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IMAGING VIGNETTE

The No-Reflow Phenomenon

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LACK OF INTRAMYOCARDIAL REPERFUSION after successful coronary recanalization has been defined as the "no-reflow" phenomenon. The phenomenon is not uncommon (39% with myocardial contrast echocardiography [MCE] and 43% using myocardial blush grade at coronary angiography) in humans after successful primary percutaneous coronary intervention (PCI) in the setting of acute myocardial infarction (AMI). Ischemia, reperfusion, and atheroembolism are the 3 major players in the pathogenesis of no-reflow, mediating microvascular obstruction through endothelial

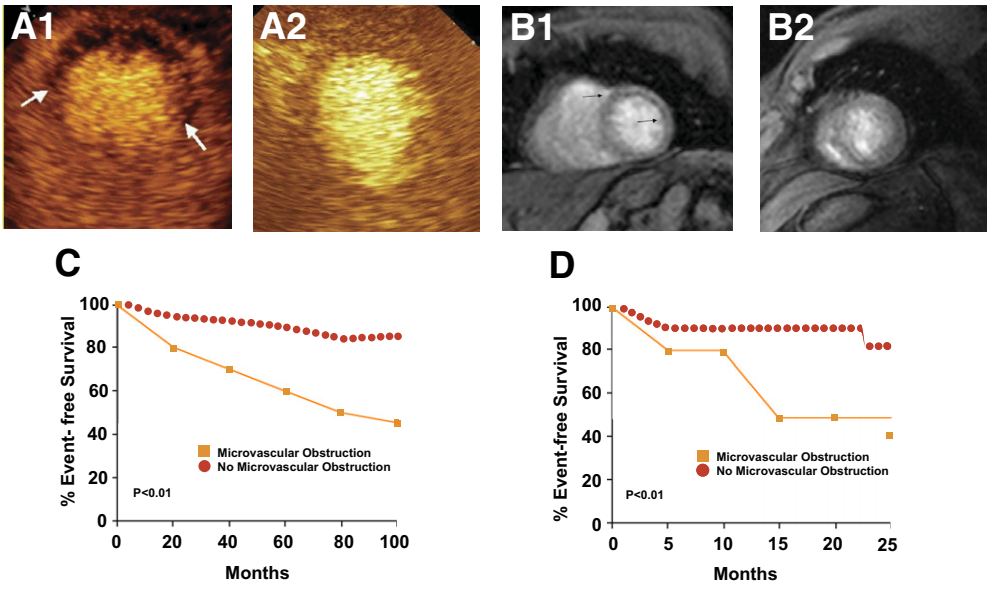

Figure 1. Visual Appearance of Microvascular Obstruction

Visual appearance of microvascular obstruction (no-reflow) as black area (between **arrows**) at myocardial contrast echocardiography (MCE) **(A1)** (also see Online Video 1) and cardiac magnetic resonance **(B1)** as compared to what a normal study would look like **(A2 and B2)**. MCE score index, a semiquantitative parameter of no-reflow, is a better predictor of left ventricular remodeling compared to end-diastolic volume at baseline, peak creatine kinase, presence of collaterals, and symptom-to-balloon time. Patients with successful primary percutaneous coronary intervention with residual microvascular obstruction have an almost 50% worse event-free survival than those without microvascular obstruction (with MCE **[C]** or with magnetic resonance imaging **[D]**).

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damage, tissue edema, platelet/fibrin/leukocyte plugs, and free radical injury. MCE and contrast-enhanced cardiac magnetic resonance (CMR) are the most common techniques for its diagnosis. The role for MCE is summarized in Figures 1 to 3. MCE can clearly delineate no reflow after primary PCI and helps in prognostication. MCE can be used to test if treating no reflow will be useful in humans.

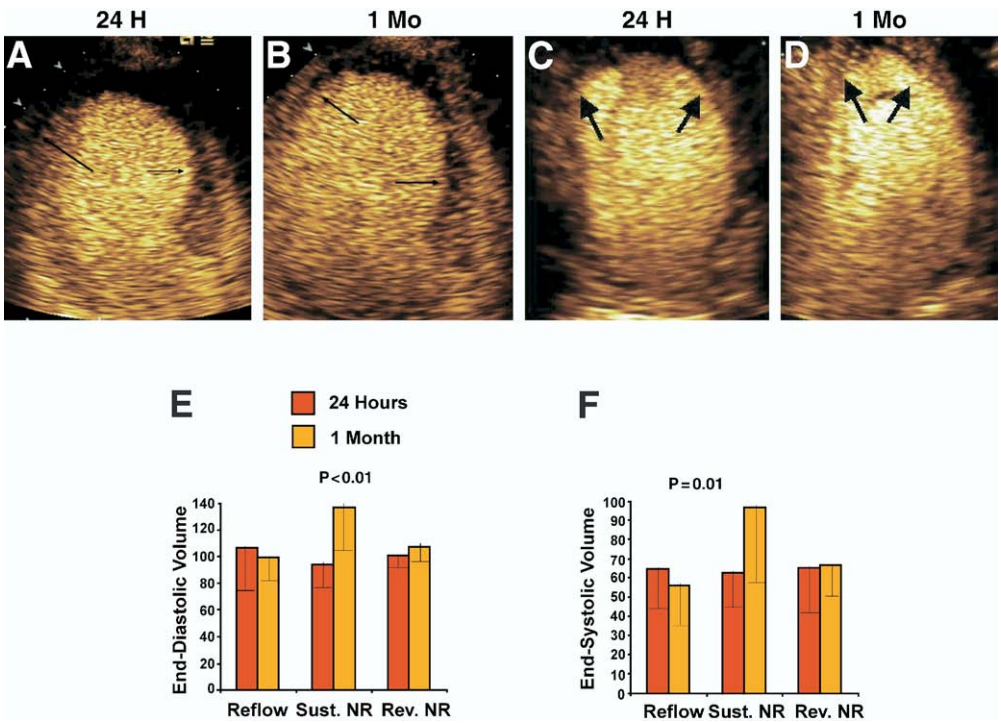

Figure 2. No-Reflow Can Be Sustained or Reversible

No-reflow area (between **arrows**) present at myocardial contrast echocardiography (MCE) performed 24 h after primary percutaneous coronary intervention (PCI) **(A)** (see Online Video 1) is confirmed with a similar extent at 1-month follow-up **(B)**. In comparison, no-reflow area (between **arrows**) present at MCE performed 24 h after primary PCI **(C)** is significantly reduced at 1-month follow-up **(D)**. No-reflow has been shown to be reversible at 1 month in 50% of patients with no-reflow at 24 h. No reflow on MCE influences left ventricular (LV) remodeling (end-diastolic **[E]** and end-systolic **[F]** LV volumes) in patients treated with primary PCI. In patients with reflow, as assessed by MCE, volumes are unchanged at 1-month follow-up. On the other hand, patients with sustained no-reflow demonstrate a progressive LV dilation. More importantly, patients with reversible no-reflow demonstrate preserved LV volumes.

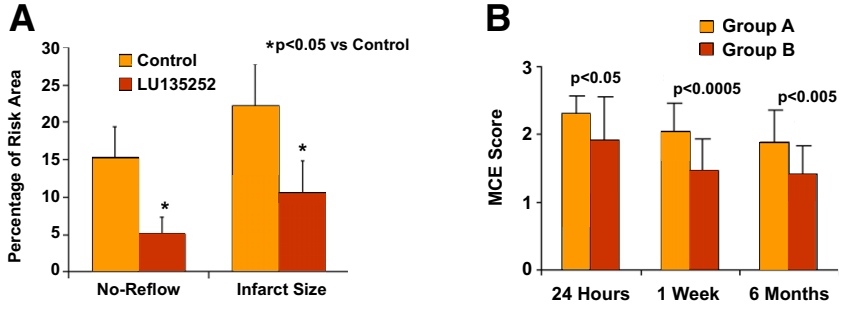

Figure 3. Plasma Levels of Endothelin-1 in a Patient With No-Reflow

In humans, plasma levels of endothelin 1 are higher in patients with no-reflow. In a canine model of ischemia-reperfusion, intracoronary administration of an endothelin-A selective antagonist (LU135252) significantly reduces both no-reflow and infarct size **(A)**. We have recently found that the atheroembolic component of no-reflow may be attenuated by mechanical interventions such as thrombus-aspiration at the time of PCI. Extent of no-reflow at MCE was significantly reduced in patients randomized to the thrombus-aspiration (group B) compared with the control (group A). Such beneficial effect demonstrated at 24 h was maintained at 1 week and 6 months **(B)**. Abbreviations as in Figure 2.