fr sheath was inserted into the radial or femoral artery, heparin 5,000 U was administered intra-arterially, and coronary angiography (CAG) was performed. angiography of the contralateral coronary artery was performed first, and after assessment of collateral circulation by the Rentrop classification, a guiding catheter was used to perform angiography of the affected coronary artery for assessment of TIMI flow grade. In the PS group, after the guide wire was crossed over the lesion, the Thrombuster thrombectomy catheter (Kaneka Co., Ltd.) was inserted for manual aspiration of 20–60 ml of blood. Following removal of the thrombectomy catheter, prior to POBA the GuardWire Plus™ system was inserted just distally to the lesion site and the occlusion balloon was inflated 3 to 5 mm in size according to the vessel diameter. After inflation, and POBA was performed. Following POBA, thrombectomy was performed with the occlusion balloon in its inflated state. After completion of aspiration, the occlusion balloon was removed.

Stenting was performed in the same manner with the occlusion balloon inflated.

After stenting, thrombectomy was performed followed by removal of the occlusion balloon.

In the CS group, after the guide wire was advanced over the lesion, stenting was performed after POBA without the use of a thrombectomy or embolic protection device. The selection of type, size, and length of stent used was determined by the operator.

In principle, antiplatelets (aspirin 162 mg/day, ticlopidine 200 mg/day) were administered orally after the procedure for at least 2 weeks or more.

3. Quantitative assessments of CAG and LVG

Left ventricular angiograms (LVG) was obtained at a 30° right anterior oblique projection with contrast medium, and was performed at the acute phase (at the end of PCI) and chronic phase (mean 4.0 ± 2.1 months after PCI procedure) to calculate left ventricular ejection fraction (LVEF) and left ventricular end diastolic volume (LVEDV) and regional wall motion (RWM) for assessment of left ventricular function.

CCIP-310 (Cathex Co., Ltd.) was used for quantitative assessments of CAG and LVG.

The difference in LVEF and RWM from acute to chronic phase were yielded, and ratio of change in LVEDV (%LVEDV) from the acute to chronic phase was yielded by %LVEDV = LVEDV (chronic phase)/LVEDV (acute phase) × 100 – 100 (%).

4. Myocardial SPECT imaging and image analysis

Myocardial perfusion SPECT using thallium-201 (^{201}Tl) or technetium-99m-sestamibi (^{99m}Tc-MIBI) was conducted at a mean 9.3 ± 4.7 days after the PCI procedure. Myocardial fatty acid metabolic SPECT using iodine-123 (15-p-iodophenyl)-3 (R,S)-methylpentadecanoic acid (^{123}I-BMIPP) was conducted at a mean 8.3 ± 3.1 days following the PCI procedure.

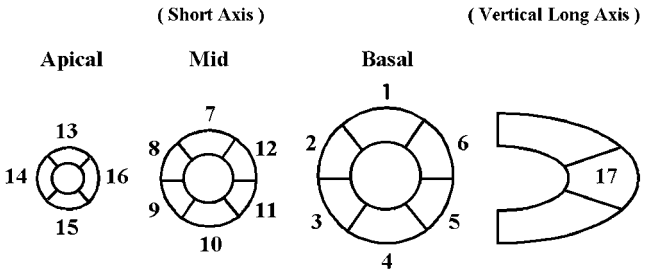

Fig. 1 The left ventricular myocardium was divided into 17 segments, and calculated for total defect score (TDS) using a 5 stage evaluation system (0: normal, 1: slightly reduced, 2: moderately reduced, 3: severely reduced, 4: defect).

Both examinations were performed after fasting and rest of 2 hours or more. Images were obtained 5 minutes after intravenous injection of 111 MBq of ^{201}Tl or 45 minutes after intravenous injection of 740 MBq of ^{99m}Tc-MIBI. Images were obtained 20 minutes after intravenous injection of 111 MBq of ^{123}I-BMIPP. The gamma camera was a triple detector PRISM-IRIX (HP Co., Ltd.) with a low-energy all-purpose collimator, using a 64 × 64 matrix, step & shoot mode, 5° step, 37.5 sec/step, and proximal activation for a 360 °acquisition. Workstation Odyssey fx820 (HP Co., Ltd.) was used for SPECT image reconstruction. Using filtered back projection, 6 mm thick slices of left ventricular short axis, vertical long axis, and horizontal long axis tomograms were generated and displayed at a 40% cut off level.

5. Semi-quantitative assessment of myocardial SPECT

From short axis and vertical long axis tomograms, the left ventricular myocardium was divided into 17 segments (Fig. 1).

Two physicians specializing in nuclear cardiology visually scored each segment into 5 grade (0: normal, 1: slightly reduced uptake, 2: moderately reduced uptake, 3: severely reduced uptake, 4: defect of uptake).

The sum total of scores was expressed as total defect score (TDS), and difference between TDS of the perfusion agent and fatty acid agent (fatty acid agent - perfusion agent) was classified a mismatch. Scoring of myocardial SPECT was undertaken by assessments blinded to the PS and CS groups.

6. Statistical analysis

Values were expressed by actual measurements, ratio (%) and mean ± standard deviation. Continuous variables were compared by the t test, and group comparisons by the χ^2-test.

Table 1. Patient characteristics

	PS group (n=17)	CS group (n=39)	p value
Age (years)	64 ± 11	66 ± 12	n.s
Male gender (%)	13 (76%)	24 (62%)	n.s
Risk factors			
Diabetes mellitus (%)	8 (47%)	16 (41%)	n.s
Hypertension (%)	11 (65%)	22 (56%)	n.s
Hyperlipidemia (%)	7 (41%)	16 (41%)	n.s
Smorking (%)	13 (76%)	24 (62%)	n.s
Elapsed time (hours)	5.6 ± 4.1	5.9 ± 3.9	n.s
Medications			
ACE or ARB (%)	13 (76%)	29 (74%)	n.s
Calcium blockers (%)	7 (41%)	14 (36%)	n.s
β-blockers (%)	2 (12%)	3 (8%)	n.s

ACE: angiotensin converting enzyme inhibitor
ARB: angiotensin receptor blockers

Table 2. Lesion characteristics

	PS group (n=17)	CS group (n=39)	p value
Reference diameter (mm)	3.2 ± 0.7	3.2 ± 0.5	n.s
Target vessel			
LAD (%)	10 (59%)	22 (56%)	n.s
RCA (%)	7 (41%)	17 (44%)	n.s
Extent of CAD			
1 vessel disease (%)	10 (59%)	24 (61%)	n.s
2 vessel disease (%)	4 (23%)	9 (23%)	n.s
3 vessel disease (%)	3 (18%)	6 (16%)	n.s
TIMI flow grade at base line CAG			
TIMI 0 (%)	11 (65%)	23 (59%)	n.s
TIMI 1 (%)	6 (35%)	16 (41%)	n.s
Rentrop classification at base line CAG			
Grade 0 (%)	11 (65%)	21 (53%)	n.s
Grade 1 (%)	6 (35%)	18 (47%)	n.s

LAD: left anterior descending artery
RCA: right coronary artery
CAG: coronary angiography
CAD: coronary artery disease
TIMI: thrombolysis in myocardial infarction

III. Results

1. Patient background

No differences existed between the groups in age, gender, coronary risk factors, interval from onset to presenting at the hospital, and agents used after the procedure (Table 1).

2. Lesion background

No differences existed between the groups in reference vessel diameter, target vessel, number of diseased vessels, TIMI flow grade or Rentrop classification of collateral circulation in pre-procedure CAG (Table 2).

Table 3. Strategy for stenting

	PS group (n=17)	CS group (n=39)	p value
Stent size (mm)	3.3 ± 0.2	3.2 ± 0.5	n.s
Stent length (mm)	17.4 ± 4.4	18.2 ± 5.1	n.s
Max inf-pressure (atm)	13.2 ± 3.1	12.4 ± 3.2	n.s

Max inf-pressure: max inflation pressure

Table 4. Maximum CK/CK-MB

	PS group (n=17)	CS group (n=39)	p value
CK (IU/l)	3,109 ± 1,714	3,996 ± 1,976	<0.05
CK-MB (IU/l)	245 ± 127	330 ± 139	<0.05

CK: creatininphosphokinase

Table 5. Comparison of total defect score

	PS group (n=17)	CS group (n=39)	p value
^{201}Tl or ^{99m}Tc-MIBI (point)	5.7 ± 4.6	10.6 ± 8.1	<0.05
^{123}I-BMIPP (point)	16.3 ± 7.7	16.7 ± 7.3	n.s
Mismatch (point)	10.8 ± 6.7	5.7 ± 5.3	<0.05

^{201}Tl: thallium-201
^{99m}Tc-MIBI: technetium-99m-sestamibi
^{123}I-BMIPP: iodine-123 (15-p-iodophenyl)-3(R,S)-methylpentadecanoic acid

3. Procedural background

No differences existed in stent diameter, stent length, or maximum inflation pressure (Table 3).

4. Comparison of maximum CK and CK-MB after PCI

Maximum CK/CK-MB after the procedure was significantly lower in the PS group with CK (PS: 3,109±1,714 vs. CS: 3,996 ± 1,976 IU/l, p<0.05) and CK-MB (PS: 245±127 vs. CS: 330 ± 139 IU/l, p<0.05) (Table 4).

5. Comparisons of TDS and mismatch of TDS

TDS in ^{201}Tl or ^{99m}Tc-MIBI perfusion scintigrams (PS: 5.7 ± 4.6 vs. CS: 10.6 ± 8.1 points, p<0.05) were significantly lower in the PS group. No significant difference existed between the two groups in ^{123}I-BMIPP TDS (PS: 16.3 ± 7.7 vs. CS: 16.7 ± 7.3 points). The PS group had a significantly higher mismatch in TDS (PS: 10.8 ± 6.7 vs. CS: 5.7 ± 5.3 points, p<0.05) (Table 5).

6. Changes in LVEF and RWM, and ratio of change in LVEDV

Although the PS group showed a larger difference in LVEF from acute phase to the chronic phase (PS: 7.3 ± 9.6 vs. CS: 3.9 ± 11.6 %), there was no significant difference between the two groups (Fig. 2). However, the difference in RWM from acute phase to chronic phase (PS: 0.38 ± 0.37 vs. CS: 0.10 ± 0.37 SD/chord, p<0.05) was significantly greater in the

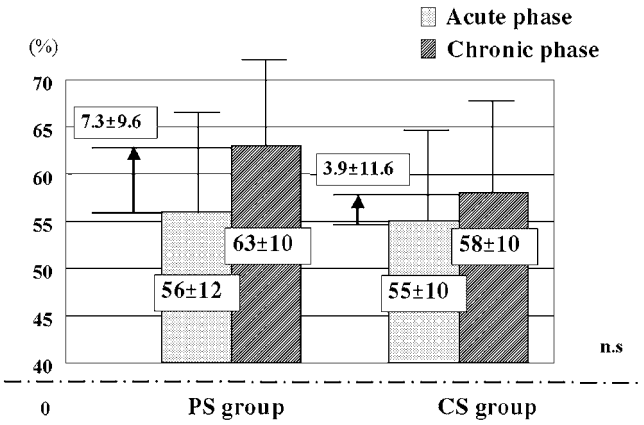

Fig. 2 The difference of ejection fraction between chronic phase and acute phase.

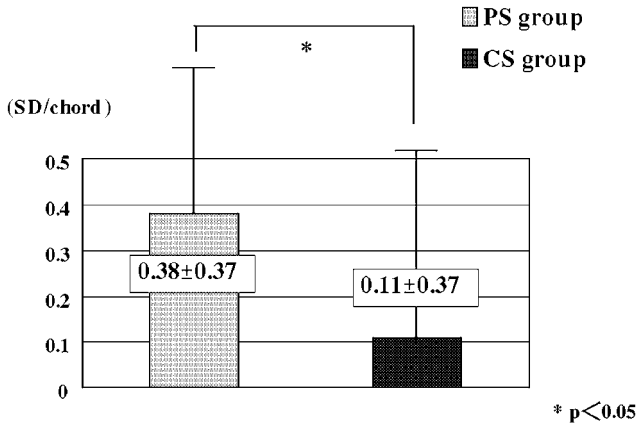

Fig. 4 The difference of regional wall motion (SD/chord) between chronic phase and acute phase.

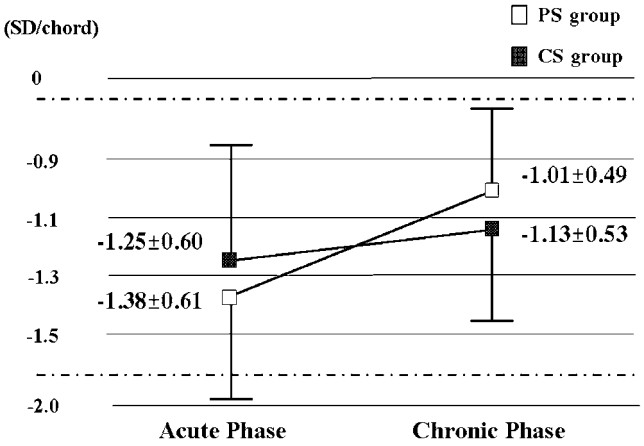

Fig. 3 Changes of regional wall motion from acute phase to chronic phase.

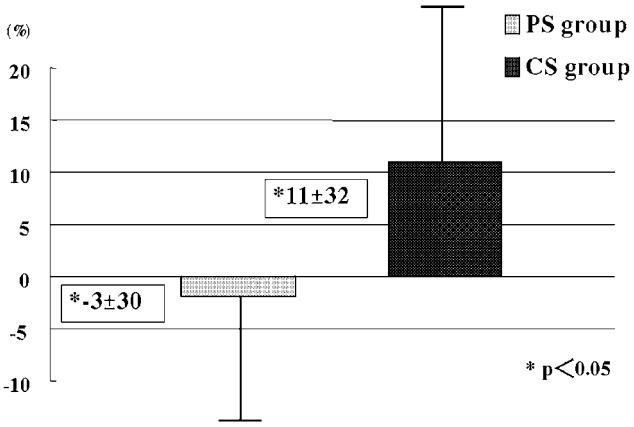

Fig. 5 Comparison of %LVEDV from acute to chronic between PS group and CS group.

PS group (Fig. 3, 4).

The PS group also had significantly lower % LVEDV from the acute to chronic phase (PS: –3 ± 30 vs. CS: 11 ± 32 %, p<0.05) (Fig. 5).

IV. Discussion

1. Benefits of PercuSurge for myocardial salvage

Many studies have demonstrated the benefits of stenting as a revascularization therapy for AMI.[6-8]

However, despite improvement of stenosis by stent implantation, there are cases where satisfactory improvement of blood flow is not achieved due to occurrence of the no-reflow phenomenon.[9, 10] In addition, it has been reported that assessment of reperfusion by TIMI flow grade is not sufficient. Although 80 to 90% of patients undergoing PCI for AMI achieved TIMI grade 3 flow in final angiography, only 20-30% achieved normal reperfusion on the myocardial level.[11, 12]

From such considerations, reperfusion assessments of angiographic findings at present use the myocardial blush grade[13] or TIMI myocardial perfusion grade (TMPG)[14]. The first study to verify that patients are not achieving reperfusion on the myocardial level despite achievement of TIMI 3 angiographically used the myocardial scintigram.[15] The myocardial scintigram, along with the myocardial contrast echocardiogram, is known to be a very useful way to assess myocardial tissue disorders following reperfusion.

In this study, myocardial SPECT was used to assess myocardial salvage using the mismatch in uptake between a fatty acid agent and perfusion agent in the post-procedure subacute phase. This mismatch phenomenon is noted distinctly in cases of myocardial infarction in the acute phase following reperfusion therapy, with the segment of mismatch known to reflect the region of myocardial salvage achieved through reperfusion therapy.[16, 17]

In addition, compared to other methods of evaluation, one of the benefits of myocardial SPECT is that the myocardial risk area at the onset of infarction can be assumed indirectly from the defect region of fatty acid agents in the subacute period.[18]

In this result, there was no difference in TDS of the subacute fatty acid agent between the two groups, indicating no significant difference between the two groups in acute risk area. On the other hand, the TDS of perfusion agents was significantly lower in the PS group, and the mismatch in TDS of the fatty acid agent and perfusion agent was also significantly higher in the PS group. This suggests that stenting with adjunctive use of the PercuSurge achieved better reperfusion on the myocardial tissue level than conventional stenting.

The mechanism in the occurrence of no-reflow phenomenon which results in reperfusion disorders is mainly attributed to microvascular embolization from platelets and neutrophils, the obstruction of capillary vessels by myocardial cell swelling, and changes in blood viscosity.[19] In particular, distal embolization by platelet thrombi and plaque constituents such as foam cells, activated leukocytes (especially neutrophils)[20] and macrophages accompanying plaque rupture are major factors contributing to the no-reflow phenomenon.[9, 21]

PercuSurge not only prevents thrombus, but also plaque fragmented by the mechanical stress of balloon inflation, from flowing to the distal coronary arteries.

Our investigation was conducted on patients with successful reperfusion. Although the CS group also achieved TIMI grade 3 flow angiographically, it is surmised that embolic protection led to greater reduction of reperfusion disorders on the myocardial level in the PS group.

2. Effects on chronic RWM and LVEDV

The region of mismatch in uptake between the fatty acid agent and perfusion agent in the subacute phase following the procedure has been acknowledged to show serial improvement of wall motion.[22, 23]

As with such previous reports, our study also saw a significant improvement of RWM in the chronic phase in the PS group which had a high degree of TDS mismatch.

It has been reported that LVEDV, as well as LVEF, is an independent predictor for prognoses of AMI patients.[24]

In this study, no significant difference was seen in change of LVEF in the PS group, but increase of LVEDV from the acute to chronic phase was significantly inhibited in the PS group compared to the CS group.

Ito, et al, in contrast echocardiographic assessment of AMI patients, reported that echo assessed no-reflow was the single predictor of left ventricular dilation (increase of 20% or more of left ventricular end diastolic volume) at 1 month.[25]

No significant differences were seen between the two groups in acute risk area assessed by the fatty acid agent in the subacute phase, elapsed time, collateral circulation, or drugs used, suggesting that inhibition of no-reflow by the PercuSurge may be associated with improvement of left ventricular dilation in the PS group.

It has been reported that reduction in size of the infarct and promotion of the healing process in the infarct bed through maintenance of distal coronary flow by inhibition of no-reflow suppress left ventricular remodeling and are associated with the improvement of prognoses.[26, 27]

We hope that by future long term follow up studies, the use of PercuSurge will improve the manifestation and prognoses of cardiac failure in AMI patients.

V. Study Limitations

This study was a non-randomized retrospective test in which the period of treatment for the two groups was not identical. In addition, indication for use of PercuSurge in the procedure was left to the discretion of the operator.

Henceforth, study by a larger prospective multi-center trial is believed necessary.

VI. Conclusion

From myocardial SPECT assessments, stenting using the PercuSurge GuardWire Plus™ system achieved better myocardial salvage results in AMI patients than conventional stenting. It also improved regional wall motion from the acute to chronic period and inhibited left ventricular remodeling.

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