Intracoronary Administration of Abciximab
Acutely Increases Flow Through Culprit Vessels of Patients With Acute Coronary Syndromes
Undergoing Percutaneous Coronary Intervention

To the Editor:
We read with interest the article by Wöhrle et al reporting the reduction of major coronary events with the intracoronary compared with the intravenous administration of abciximab in patients with acute coronary syndromes undergoing percutaneous coronary interventions. Some cases of rapid reduction of coronary thrombus after intracoronary administration of abciximab have been previously reported. Yet, to date, it has not been determined whether such dethrombosis translates into an improvement of coronary blood flow.

To address this issue, we have measured, before and after intracoronary abciximab (0.25 mg · kg$^{-1}$) administration, corrected Thrombolyis in Myocardial Infarction (TIMI) frame count (CTFC) in a cohort of patients with acute coronary syndromes (acute ST-elevation myocardial infarction or IIIB Braunwald class unstable angina) referred to our catheterization laboratory for urgent percutaneous coronary intervention. To enter the analyses, patients had to have angiographic evidence of a culprit lesion with complex morphology defined as evident thrombus or ulceration. Ten patients matched these criteria and constituted the study population (7 males and 3 females, 62 ± 12 years of age). All patients received standard doses of aspirin, heparin, and nitrates at the beginning of the procedure. CTFC was measured, according to Gibson and colleagues, in the culprit vessel (5 left anterior descending, 1 circumflex, 3 right coronary arteries, and 1 saphenous vein graft) and in the nonculprit vessel (only in the 6 patients with a target lesion located in the left coronary artery) before and after intracoronary administration of abciximab.

Baseline CTFC was 25 ± 16 in culprit vessels and 17 ± 9 in nonculprit ones ($P = 0.08$). CTFC in the culprit vessel significantly decreased from 25 ± 16 before to 16 ± 10 after intracoronary abciximab administration ($P = 0.024$), whereas in the corresponding nonculprit vessel, no evidence of flow modification was observed ($17 ± 9$ before and $16 ±11$ after).

The drop in CTFC was confined to the 6 patients with angiographically evident thrombus (from 35 ± 13 before to 13 ± 10 after abciximab administration, $P = 0.034$). Three of these patients also exhibited an appreciable reduction in the haziness of the thrombotic lesion after intracoronary abciximab.

Our angiographic data suggest that in patients with acute coronary syndromes, the reduction of angiographically evident thrombus obtained with intracoronary administration of abciximab translates into an acute improvement of coronary blood flow. This fits with, and extends, the findings of Wöhrle et al who observed a more pronounced clinical benefit with intracoronary administration of abciximab in those patients with unpaired TIMI flow.

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Response
We thank Dr Burzotta and colleagues for their letter. The improved corrected TIMI frame count after intracoronary abciximab indicates dethrombosis at the culprit lesion and/or in the distal microcirculation. Their observation fits with our subgroup analysis indicating a more pronounced benefit of intracoronary abciximab in patients with preprocedure TIMI 0/1 flow.

Dethrombosis with abciximab has been related to partial displacement of platelet-bound fibrinogen. In addition to its ability to disperse platelet aggregates, abciximab has additional properties that impede the formation and stability of clot structure. Abciximab has been shown to allow penetration of endogenous fibrinolytic agents into the clot, thereby promoting spontaneous thrombolysis. The intravenous standard bolus of 0.25 mg/kg achieves 80% blockade of all circulating platelets within 10 minutes. The higher efficacy of intracoronary abciximab could be explained by additional thrombus disaggregation properties dependent on very high local concentrations of abciximab not achievable with intravenous application, or by the reduced blood flow distal to the culprit lesion requiring local bolus application to achieve local drug levels similar to that of the circulating blood. The data from Marciniak et al indicate that the dose-dependent dispersion of platelet aggregates back to single cells requires 6.25 μg/mL of abciximab, a concentration superior to what is achieved with the recommended intravenous dose for coronary procedures.

Burzotta et al and we administered a single intracoronary bolus of abciximab. To optimize local drug concentration and to avoid draining off the drug into nonculprit vessels, fractionated application or continuous injection over several minutes may be even more efficient. Although clinical experience with intracoronary application of GpIIb/IIIa receptor antagonists is currently limited to abciximab, in vitro data demonstrate dose-dependent disaggregation of platelet-rich clots also with eptifibatide and tirofiban.

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