心原性ショックを伴ったAMI患者におけるabciximabの効果は失望させられる結果であった

PRAGUE-7 Study：GP IIb/IIIa阻害薬abciximabは心原性ショックを伴った急性心筋梗塞患者に対し有益ではない

PRAGUE-7 Study: GP IIb/IIIa inhibitor abciximab shows no benefit in patients with acute myocardial infarction and cardiogenic shock

心原性ショックを伴った急性心筋梗塞患者に対する初回経皮的冠動脈インターベンション（PCI）の際に、GP IIb/IIIa阻害薬abciximabをルーチンにup-frontで使用することは有益ではないとのPRAGUE-7スタディの結果がESC 2009ホットラインセッションで発表された。80人の患者が移送中またはカテ室で直に標準的な抗血栓薬および抗凝固薬を投与され冠動脈造影を施行された。その後患者らはup-frontでabciximabをボーラス投与後に点滴を12時間施行される群または標準的な周術治療を施行される群に無作為に割り付けられた。PCI中のabciximabの使用はインターベンションの術者の裁量に任された。Abciximabはup-front治療群患者全員に使用されたのに対し、標準治療群患者で使用されたのは35%であった。一次エンドポイント（30日間の死亡／再梗塞／脳卒中／新規の腎不全の合計）に達したのはup-front治療群患者のうち17人（42.5%）であり、標準治療群患者のうち11人（27.5%；p=0.24）であった。入院中に死亡したのはup-front群患者のうち15人（37.5%）であり、それに対し標準治療群患者では13人（32.5%；p=0.82）であった。他の項目に関しては両群間で有意差はなかった。

Full Text

Routine upfront use of the GP IIb/IIIa inhibitor abciximab during primary percutaneous coronary intervention (PCI) was of no benefit in patients with acute MI (AMI) complicated by cardiogenic shock, according to the results of the PRAGUE-7 study reported during a hotline session at the European Society of Cardiology Congress 2009.

The outcome of patients with acute myocardial infarction (AMI) complicated by cardiogenic shock is generally very poor. Although early mechanical revascularization by primary PCI has been shown as superior to medical treatment, the mortality range remains high (at about 45-60%). Registries have shown further therapeutic benefit from the administration of glycoprotein (GP) IIb/IIIa inhibitors during PCI in AMI patients with cardiogenic shock. However, there are no randomized data to support this approach in these high risk patients. The PRAGUE-7 study was designed to determine whether the routine upfront administration of abciximab (a IIb/IIIa GP inhibitor) improves outcome when compared with conventional selective administration.

This study, which is part of a series of randomized trials in cardiology and cardiac surgery performed in the Czech Republic, enrolled 80 of these most critically ill patients (AMI complicated by cardiogenic shock) but failed to show any benefit from the routine upfront administration of abciximab to all patients (before coronary angiography) over a more conventional selective use of abciximab during subsequent primary PCI.

All 80 patients in this open-label multicentre trial received standard antithrombotic and anticoagulant treatment (either during transport or directly at the catheterization laboratory) and coronary angiography. Patients in the upfront treatment group (group A) received a bolus of abciximab immediately after randomization followed by an infusion for 12 hours. PCI was performed immediately after coronary angiography. Group B received standard therapy with optional abciximab administration during PCI according to the interventional cardiologist.

The study's primary endpoint was a 30-day combined outcome of death/reinfarction/stroke/new renal failure. Secondary objectives were left ventricular ejection fraction assessed by echocardiography on day 30, major bleeding complications, myocardial blush grade after PCI, and TIMI-flow after PCI.

Results showed that PCI was technically successful in 90% of group A and 87.5% of group B patients. Abciximab was used in 100% of group A and 35% of group B. The primary endpoint was reached in 17 group A patients (42.5%) and 11 group B patients (27.5%) (p=0.24). Fifteen patients (37.5%) died during hospitalization in group A and 13 patients in group B (32.5%) (p=0,82). Ejection fraction among survivors after 30 days was 44 ± 11% (A) vs. 41 ± 12% (B) (p=0.205). Major bleeding occurred in 17.5% (A) vs. 7.5% (B) (p=0.310) and stroke in 2.5% (A) vs. 5% (B). No differences were found in TIMI-flow and MBG after PCI.

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The diabetic sub-group analysis was presented by Stephen Wiviott, M.D., Assistant Professor of Medicine at Harvard Medical School and investigator with the Thrombolysis in Myocardial Infarction (TIMI) Study Group, Brigham & Women's Hospital, Boston, USA, at the Congress of the European Society of Cardiology (ESC) in Munich, Germany. In addition, the manuscript was simultaneously published online in Circulation, the medical journal of the American Heart Association.

"The results observed from this sub-group analysis showed that antiplatelet therapy with prasugrel resulted in significantly greater reduction of cardiovascular events among patients with diabetes when compared to those who were treated with clopidogrel," said Wiviott.

The reduction of cardiovascular events was consistent across the sub-group of diabetes patients regardless of diabetic therapies (insulin versus no insulin). The study showed a significant relative risk reduction in the primary endpoint of cardiovascular death, non-fatal heart attack and non-fatal stroke with prasugrel, 37 percent for insulin treated and 26 percent (p=0.001) for non-insulin treated diabetics. There was also a significantly lower rate of stent thrombosis among diabetes patients treated with prasugrel, resulting in a 48 percent relative risk reduction in stent thrombosis compared with clopidogrel (3.6 percent vs. 2.0 percent, p=0.007).

"These findings are interesting in view of previous studies that showed higher levels of platelet aggregation in insulin-treated diabetes patients after dual antiplatelet therapy compared to diabetes patients not treated with insulin," said Dr. Wiviott.

The main TRITON-TIMI 38 clinical trial, previously published in the New England Journal of Medicine in November 2007 (Vol. 357, No. 20), compared prasugrel with clopidogrel in patients with ACS undergoing percutaneous coronary intervention (PCI). In the primary analysis of the trial, prasugrel reduced the risk of the composite endpoint of cardiovascular death, heart attack or stroke by 19 percent, with an increased risk of major bleeding compared with clopidogrel (2.4 percent vs. 1.8 percent).

In this sub analysis, the rates of major bleeding events were similar for prasugrel (2.5 percent) and clopidogrel (2.6 percent) among patients with diabetes, regardless of diabetes therapies (insulin versus no insulin).

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