高齢者には初期治療としてのPCIは血栓溶解療法よりも有効性が高い

TRIANA：非常に高齢のAMI患者には初期治療としてPCIを施行した方が血栓溶解療法よりも有効性が高いことが示唆された

TRIANA: Primary angioplasty may be more effective than thrombolysis in very elderly patients with AMI

非常に高齢の急性心筋梗塞（AMI）患者には初期治療としてPCIを施行した方が血栓溶解療法よりも有効性が高いことが、スペイン心臓協会の後援で施行された無作為化トライアルTRIANA（TRatamiento del Infarto Agudo de miocardio eN Ancianos）スタディの結果示唆され、ESC 2009ホットラインセッションで発表された。このトライアルは75歳以上で発症後6時間未満の急性心筋梗塞患者226人を対象に施行され、2005～2007年にスペインの23の病院において組み入れられた。このスタディは患者の組み入れ率不良のために早期に終了したが、一次エンドポイント（30日間の死亡、再梗塞または障害を伴う脳卒中）は両群間で差がなかった（血栓溶解療法群で25.4%に対し血管形成術群で18.9%、p=0.21）。両群ともにイベント発現率が予測より高かったにもかかわらず、患者組み入れが遅かったために有意差の検出力は十分ではなかった。しかし、あらかじめ指定された二次エンドポイントにおいては、血管形成術群のほうが再虚血に対するカテーテル施行率が有意に低かった（0.8%対9.7%、p<0.001）。

Full Text

Primary angioplasty is superior to thrombolysis in the treatment of very old patients with acute myocardial infarction (AMI), according to results from the TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) study, a randomized trial sponsored by the Spanish Society of Cardiology.

The trial was designed to compare the two principal available treatments to open blocked coronary arteries in AMI patients: immediate primary PCI with angioplasty, and thrombolysis with clot-dissolving drugs. The trial was performed in 226 patients all aged 75 years or older and all with acute myocardial infarctions (AMIs) of less than six hours' evolution. They were recruited in 23 Spanish hospitals between 2005 and 2007.

The study, which was closed prematurely because of slow patient recruitment, found no differences between the two groups in its primary endpoint — the incidence of death, reinfarction or disabling stroke at 30 days (25.4% in the thrombolysis group and 18.9% in the primary angioplasty group, p=0.21). Despite the higher-than-anticipated rate of events in both arms, the study became underpowered to detect such differences because of its reduced recruitment. However, in a pre-specified secondary endpoint there was a significantly lower need of new catheterization for recurrent cardiac ischemia in the primary angioplasty arm (0.8% versus 9.7%, p<0.001).

Reviewing the findings principal investigator Professor Héctor Bueno from the Hospital General Universitario "Gregorio Marañón" in Madrid reported that:

- The effect of primary angioplasty on reducing recurrent ischemia was so strong that it could still be easily detected in the study, despite its limited statistical power.
- Contrary to what might have been anticipated, there was no clear evidence that thrombolysis, which is considered controversial in older patients because of their increased bleeding risk, was unsafe in a population whose median age was 81 years; the study found no intracranial bleeding directly related to the use of thrombolysis, and no significant differences between groups in major bleeding (4.5% versus 3.8%; p=0.78), or need for transfusions (3% vs. 5.3%, p=0.35).
- There was no increase in renal failure associated with primary angioplasty (6.1% versus 7.5% with thrombolysis), a feared complication of catheterization in older patients.

Professor Bueno added: "All efficacy outcomes showed concordant trends in favor of primary angioplasty, suggesting that the potential advantage of an invasive strategy over thrombolysis in very old patients is because of its greater efficacy rather than its superior safety. However, patients in both groups tended to have a comparable prognosis one year later."
The TRIANA study was funded by the Fondo de Investigaciones Sanitarias (Instituto Carlos III, Ministry of Health, Spain), and unrestricted grants from Sanofi, Medtronic, Boston Scientific, Guidant, and Johnson & Johnson.

The pathophysiology of a PMI is complex. While cardiac oxygen demand / supply mismatch in patients with coronary artery disease might be counteracted by appropriate beta-blocker use or coronary revascularization in these patients, coronary plaque instability leading to plaque rupture and thrombosis remains a significant problem. Recent retrospective studies suggested a potential beneficial role of statins in the prevention of PMI, in particular by "stabilizing" coronary plaques due to their pleiotropic, anti-inflammatory effects. Therefore the aim of the randomized, double blind, Dutch Echographic Cardiac Risk Evaluation Applying Stress Echo (DECREASE) III trial was to assess the cardioprotective effect of fluvastatin XL on top of beta-blocker therapy in vascular surgery patients.

Between June 2004 and April 2008 497 statin-naive patients (median age 65.7 years, 75% men, 39% prior coronary artery disease, 29% prior stroke, 20% diabetic) scheduled for vascular surgery were included in the trial at Erasmus MC Rotterdam, the Netherlands. Patients were randomized to receive either placebo or fluvastatin extended at a dose of 80 mg once daily. Treatment was started at the outpatient clinic on the day of randomization, median 37 days prior to the surgical procedure and was continued at least during the first 30 days after surgery. Inflammatory markers at baseline, including hs-CRP and IL-6 were assessed in patients allocated to fluvastatin or placebo. At hospital admission levels of hs-CRP and IL-6 were significantly lower in patients on fluvastatin (respectively 6.00 mg/L vs 4.66 mg/L, p=0.030 and 8.45 pg/ml vs 5.75 pg/ml, p=0.024). The primary analysis was intention-to-treat and involved all patients who were randomly assigned to either fluvastatin or placebo. Directly after surgery, study treatment was temporarily discontinued in 115 (23%) patients for a median duration of 2 days because of the inability to take the study drug orally. A total of 34 patients discontinued study medication because of laboratory abnormalities; 16 (3.2%) because of ALAT exceeding 3x upper limit of normal, 13 (2.6%) because of CK exceeding 10x upper limit of normal, and 5 (1.0%) because of a combination of elevated ALAT and CK.

Myocardial ischemia was detected in 74 (14.9%) patients within 30 days of the initial vascular surgical procedure. A total of 27/250 (10.9%) patients allocated to fluvastatin reached the primary endpoint compared to 47/247 (18.9%) patients allocated to placebo treatment (OR 0.53; 95% CI 0.32-0.88). Hence, the number needed to treat (NNT) to prevent one patient experiencing myocardial ischemia was 12.5 patients.

A total of 18 (3.6%) patients died within 30 days after surgery of which 12 (2.4%) were attributable to cardiovascular causes. 25 (5.0%) patients experienced a nonfatal myocardial infarction during that same period. The combined endpoint of cardiovascular death and nonfatal myocardial infarction was reached in 37/497 (7.4%) patients. A total of 12/250 (4.8%) patients allocated to fluvastatin therapy reached the combined endpoint, compared to 25/247 (10.1%) allocated to placebo. Hence, fluvastatin therapy was associated with a 52% relative reduction in the incidence of cardiovascular death or MI (OR 0.48; 95% CI 0.24-0.95). The NNT for the composite endpoint of cardiovascular death or nonfatal MI is 18.9 patients.

The proportion of patients experiencing any adverse event was similar between the fluvastatin and placebo groups. The proportion of patients experiencing a CK rise > 10x the upper limit of normal was 4.1% in the fluvastatin group and 3.0% in the placebo group. The median peak CK level was 141 U/Lin patients on fluvastatin and 113 U/L in patients on placebo (p=0.24). The proportion of patients with significant increase in ALAT levels, ie > 3x times upper limit of normal, was 3.1% in the fluvastatin group and 5.2% in the placebo group. The median peak ALAT level was 23 U/L in patients on fluvastatin and 24U/L in patients on placebo.
The study authors conclude that fluvastatin XL therapy was associated with improved postoperative cardiac outcome in high-risk patients undergoing elective vascular surgery.

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