Current Approach to Slow Flow and No-Reflow

A preventive approach appears to be the best strategy based on current understanding of this phenomenon.

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Slow flow and the no-reflow phenomenon are feared complications after percutaneous coronary interventions (PCIs). In general terms, both phrases refer to impaired epicardial coronary flow and myocardial perfusion despite patency of the epicardial arteries during PCI. Slow flow and no-reflow usually manifest as a failure of the affected artery to opacify after angioplasty or stenting of the occluded segment during acute myocardial infarction (AMI) (no-reflow), or as a reduction in flow in the affected artery after PCI of a nonoccluded segment. No-reflow is associated with a worse prognosis and has been shown to be an independent predictor of death, MI, and impaired left ventricular function.[1-5] Several key pathophysiological processes, usually in combination, are believed to be responsible for this complication, including distal embolization of atherothrombotic debris, thrombus formation, and endothelial dysfunction of the distal arteriolar and capillary bed, including endothelial desquamation and microcirculatory vasospasm.[6] The incidence of this complication varies with the type of PCI, being highest in the setting of primary PCI, saphenous vein graft (SVG) intervention, and rotational atherectomy (Table 1).[7] Several management strategies have undergone evaluation in trials with variable success rates, and continued understanding of this phenomenon suggests that prevention might be better than the cure in most settings.[8]

TABLE 1. INCIDENCE OF ANGIOGRAPHIC NO-REFLOW IN VARIOUS PCI SETTINGS

PCI Type	Incidence of No-Reflow
All PCI	0.6%–2%[7,104]
Primary PCI	8.8%–11.5%[1,7]
SVG PCI	8%–15%[68,105]
Rotational atherectomy	≤16%[75,76]

PATHOPHYSIOLOGY

An understanding of the pathophysiology of slow flow and no-reflow is critical in understanding the various preventive and treatment strategies. The no-reflow concept was first described in animal brain ischemic models in 1967.[9] Brains of rabbits exposed to long periods (>2.5 minute) of ischemia did not have normal blood flow restored when the ischemia was relieved. This was pathologically correlated with changes in brain microvasculature that impeded normal flow to brain cells.[10,11] Kloner et al demonstrated a similar phenomenon in canine hearts, in which prolonged periods (>90 minutes) of proximal coronary occlusion were associated with only partial restoration of coronary flow despite removal of the coronary occlusion.[11] Electron microscopy of the coronary microvasculature within the no-reflow zones showed significant capillary damage with endothelial swelling and intraluminal protrusions, which could occlude the capillary lumen. Other studies highlighted the role of intravascular plugging with fibrin, platelets, leukocytes, and atherothrombotic debris as potential contributors to the no-reflow phenomenon.[12-16] The etiology of no-reflow and slow flow in any patient is, therefore, likely multifactorial, with endothelial damage in the microvasculature during ischemia and distal emboliza-

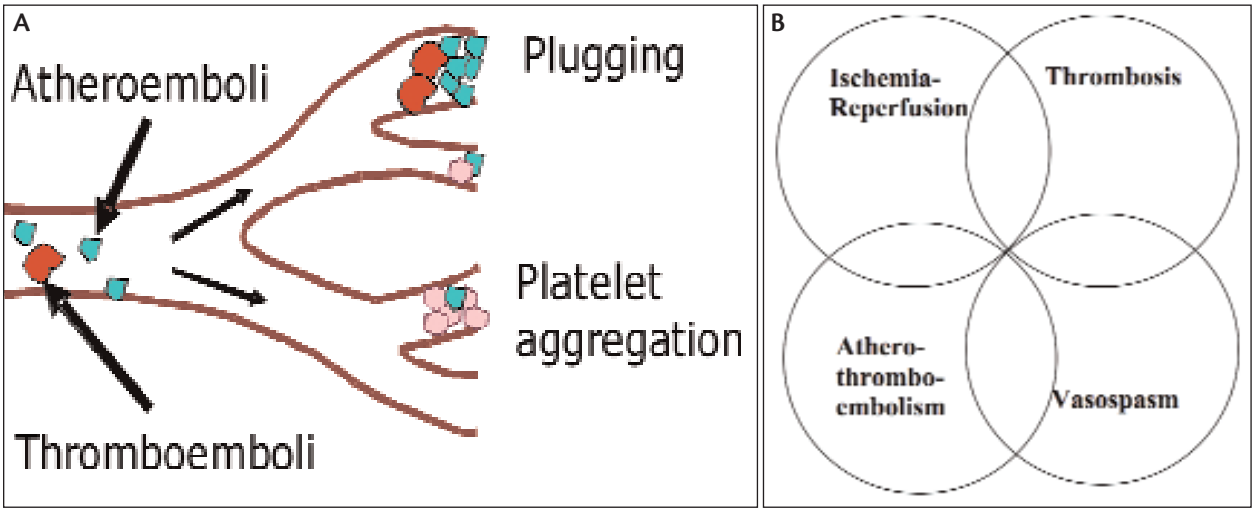

Figure 1. Multifactorial causation of no-reflow and slow-flow following percutaneous coronary intervention. A and B illustrate the complex interaction of several pathophysiologic processes in the causation of slow flow and no-reflow. Current understanding suggests more than one mechanism may be responsible in any given situation. (Adapted and reprinted with permission from Hori M, Inoue M, Kitakaze Y, et al. Role of adenosine in hyperemic response of coronary blood flow in microembolization. Am J Physiol. 1986;250:H509-518.)

tion of microparticles during reperfusion, resulting in diminished myocardial perfusion. This complex interaction is illustrated in Figure 1.

DIAGNOSIS OF SLOW FLOW AND NO-REFLOW

Slow flow and no-reflow with impaired myocardial perfusion can be diagnosed angiographically or by using adjunctive imaging modalities that can quantify myocardial perfusion, such as myocardial contrast echocardiography. Angiographically, the most widely used schemes to describe coronary flow and myocardial perfusion, both qualitatively and semiquantitatively, include the TIMI blood flow grades, the corrected TIMI frame count (TFC), and the myocardial blush grade (MBG).[17-19] These schemes are summarized in Table 2.

The TIMI coronary flow grade was introduced by the TIMI study group in 1985 as a simple, qualitative tool to assess angiographic coronary flow rates to gauge the efficiency of thrombolytic therapy.[17] Coronary flow is graded on a scale of 0 through 3 depending on flow characteristics, as summarized in Table 2. Improved TIMI grades have been shown to be correlated with improved outcomes.[20,21] No-reflow is traditionally defined as TIMI grade 0 or 1, and slow flow is defined as TIMI grade 2 in this scheme.[17] The TFC method, first described by Gibson et al, provided a semiquantitative method of assessing coronary flow.[22] The number of angiographic frames for contrast to reach a specified distal segment in the coronary artery with cineangiography performed at 30 frames per second through a 6-F catheter was designated the TFC. The distal landmarks and normal reference ranges are summarized in Table 1. A further correction is made in the TFC for the left anterior descending artery (LAD), given its longer length relative to the other coronary arteries, by dividing the TFC in the LAD by a factor of 1.7, which yields the corrected TFC (cTFC). Normal coronary and microvascular function usually yield a cTFC of <20, a slow flow of cTFC of 20 through 40, and a no-reflow cTFC of >40.[21] The prognostic significance of the cTFC was studied in an analysis of patients enrolled in the TIMI studies, in which it was shown to be an independent predictor of mortality.[22]

The concept of MBG was developed as a means of describing myocardial perfusion at the level of the capillary, in addition to describing epicardial artery flow.[18] Myocardial microvascular perfusion, as assessed by an MBG score, has been shown to be one of the strongest predictors of mortality after primary PCI, independent of infarct artery patency.[23] MBG is scored 0 to 3, as summarized in Table 2. In this scheme, true no-reflow would correlate with an MBG of 0 and 1, and slow flow would correspond with an MBG of 2. Of course, the accuracy of these three methods depends on several factors, such as amount of contrast injected, length of injection, and fluoroscopic time, as well as systemic blood pressure. For example, a contrast injection rate increase of more than 1 mL/s by hand injection can decrease the cTFC by two frames.[24]

Adjunctive imaging modalities that can assess myocar-

TABLE 2. SCHEMES TO DESCRIBE CORONARY AND MYOCARDIAL BLOOD FLOW DURING CORONARY ANGIOGRAPHY

TIMI Flow Grades[17]
- TIMI 0: No contrast flow beyond the site of occlusion (no perfusion)
- TIMI 1: Contrast flow beyond the site of occlusion but failing to opacify entire artery (penetration with minimal perfusion)
- TIMI 2: Contrast flow beyond the site of occlusion and opacification of the entire artery but at a rate slower than normal (partial reperfusion)
- TIMI 3: Normal flow, with opacification of the entire artery at a normal rate

cTFC[19]
- LAD: Normal TFC 36±3
- Normal cTFC 21±2
- LCx: Normal TFC 22±4
- RCA: Normal TFC 20±3

Normal flow: cTFC <20–22
- Distal landmarks: LAD, distal bifurcation; LCx, distal bifurcation of the branch segments with the longest total distance; RCA, first branch of the posterolateral artery

MBG[18]
- Blush 0: No appearance of blush or contrast density (also persistent staining of myocardium)
- Blush 1: Minimal myocardial blush or contrast density
- Blush 2: Moderate myocardial blush or contrast density
- Blush 3: Normal myocardial blush or contrast density

LCx, left circumflex artery; RCA, right coronary artery.

dial perfusion and have found clinical utility in identifying no-reflow zones include myocardial contrast echocardiography,[25,26] nuclear imaging,[27,28] contrast-enhanced MRI,[29,30] and PET imaging.[31] However, despite the availability of these adjunctive imaging modalities, the diagnosis of coronary slow flow and no-reflow after PCI remains largely an angiographic one. Importantly, no-reflow must be suspected clinically if there is a lack of ST-segment resolution after PCI.

SLOW-FLOW AND NO-REFLOW IN AMI

PCI in the setting of AMI is associated with high rates of distal embolization due to the relatively high thrombus burden associated with plaque rupture and coronary occlusion. The sequelae of distal embolization results in reduced myocardial perfusion and increased myocyte damage, which portends a worse prognosis.[32] Macroscopic distal embolization may be seen in up to 16% of patients undergoing primary PCI,[32] and suboptimal tissue perfusion may be seen in 20% to 40% of patients despite restoration of TIMI 3 epicardial flow.[18,33] A number of strategies may be employed to prevent slow flow and no-reflow during primary PCI. First, given the central role of duration of ischemia in the pathogenesis of impaired flow, primary PCI should be performed as soon as possible to limit ischemia reperfusion injury. In the catheterization laboratory, two technologies have emerged as potentially beneficial in improving epicardial and myocardial perfusion: adjunctive pharmacotherapy with glycoprotein IIb/IIIa inhibitors (GPIIb/IIIa) and mechanical devices to prevent distal embolization.

GPIIb/IIIa inhibitors block the final common pathway in the platelet activation and aggregation cascade, and as such, exert a powerful antithrombotic effect. Abciximab remains the most studied agent in this class in the treatment of AMI. In the Abciximab before Direct Angioplasty and Stenting in Myocardial Infarction Regarding Acute and Long-Term Follow-up (ADMIRAL) trial, upstream use of abciximab resulted in a higher rate of TIMI 3 flow after primary PCI compared to placebo in patients with STEMI undergoing primary PCI (95.1% vs 86.7%; P=.04) and was associated with reduced major adverse cardiac events (MACE) at 30 days (6% vs 14.6%; P<.01).[34] The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial, by comparison, did not demonstrate a benefit with abciximab on final TIMI 3 flow in patients with STEMI undergoing primary PCI.[35] However, abciximab was only given at the time of PCI in the CADILLAC trial, compared to upstream administration in the ADMIRAL trial. Other studies have demonstrated specifically the beneficial impact of using GPIIb/IIIa inhibitors during primary angioplasty on coronary microvascular flow using the coronary flow wire measurements[36] and myocardial contrast echocardiography.[37] This strongly suggests that the beneficial effect of abciximab results, at least partly from reduction of no-reflow zones in the myocardium. Moreover, a recent meta-analysis of all trials of abciximab in STEMI (11 trials; 27,115 patients) showed that abciximab administration during primary angioplasty is associated with a significant mortality reduction.[38] These data from randomized controlled trials confirm improved epicardial flow, better tissue perfusion with less no-reflow phenomenon, and improved clinical outcomes with abciximab use in STEMI, and therefore make a compelling case for the use of abciximab as a standard of care in patients undergoing primary PCI.

The use of adjunctive mechanical devices to prevent

TABLE 3. ADJUNCTIVE MECHANICAL DEVICES TO PREVENT DISTAL EMBOLIZATION DURING PRIMARY PCI

Device	Study	Date*	n	Primary Endpoint	Improvement in Post-PCI TIMI 3 Flow	Improvement in Post-PCI MBG 3	30-Day Mortality Benefit
X-sizer (ev3 Inc.)	Napodono et al[39]	2003	92	MBG	N	Y	N
	X-Amine ST[40]	2005	201	STSR	N	N	N
	Beran et al[41]	2002	61	cTFC	N	n/a	N
AngioJet (Possis Medical Inc.)	Antoniucci et al[42]	2004	100	STSR	N	n/a	N
	AIMI[43]	2006	480	Infarct size	N	N	N
Diver (ev3 Inc.)	REMEDIA[44]	2005	99	MBG/STSR	N	n/a	N
	De Luca et al[45]	2006	78	LV remodeling	N	Y	N
Rescue Catheter (Boston Scientific Corporation)	Dudek et al[46]	2004	72	n/a	N	Y	n/a
	NON-STOP[107]	2004	258	n/a	N	n/a	N
	Kaltoft et al[47]	2006	225	Infarct size	N	n/a	N
Pronto Catheter (Vascular Solutions, Inc.)	DEAR–MI[50]	2005	148	STSR/MBG	N	Y	N
Export Catheter (Medtronic CardioVascular)	EXPORT[58]	2005	50	STSR	N	N	N
TVAC Catheter	VAMPIRE[49]	2005	355	MBG	N	Y	N
Guardwire Plus (Medtronic CardioVascular)	EMERALD[52]	2005	501	MBG/STSR	N	N	N
	ASPARAGUS[53]	2004	341	MBG/STR	N	N	N
	Tahk et al[108]	2004	96	APV	Y	Y	n/a
	Nanasato et al[109]	2004	64	n/a	N	Y	n/a
FilterWire EX (Boston Scientific Corporation)	PROMISE[53]	2005	200	APV	N	n/a	N
AngioGuard (Cordis Corporation)	DIPLOMAT[56]	2003	60	STSR	N	Y	N
SpideRX (ev3 Inc.)	PREMIAR[57]	2007	140	STSR	N	N	N
FilterWire EZ (Boston Scientific Corporation)	UPFLOW[55]	2006	100	STSR/MBG	N	N	N

**Year of publication or presentation.*
TVAC, thrombus aspiration vacuum catheter; STSR, ST-segment resolution; APV, average peak velocity.

distal embolization during primary PCI appears intuitive. Several devices have now been evaluated in randomized clinical trials,[39-58] the results of which are briefly summarized in Table 3. As illustrated in Table 3, a number of devices have been tested, generally in small trials that used surrogate endpoints as the primary outcome measure. Most trials were generally underpowered to detect a mortality benefit and failed to do so. The results of many of these randomized trials were summarized in a recent meta-analysis (21 trials, 3,721 patients) by De Luca et al,[45] which showed that adjunctive mechanical devices to prevent distal embolization in patients with AMI treated with primary PCI were associated with higher rates of postprocedural TIMI 3 flow and MBG 3, as well as less distal embolization.[59] However, despite these improvements in epicardial flow and myocardial perfusion, no benefit was noted in terms of 30-day mortality. Although the reasons for this discrepancy in trial findings are not

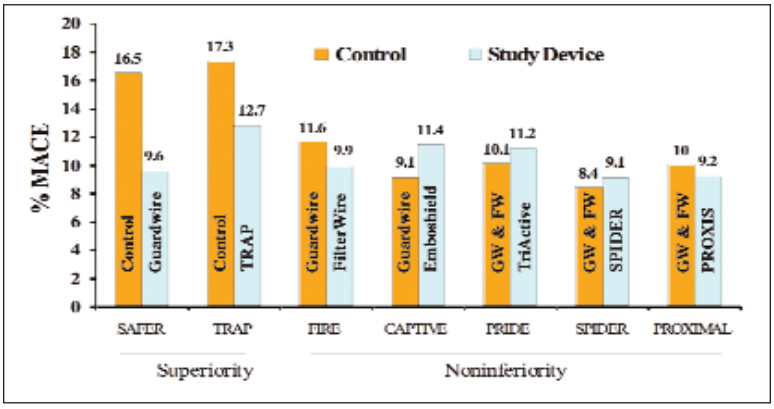

Figure 2. Studies of adjunctive mechanical devices to prevent distal embolization in SVG PCI.

clear, it highlights the need for larger trials with higher-risk patients and longer-term follow-up to optimally define the role of adjunctive mechanical devices in primary PCI. Until such data are available, routine use of adjunctive devices to prevent distal embolization during primary PCI remains a controversial and unresolved issue.

A number of vasodilator agents have been shown to improve surrogate endpoints, such as TIMI flow rate, corrected TIMI frame counts, and wall motion scores, among others, when used as an adjunct in treating AMI. Such vasodilator agents include adenosine, verapamil, nicorandil, and sodium nitroprusside.[1,60-63] However, the results of the Acute Myocardial Infarction Study of Adenosine (AMISTAD) trials highlight the pitfalls in accepting these surrogate endpoints. The AMISTAD studies investigated the utility of adenosine in primary PCI. In the first (and smaller) AMISTAD study, which was not powered to evaluate clinical endpoints, a 3-hour intravenous infusion of adenosine (70 µg/kg per minute) resulted in a relative reduction in infarct size of 33% in patients treated with thrombolysis.[63] This result formed the basis of the larger AMISTAD-II study (n=2,118), which was powered to evaluate clinical endpoints in patients treated with either thrombolysis or primary PCI.[64] Although a significant 57% relative reduction in infarct size was again demonstrated with the 70 µg/kg per minute infusion, the study did not show any benefit in clinical endpoints, including mortality rates. In this instance, improvement in validated surrogate endpoints did not appear to translate into meaningful clinical benefits. An exception in this category would appear to be nicorandil, which was shown to significantly reduce the primary clinical endpoint of death or heart failure (6.5% vs 16.4%; *P*=.05) when administered as a single intravenous dose of 12 mg in a 368-patient randomized study of acute STEMI patients undergoing primary PCI.[60]

Therefore, although some of the results are encouraging, there would not appear to be sufficient evidence to recommend routine use of any vasodilator agents during primary PCI. Their use should be reserved for the treatment of no-reflow when preventive measures have failed.

SLOW FLOW AND NO-REFLOW IN SVG PCI

SVG PCI is associated with high rates of distal atherothromboembolism due to graft degeneration, higher atherosclerotic and thrombotic burden, and a softer plaque composition.[65] A high incidence of no-reflow (approximately 8%), as well as a high incidence of periprocedural MI (up to 28%), has been reported with SVG PCI.[7] Because patients with SVG tend to have a higher burden of coronary disease and impaired left ventricular function, they have a tendency to have a particularly adverse prognosis after these distal embolic complications.[66] Therefore, prevention of distal embolization in SVG PCI is a relatively more important goal.

Several embolic protection devices have demonstrated efficacy in reducing atheroembolic complications during

Figure 3. Atherothrombotic debris retrieved with the FilterWire EZ device (Boston Scientific Corporation, Natick, MA) after elective SVG PCI. The distal filter with clot remnants and retrieved clot are shown side by side.

SVG interventions. The pivotal Saphenous Vein Graft Angioplasty Free of Emboli Randomized (SAFER) trial randomized 801 patients undergoing SVG PCI to conventional stenting versus stenting over the PercuSurge GuardWire (Medtronic CardioVascular, Santa Rosa, CA) distal balloon protection device.[67] A substantial reduction in 30-day MACE (16.9–9.6%) and no-reflow (8.3% to 3.3%) was noted in this study. This single trial established distal protection in eligible SVG lesions as a standard of care. The EPI FilterWire distal protection device (Boston Scientific Corporation) was shown to be noninferior with respect to 30-day MACE to the PercuSurge GuardWire in a 656-patient, head-to-head randomized comparison[68] and is thus an acceptable alternative. Several other devices have since been shown to be noninferior to either the GuardWire or the FilterWire EX (Boston Scientific Corporation) in randomized controlled trials. Figure 2 provides a summary of the trials of devices to prevent distal embolization in SVG PCI. Figure 3 shows embolic debris retrieved from an SVG intervention case. Predicting which SVGs are more prone to distal embolization remains a challenge,[69,70] and therefore, embolic protection in all cases in which device deployment is feasible should be considered the standard of care. Importantly, despite significant benefits with these devices compared to placebo, the MACE rate still remains approximately 10%, as illustrated in Figure 2, and suggests either the need for better distal embolic protection, or perhaps another mechanism for the high rates of distal myocardial damage.

GIIb/IIIa inhibitors have not been shown to reduce atheroembolic complications in SVG interventions.[71,72] Limited data are also available for a small number of pharmacological agents other than GPIIb/IIIa inhibitors in preventing no-reflow in SVG PCI. Intragraft adenosine did not reduce the incidence of no-reflow in a retrospective study of 143 patients undergoing SVG PCI.[73] In the Vasodilator Prevention of No-Reflow (VAPOR) randomized study, a significant reduction in no-reflow was noted with 200 µg of intragraft verapamil, with no-reflow observed in none of the patients in the treatment arm compared to one third of the patients in the control group.[74] However, this small study consisted of only 22 patients. Fischell et al reported a low incidence of no-reflow (2.4%) in an observational registry of 83 consecutive SVG PCIs performed without distal embolic protection, all of which received intragraft nicardipine at a dose of 200 to 300 µg.[75] Although the available data are limited and not sufficient to support the routine use of these medications for the prevention of slow or no-reflow during SVG PCI, these results are promising. Given that MACE rates with SVG PCI remain approximately at 10%, even with the use of embolic protection devices, it is feasible that these agents may find a role as adjunctive therapy with embolic protection devices in SVG PCI in the future.

TABLE 4. ACTION PLAN FOR NO-REFLOW

Step 1. Resuscitate patient as required
- Analgesia
- Fluids
- Inotropes
- Temporary pacing
- Intra-aortic balloon pump

Step 2. Exclude mechanical cause for impaired flow
- Dissection at angioplasty or stent site
- Thrombus
- Spasm at lesion site: administer nitroglycerin

Step 3. Check ACT and top up heparin as required
- Aim ACT >300 seconds without GPIIb/IIIa agent
- Aim ACT 250–300 seconds with GPIIb/IIIa agent

Step 4. GPIIb/IIIa should be administered for presumably beneficial antiplatelet effects

Step 5. Vasodilator agents via intracoronary route
- Dosage as per Table 5

ACT, activated clotting time.

SLOW FLOW AND NO-REFLOW IN ROTATIONAL ATHERECTOMY

Rotational atherectomy is associated with a high rate of slow flow and no-reflow, with the incidence of no-reflow up to 16%.[76,77] The pathogenesis of this relates mainly to distal embolization of particulate debris generated during rotational atherectomy[76,77] but also to platelet activation with burr rotation.[78] It is more common in longer and heavily calcified lesions.[76,77] Several precautions related specifically to procedural technique are recommended to prevent no-reflow, including avoiding speeds above 150,000 rpm, avoiding drops in burr speeds of more than 5,000 rpm, beginning with a smaller burr size (burr:artery ratio <0.6 or a burr size of 1.25 to 1.5 mm), and limiting runs to short intervals (20–30 seconds).[78-80] The Cocktail Attenuation of Rotational Atherectomy Flow Effects (CARAFE) study established the standard of continuous flushing of the treated vessel with a saline solution containing verapamil, glycerlyl trinitrate, and unfractionated heparin.[81] Recent studies have suggested that nicorandil in the flush solution may be more effective in reducing no-reflow compared to verapamil.[82,83] Although GPIIb/IIIa inhibitor use during rotational atherec-

TABLE 5. SUGGESTED INTRACORONARY DRUG ADMINISTRATION REGIMENS FOR TREATMENT OF SLOW FLOW AND NO-REFLOW

Drug	Administration
Verapamil[7]	Boluses of 100–200 µg up to four doses
Adenosine[96]	Boluses of 24 µg up to four doses
Sodium nitroprusside[97]	Boluses of 100 µg up to total of 1,000 µg
Nitroglycerin[106]	Boluses of 100–200 µg up to four doses
Epinephrine[101]	Intracoronary dose 50–200 µg

tomy has been shown to reduce periprocedural myonecrosis,[84,85] caution must be exercised with up-front administration given the risk of coronary perforation.

MANAGEMENT OF SLOW FLOW AND NO-REFLOW

When slow flow and no-reflow are encountered in the catheterization laboratory after PCI, the mainstay of treatment is pharmacologic. A systematic and algorithmic approach is suggested in Table 4. As an important first step, the operator must exclude a mechanical cause, such as coronary spasm, dissection, or thrombus formation, as a cause of impaired flow. Attention to supportive treatment for the patient should also be emphasized because patients frequently experience chest pain, hypotension, and cardiac dysrhythmias. There is limited evidence for a small number of vasodilator agents that have been shown to improve coronary flow in this setting. At least one of these agents should be administered because the ability to reverse slow flow and no-reflow has been shown to have important prognostic implications.[86] Table 5 summarizes the commonly used vasodilators in the catheterization laboratory. For refractory slow flow and no-reflow, we advocate ongoing supportive treatment with GPIIb/IIIa inhibitors, intra-aortic balloon pump, and ionotropic support as required.

In terms of vasodilator therapies for slow flow and no-reflow, the two most studied agents are adenosine and verapamil, with the evidence for their use derived from both animal studies and small clinical studies. Calcium-channel blockers have been shown to attenuate no-reflow in both laboratory animal models[87,88] and clinical studies,[89-91] putatively on the basis of vasodilation of the distal microcirculation. In a prospective study of verapamil for the treatment of no-reflow, approximately 90% of patients demonstrated prompt response to verapamil with improvements in TIMI flow grade and corrected TIMI frame count.[7] In another prospective study of no-reflow in 36 SVG lesions, intragraft verapamil was associated with improved flow in all patients.[92] However, in another study, intracoronary verapamil was not superior to conservative treatment (including intracoronary nitrates) in improving coronary flow, as measured by cTFC in patients with established no-reflow.[1] Importantly, in a recent study comparing intracoronary verapamil and adenosine for slow flow and no-reflow prophylaxis in patients with acute coronary syndromes, verapamil was associated with hypotension and complete heart block lasting up to 3 hours in 18% of patients.[91]

Adenosine is commonly used to manage no-reflow, and has also been shown to attenuate no-reflow in both laboratory animal models[93] and clinical studies.[63,64,94,95] In a canine model, intracoronary adenosine infusion after prolonged coronary occlusion resulted in significantly improved regional myocardial flow.[93] The putative benefit of adenosine was attributed to a combination of distal vasodilatation, decrease in neutrophil count, and preservation of endothelial structure. Sringdola et al and Fischell et al demonstrated the efficacy of rapid 24-µg boluses of intragraft adenosine in reversing established no-reflow in SVG intervention.[73,96] Because adenosine has a short half-life and is not associated with prolonged hypotension and conduction disturbances, as described previously with verapamil, it is the agent that is favored at our institution.

Nitroglycerine is frequently administered to exclude underlying spasm as a cause of no-reflow. Although this is an appropriate step, once spasm has been excluded, there is no evidence to support the use of nitroglycerine in reversing no-reflow, and it is most operators' experience that its administration is not useful.[9]

There are limited data for other agents, which might be beneficial, that are not as widely used for the treatment of no-reflow and are therefore not discussed in detail here. These agents include nitroprusside,[97] nicardipine,[98] nicorandil,[99] papaverine,[100] and epinephrine.[101] Other agents that have undergone trials and have been shown to have limited efficacy in treating no-reflow include urokinase,[102] streptokinase,[103] and tissue-type plasminogen activator.[104]

CONCLUSION

Slow flow and no-reflow result from a complex interaction of several pathophysiological processes. Prevention of impaired flow in patients at highest risk remains the best strategy. In AMI, timely reperfusion should be achieved, and GPIIb/IIIa agents should be strongly considered in all patients. Adjunctive mechanical devices to prevent distal embolization during AMI should be considered in patients with a high thrombus burden,

although the clinical benefits of these devices have not been clearly established in primary PCI at present. In SVG PCI, distal protection of all suitable grafts should be employed. Procedural precautions aimed at preventing impaired flow states should be employed during rotational atherectomy. When slow flow or no-reflow is encountered after PCI, vasodilatory agents shown to improve epicardial and myocardial flow after the occurrence of this complication should be administered in an effort to improve myocardial perfusion, as this may improve prognosis. The best approach to slow flow and no-reflow in the present day remains one that incorporates the philosophy "prevention is better than the cure." ■

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