(AMI), according to findings from the Tratamiento del Infarto Agudo de Miocardio en Ancianos (TRIANA) trial (NCT00257309), which was halted early due to slow enrollment. Although TRIANA failed to meet its primary endpoint, it did show favorable (albeit nonsignificant) trends with an invasive strategy in this relatively unstudied group with a relatively small sample size.

PCI is the preferred therapy for ST-segment elevation MI (STEMI); yet the majority of very elderly patients (aged ≥75 years) with STEMI is treated with fibrinolytic therapy or no reperfusion therapy. Many physicians may be reluctant to use any reperfusion strategy in the elderly, given the sparse evidence that supports primary PCI and the fear of increased bleeding risk with fibrinolytic therapy in very elderly patients, said Professor Héctor Bueno, MD, PhD, Hospital General Universitario Gregorio Marañón, Madrid, Spain. Dr. Bueno presented results of the TRIANA trial, which was designed to compare the efficacy and safety of primary PCI and fibrinolytic therapy in patients aged ≥75 years.

TRIANA included patients aged ≥75 years (mean age, 81 years) who presented within 6 hours of symptom onset with STEMI and without contraindications for fibrinolysis at centers that offered primary angioplasty in Spain. Patients were randomly assigned to fibrinolytic therapy that consisted of weight-adjusted tenecteplase, unfractionated heparin, and clopidogrel (n=134) or primary angioplasty with clopidogrel and, at the physician's discretion, abciximab (n=132). The primary endpoint was the cumulative incidence of all-cause death, reinfarction, or disabling stroke at 30 days. Initially, the study was powered to detect a 40% relative risk reduction in the primary endpoint, based on a sample size of 560 patients. However, TRIANA was discontinued early due to slow recruitment after enrolling only 266 patients.

At 30 days, there were numerically fewer (but statistically not significant) primary endpoint events in the primary PCI group (18.9%) than in the fibrinolytic therapy group (25.4%; OR, 1.46; p=0.21). Each component of the primary endpoint tended to occur less frequently with PCI, including death (13.6% vs 17.2%; p=0.43), reinfarction (5.3% vs 8.2%; p=0.35), and disabling stroke (0.8% vs 3.0%; p=0.18). At 12 months, results for the primary endpoint again showed no statistically significant difference between treatment groups (27.3% vs 32.1%; p=0.31)

Among secondary outcomes, primary PCI significantly reduced the risk of recurrent ischemia compared with fibrinolysis (0.8% vs 9.7%; p<0.001). No differences were found between the primary PCI and fibrinolytic therapy groups in a range of safety outcomes, including major bleeding (3.8% vs 4.5%; p=0.78), need for transfusion (5.3% vs 3.0%; p=0.35), and renal failure (6.1% vs 7.5%; p=0.64).

Although TRIANA lacked the statistical power to demonstrate the superiority of PCI over fibrinolytic therapy, the observed risk reduction was consistent with the benefit that had been anticipated with primary PCI in the initial design of the study. Primary angioplasty should be considered the treatment of choice even in very old patients with STEMI. In situations in which primary PCI is not available, safety findings from TRIANA indicate that fibrinolysis may be considered as an alternative, with an acceptable rate of intracerebral hemorrhage among old patients who are carefully selected for fibrinolytic therapy.

Results from the AAA Study

Results from the Aspirin for Asymptomatic Atherosclerosis (AAA) study, presented by Professor Gerry Fowkes, MD, University of Edinburgh, Edinburgh, Scotland, showed no support for the routine use of aspirin for the primary prevention of vascular events in people with asymptomatic atherosclerosis.

The objective of the AAA study was to evaluate whether the routine use of low-dose (100 mg) aspirin was as effective as primary prevention of vascular events in individuals at high risk of a future event, as determined by ankle brachial index (ABI) score. The primary endpoint was a composite of initial fatal or nonfatal coronary event or stroke or revascularization. Secondary endpoints were all initial vascular events (defined as a composite of a primary endpoint event or angina, intermittent claudication, or transient ischemic attack) and all-cause mortality.

The study population consisted of 3350 men and women who were recruited from general practice registers in Scotland who had a low (≤0.95) ABI score, were free of cardiovascular disease, and were not already taking routine aspirin or warfarin. Subjects were randomly assigned to receive 100 mg enteric-coated aspirin (n=1675) or matching placebo (n=1675) and were followed for a mean of 8.2 years. The mean ABI at study entry was 0.86; mean age was 62 years, and 29% was male.

There was no difference between treatment groups for either the primary or secondary endpoints (Table 1). There was, however, an increase in major hemorrhages that required hospitalization in the aspirin group (2% of subjects in the aspirin group vs 1.2% of subjects in the placebo group; HR,1.71; 95% CI, 0.99 to 2.97). Gastrointestinal ulcers were also more frequent in subjects

who were taking aspirin (0.8% of subjects in the aspirin group vs 0.5% of subjects in the placebo group).

Table 1. Primary and Secondary Outcome Events.

Endpoint	No. of Events		HR (95% CI)
	Aspirin 100 mg	Placebo	
Primary Endpoint			
Composite of initial fatal/nonfatal coronary event or stroke or revascularization	181	176	1.03 (84, 1.27)
Secondary Endpoint			
Vascular event	288	290	1.00 (0.85, 1.17)
All-cause mortality	176	186	0.95 (0.77, 1.16)

Commenting on the use of ABI as a screening method, Prof. Fowkes said, "Although the AAA trial was not to test screening, the results would suggest that using the ABI as a tool to screen individuals free of cardiovascular disease in the community is unlikely to be beneficial if aspirin is the intervention to be used in those found to be at higher risk. Other more potent antiplatelets might be considered, but only if increased effectiveness in avoiding ischemic events is not matched by increased bleeding."

In his discussion of the AAA study, Professor Carlo Patrono, MD, University of Rome, Rome, Italy, compared the results with those of the Antithrombotic Trialists' collaborative meta-analysis of aspirin trials [ATT Collaboration. *Lancet* 2009], in which treatment with aspirin resulted in a 12% proportional reduction in serious vascular events in individuals at low to moderate risk. Prof. Patrono suggested lack of statistical power, perhaps amplified by poor compliance, as the primary cause of the null response of the AAA trial.

Results from CURRENT-OASIS 7

The Clopidogrel optimal loading dose Usage to Reduce Recurrent EveNTs-Organization to Assess Strategies in Ischemic Syndromes (CURRENT-OASIS 7) trial was a 2×2 factorial, open-label, randomized trial to determine optimal clopidogrel and aspirin dosing in subjects with acute coronary syndrome (ACS) within 24 hours of ischemic symptoms. Subjects were randomly assigned to either double-dose clopidogrel for 7 days (600-mg loading dose, followed by 150 mg daily on Days 2 to 7, then 75 mg daily to Day 30) or the standard-dose regimen (300-mg loading dose, followed by 75 mg daily). The second randomization was to open-label, high-dose (300-325 mg) or low-dose (75-100 mg) aspirin daily for 30 days. The primary outcome was a composite of cardiovascular (CV) death, myocardial infarction (MI), or stroke to Day 30. The primary safety outcome was major bleeding. The results were presented by Professor Shamir Mehta, MD, McMaster Clinic, Hamilton, Ontario, Canada.

Primary Analysis

A total of 25,087 subjects were enrolled, including 71% with UA/NSTEMI and 29% with STEMI. PCI was performed at the discretion of the treating physician in 70% of the trial cohort. The primary analysis for this 2x2 factorial trial showed a significant interaction for the primary endpoint between high-dose and low-dose aspirin and double-dose and standard-dose clopidogrel groups (p=0.043). Subjects who were randomized to high-dose aspirin had lower rates of the primary endpoint on double-dose clopidogrel compared with standard-dose clopidogrel (3.8% vs 4.6%; RR, 0.83; 95% CI, 0.70 to 0.99; p=0.036). This difference was not seen with double-dose versus standard-dose clopidogrel in the low-dose aspirin strata (4.5% vs 4.2%; RR, 1.07; 95% CI, 0.91 to 1.27; p=0.42). For the aspirin dose comparison, there was no difference in rates of the primary endpoint between high-dose and low-dose aspirin (4.2% vs 4.4%; HR, 0.96; 95% CI, 0.85 to 1.08; p=0.47). On pooling subjects across aspirin strata, there was no difference in the primary endpoint between double-dose and standard-dose clopidogrel (4.2% vs 4.4%; HR, 0.95; 95% CI, 0.84 to 1.07; p=0.37).

PCI Subgroup Analyses

In a postrandomization (improper subgroup) analysis of the pooled cohort that examined patients who were undergoing PCI only (17,232 subjects), there were lower rates of the primary endpoint with double-dose compared with standard-dose clopidogrel (3.9% vs 4.5%). In patients who were not undergoing PCI, the rate of the primary endpoint did not favor double-dose clopidogrel (4.9% vs 4.2%). The main reduction in events with double-dose clopidogrel among subjects who were undergoing PCI was for MI (2.0% vs 2.6%), with no difference in the rate of CV death. Definite or probable stent thrombosis was also lower with double-dose clopidogrel (1.6% vs 2.3%).

Safety Analysis

The primary safety endpoint of CURRENT major bleeding was increased with double-dose clopidogrel (2.5% vs 2.0%; HR, 1.25; 95% CI, 1.05 to 1.47; p=0.01), with an associated increased need for transfusion (2.2% vs 1.8%; HR, 1.26; 95%