Use of Distal Protection Device for Percutaneous Intervention in Native Coronary Arteries

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LAM and LI: ***Use of Distal Protection Device for Percutaneous Intervention in Native Coronary Arteries.*** *Microembolization of particulate debris during percutaneous coronary intervention (PCI) will lead to various degree of microvascular obstruction, terminating in no-reflow phenomenon observed angiographically. Different methods, including angiography, non-invasive imaging, and assays of myocardial injury markers, have been used for detection of occurrence of microvascular obstruction. The prevalence of, and the adverse prognosis associated with microvascular obstruction have led to the concept and application of distal protection for coronary interventions. While its value has been confirmed in saphenous vein grafts intervention, data is now growing to support use of distal protection devices in native coronaries. Findings from a local registry that reveals the initial experience on use of GuardWire Plus System, a kind of occlusive distal protection device, for elective PCI are discussed herein. (J HK Coll Cardiol 2002;10:191-197)*

Distal protection, microembolization, microvascular obstruction, percutaneous coronary intervention

摘要

在經皮冠脈介入干預（PCI）中破碎的斑塊引起的微栓塞將導致不同程度的微血管阻塞，冠脈造影上出現無複流現象。有不同的方法，如冠脈造影、無創性顯像技術、心肌損傷標誌物用以檢查微血管阻塞的發生。微血管阻塞現象的頻繁發生及其不良預後帶來了冠脈介入遠端保護的概念與技術應用。這種技術的價值在大隱靜脈移植血管介入干預中得到證實後，現在有越來越多的資料支援其在冠脈介入干預中使用血管遠端保護裝置。從一個地區的註冊登記中顯示了 GuardWire Plus 系統 －一種遠端閉塞性保護裝置使用的初步經驗，本文就擇期 PCI 中使用這一裝置進行討論。

關鍵詞：遠端保護　微栓塞　微血管阻塞　經皮冠脈介入干預

Introduction

Microembolization, Microvascular Obstruction and No-Reflow: Pathophysiology

With the advances seen in various devices used for percutaneous coronary intervention (PCI) and the widespread use of stents, acute complications are uncommon during the procedure. However, slow distal flow or no-reflow phenomena remain one of the frustrations facing interventional cardiologists. The pathophysiology underlying such phenomena seen during PCI is likely to be complex, but probably starts off with microembolization of particulate debris dislodged from atherosclerotic/thrombotic lesions down to distal capillary bed, causing microvascular obstruction.[1] This in turn results in microvascular plugging, microvascular spasm or edema, and/or platelet aggregation. Experiments in canine models had shown that embolization of a coronary artery with minute particles/microspheres measuring less than 100 μm resulted in regional contractile dysfunction and perfusion-contraction mismatch.[2] Following microvascular obstruction, epicardial flow is initially

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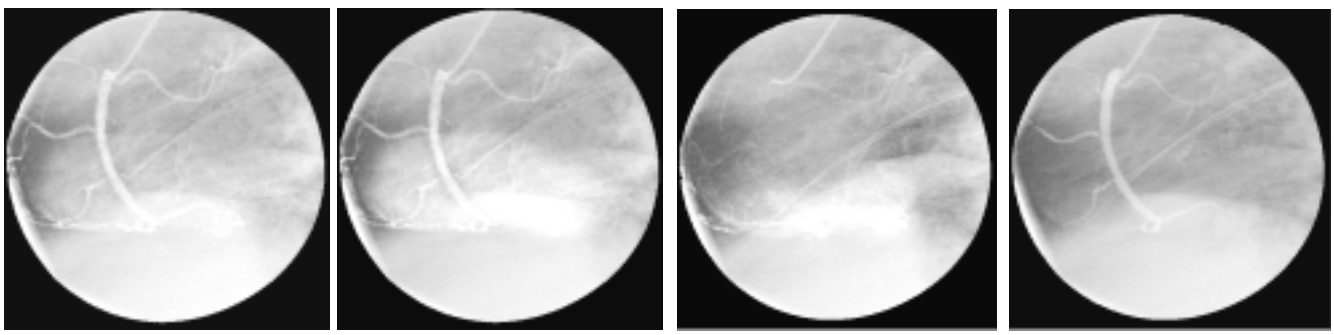
maintained or even enhanced due to an adenosine-related hyperaemia of the myocardium surrounding the embolized microregions, with blood shunting around the areas of microvascular obstruction.[1] However, as the total embolized burdens increase, the epicardial flow will eventually become reduced, corresponding to the angiographic manifestation of slow distal flow or no-reflow. In other words, no-reflow represents an advanced stage of significant degree of microvascular obstruction.

Detection of Microembolization and Microvascular Obstruction

The presence and extent of microvascular obstruction can be assessed by examining the degree of impairment of myocardial perfusion. Several methods have been used for this purpose. The angiographic method is perhaps the simplest way in the catheterization laboratory. Two different approaches have been derived: first, to record the Corrected TIMI Frame Count (CTFC) which is defined as the number of cine frames required for contrast to first reach distal coronary landmarks in that artery;[3] and second, to report on the TIMI Myocardial Perfusion (TMP) Grades (0-3) by noting the appearance of blush, and the rate at which the blush disappears (Figure 1).[4] Myocardial contrast echocardiography constitutes another method for assessing myocardial perfusion by intravenous or intracoronary injection of sonicated bubbles. Ito et al[5] showed that myocardial perfusion defects was detectable in up to 26% of patients who had TIMI 3 flow in the infarct-related artery after reperfusion therapy (either thrombolysis or primary angioplasty). Nuclear imaging using Sestamibi Single-Photon Emission Computerized Tomography (SPECT) has also been used for detection of myocardial perfusion defects. Koch et al[6] demonstrated that up to 87% of patients undergoing rotational atherectomy had detectable perfusion defects on SPECT, but the figure dropped to 33% with infusion of abciximab, thereby providing evidence that platelet emboli were at least partly involved. Magnetic Resonance Imaging (MRI), on the other hand, is able to demonstrate subendocardial microvascular obstruction by showing regions of hypoenhancement after contrast injection.[7] Finally, reduction in relative coronary flow velocity reserve (as measured by intracoronary Doppler flow analysis) after successful coronary intervention has been observed, and has been related to microvascular obstruction.[8,9]

Abnormal levels of myocardial injury markers represent the sequelae (when other confounding factors like acute closure during the procedure or jailing of side-branch are absent), and also serve as circumstantial evidence for occurrence of microvascular obstruction during PCI. In a study by Hong et al[10] recording successful,



TMP Grade 3
Normal ground-glass appearance of blush. Contrast mildly persistent at end of washout

TMP Grade 2
Contrast strongly persistent at end of washout. Disappears by next injection

TMP Grade 1
Stain present. Blush persists on next injection

TMP Grade 0
No or minimal blush

Figure 1. *TIMI Myocardial Perfusion (TMP) Grades (Graphics supplied by Medtronic Inc.).*

angiographically and clinically uncomplicated PCI in over 700 patients with saphenous vein graft (SVG) lesions, raised creatine kinase-MB fraction (CK-MB) levels, defined as levels above upper normal limit, were detected in 38.5% of patients. In a recent study which measured serum troponin T and I levels after successful uncomplicated elective PCI in native coronary arteries, up to 14% of patients had raised troponin T or I levels in absence of side-branch occlusion.[11] More evidence to suggest microembolization during PCI comes from the observation of a higher incidence of microvascular obstruction associated with more aggressive coronary intervention. Directional atherectomy, for instance, was the strongest correlate of post-procedure CK-MB elevation in a series of patients who underwent successful PCI (odds ratio 4.1 when compared to balloon angioplasty).[12] The paradoxical finding of a decrease in TIMI 3 flow in patients after stenting as compared to balloon angioplasty in the Primary Angioplasty in Myocardial Infarction (PAMI) trial lends more support to the occurrence of microembolization.[13]

Impact of Microvascular Obstruction on Outcomes Post-PCI

It is well known that occurrence of no-reflow during PCI is associated with higher incidence of major adverse cardiac events (MACE). In a study addressing this issue, the incidences of non-Q myocardial infarction and in-hospital mortality were reported as 31% and 15% respectively.[14] Even when epicardial flow is preserved, the occurrence of microvascular obstruction will lead to a worse outcome. In a study which recruited patients with normal or mildly raised (<2 times upper limit of normal) creatine kinase after successful PCI, Abdelmeguid et al[12] showed that the subgroups with elevated CK-MB carried a higher incidence of MACE over a median follow-up period of 3 years. Hong et al[10] in the study on SVG interventions showed that the 1-year mortality rate in patients with post-procedure CK-MB 1-5 times upper limit of normal and those with CK-MB more than 5 times normal were, respectively, at least 2 times and 4 times higher than patients with normal CK-MB levels. In another study, Stone et al[15] discovered that only 29.4% of patients who had TIMI 3 flow in the infarct-related artery after primary angioplasty achieved a TMP Grade of 3. More importantly, the 1-year mortality rates in this group of patients were closely correlated to the TMP Grades: 6.8% for TMP Grade 3; 13.2% for TMP Grade 2; and up to 18.3% for TMP Grade 0/1.

Distal Protection for PCI

Distal Protection Devices

It is therefore reasonable to hypothesize that protecting distal vessels from particulate embolization can improve immediate and long-term outcome after PCI. Different distal protection devices have been designed. As of today, they fall into one of two categories: a) distal occlusion balloon on a wire; any particulate debris within the column of occluded blood will be aspirated after intervention on target lesion; and b) filter that can be deployed distal to target lesion, trapping any particulate debris; the filter with the entrapped debris are then retrieved with a capture sheath. The former, as exemplified by the GuardWire Plus System (Medtronic®) (Figure 2), has the advantages of having a low crossing profile and completeness of debris retrieval, but vessel occlusion is inevitable during the procedure. The latter, as exemplified by the AngioGuard Emboli Capture Guidewire (Cordis®) (Figure 3) and the EPI FilterWire (Boston Scientific®) (Figure 4) have the advantages of allowing continued blood flow during the procedure, but suffer from having a larger crossing profile (4.0F or more) and uncertainties in offering complete protection or retrieval of entrapped particulates.

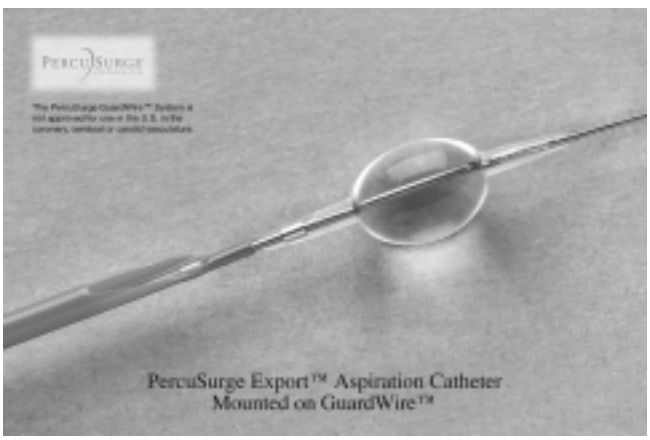


Figure 2. *The GuardWire Plus System (Medtronic®).*

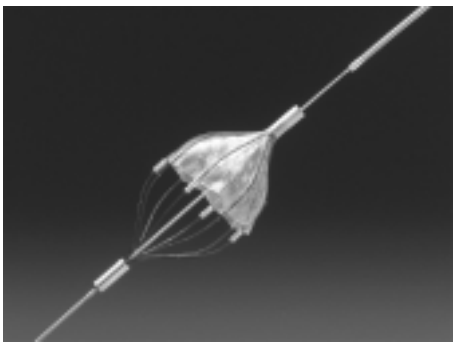


Figure 3. *The AngioGuard Emboli Capture Guidewire (Cordis®).*

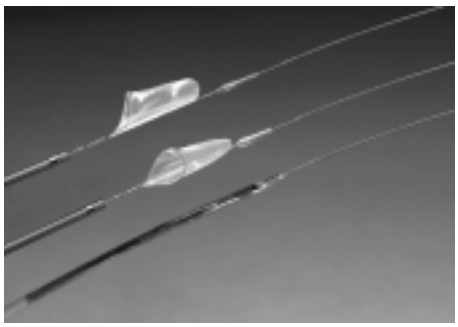


Figure 4. *The EPI FilterWire (Boston Scientific®).*

Clinical Data on Use of Distal Protection for PCI

The value of distal protection has been/is being tested in two high-risk areas for microembolization: interventions in saphenous vein grafts and on culprit lesions of acute coronary syndromes. The SAFER trial[16] is the first randomized clinical trial examining the benefit of distal protection using GuardWire System (Medtronic®) during interventions in SVG. Over 800 patients were enrolled in the trial. The incidence of no-reflow was 3.4% using distal protection versus 8.8% without distal protection. Incidences of in-hospital MACE and 30-day MACE were decreased by 38% and 42% respectively with the use of distal protection. In the setting of intervention for acute ST elevation myocardial infarction (STEMI), a multicentre registry in Europe recorded in 37 patients an improvement in TIMI 3 flow from 24.3% to 86.1% and improvement in TMP Grade 3 from 2.7% to 58.8% of patients post-intervention with the use of GuardWire System.[17] Similarly, in a single-centre cohort of 51 STEMI patients, an improvement in TIMI 3 flow from 0% to 96% of patients was noted post-intervention using the same GuardWire System,[18] with 54.5% of patients who had TIMI 3 flow achieving TMP Grade 3. Though randomized comparison was not available, this 54.5% of TMP Grade 3 was a significant improvement over the 18.8% figure obtained from historical trial data. In 96% of this cohort, either thrombus or atherosclerotic materials were successfully aspirated.

Use of Distal Protection for Elective PCI in Native Coronary Arteries

Slow distal flow or no-reflow does occur occasionally in the setting of elective PCI (excluding interventions during acute phase of acute coronary syndromes). In a review on all elective PCI in native coronary arteries conducted in the authors' catheterization laboratory in year 2001, the incidence of slow distal flow/no-reflow was up to 3% when vessels ≥3.5 mm in diameter were counted, and up to 13% in vessels ≥4.0 mm in diameter. As from deduction and also from observation, larger plaque burden and more friable plaque predispose to occurrence of such adverse phenomena. However, there is as yet little controlled data on the use of distal protection for elective PCI in native coronary arteries. A recent report from Grube et al[19] included the experience of using the AngioGuard Emboli Capture Guidewire (Cordis®) for distal protection in 15 native coronary lesions. Particles retrieved from the filters were sent for histochemical staining, and the study constitutes "the first direct evidence that embolization of arterial plaque components occurs routinely during native coronary artery interventions".

Local Registry on Use of Distal Protection for Elective PCI in Native Coronaries

In view of the potential value of distal protection for elective PCI in native coronaries, a registry on the use of GuardWire Plus System (an improved version of the original GuardWire System) has been set up in the authors' hospital. Lesions included are those within large native coronary arteries (≥3.5 mm), or lesions with heavy plaque load/complex morphology/overlying thrombus in coronary arteries ≥3.0 mm. Exclusion criteria are: a) the presence of significant (≥1.5 mm)

side-branch between the target lesion and potential location of distal protection balloon on the GuardWire (as otherwise most of the dislodged particulates may embolize down the side-branch); b) diameter of distal vessel segment where protection balloon would be inflated is <3.0 mm; c) planned use of adjunctive devices other than coronary stents, which would lengthen the procedure and also the occlusion time; and d) anticipated difficult stenting procedure (e.g. proximal calcified segment or excessive proximal tortuosity), as the protection balloon is usually only positioned 20-40 mm distal to the lesion, and support from the GuardWire is not as good as ordinary coronary wires. The first three exclusion criteria are specific to the GuardWire Plus System, and serve to illustrate that each protection system available in market bears its own characteristics and limitations. Two or three operators co-operated in using the system. Basically the procedure can be divided into 4 parts (Figure 5): a) passing the GuardWire across the lesion and inflating the distal protection balloon; b) performing intervention on the lesion as is required; c) aspirating any particulate debris which may be present in the column of occluded blood; and d) deflating the distal protection balloon. In cases of tight lesions or in totally occluded vessels, an ordinary coronary guidewire may be used to cross the lesion first (as "buddy" wire), with or without gentle predilatation with a small diameter balloon to allow subsequent passage of the GuardWire. Three different strategies could be employed for target lesion intervention, depending on coronary anatomy and expected patient's tolerance on vessel occlusion during distal protection: a) direct stenting; b) balloon angioplasty followed by an interim period of rest before stenting (referred here as balloon-rest-stent); c) combined balloon angioplasty and stenting (balloon+stent) without interruption.

So far, distal protection for elective PCI in native coronaries has been performed for 20 lesions in 17 patients (Table 1). Majority of the lesions were in RCA, as expected because of the large size of this vessel often encountered (Table 2).

Predilatation for initial passage of the GuardWire was required only in 3 lesions. In fact, with more experience in manipulating the GuardWire and in the presence of good guiding catheter support, it is possible to pass it through critical lesions without the need for predilatation. Direct stenting was performed on 11 lesions; balloon-rest-stent on 7 lesions; and

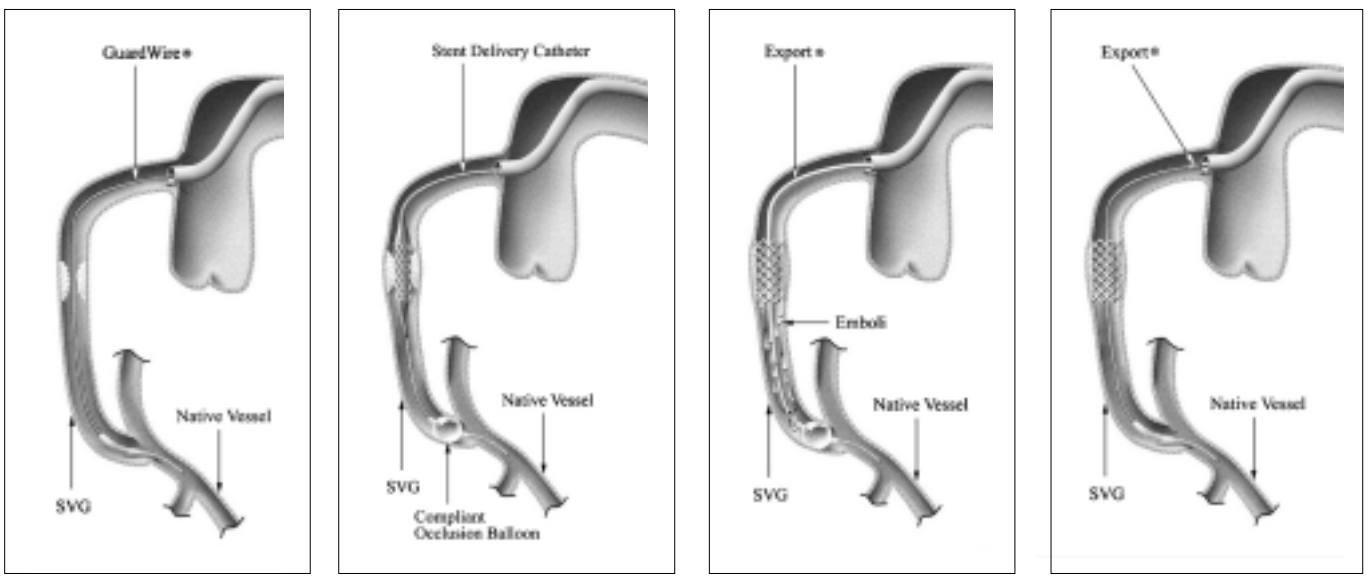


Figure 5. *Use of the GuardWire Plus System in a SVG is illustrated. (A) Crossing the lesion with the GuardWire. (B) Performing intervention on target lesion while distal protection balloon is inflated. (C) Aspirating particulate debris through the aspiration catheter. (D) Deflating the distal protection balloon.*

Table 1. Patients undergoing distal protection for elective PCI

Total no.	17
M:F ratio	14:3
Mean age (yrs)	65.9±11.7
Indication for PCI	
Stable angina	10
Stabilized after recent ACS	7

Table 2. Lesion characteristics

Vessel	
RCA	15
LCx	3
LAD	2
Mean vessel size (mm)	3.56±0.36
Lesion type	
A	3
B1	11
B2	11
C	6
Mean % stenosis	87.4±9.6

balloon+stent on 2 lesions. Mean vessel occlusion time was 181 seconds for stenting in direct stenting and balloon-rest-stent; 182 seconds for balloon angioplasty during balloon-rest-stent; and 354 seconds for balloon+stent. There is definitely a learning curve in using the system. The mean occlusion time for stenting in the last 5 lesions, for instance, has dropped to 146 seconds. The incidence of chest pain during distal protection occurred in about half of patients, bradycardia and BP drop (>20 mmHg from baseline) in around 60% and 50% respectively; and ST segment changes in about 90%. All these symptom and changes disappeared on relief of the vessel occlusion. Distal protection was successfully performed for all lesions. TIMI 3 flow and TMP Grade 3 were noted in every case. Amount of plaque debris retrieved was recorded in a semi-quantitative manner: small, moderate, and large. In around two-thirds of instances, the amount retrieved was either moderate or large (Figure 6). In none of the cases was the yield negative. Problems encountered were: one dissection at site of distal protection balloon caused by over-sizing, handled by stenting; one incident of initial difficulty in retracting the GuardWire due to the protection balloon impinging on stent struts; and one incident of non-deflating protection balloon, handled by cutting the GuardWire. The first two problems could have been avoided by more careful use, while the last problem is reportedly rare according to manufacturer. There was no in-hospital MACE related to the use of distal protection. It thus appears that distal protection using GuardWire Plus System for elective PCI in native coronaries is a feasible option. The successful retrieval in virtually all cases of particulate debris which would otherwise have embolized down the distal (micro) vasculature reflected the system's efficacy in providing myocardial protection. Indeed, the system has probably avoided several incidents of adverse slow flow/no-reflow phenomenon, judging

Figure 6. *Plaque debris retrieved.*

from the large size of the debris retrieved in some cases. Whether these benefits would transcribe into better clinical outcome would require confirmation by randomized studies. On the other hand, there is definitely a learning curve in the use of the device. Operators are expected to encounter problems in their early experience, and should be prepared to overcome them if they do occur. In fact, with careful use and as experience grows, most problems can be avoided. It should be emphasized, however, that as the benefit-risk ratio is comparatively lower in the setting of elective PCI than in PCI for acute coronary syndromes, proper case selection, as well as acquaintance with and proper use of the system are important issues.

Conclusion

Evidences are now growing in support for distal protection during PCI in native coronary arteries. Well-controlled randomized studies may eventually confirm its clinical value, just as in the case of intervention in saphenous vein grafts, especially in the area of primary angioplasty for STEMI. In the setting of elective PCI in native coronaries, further studies are required to identify lesions that are prone to distal microembolization in order to justify its use. With distal protection devices becoming user-friendlier, they may one day turn into a frequently used gadget that will help prevent adverse consequences secondary to particulate embolization that cannot be effectively prevented or handled by pharmacological means.

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