Balloon-Based Distal Protection Device Improves the Recovery of Left Ventricular Function after Primary Coronary Angioplasty

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ABSTRACT

Background and Objectives: Despite the high success rate of primary angioplasty in cases of acute myocardial infarction (AMI), myocardial reperfusion can frequently be compromised, mainly due to distal embolization, which can be effectively prevented with the use of distal protection devices. The goal of this study was to see whether PercuSurge®, a balloon-based distal protection device, could improve myocardial reperfusion and late clinical outcomes after primary coronary angioplasty.

Subjects and Methods: Between April 2002 and July 2003, 29 patients with AMI, within 12 hours of the onset of symptoms, were scheduled to undergo primary angioplasty using PercuSurge® (PS group). Thirty patients were selected as a control group by matching the 5 clinical and angiographic variables; the clinical status and coronary angiograms were also prospectively reviewed and analyzed.

Results: There were no significant differences in the baseline clinical and angiographic characteristics, including the left ventricular ejection fraction (LVEF) between two groups. The procedures were successful, without complications, in all patients from both groups. However, the PS group was associated with a significantly higher incidence of myocardial blush score of 3 (PS 58%, control 30%, p=0.001) and early ST-segment elevation resolution (PS 76%, control 47%, p=0.02) compared to the control group. The PS group also showed a greater LVEF at 60 days after the procedure (PS 51 ± 5%, control 46 ± 8%, p=0.007). There was no significant difference in the incidences of death or myocardial infarction between the two groups during the follow-up period.

Conclusion: The use of the PercuSurge® was found to be safe and feasible during primary angioplasty, and this system also improved the recovery of the left ventricular function as well as myocardial reperfusion following primary coronary angioplasty.

KEY WORDS: Angioplasty; Transluminal; Percutaneous coronary; Myocardial infarction; Thromboembolism; Balloon occlusion.
the PercuSurge® Guard-Wire system may help the LV functional recovery by improving the myocardial tissue reperfusion during primary angioplasty in AMI patients.

Subjects and Methods

Patients population
This study was designed as a single center prospective non-randomized comparative study. The patients who presented with acute anterior chest pain of more than 30 minutes duration and ST-segment elevation >0.1 mV in at least 2 contiguous leads on the 12-lead electrocardiograms (ECGs), and who had undergone primary PCI within 12 hours of the onset of symptoms were included. The infarct-related lesion had to be in the mid or proximal segment of the major artery and the reference diameter more than 2.5 mm to accommodate the Guard-Wire balloon. The exclusion criteria were: unprotected left main coronary disease >50%, or after thrombolytic therapy, cardiogenic shock, a known allergy to aspirin, clopidogrel, or heparin, current neutropenia, thrombocytopenia or a history of serum creatinine >2.5 mg/dl.

Primary PCI was performed with distal protection using the PercuSurge® Guard-Wire system in PercuSurge® group (PS group). The matched control group was selected from patients who had undergone primary PCI without a distal protection device. The following parameters were matched; 1) the location of infarct-related artery (IRA), 2) pre-PCI TIMI flow grade, 3) gender, 4) age and 5) pain-to-balloon time.

Data collection
We reviewed the medical records of the patients to identify their clinical characteristics. The 12-lead ECGs were analyzed both before and at the end of the procedure by a blinded observer. The total STE was measured manually from the leads exploring the infarct area, as previously described.12) The early resolution of the STE after PCI was defined as >50% reduction in the initial value on the ECG 90 minutes after the procedure. Echocardiography was performed both before and 60 days after PCI, with the echocardiograms analyzed by 2 observers blinded to the clinical and angiographic data. Left ventricular wall motion score index (WMSI) and left ventricular ejection fraction (LVEF) were calculated using Simpson’s methods. The creatine kinase MB fraction (CK-MB) was measured every 8 hours during the first day, and then daily thereafter until discharge.

Primary PCI with PercuSurge®
The PercuSurge® Guard-Wire system is a balloon-based distal protection system, composed of three separate elements: the Guard-Wire®, the Micro-seal® inflation adaptor and the Export® aspiration catheter (EAC). The Guard-Wire® is a temporary occlusive device, consisting of a hollow 0.014 inch nitinol hypo-tube, with a distal, low profile, elastomeric occlusion balloon. The EAC is a 135 cm long 4 Fr catheter, with a dual lumen, which allows the aspiration and removal of particulate debris.

All patients received 100 IU/kg of unfractionated heparin, 300 mg of chewable aspirin and 300 mg of clopidogrel. Intra-aortic counter-pulsation was performed in the case of hemodynamic instability. The activated clotting time was maintained at more than 300 seconds during the procedure. After the diagnostic coronary angiography, an 8 Fr guiding catheter was to engage into the infarct-related artery. An initial attempt to cross the culprit lesion was performed with the Guard-Wire, but when this was not possible, the operator used a conventional wire to help the Guard-Wire to cross the lesion. When required, predilatation with a small-diameter balloon was performed before placement of the Guard-Wire. Once in place, the Guard-Wire was about 1-2 cm distal of the target lesion, with the position checked using fluoroscopy. The balloon was then inflated and proper placement of the Guard-Wire confirmed by the lack of distal antegrade flow. The inflation of the distal occluding balloon was maintained while the EAC was connected to a 20 ml suction syringe for manual aspiration, followed by initial balloon predilatation and the subsequent aspiration of debris. Following aspiration, the aspirate was rinsed over a 40 mm nylon cell strainer, with the protective distal balloon then inflated again; stenting was performed only in the IRA in all patients, followed by further aspiration at the conclusion of the stenting procedure. Finally, the balloon was deflated in order to visualize the angiographic results. If additional intervention was required, this was always performed under distal protection.

Glycoprotein Ill/IIa inhibitors were given at the operator’s discretion. Aspirin, 100 mg per day, was given after the PCI, as was clopidogrel, 75 mg, once a day. The When the post-procedural diameter stenosis of the infarct artery was <20%, with adequate restoration of coronary patency (TIMI flow grade 3), the PCI was considered successful.

Angiographic analysis
The angiograms were analyzed separately by 2 experienced observers blinded to both the patient groups and clinical data. The basal TIMI flow was evaluated on the first angiogram, with the post-procedure TIMI flow and myocardial blush score graded on those taken immediately after PCI. In each patient, the best projection was chosen to assess the myocardial region of the infarct-related coronary artery. Quantitative coronary angiography parameters, TIMI flow grade, corrected TIMI frame count (cTFC) and myocardial blush were measured, as previously described.40-18 With regard to the cTFC, the
number of frames was multiplied by 30, and then divided by 12.5, to report a cine frame count in accordance with the standard methods. Myocardial blush was graded according to the dye density score proposed by van’t Hof et al: grade 0 to 1 was minimal to no myocardial blush or contrast density, grade 2 was moderate blush, and grade 3 was normal blush in comparison to the dye density in the uninjured area. In the case of any disagreement, a third observer evaluated the angiographic images, with consensus obtained by discussion. Intra-observer agreement was measured by having an observer repeat the assessment on 20 angiographic images (presented in random order) after one week. The inter-observer agreement was measured by comparing the assessment of the 20 angiographic images by two observers. The kappa values for intra-observer agreement of the TIMI flow grade, cTFC and myocardial blush score were 1.00, 0.90 and 0.78, respectively. In addition, the kappa values for grade, cTFC and myocardial blush score were 1.00, 0.90 and 0.74, respectively.

Study End-points

The primary end point was the change in the LVEF at 60 days compared to that prior to discharge. The secondary end-points were the feasibility and safety of the adjunctive use of the PercuSurge® during primary PCI, 90 minutes resolution of the STE, the myocardial blush score and cTFC.

Statistical analysis

Data are expressed as the mean ± standard deviation for continuous variables, and as the absolute and relative frequencies for categorical variables. An unpaired Student’s t test was used to compare the continuous variables between groups, with a paired Student’s t test used to assess changes between the baseline and the follow-up data obtained at 60 days. Categorical variables were compared using the Chi-squared test. Predictors of the occurrence of STE resolution and of a myocardial blush score of 3 were identified by a univariate analysis. Probability values <0.05 were considered statistically significant.

Results

Matched comparison of baseline characteristics and procedural results

The PS and control groups included 29 and 30 patients, respectively. The baseline clinical and angiographic characteristics of the 2 groups are shown in Table 1. There were no significant differences between the two groups with regard to age, gender, peak CK-MB, culprit location, incidence of coronary risk factors, TIMI flow grade before reperfusion and pain to balloon time, as well as the mean baseline LVEF and WMSI values on admission. Intravenous Abciximab was used more frequently in the control group, although this did not reach statistical significance (p=NS). The procedural characteristics are presented in Table 2. There were no significant differences between the two groups in terms of the diameter of stenosis, reference vessel diameter, minimal luminal diameter and TIMI flow 3 after PCI. There were 3 cases of incomplete procedure in the control group, resulting in residual stenosis and low-grade TIMI flow, but these were resolved by successful PCI after a few days. After PCI; however, the frequency of a myocardial blush score of 3, as well as the STe resolution were significant.

Table 1. Clinical and angiographic characteristics on admission of the patients in the PercuSurge® (PS) and control groups

<table>
<thead>
<tr>
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<th>PS (n=29)</th>
<th>Control (n=30)</th>
<th>p</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>58±11</td>
<td>59±14</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>23/6</td>
<td>22/8</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>17 (59)</td>
<td>18 (60)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>5 (17)</td>
<td>4 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>7 (24)</td>
<td>8 (27)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking history, n (%)</td>
<td>6 (21)</td>
<td>8 (27)</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>46±9</td>
<td>43±9</td>
<td>NS</td>
</tr>
<tr>
<td>LV WSMI</td>
<td>1.5±0.3</td>
<td>1.6±0.4</td>
<td>NS</td>
</tr>
<tr>
<td>IRA, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>13 (45)</td>
<td>11 (37)</td>
<td>NS</td>
</tr>
<tr>
<td>RCA</td>
<td>15 (60)</td>
<td>18 (52)</td>
<td>NS</td>
</tr>
<tr>
<td>LCX</td>
<td>1 (4)</td>
<td>1 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>TIMI flow grade, 0-1/2/3</td>
<td>19/4/6</td>
<td>20/4/6</td>
<td>NS</td>
</tr>
<tr>
<td>Pain-to-balloon time (min)</td>
<td>267±57</td>
<td>263±36</td>
<td>NS</td>
</tr>
<tr>
<td>Use of abciximab, n (%)</td>
<td>3 (10)</td>
<td>10 (33)</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF: left ventricular ejection fraction, WMSI: wall motion score index, IRA: infarct-related artery, LAD: left anterior descending artery, RCA: right coronary artery, LCX: left circumflex artery, TIMI: thrombolysis in myocardial infarction, NS: not significant</td>
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Table 2. Procedural results in the 2 study groups

<table>
<thead>
<tr>
<th></th>
<th>PS (n=29)</th>
<th>Control (n=30)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural success, n (%)</td>
<td>29 (100)</td>
<td>27 (90)</td>
<td>NS</td>
</tr>
<tr>
<td>Reference diameter (mm)</td>
<td>3.4±0.5</td>
<td>3.3±0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Minimal luminal diameter (mm)</td>
<td>1.85±0.4</td>
<td>1.42±0.63</td>
<td>NS</td>
</tr>
<tr>
<td>Diameter stenosis (%)</td>
<td>9±8</td>
<td>8±9</td>
<td>NS</td>
</tr>
<tr>
<td>Stent length (mm)</td>
<td>19±9</td>
<td>17±7</td>
<td>NS</td>
</tr>
<tr>
<td>TIMI flow grade &lt;3, n (%)</td>
<td>3 (10)</td>
<td>4 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>cTFC, frames</td>
<td>23.5±2.4</td>
<td>25.1±2.9</td>
<td>0.054</td>
</tr>
<tr>
<td>Myocardial blush score, n (%)</td>
<td>0-1</td>
<td>2 (7)</td>
<td>9 (30)</td>
</tr>
<tr>
<td>2</td>
<td>10 (35)</td>
<td>12 (40)</td>
<td>0.001</td>
</tr>
<tr>
<td>3</td>
<td>17 (58)</td>
<td>9 (30)</td>
<td></td>
</tr>
<tr>
<td>STE resolution &gt;50% at 90 min, n (%)</td>
<td>22 (76)</td>
<td>14 (47)</td>
<td>0.02</td>
</tr>
<tr>
<td>Peak CK-MB (U/L)</td>
<td>202±45</td>
<td>242±54</td>
<td>0.01</td>
</tr>
<tr>
<td>PCI: percutaneous coronary intervention, cTFC: corrected TIMI frame count, MB: myocardial blush grade, PS: PercuSurge®, TIMI: thrombolysis in myocardial infarction</td>
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Feasibility and safety of the use PercuSurge® during primary PCI

The PercuSurge® Guard-Wire system was successfully used in all the patients of the PS group, with no case of major in-hospital complications attributable to the PercuSurge® system. In 26 of the 29 PS cases (92%), aspiration with the EAC® yielded grossly visible particles and thrombotic material, which were reddish or white in color, and sometimes admixed with partially organized clots (Fig. 1).

Left ventricular function and clinical course

The LVEF at day 60 was significantly higher in the PS than in the control group (Fig. 2A, PS group 51 ± 5%, C group 46 ± 8%, p = 0.007), whereas the baseline LVEF was not statistically different between the 2 groups (PS group 46 ± 9%, C group 43 ± 9%, p = NS). The LVEF had improved significantly at 60 days in both groups (PS group p < 0.001, C group p < 0.001), but there was a tendency for a larger improvement in the PS group (PS 5.2 ± 1.6%, C group 3.3 ± 3.2%, p = 0.089). The WMSI was not significantly improved in either group (Fig. 2B, PS group: 1.5 ± 0.3 to 1.4 ± 0.3, p = NS, C group: 1.6 ± 0.4 to 1.6 ± 0.4, p = NS).

One patient in the control group died in hospital due to the development of refractory cardiogenic shock and mitral regurgitation. There were no significant differences in the incidence of death, myocardial infarction or revascularization at 30-day between the 2 groups (PS group 5%, C group 11%, p = 0.49).

Discussion

This study demonstrates that a balloon-based distal protection device, the PercuSurge® Guard-Wire system, can be effectively used during primary PCI, with a high rate of success and without significant complications, which was followed by improved myocardial reperfusion and LV functional recovery.

Distal embolization to the coronary circulation, as well as impaired microvascular reperfusion, are serious complications during primary PCI in AMI patients. Angiographic evidence of distal embolization during pri-
Distal embolization and/or the no-reflow phenomenon during primary PCI have an adverse effect on the prognosis. The 5-year mortality rate can be as high as 44% in patients with distal embolization, whereas this is only 9% in those without. Thus, the mechanical prevention of distal embolization during primary PCI might prevent myocardial reperfusion and improve clinical outcomes.

Glycoprotein IIb/IIIa inhibitors have been reported to be effective in preventing distal microembolization and improving myocardial perfusion during PCI. However, the clinical outcomes in large randomized trials were not shown to be improved. The CADILLAC trial showed that Abciximab was not effective at reducing the incidence of distal embolization, whereas this increase being greater in the PS compared with the control group.

Figure 2. Changes in the LVEF and LVWMSI during follow-up. LVEF: left ventricular ejection fraction, WMSI: wall motion score index, NS: not significant.

The PercuSurge® has been recently shown in the SAFER study to improve the clinical outcomes in patients undergoing saphenous vein graft intervention. The beneficial effect of distal protection was noted to be independent of the use of GP IIb/IIIa inhibitors. However, not much data exists on the efficacy of distal protection in native coronary arteries during primary PCI in AMI.

The use of PercuSurge® has been discouraged due to the technical limitations of the available device: 1) The design of the Guard-Wire®, which is less trackable and maneuverable than routine 0.014" guide-wires, 2) Its incomplete protection of proximal side branches from atheroembolization and its limited utility for preexisting distal embolization, 3) Cessation of distal flow, with ischemia, during intervention, 4) A mismatch of the balloon and vessel diameters due to difficulty in estimating the actual distal vessel size, and 5) Excessive time required for its use. Our series, however, showed that use of the PercuSurge® was feasible and safe, with a high rate of success, even during emergent angioplasty in AMI.

Some small studies have reported favorable immediate angiographic results using the PercuSurge® as an adjunct to primary PCI, and without procedural complications; conversely, the EF in the acute phase did not change, although the EF in the chronic phase was significantly higher in the PS compared with the control group.

However, this prospective study has demonstrated that, after the use of the PercuSurge® in native coronary arteries during primary PCI, the integrated analysis of the cTFC, MB and STe changes in a single patient allows for better characterization of the microvascular reperfusion of the infarct area, and also predicts a 2-month LV functional recovery in patients with AMI. In this study, the LVEF was significantly improved at 60 days with respect to the baseline values, with this increase being greater in the PS group.

We evaluated simple tools that significantly correlate with the tissue-level perfusion shortly after recanalization of the IRA, early recovery of the LV function and survival. The MB score and STe resolution have been validated as markers of effective myocardial reperfusion and as predictors of the clinical outcome. A cTFC cutoff value of 23 has also been demonstrated as being highly predictive of a greater LV functional recovery and favorable clinical outcomes, including a lower incidence of in-hospital complications compared to those patients with a higher cTFC; in the present study, a cTFC >23 was observed in 62 and 73% of the patients treated with PS and in the control groups (p=NS), respectively.

However, a recent large scale randomized study showed no benefit from the use of the Guard-Wire system either in terms of myocardial perfusion and STe resolution or 30-day cardiac event, and even using the infarcted size suggested by Tc-sestamibi, the myocardial SPECT
might not be sensitive or accurate enough to demonstrate the extent of subendocardial infarction. However, the inclusion criteria for subjects to that study resulted in the enrollment of patients with a shorter pain-to-balloon time, a greater number of low-risk patients, a much higher incidence of abciximab use, lower cTFC and a greater number with a MB score of 3 in the control group. Moreover, PCIs were fully protected, with occlusion balloon inflation in only 79%.

This study suggests that mechanical prevention of distal embolization might prevent no-reflow and unfavorable clinical results during primary PCI, with a substantial benefit expected.

Study limitations
The results of this study should be considered in the light of the following limitations: Firstly, the non-randomized small sample size should be noted with caution when interpreting our data. However, the case-matched design of the present study allowed a balanced between-group distribution of the main baseline parameters that are known to affect the prognosis after primary PCI (Table 1). Secondly, the principal end points of the present study were not evaluated by an independent, validated core laboratory, although the angiography, echocardiography and ECG data were analyzed by reviewers other than the operators; these were also blinded to the treatment.

Conclusions and clinical implications
The adjunctive use of the PercuSurge® Guard-Wire system is feasible and safe during primary PCI in AMI, and seems to reduce microcirculatory damage and improve the recovery of the LV function. A larger randomized study will be needed to see whether distal protection devices can reduce the major cardiac events, as well as myocardial damage, after primary PCI.

Acknowledgments
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