

# CRP Level Before PCI Predicts Clopidogrel Benefit

*A year of clopidogrel cut the risk of atherosclerotic events in those with elevated CRP pre-angioplasty.*

BY BRUCE JANCIN  
Denver Bureau

NEW ORLEANS — Measuring high-sensitivity C-reactive protein prior to elective percutaneous coronary intervention may be useful for identifying the subset of patients who will derive greatest benefit from long-term clopidogrel, Steven R. Steinhubl, M.D., reported at the annual scientific sessions of the American Heart Association.

He presented a secondary analysis involving the 1,469 participants in the Clopidogrel for the Reduction of Events During Observation (CREDO) trial for whom baseline C-reactive protein (CRP) values were available. The subanalysis showed that an elevated CRP level prior to percutaneous intervention (PCI) was an independent predictor of poor outcome at 1-year follow-up—and that a full year of clopidogrel in such patients markedly reduced their risk of atherosclerotic events, compared with just a month of clopidogrel immediately post PCI.

CREDO was a double-blind clinical trial involving more than 2,100 patients who underwent planned elective PCI. They were randomized to receive a pre-PCI loading dose of 300 mg clopidogrel or placebo. Afterward, all patients received 75 mg/day of clopidogrel for 28 days. Thereafter out to 12 months, patients who had gotten the loading dose of clopidogrel continued on 75 mg/day of the an-

tiplatelet agent, while those in the control arm got placebo. All CREDO participants also received the standard 75 mg/day of aspirin during the follow-up period.

Previously reported primary results of CREDO showed that patients who received a year of clopidogrel had a statistically significant 27% reduction in the combined end point of death, MI, or urgent target vessel revascularization (JAMA 2002;288:2411-20). The new subanalysis was conducted to see whether CRP could be utilized to target long-term clopidogrel therapy more precisely, explained Dr. Steinhubl, CREDO principal investigator

and a cardiologist at the University of Kentucky, Lexington.

This indeed proved to be the case. Patients in the highest baseline tertile for CRP—those with a CRP level higher than 5.1 mg/L—had a 15% incidence of the combined end point of death, MI, or stroke at 1 year if they received only 1 month of clopidogrel followed by placebo after PCI. The incidence of the combined end point dropped to 8% in highest-tertile CRP patients who got a full year of the antiplatelet agent, a 44% reduction in relative risk.

An elevated CRP level is conventionally defined as higher than 3 mg/L. Among the 704 CREDO participants known to have CRP levels higher than this threshold pre-PCI, the 1-year rate of the combined end point was 9% in those who received

long-term clopidogrel, a highly significant 36% reduction in risk compared with the 14% incidence in the group who got a month of clopidogrel.

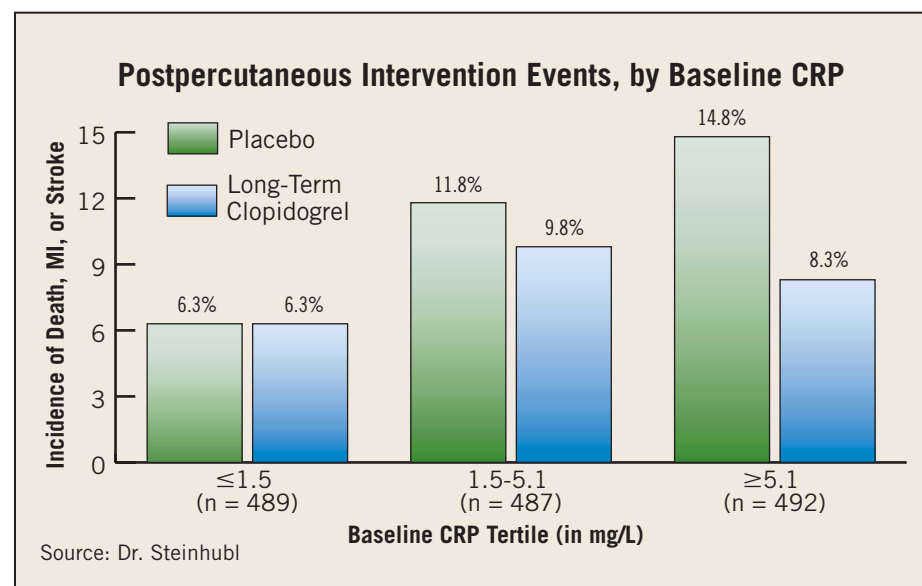
Although these data are promising, Dr. Steinhubl noted the findings require replication, as this was a post hoc analysis.

In another CREDO substudy presented at the conference, W.H. Wilson Tang, M.D., reported that pre-PCI plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels were useful in stratifying patients in terms of risk of atherosclerotic events at 1 year. Even NT-proBNP levels that were lower than the standard diagnostic threshold for heart failure were associated with increased risk independent of left ventricular ejection fraction.

“These data support the notion that the prognostic value of NT-proBNP in patients with coronary ischemia may not necessarily be specific to the setting of acute coronary syndrome,” observed Dr. Tang of the Cleveland Clinic Foundation.

CREDO participants in the lowest tertile for NT-proBNP levels—52 pg/mL or lower—had a 4.8% incidence of the combined end point of death, MI, or stroke at 1 year. The incidence climbed in stepwise fashion with increasing BNP. Patients with a BNP level of 53-130 pg/mL had an 8.3% event rate, those in the 131-340 pg/mL range had a 9.6% event rate, and those in the highest BNP tertile had a 16% event rate. The standard diagnostic threshold for heart failure using this commercial assay is 125 pg/mL.

The substudy received no commercial funding. The main CREDO trial was sponsored by Sanofi-Synthelabo. ■



## Rescue PCI Beats Repeat Thrombolysis for Myocardial Infarction

BY MITCHEL L. ZOLER  
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NEW ORLEANS — When thrombolysis fails to fully unblock the infarct-related artery of a patient with an acute myocardial infarction, percutaneous coronary intervention is the best next step, according to the results of a controlled study with 427 patients.

Up to now, some physicians have treated MI patients who failed thrombolysis with percutaneous coronary intervention (PCI) because they intuitively believed that it was the right thing to do, but there was no evidence to back it up, Anthony H. Gershlick, M.B., said at the annual scientific sessions of the American Heart Association.

About 40% of patients treated with thrombolysis for an acute MI fail this initial treatment and do not show full resolution of their ST-segment abnormality, said Dr. Gershlick, a cardiologist at University Hospital in Leicester, England. The results “tell us that you need to assess patients 90 minutes after thrombolysis with ECG to see if thrombolysis was successful.”

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“These results should have an impact on practice,” commented Eric R. Bates, M.D., a professor of internal medicine at the University of Michigan in Ann Arbor. Community hospitals that use thrombolysis but lack a catheterization laboratory will need to collaborate with an angioplasty center that can treat their patients who fail thrombolysis, Dr. Bates said.

The study was done at 35 United Kingdom hospitals. Patients with an acute MI

who received standard lytic therapy and aspirin underwent a repeat ECG 90 minutes after receiving their initial thrombolytic drug. (About 60% of patients received streptokinase, 27% received reteplase, and the remaining patients received other agents.) Patients with less than 50% resolution of their ST changes were randomized to one of three treatment strategies: conservative management in the hospital, repeat treatment with thrombolysis, or PCI (about 69% of the PCI-treated patients received coronary stents).

The study’s primary end point was the incidence of death, repeat MI, stroke, or severe heart failure at 6 months after treat-

ment. This end point occurred in 15% of the 144 patients treated with PCI, 30% of 141 patients treated with conservative therapy, and 31% of 142 patients treated with repeat thrombolysis, a statistically significant difference in favor of PCI. PCI led to consistent reductions in death, repeat MI, and severe heart failure. The incidence of stroke was similar in all three groups.

Treatment with PCI also led to a higher rate of major bleeding events, 19%, compared with a 5% in the repeat lysis group and 2% in the conservatively managed group. Of the 27 patients with major bleeds in the PCI group, 22 cases involved sheath complications during coronary

catheterization. Severe complications from bleeding were similar in the three groups.

The average time from the onset of pain to when patients received the first thrombolytic treatment was 140 minutes. Patients who received a second dose of a lytic drug got it 190 minutes later; patients who received PCI were treated an average of 274 minutes later, an average delay of 84 minutes beyond the thrombolytic group.

Thus, the patients treated by rescue PCI got their definitive treatment after 414 minutes, nearly 7 hours, after their onset of chest pain. Despite this delay, these patients still did better than the comparator groups, Dr. Gershlick said. ■

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*‘We can talk about improving ductal drainage. We can talk about ... improving functional deficits. We can talk about weight gain. We can talk about improving quality of life. But the fact of the matter is, the main issue is pain.’*

Dr. Robert H. Hawes,  
on treating patients with  
chronic calcific pancreatitis, p. 71