

Best of the ESC 2004

*Highlights from the European Society of Cardiology Congress,
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The European Society of Cardiology meeting was held in Munich, Germany from August 28–September 1, 2004. The Hot Line sessions, where a number of important clinical trials were presented, including Invasive Versus Conservative Treatment of Unstable Coronary Syndromes (ICTUS), Joint Utilization of Medications to Block Platelets Optimally-TIMI 28 (JUMBO-TIMI 28), INTERHEART, and Reassessing European Attitudes About Cardiovascular Treatment (REACT), were the most popular.

ICTUS was a multicenter trial con-

ducted in 42 centers in Europe to evaluate the benefit of an early invasive strategy versus a selective invasive strategy on clinical outcome in 1201 patients with acute coronary syndromes (ACS). Patients were included if they had chest pain within 24 h, positive troponin levels, and a history of prior coronary artery disease or electrocardiogram (ECG) changes. The early invasive group underwent percutaneous coronary intervention (PCI) within 24–48 h and both arms were treated with aspirin, enoxaparin, clopidogrel, and a statin. The primary endpoint was death, recurrent myocardial infarction (MI), and rehospitalization for acute coronary syndrome at 1 year. Surprisingly, there was no difference in the primary endpoint

(21.7% for the early invasive group and 20.4% for the selective group, relative risk [RR] = 1.06, $P = 0.59$). There was a significantly higher incidence of MI in the early invasive group (14.65% vs 9.4%; see Figure 1). Part of the explanation for the lack of difference was the high crossover rate in the selective group with 47% of patients undergoing PCI as compared to 73% in the invasive group. Thus, the difference between the groups was only 26%. In addition, the major difference in outcome was in the incidence of MI, the definition of which was much more lenient than in other trials. When the Thrombolysis and Counterpulsation to Improve Cardiogenic Shock Survival (TACTICS) definition of

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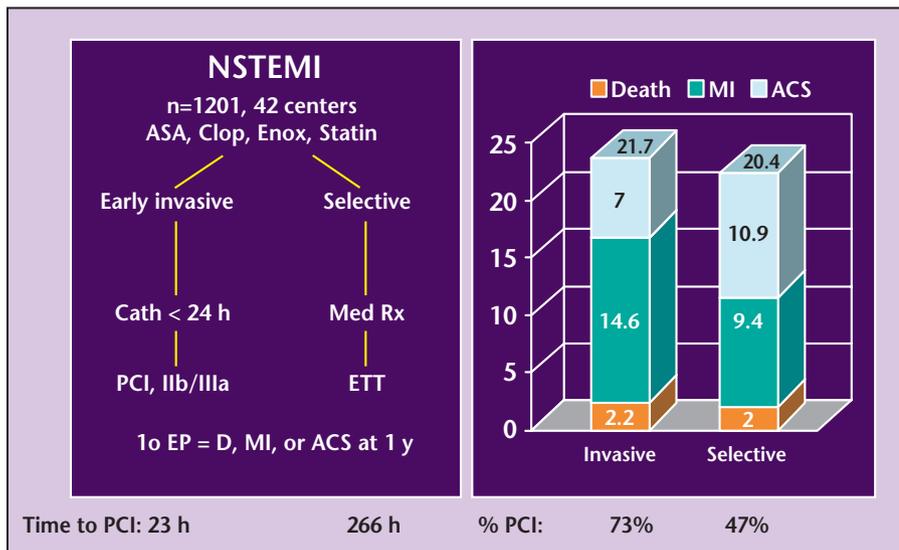


Figure 1. Early invasive strategy versus selective strategy in acute coronary syndromes — the ICTUS trial. 1o EP, primary endpoint; ACS, acute coronary syndrome; Cath, catheterization; Clop, clopidogrel; D, death; Enox, enoxaparin; ETT, exercise tolerance test; IIb/IIIa, glycoprotein IIb/IIIa inhibitor; MI, myocardial infarction; PCI, percutaneous coronary intervention.

acute MI was used, no difference in MI rates was seen.

Given the prevalence of PCI procedures in both groups and the small difference between groups, the trial provides additional insights into the role of early versus late PCI in ACS patients. Interestingly, there appeared to be an early risk of death, MI, or rehospitalization in the early invasive arm. This supports delaying PCI in such patients to allow them to stabilize and then to consider revascularization when risks are lower. The trial was not specifically designed to evaluate the optimal timing of intervention in ACS and we will need to await the outcome of the larger Organization to Assess Strategies for Ischemic Syndromes (OASIS) 5 trial.

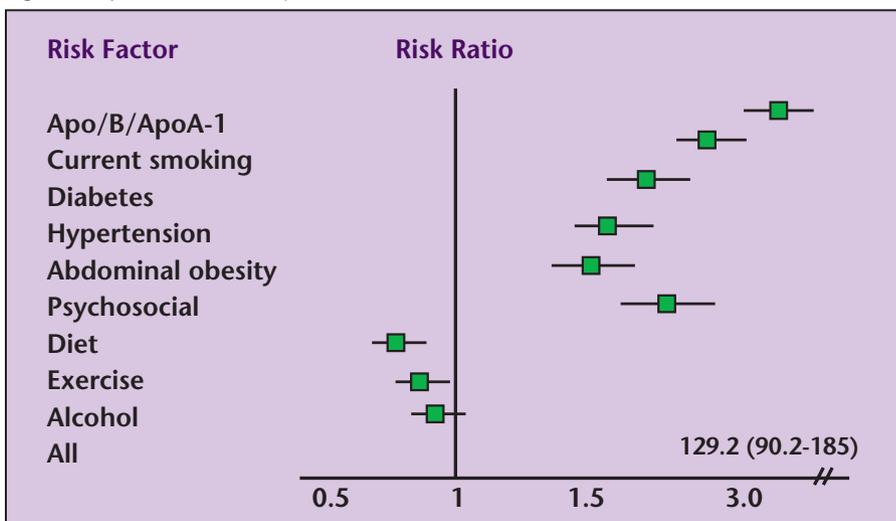
The JUMBO-TIMI 28 trial was a multicenter trial to evaluate the safety of a new thienopyridine, prasugrel, in 904 patients undergoing coronary stent placement. Patients were randomized to either prasugrel or clopidogrel. The primary endpoint was major bleeding at 30 days that was

not different between the groups (1.7% vs 1.2%, respectively). Likewise, there was no difference in major adverse coronary events (7.5% vs 9.4%). However, target vessel revascularization (TVR) was lower in the prasugrel group (0.6% vs 2.4%, $P = 0.03$). One potential advantage of this drug over clopidogrel is a lower incidence of drug resistance.

The larger efficacy trial, TITAN TIMI 38, will enroll over 30,000 patients and is now underway based on these favorable early results.

Dr. Salim Yusuf of McMaster University and Hamilton Civic Hospitals Research Center in Hamilton, Ontario, Canada, presented one of the most interesting trials of the meeting, the INTERHEART trial, results of which were recently published.¹ The study was a case controlled trial of over 30,000 patients from 52 countries with over 10,000 patients from South Asia and China. One half of the patients (15,152) had a prior MI and the other half (14,820) served as matched controls. The primary goal of the study was to determine the risk factors for MI and the predictive value of these factors in a broad group of patients from all over the world. The study identified nine-factors that predicted the risk of an MI. Using a weighted model, over 90% of the risk could be accounted for by these factors, refuting previous estimates that these factors could only predict 50% of the risk. The most powerful predictor was the ratio of apolipoprotein B versus apolipoprotein A-1, a measure of low-density

Figure 2. Adjusted risk of acute myocardial infarction — the INTERHEART trial.



lipoprotein (LDL). Other factors included current smoking, diabetes, hypertension, abdominal obesity (waist-to-hip ratio), psychosocial factors (depression), and a diet that included daily fruits and vegetables and modest alcohol intake. Risk was increased even with very minimal increases in lipids or cigarette smoking

The REACT trial was a multicenter randomized trial conducted in the United Kingdom that evaluated the role of rescue angioplasty in patients with acute ST-segment elevation MI who failed initial thrombolytic therapy. The study randomized 428 patients to conservative therapy, repeat thrombolytic therapy, or res-

domized to rescue angioplasty as compared to either conservative therapy or repeat lytic therapy (6.8% vs 21.7% vs 16%, respectively, RR = 0.38, $P = 0.00003$). Rescue angioplasty was performed an average of 4 h after lytic therapy and crossover occurred in approximately 10% of each group. These preliminary results strongly support the use of rescue angioplasty but given the preliminary nature of the report and the limited number of patients, full presentation of the study will prove more conclusive. In addition, the larger Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial is ongoing in Europe and should provide further information on the role of rescue angioplasty. ■

The majority of ischemic heart disease worldwide can be prevented by major reduction in known risk factors.

and together predicted 66% of the risk of heart disease. Small amounts of alcohol and eating fruits and vegetables daily reduced risk (see Figure 2). The study has some limitations despite its size and global scope, and it likely underestimated the incidence of diabetes and hypertension because these were self-reported. However, the study provides powerful evidence that the majority of ischemic heart disease worldwide can be prevented by major reduction in known risk factors.

cue angioplasty. Failed lytic therapy was defined as less than a 50% decrease in ST-segment elevation 90 minutes after lytic administration. The primary endpoint was death, reinfarction, cardiovascular accident (CVA), or congestive heart failure (CHF) at 6 months. Although a full analysis was not available until presentation at the American Heart Association scientific sessions in November 2004, the interim results showed that the primary endpoint was significantly better in those ran-

Reference

1. Yusuf S, Hawken S, Ounpuu S, et al. for the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:937-952.

Main Points

- The Invasive versus Conservative Treatment of Unstable Coronary Syndromes (ICTUS) trial was a multicenter trial conducted in 42 centers in Europe to evaluate the benefit of an early invasive strategy versus a selective invasive strategy on clinical outcome in 1201 patients with acute coronary syndromes (ACS). There was a significantly higher incidence of MI in the early invasive group (14.65% vs 9.4%).
- The JUMBO-TIMI 28 trial was a multicenter trial to evaluate the safety of a new thienopyridine, prasugrel, in 904 patients undergoing coronary stent placement. Patients were randomized to either prasugrel or clopidogrel. There was no difference in major adverse coronary events (7.5% vs 9.4%, respectively). However, target vessel revascularization (TVR) was lower in the prasugrel group.
- The INTERHEART study provides powerful evidence that the majority of ischemic heart disease worldwide can be prevented by major reduction in known risk factors.
- The REACT trial was a multicenter randomized trial conducted in the United Kingdom that evaluated the role of rescue angioplasty in patients with acute ST-segment elevation MI who failed initial thrombolytic therapy. The interim results showed that the primary endpoint was significantly better in those randomized to rescue angioplasty as compared to either conservative therapy or repeat lytic therapy.