

Differential Effects by Age of an Early Invasive Strategy for Non-ST-Segment Elevation Acute Coronary Syndromes

Bach RG, Cannon CP, Weintraub WS, et al. The effect of routine, early invasive management on outcome for elderly patients with non-ST-segment elevation acute coronary syndromes. *Ann Intern Med* 2004;141:186–95.

Study Overview

Objective. To compare the outcomes of early invasive management and conservative management for patients with non-ST-segment elevation acute coronary syndromes (ACS) by age-group.

Design. Subgroup analysis of a randomized controlled trial.

Setting and participants. 2220 patients admitted to 169 hospitals in 9 countries with unstable angina or non-ST-segment elevation myocardial infarction (MI) from December 1997 to 1999. Exclusion criteria included ST-segment elevation MI, secondary angina, revascularization in the past 6 months, prior gastrointestinal bleeding, platelet disorders, thrombocytopenia, any hemorrhagic cerebrovascular disease, nonhemorrhagic cerebrovascular disease in the past year, left bundle-branch block, severe heart failure, or serum creatinine level > 2.5 mg/dL. Subgroup analysis of patients aged < 65 years of age versus those ≥ 65 years was prespecified in the study protocol. A 4-age-group analysis was performed post hoc.

Intervention. Medical therapy followed by coronary angiography within 4 to 48 hours after presentation with revascularization (early invasive strategy), if appropriate, was compared with medical management followed by exercise stress testing with or without imaging (conservative management strategy). For the conservative group, angiography was performed for patients with clinical progression or high-risk features on noninvasive testing. All patients received aspirin, heparin, and tirofiban.

Main outcome measures. Death, nonfatal MI, rehospitalization for ACS, stroke, and major bleeding.

Main results. 1258 patients were < 65 years (mean age, 53.4 years), and 962 were ≥ 65 years (mean age, 72.9 years). Older patients were more likely than younger patients to have high-risk prognostic features. Across age-groups, coronary angiography was performed for at least 95% of patients assigned to the early invasive group and for 48% to 55% of

patients in the conservative management group. Among patients aged ≥ 65 years, death or MI occurred less often in the early invasive group as compared with the conservative group (4.9% versus 9.6%; odds ratio [OR], 0.61 [95% confidence interval {CI}, 0.41–0.92]). For patients < 65 years, there was no difference in death or MI between groups (6.1% versus 6.5%; OR, 0.94 [95% CI, 0.60–1.48]). For patients ≥ 75 years, the reduction in death or MI was 10.6% (absolute rate 10.8% in the invasive group versus 21.6% in the conservative group; $P = 0.016$). In multivariable analysis, there was a significant interaction between age and treatment strategy ($P = 0.044$). Bleeding rates were higher among older patients. In patients aged > 75 years, the early invasive strategy was associated with an increased risk of major bleeding (16.6% versus 6.5%; $P = 0.009$). There was no significant difference in stroke by treatment group for any age-group. The estimated cost per death or MI averted using the invasive strategy was \$39,067 for patients aged < 65 years and \$10,393 for patients ≥ 65 years.

Conclusion. The rate of death or MI was decreased in elderly patients undergoing early invasive management for ACS, but bleeding rates were higher.

Commentary

Older patients with ACS have more high-risk features and, therefore, a worse prognosis than do younger patients. This subgroup analysis by age of the TACTICS-TIMI 18 (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction) trial reveals that in an era of coronary stenting and glycoprotein IIb/IIIa antagonism, an early intervention strategy benefits elderly patients most in terms of the reduction of death or MI. While there were more episodes of major bleeding and blood transfusions for elderly patients, it seems unlikely that this potential adverse effect outweighs the possible benefits for elderly patients with ACS.

Bach and colleagues openly acknowledge the limitations of this study. There were many exclusion criteria used, most of which are more common in elderly patients presenting with ACS. Therefore, it is not clear how these results should

be applied to elderly patients with comorbid conditions such as prior bleeding episodes, renal failure, or cerebrovascular disease.

One point the authors do not discuss is whether the results from this prespecified subgroup analysis should dampen our enthusiasm for an early invasive strategy for ACS in the youngest patients. Another recent study comparing an early invasive strategy with a conservative strategy also showed that the reduction in death or MI with early intervention was largely confined to patients over age 65 years, while the reduction in angina with the early intervention was similar in both age-groups [1]. If an early intervention strategy is chosen for middle-aged adults, Bach et al's findings suggest that the cost per death or MI averted will be much greater than it is for older adults.

Applications for Clinical Practice

Elderly patients with ACS have better ischemic outcomes

with an early invasive strategy. Clinicians should make efforts to minimize the risk of bleeding and manage this predictable complication appropriately when it occurs. It is not clear if an early invasive strategy will produce the same favorable results for patients with the excluded comorbidities. For middle-aged patients with ACS, an early invasive strategy is not clearly superior to a conservative medical strategy with angiography and revascularization reserved for those with clinical progression or abnormal results on noninvasive cardiac testing.

—Review by Stephen D. Persell, MD, MPH

References

1. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. FRagmin and Fast Revascularisation during InStability in Coronary artery disease Investigators. *Lancet* 1999;354:708–15.

Copyright 2004 by Turner White Communications Inc., Wayne, PA. All rights reserved.