Coronary Intervention in Thrombus-Rich Lesions: Beyond Stents and Glycoprotein IIb/IIIa Inhibitors

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Percutaneous coronary intervention of thrombus-rich coronary lesions is still associated with high rates of adverse events, despite the frequent use of stents and glycoprotein IIb/IIIa antagonists. The mechanical trauma to the thrombus inflicted by interventional devices results in excessive rates of periprocedural and late complications.

As stated, PCI of the thrombus-rich lesion in the setting of acute coronary syndromes is associated with a high complication rate. The widespread use of stents and glycoprotein IIb/IIIa antagonists in clinical practice has decreased the number of adverse events following PCI in acute coronary syndromes. However, randomized clinical trials, corroborated by data from large observational registries, have demonstrated that the occurrence of periprocedural and late complications remains high when an angiographically evident thrombus-rich lesion is present [1].

In this article, we review the available data on current PCI in the setting of intracoronary thrombosis and describe the impact of novel dedicated devices on the management of intracoronary thrombus.

Pathophysiology of PCI in thrombus-rich lesions

Atherosclerotic plaque rupture is usually the precipitating factor for intracoronary thrombosis [2]. The propensity of vulnerable plaque to rupture depends on multiple factors, such as plaque composition, plaque structure, stress-strain distribution, blood pressure, and presence of inflammation [3,4]. Plaque rupture exposes thrombogenic plaque content to blood components, initiating thrombosis [5]. During its development and growth, a coronary thrombus undergoes changes in size and composition that ultimately correlate with differing clinical syndromes [6]. DeWood and colleagues [7] conclusively demonstrated that thrombotic occlusion of an epicardial artery is the most common cause of acute myocardial infarction. The causative role of non-occlusive thrombi was later documented in unstable angina and non-ST segment elevation MI [8]. Pathologic and angioscopic findings in ACS patients demonstrated that occlusive clots are almost always "red" (consisting mainly of loose fibrin and erythrocytes) and that non-occlusive thrombi are "white" (rich in platelets and densely packed fibrin, with relatively few erythrocytes) [2,9] – independently of the clinical presentation (i.e., AMI or unstable angina).

Unlike PCI for stable coronary lesions, PCI for thrombus is performed in the presence of friable clot material and activated platelets. These factors have implications for the choice of adjunct antiplatelet therapy and the development of events that occur "downstream" in the distal microcirculation as a result of microembolization [Figure 1]. Fragmentation of coronary thrombus

PCI = percutaneous coronary intervention
AMI = acute myocardial infarction
ACS = acute coronary syndromes

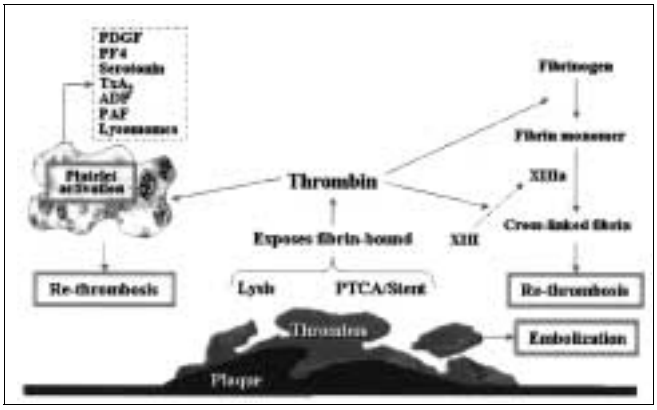

Figure 1. Manipulation of thrombus by mechanical devices and thrombolytic agents leads to clot fragmentation, microembolization and exposure of fibrin-bound thrombin. Fibrin-bound thrombin is the strongest activator of platelets. It activates factor V to Va, converts fibrinogen to fibrin and activates factor XIII to XIIIa which cross-links fibrin. The parallel stimulation of these combined processes by thrombin produces a potent stimulus for thrombosis. Following mechanical fragmentation of clots by percutaneous transluminal coronary angioplasty or stenting, additional fibrin-bound thrombin is exposed, further increasing platelet activation (Reproduced with permission from *J Am Coll Cardiol* 1991;17:77–88B).

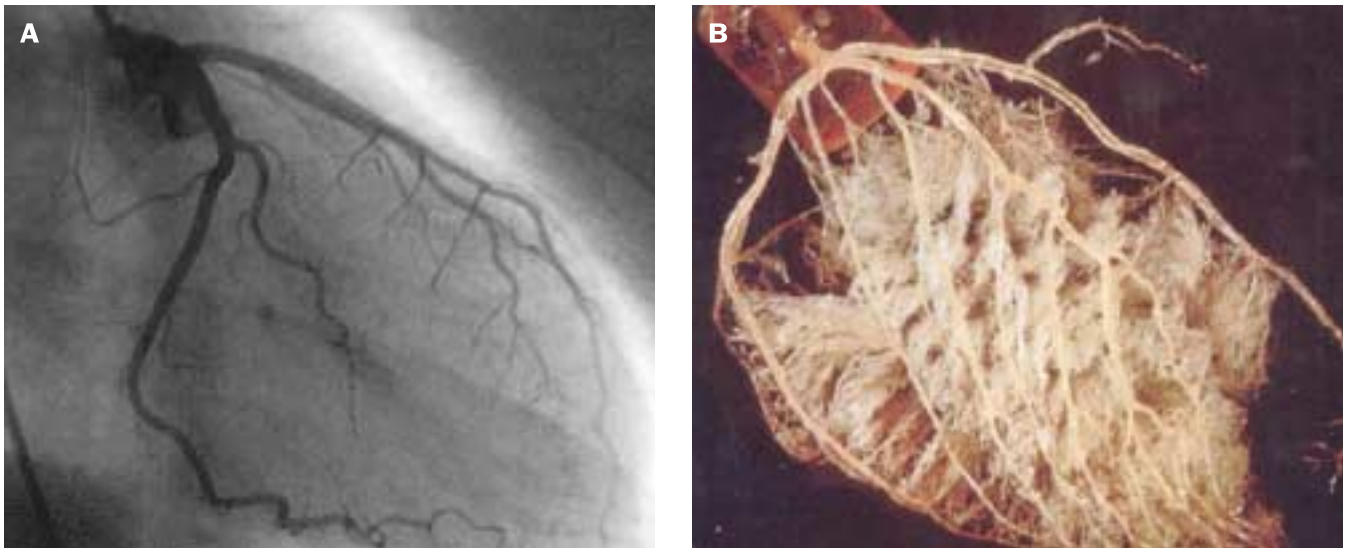

Figure 2. [A] Coronary angiography is limited in resolution to large vessels ($\geqslant$ 500 μ in diameter) **[B]** Hence, angiography is suboptimal for assessment of the myocardial microvasculature (Courtesy of Dr. G. Guagliumi). Since flow in the epicardial artery is not necessarily affected by microembolization, this process is mostly angiographically silent. Only massive microembolization may manifest as the "no-reflow" phenomenon.

occurring spontaneously [10], or as a result of therapeutic interventions, can result in macro or microemboli that occlude the distal microcirculation. In a postmortem study by Saber et al. [11] of AMI patients treated with thrombolytic agents and/or percutaneous transluminal coronary angioplasty, 83% had multiple distal microemboli, mostly thrombotic, in small coronary branches. The clinical consequences of coronary microembolization ranged from a cardiac enzyme elevation to profound myocardial necrosis, left ventricular dysfunction, and death. The median diameter of the microemboli was found to be smaller than the resolution of standard radiographic equipment [12]. Since flow in the epicardial coronary vessel is not necessarily affected by distal capillary plugging, events caused by microembolization are often angiographically silent [Figure 2]. Only massive microembolization manifests as the "no reflow" phenomenon [Figure 3]. In patients with AMI treated by primary angioplasty, "no reflow" occurs in up to 15.7% of patients [13], while rarely occurring after PCI in stable coronary artery disease [14]. "No reflow" phenomenon is a strong

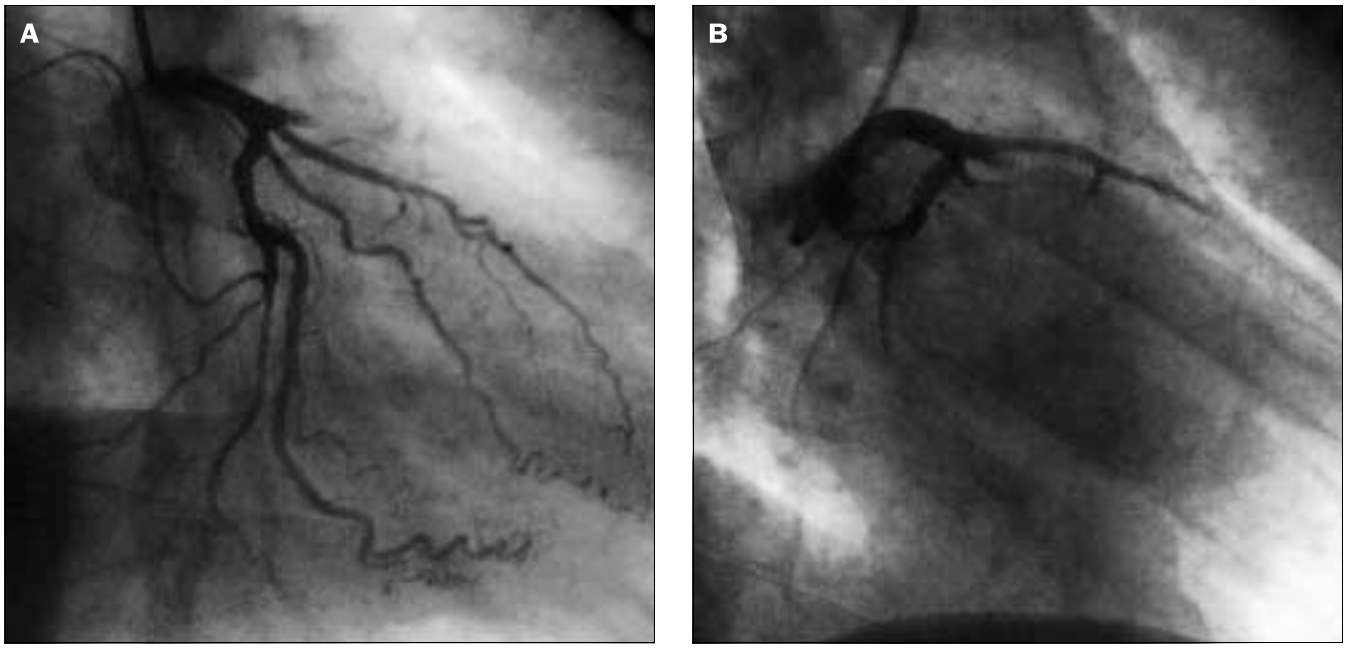

Figure 3. A baseline angiography of a 57 year old man who presented with chest pain and ST segment elevation in the precordial leads. **[A]** The left anterior descending coronary artery is totally occluded (TIMI grade flow 0) proximally. **[B]** Primary PTCA leads to massive microembolization both downstream and backward to the left circumflex artery circulation, leading to "global" no reflow in the left coronary system.

predictor of late-stage mortality and left ventricular dysfunction [15].

The adverse effect of embolization on the microcirculation during PCI of thrombus-rich lesions was first highlighted by Ito et al. [16], who used contrast echocardiography to evaluate myocardial perfusion in AMI patients treated with primary angioplasty. Of the patients in whom epicardial TIMI grade 3 flow was restored, 16% had echocardiographic evidence of "no reflow." All patients with TIMI grade 2 had "no reflow." In another study of patients with first anterior AMI, Kondo et al. [17] evaluated myocardial perfusion immediately after angioplasty using a nuclear method. Absent or severely reduced perfusion at the myocardial level was found in 56% of patients with TIMI grade 3 flow in the infarct-related artery; normal myocardial perfusion was documented in only 16% of patients. Van 't Hof et al. [18] studied the angiograms of 777 consecutive patients after primary angioplasty using a new angiographic measure for assessment of myocardial perfusion – the "myocardial blush score." Normal myocardial perfusion was observed in only 20% of patients. In a confirmatory study of 173 high risk patients undergoing primary and rescue PCI, Stone and colleagues [19] reported that normal myocardial perfusion was present in only 28% of patients, despite the restoration of epicardial TIMI 3 flow in 94% by core lab analysis. Among patients achieving TIMI 3 flow, the myocardial blush grade was a powerful determinant of long-term survival.

Primary stenting does not appear to improve myocardial perfusion. In fact, in the PAMI-Stent trial, stent implantation was associated with a lower incidence of TIMI 3 flow than angioplasty alone [20]. Coronary embolization and its clinical sequelae may correlate with the degree of thrombus burden at the time of intervention. In ACS, angiographically evident clot is strongly associated with evidence of myocardial necrosis [21] and increased major adverse coronary events [13]. Furthermore, in patients with AMI undergoing primary PTCA, high clot burden has been associated with a greater risk of "no-reflow" and adverse clinical events [13,22].

Thus, failure to establish normal myocardial perfusion in AMI is common, occurring in up to 60% of patients "successfully" treated with current catheter-based methods of reperfusion. This phenomenon, which is mainly the result of distal microembolization, seriously limits myocardial salvage despite successful restoration of antegrade epicardial blood flow.

Impact of PCI on thrombus-rich lesions

Treatment of coronary thrombus by PTCA is associated with a high rate of early and late complications [23,24]. In a study by Waxman et al. [23], who used angioscopy to accurately diagnose thrombi at the culprit lesion, the presence of thrombus prior to PTCA was associated with an 8.8-fold increase in the risk of an early adverse event.

The use of GP IIb/IIIa antagonists reduced the periprocedural complications of PCI [25,26]. Given the underlying mechanism of these agents, such results have frequently been extrapolated to PCI for thrombus-rich lesions. However, analyses focusing on the role of GP IIb/IIIa inhibitors in these lesions are not conclusive. In the EPIC trial [26], treatment with abciximab in patients undergoing angioplasty was not superior to standard aspirin and heparin therapy when a thrombus was angiographically documented. In the RAPPORT trial, AMI patients treated with primary PTCA and concomitantly with abciximab did not affect the combined primary endpoint. Of interest, the rate of need for target vessel revascularization was lower in the abciximab-treated patients [27]. Furthermore, the presence of thrombi on the baseline angiogram predicted procedural failure, while the use of abciximab had no predictive value for procedural success. In the PRISM-PLUS study, patients with non-ST elevation ACS were randomized to treatment with tirofiban, heparin, or both [1]. Sixty hours after treatment, thrombus was evident in more than 40% of patients, regardless of their therapeutic assignment. Further, PCI in the presence of thrombus significantly increased major adverse clinical events, regardless of the status of the GP IIb/IIIa blockade.

In the PAMI-Stent Trial, AMI patients were randomized to receive primary angioplasty with or without stenting [20]. The stent group had a non-significant trend towards increased mortality. Among patients with an occluded IRA, stenting was associated with significantly increased early and late mortality [28]. The PAMI-Stent results suggest that stent implantation in lesions with a large thrombus burden that is reflected in occlusion of the IRA may actually be detrimental.

Currently, the most widely used therapeutic approach in the treatment of coronary thrombus is a combined strategy of GP IIb/IIIa antagonists and stent deployment. The efficacy of this combination was tested in the CADILLAC trial, where AMI patients were randomized in a 2 x 2 factorial design to receive primary PTCA, PTCA with abciximab, stenting, or stenting with abciximab [6]. Abciximab had no significant long-term benefits on the primary endpoint in either the PTCA or stent-assigned patients [Figure 4]. In the ISAR-2 trial, where patients underwent stenting within 48 hours of AMI, the abciximab group was associated both with improved early myocardial recovery and greater peak coronary blood flow velocity, suggesting improved microvascular perfusion [29]. However, in the final report, these findings did not translate into clinical benefit, either at 30 days or after 1 year [7].

Moreover, data from recent large prospective registries provide limited support for the use of stents and the GP IIb/IIIa blockade for thrombus-rich lesions. Ellis et al. [30] identified lesion characteristics predictive of PCI complications in 6,327 consecutive patients who were treated in the era of stenting and GP IIb/IIIa antagonists. In this group, abciximab was used in 41% of cases and stents in 64%. Interventions on thrombotic occlusions were associated with the highest complication rates (12.6%). Another recent report from the Mayo Clinic documents interventions in more than 3,900 consecutive patients in the stent and GP IIb/IIIa antagonist era. Here thrombus-rich lesions were strongly associated with an

PTCA = percutaneous transluminal coronary angioplasty
GP = glycoprotein

IRA = infarct-related artery

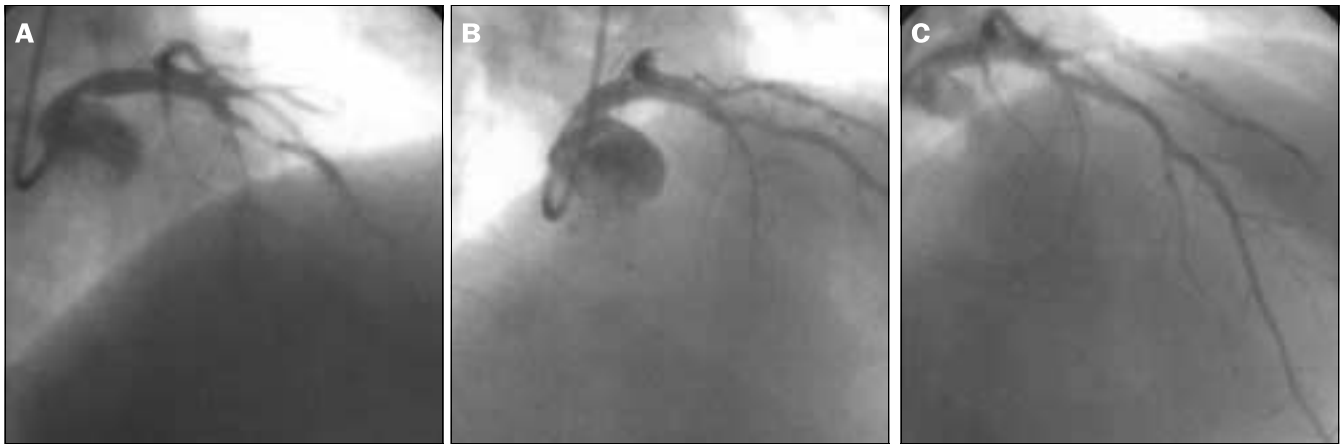

Figure 4. Angiogram of a 43 year old man who presented with chest pain of 2 hours duration and precordial lead ST elevations. **[A]** The diagnostic angiogram demonstrated a filling defect in the mid-portion of the left anterior descending coronary artery, consistent with a large thrombus and TIMI 1 flow. **[B]** Following therapeutic ultrasound thrombolysis, the filling defect has largely resolved, revealing a residual stenosis of approximately 40%. **[C]** Stent deployment eliminated the residual stenosis with TIMI 3 flow restored in the distal artery.

increased risk of in-hospital death or major adverse cardiovascular events [9]. Thus, large consecutive registries support the findings of randomized trials and demonstrate that complication rates following PCI for thrombus-rich lesions remain high, despite the widespread use of stents and GP IIb/IIIa antagonists.

Catheter-based approaches to thrombus-rich lesions

The negative impact of angiographically evident thrombi on PCI outcomes has prompted attempts to reduce clot burden prior to intervention in order to minimize embolization and clinical complications. Novel catheter-based devices have been designed for this purpose. These devices operate either by debulking thrombi prior to PCI (active protection), or by creating a barrier to limit distal embolization (passive protection).

For many years the transluminal extraction catheter (InterVentional Technologies Inc., San Diego, CA, USA) was employed for the treatment of thrombus-rich lesions in native coronary arteries and saphenous vein grafts. However, use of this device was restricted by its difficult set-up, large profile and propensity to cause dissections.

Several new dedicated catheter-based methods for intracoronary thrombus debulking have recently been introduced. Expanding clinical experience with these technologies suggests they may play an important role as adjuncts to PCI for thrombus-rich lesions.

Coronary ultrasound thrombolysis

Several devices are now employed that use ultrasound to achieve thrombo-ablation. Of these, the Acolysis system (Angiosonics Inc., Morrisville, NC, USA) has been most extensively studied. It consists of a control unit that generates ultrasound energy at 35–50 kilohertz, which is transmitted to the distal tip of a catheter. Clinical assessment of intracoronary ultrasound thrombolysis with this system has recently been described in both native coronary arteries and saphenous vein grafts.

In the ACUTE study, consecutive patients with first anterior myocardial infarction and occluded left anterior descending coronary artery were recruited. Ultrasound thrombolysis was successful (TIMI 2-3) in 94% of patients. At the 6 month follow-up, the left ventricular ejection fraction increased from 45 $\pm$ 11% at baseline to 58 $\pm$ 7% (P = 0.0005) [31,32]; this suggests that safe, effective reperfusion and significant myocardial salvage can be achieved in high clot burden lesions in the native coronary arteries through primary coronary ultrasound thrombolysis.

In the Acolysis Registry, data were prospectively collected in a multicenter registry of consecutive ACS patients (n=160), with the culprit vessel being mostly in native coronary arteries (n=126). The culprit vessels were almost totally occluded in 84% of the patients. The median age of clot was 3 days (range 0–60 days). Device success was obtained in 112 patients (89%). Adjunct PTCA or stenting was used in 97% of the patients. There was a low rate of adverse angiographic events during the procedure, with distal embolization observed in four patients (3%) that was not device-related. No major adverse clinical events occurred during hospitalization [33].

Rheolytic thrombectomy

Dissolution and removal of clots from coronary and peripheral arteries is achieved by the creation of a flow-mediated vacuum in the vicinity of the treated lesion. High speed injection of saline fluid into an aspiration catheter forms a low pressure zone at its orifice (the Bernoulli effect). The pressure gradient between the thrombus and the catheter tip draws clot particles into the lumen of the device, where they are further fragmented by the high speed saline jets and then aspirated. The double lumen device allows both saline injection and aspiration of particulate matter into its collection system.

Two currently available devices that incorporate this principle have been tested, namely the Possis Angiojet (USA) and Cordis Hydrolyser (USA) catheters. In the VeGAS 2 trial, the Angiojet device was compared with urokinase prior to percutaneous treatment of 346 patients with thrombus-rich lesions in native coronary arteries or saphenous vein grafts. In this high risk population, procedural

success and hospital course without a major adverse cardiac event were achieved with the Angiojet catheter in 86% of cases, significantly more frequently than with urokinase (66%, $P = 0.01$) [34]. Silva and co-workers [35] used the Angiojet system in 70 AMI patients prior to angioplasty of the culprit lesion. The procedure was successful in more than 90% of patients. In-hospital survival exceeded 90%, and 87% of this group remained free of major adverse cardiac events throughout their hospital course, although 16% had cardiogenic shock at the time of the procedure.

The largest study with the Cordis Hydrolyser in coronary PCI included 31 patients [36]. TIMI 2-3 flow was achieved with the Hydrolyser in 58% of initially occluded vessels. Ninety percent of the patients received additional PCI (PTCA and stent). A major adverse cardiac event occurred in three patients (in-hospital mortality in two, non-Q AMI in one).

Aspiration thrombectomy

The X-Sizer (EndicCOR Medical, Inc., USA) is a thrombo-atherectomy catheter of varying dimensions. Rotation of a distal helical cutter results in thrombus maceration and extraction into a distal vacuum collection bottle. Experience in several hundred patients has shown this catheter to be effective in debulking thrombus and degenerating saphenous vein graft lesions [37]. An 800 patient randomized trial (X-TRACT) to evaluate this device in saphenous vein grafts and thrombus-rich lesions is currently underway in the United States.

In the X-TRACT AMI registry, thrombectomy with the X-Sizer was performed in 220 consecutive patients with AMI, prior to stenting. Preliminary analysis showed that normal microvascular perfusion (as assessed by the myocardial blush grade) was restored in about 60% of these patients, compared to approximately 30% in historical controls [38].

Thus, the early results of mechanical thrombectomy devices in thrombus-rich lesions are encouraging. Additional studies are required to establish the utility of device-mediated thrombus debulking and indications for the procedure

Role of distal protection for thrombus-rich lesions

Two classes of devices designed to trap embolic matter downstream from the site of intervention are the occlusive type (e.g., PercuSurge, USA) and the filter wires type (e.g., Angioguard, USA). With the PercuSurge system, a balloon is incorporated into a 0.014" wire, passed across the lesion and then inflated, occluding the distal vessel. Angioplasty and/or stenting is then performed over the guidewire. Following intervention, an aspiration catheter is introduced over the device wire, aspirating embolized material trapped by the distal balloon. Preliminary experience in vein graft angioplasty was promising [39] and, subsequently, the 800 patient multicenter randomized SAFER trial demonstrated a 50% reduction in in-hospital adverse events with PercuSurge distal protection during saphenous vein graft stenting, when compared to stenting without protection [G. Stone, personal communication]. Preliminary experiences with the PercuSurge in AMI patients undergoing percutaneous intervention suggest that normal myocardial blush may be achieved in more than 60% [G. Stone, personal communication].

In filter wire-type devices, an emboli entrapment net is mounted on a 0.014" guidewire and expanded distally to the lesion. Intervention is then performed over the guidewire. Unlike occlusive devices, filters do not block distal blood flow when first deployed. Dislodged material is caught by the distal filter, which is then closed and retracted only at the end of the procedure. These filter devices are currently being tested in several randomized clinical trials of patients with vein graft disease. A limitation of these devices in thrombus-rich lesions is that thrombotic emboli can partially block the filter and accelerate thrombus accumulation on it, thereby diminishing flow. The efficacy of all distal protection systems in native coronary arteries is potentially limited by side branches originating proximally to the location of the device, which may not be protected from embolization. More data are required before the use of distal protection devices is indicated in the treatment of thrombus-rich lesions.

Summary

Despite widespread use of stents and GP IIb/IIIa antagonists, complications following percutaneous treatment of thrombus-rich lesions continue to plague patients with ACS. In these patients the angiographically evident coronary thrombosis may represent a high degree of thrombus burden, which leads to a higher level of microembolization and its clinical sequelae. New catheter-based thrombus burden reduction systems and distal protection devices show promise for improving the prognosis of these high risk patients by decreasing distal microembolization, and thereby preventing myonecrosis. Careful procedural timing and patient selection are also likely to improve outcomes and resource utilization in the management of ACS patients.

References

1. The PRISM-PLUS Study Investigators. Inhibition of the glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial infarction. *N Engl J Med* 1998;338:1488–97.
2. Davies MJ. Stability and instability: two faces of coronary atherosclerosis. *Circulation* 1996;94:2013–20.
3. Lee RT, Grodzinsky AJ, Frank EH, et al. Structure-dependent dynamic mechanical behavior of fibrous caps from human atherosclerotic plaques. *Circulation* 1991;83:1764–70.
4. Van de Wal AC, Becker AE, Van de Loos CM, et al. Site of intimal rupture or erosion of thrombosed coronary atherosclerotic plaques is characterized by an inflammatory process irrespective of the dominant plaque morphology. *Circulation* 1994;89:36–44.
5. Hawiger J. Formation and regulation of platelet and fibrin hemostatic plug. *Hum Pathol* 1987;18:111–22.
6. Davies MJ. A macro and micro view of coronary vascular insult in ischemic heart disease. *Circulation* 1990;82(Suppl II):38–46.
7. DeWood MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. *N Engl J Med* 1980;303:897–902.
8. Sherman CT, Litvack F, Grundfest W, et al. Coronary angioscopy in patients with unstable angina pectoris. *N Engl J Med* 1986;315:913–19.
9. Mizuno K, Satomura K, Miyamoto A, et al. Angioscopy of coronary artery thrombi in acute coronary syndromes. *N Engl J Med* 1992;326:287–91.
10. Davies M, Thomas A. Knapman P, et al. Intramyocardial platelet aggregation in patients with unstable angina suffering sudden ischemic cardiac death. *Circulation* 1986;73:418–27.

11. Saber RS, Edwards WD, Bailey KR, et al. Coronary embolization after balloon angioplasty or thrombolytic therapy: an autopsy study of 32 cases. *J Am Coll Cardiol* 1993;22:1283–8.
12. Bruschke AV, Padmos I, Buis B, et al. Arteriographic evaluation of small coronary arteries. *J Am Coll Cardiol* 1990;15:784–9.
13. Giri S, Kiernan FJ, Mitchel JF, et al. Intracoronary thrombus is a marker for adverse angiographic and clinical outcomes in patients undergoing primary angioplasty [Abstract]. *Circulation* 1998;98(Suppl):324A.
14. Abbo KM, Dooris M, Glazier S, et al. Features and outcome of no-reflow after percutaneous coronary intervention. *Am J Cardiol* 1995;75: 778–82.
15. Morishima I, Sone T, Tsuboi H, et al. Long-term prognostic impact of angiographic no-reflow phenomenon in patients treated with coronary angioplasty for acute myocardial infarction: possible involvement of left ventricular remodeling [Abstract]. *Circulation* 1999;100(Suppl):112A.
16. Ito H, Okamura A, Iwakura K, et al. Myocardial perfusion patterns related to thrombolysis in myocardial infarction perfusion grades after coronary angioplasty in patients with acute anterior wall myocardial infarction. *Circulation* 1996;93:1993–9.
17. Kondo M, Nakano A, Saito D, et al. Assessment of "microvascular no-reflow phenomenon" using technetium-99m macroaggregated albumin scintigraphy in patients with acute myocardial infarction. *J Am Coll Cardiol* 1998;898–903.
18. Van 't Hof A, Liem A, Suryapranata H, et al., on behalf of the Zwolle Myocardial Infarction Study Group. Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction. Myocardial Blush Grade. *Circulation* 1998;97:2302–6.
19. Stone GW, Lansky AJ, Mehran R, et al. Beyond TIMI-3 flow: the importance of restored myocardial perfusion for survival in high risk patients undergoing primary or rescue PTCA. *J Am Coll Cardiol* 2000;35(2):403A.
20. Grines CL, Cox DA, Stone GW, et al. Coronary angioplasty with or without stent implantation for acute myocardial infarction. *N Engl J Med* 1999;341:1949–56.
21. Zhao XQ, Snappin S, Jang IK, Sax R, Theroux P. Association of presence of thrombus and troponin I levels in patients with unstable angina or non-Q-wave myocardial infarction in PRISM-PLUS [Abstract]. *J Am Coll Cardiol* 2000;35(Suppl A):362A.
22. Brodie BR, Stuckey TD, Hansen C, et al. Benefit of coronary reperfusion before intervention on outcomes after primary angioplasty for acute myocardial infarction. *Am J Cardiol* 2000;85:13–18.
23. Waxman S, Sassower SA, Mittleman MA, et al. Angioscopic predictors of early adverse outcome after coronary angioplasty in patients with unstable angina and non-Q-wave myocardial infarction. *Circulation* 1996;93:2106–13.
24. Ellis SG, Vandormael MG, Cowley MJ, et al. Coronary morphologic and clinical determinants of procedural outcome with angioplasty for multivessel disease: implications for patient selection. *Circulation* 1990;82:1193–202.
25. The EPISTENT Investigators. Randomized placebo-controlled and balloon angioplasty-controlled trial to assess safety of coronary stenting with use of platelet glycoprotein IIb/IIIa blockade. *Lancet* 1998;352:87–92.
26. The EPIC Investigators. Use of monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high-risk coronary angioplasty. *N Engl J Med* 1994;330:951–6.
27. Brener SJ, Barr LA, Burchenal JEB, et al., on behalf of RAPPORT Investigators. Randomized, placebo-controlled trial of platelet glycoprotein IIb/IIIa blockade with primary angioplasty for acute myocardial infarction. *Circulation* 1998;98:734–41.
28. Lansky AJ, Stone GW, Mehran R, et al. Impact of baseline TIMI flow on outcomes after primary stenting vs. primary PTCA in acute myocardial infarction. Results from PAMI stent [Abstract]. *J Am Coll Cardiol* 1999;33(Suppl A):368A.
29. Neumann JF, Blasini R, Schmitt C, et al. Effect of glycoprotein IIb/IIIa receptor blockade on recovery of coronary flow and left ventricular function after placement of coronary-artery stents in acute myocardial infarction. *Circulation* 1998;98:2695–701.
30. Ellis SG, Guetta V, Miller D, et al. Relation between lesion characteristics and risk with percutaneous intervention in the stent and glycoprotein IIb/IIIa era. *Circulation* 1999;100:1971–6.
31. Rosenschein U, Roth A, Rassin T, et al. Analysis of coronary ultrasound thrombolysis endpoints in acute myocardial infarction (ACUTE Trial): results of the feasibility phase. *Circulation* 1997;95:1411–16.
32. Rosenschein U, Hertz I, Tenenbaum-Koren E, et al. Coronary ultrasound thrombolysis in acute myocardial infarction: results from the ACUTE Study [Abstract]. *J Am Coll Cardiol* 1998;31:192A.
33. Brosh D, Bartorelli AL, Cribier C, et al., for the Acolysis Registry Study Group. Percutaneous transluminal therapeutic ultrasound for high-risk thrombus containing lesions in native coronary arteries. *Cardiovasc Coronary Intervent* 2002;55:43–9.
34. Savage MP, Ramee SR, Ho KKL, et al. Rheolytic thrombectomy for the treatment of aortocoronary venous bypass graft thrombosis: results from the VeGAS II trial [Abstract]. *Circulation* 1999;100: 79A.
35. Silva JA, Ramee SR, Cohen DJ, et al. Rheolytic thrombectomy during percutaneous revascularization for acute myocardial infarction: experience with the Angiojet catheter. *Am Heart J* 2001;141:353–9.
36. van Ommen VG, van den Bos AA, Pieper M, et al. Removal of thrombus from aortocoronary bypass grafts and coronary arteries using the 6Fr hydrolyser. *Am J Cardiol* 1997;79:1012–16.
37. Stone GW, Cox D, Lowe RI, et al. First United States experience with a novel atherectomy and thrombectomy device in thrombotic lesions in native coronary arteries and saphenous vein grafts. *J Am Coll Cardiol* 2000;35(2):40A.
38. Cox DA, Stuckey T, Low R, et al. Adjunctive thrombectomy combined with stenting for AMI: The Endicor X-SIZER AMI Registry. *J Am Coll Cardiol* 2001;37:648A.
39. Carlino M, Gregorio JD, Di Mario C, et al. Prevention of distal embolization during saphenous vein graft lesion angioplasty: experience with a new temporary occlusion and aspiration system. *Circulation* 1999;99:3221–3.

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