Cardiology Grand Rounds from
The University of North Carolina at Chapel Hill

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Incidence and Management of "No-Reflow" Following Percutaneous Coronary Interventions

ABSTRACT: No-reflow is a complex condition associated with inadequate myocardial perfusion of the coronary artery in the absence of epicardial obstruction. It can occur in several settings, including percutaneous coronary intervention, especially in complex thrombotic lesions of native arteries and vein grafts and in primary angioplasty. The causes of no-reflow are not completely understood, and current treatments consist of intracoronary vasodilators, antithrombotic therapies, and mechanical devices (including aspiration thrombectomy catheters and embolic protection devices). **KEY INDEXING TERMS:** No-reflow; Percutaneous coronary intervention; Myocardial infarction; Myocardial perfusion; Distal embolic protection. **[Am J Med Sci 2005;329(2):78–85.]**

No-reflow is a complex phenomenon in which there is inadequate myocardial perfusion of a given segment of the coronary circulation without evidence of epicardial vessel obstruction.[1] Clinically, there is sudden onset of symptoms (usually chest pain), often with electrocardiogram (ECG) changes and sometimes with hemodynamic compromise. No-reflow usually occurs in the setting of percutaneous coronary intervention (PCI), but it can also be seen in patients who have received thrombolytic therapy for acute myocardial infarction (AMI). If it persists, there is a significant increase in the risk of death, myocardial infarction, and left ventricular (LV) systolic dysfunction.[2–4]

No-reflow is diagnosed by a combination of clinical suspicion and classic coronary angiography findings of a column of contrast dye that fails to exit the epicardial artery. There is slow back-and-forth movement of the dye within the vessel, without progression of the contrast medium to the distal portions of the coronary artery. No-reflow can also be diagnosed by characteristic findings on intracoronary Doppler, which include reversal of systolic flow and rapid deceleration of diastolic flow.[5] In fact, Doppler may provide a more accurate indication of true myocardial perfusion when compared with angiography.[6]

Case Report

A 44-year-old man without any prior cardiac history awoke with chest pain and was brought to the emergency room via rescue squad. An ECG showed inferior ST elevation (Fig. 1), and the patient was treated with aspirin and heparin and referred for emergency coronary angiography. On arrival in the catheterization laboratory, the patient's chest pain had improved (decreased from 10/10 to 3/10) and initial angiography showed severe right coronary artery disease with Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow (Fig. 2A). Following the administration of intravenous abciximab (ReoPro), balloon angioplasty was performed with minimal improvement in the lesion. An intracoronary stent was placed. Coronary flow deteriorated immediately and the patient had worsening chest pain and ST elevation. No-reflow was diagnosed and intracoronary vasodilators and intracoronary lytics (tenecteplase) were administered. Within 10 minutes, coronary flow improved, the chest pain resolved, and the ECG normalized. Final angiography showed a widely patent right coronary artery with TIMI 3 flow (Fig. 2B).

Background

No-reflow was first described in humans almost 20 years ago. Schofer et al,[7] using thallium and technetium myocardial imaging, demonstrated progressive abnormal myocardial perfusion in one patient with AMI who had received thrombolytic therapy and suggested that this might be due to no-reflow. In 1986, Bates et al[8] reported the correlation between abnormal myocardial perfusion on nuclear scanning and angiographic no-reflow. In 1989, Wilson et al[9] observed persistent angina and ST elevation associated with slow antegrade flow despite a widely patent epicardial artery in five patients immediately after balloon angioplasty of a thrombus-containing lesion. Coronary dissection was excluded by the absence of a pressure gradient across the treated lesion.

Epidemiology

No-reflow is seen in 0.6% to 3.1% of PCI cases (Table 1). However, it has been reported to occur in up to 50% of PCI cases, especially in those that involve the treatment of thrombotic lesions.[10] No-

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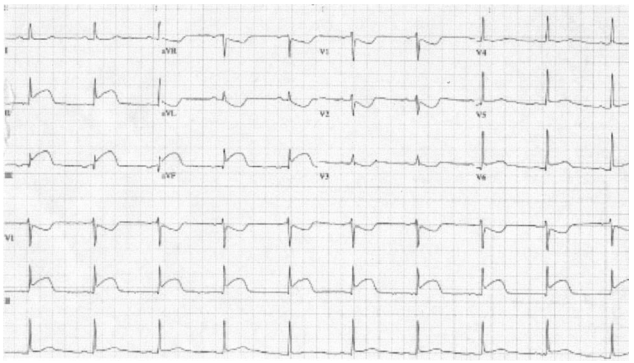

Figure 1. Electrocardiogram showing inferior-lateral ST elevation and anterior ST depression.

reflow is more common in AMI patients undergoing primary PCI, in patients undergoing saphenous vein graft interventions, and in patients who undergo rotational atherectomy.[9]

Clinically, older men undergoing PCI, who have a history of hyperglycemia and the absence of preinfarction angina, are at an increased risk for no-reflow.[11] At coronary angiography, the presence of an ulcerated plaque, intracoronary thrombus, vessel calcification, long lesions, and an occluded artery at baseline also increase risk.

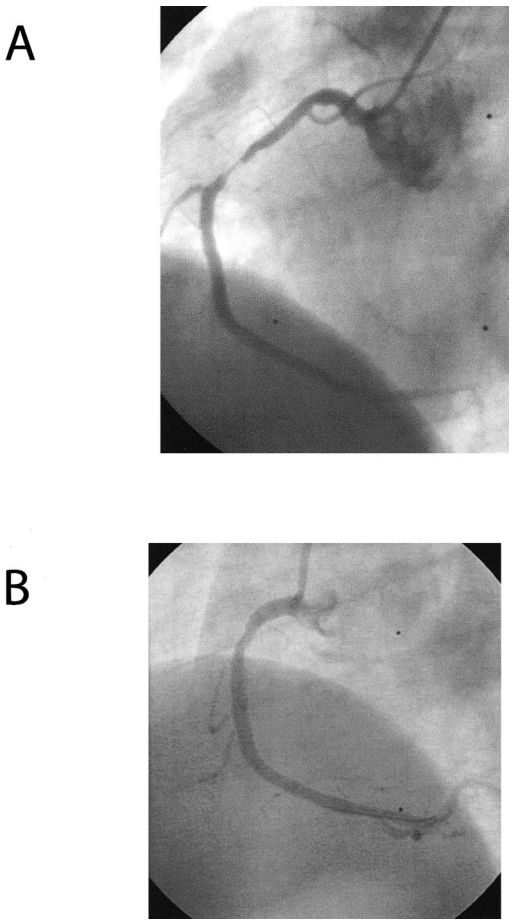

Figure 2. Right coronary artery angiograms in a left anterior oblique projection. (A) Prior to intervention. (B) After treatment.

Table 1. Incidence of No-Reflow after Percutaneous Coronary Intervention

Study Series	Incidence, %	Definition of No-Reflow	Procedure and Patients
Leopold[47]	5.8	TIMI ≤2	All PCI devices
Diez[48]	8.6	TIMI ≤2	Rotational atherectomy
Tsubokawa[49]	13	TIMI ≤2	Rotational atherectomy
Kaplan[50]	42	TIMI ≤2	Vein grafts
Abbo[3]	0.6	TIMI ≤1	All PCI devices, MI patients
Wyrens[51]	4	TIMI ≤1	All PCI devices
Pianna[4]	2	TIMI ≤2	PCI, DCA
Shani[53]	12.2	Slow flow	Primary PCI
Wilson[52]	1.3	Slow flow	PCI; MI and non-MI

DCA, directional coronary atherectomy; MI, myocardial infarction; PCI, percutaneous coronary intervention; PTCA, angioplasty; SVG, saphenous vein graft; TIMI, Thrombolysis in Myocardial Infarction.

As a result of no-reflow, patients are more likely to experience adverse cardiac events, including myocardial infarction (MI), LV systolic dysfunction, ventricular arrhythmias, congestive heart failure, and cardiac rupture.[9] An observational study reported a fivefold increased risk of MI and a fourfold increased risk of death in the 3.1% of patients who experienced no-reflow during PCI (odds ratio, 3.6).[12] A smaller study found that no-reflow was associated with a 10-fold higher incidence of myocardial infarction and death compared with patients who had normal flow during PCI.[3]

The Importance of Myocardial Perfusion

It is clear that clinical outcomes are related to both coronary blood flow and to myocardial tissue perfusion.[6] Coronary perfusion in the setting of PCI occurs on a spectrum from normal flow through completely impaired flow (ie, no-reflow). Therefore the absence of no-reflow does not imply normal perfusion. As a result, great efforts have been made to quantify myocardial and coronary blood flow to improve our understanding of these processes. Coronary angiography and various noninvasive imaging modalities (including myocardial contrast echocardiography and magnetic resonance imaging) are among the methods that have been used (Table 2).

Coronary angiography primarily measures the patency of the coronary artery, but it can also be used to estimate flow. Various indices have been developed to this end, including TIMI flow grade, TIMI frame counts, and TIMI myocardial blush. These measures of coronary flow correlate with mortality after MI and primary angioplasty. The most widely