

An early invasive strategy reduced death or MI better than a conservative strategy in unstable angina and non-STEMI at advanced age

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.

QUESTION

Is an early invasive strategy more effective than a conservative strategy for reducing clinical outcomes in unstable angina and non-ST-segment elevation myocardial infarction (MI) according to patient age?

METHODS

Design: Randomized controlled trial (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction [TACTICS-TIMI] 18 trial).

Allocation: Concealed.*

Blinding: Blinded (outcome assessors).*

Follow-up period: 6 months.

Setting: 169 hospitals in 9 countries.

Patients: 2220 patients ≥ 18 years of age (mean age 62, 66% men) who had an episode of angina in the previous 24 hours; were a candidate for coronary revascularization; had ≥ 1 of ST-segment depression ≥ 0.05 mV, transient (< 20 min) ST-segment elevation (≥ 0.1 mV), or T-wave (≥ 0.3 mV) inversion in ≥ 2 leads not known to be old; elevated levels of cardiac markers; or documented history of coronary disease. Exclusion criteria included persistent ST-segment elevation, secondary angina, percutaneous coronary revascularization or coronary bypass surgery within the previous 6 months, and a history of gastrointestinal bleeding.

Intervention: Patients were stratified by center and age (< 65 y and ≥ 65 y) and allocated to early invasive strategy (coronary angiography 4 to 48 h after randomization, and revascularization when appropriate) ($n = 1114$) or early conservative strategy (treated medically and given an exercise tolerance test before discharge, if stable) ($n = 1106$).

Outcomes: Death and nonfatal MI, and bleeding complications.

Patient follow-up: 99% (intention-to-treat analysis).

MAIN RESULTS

1258 patients (57%) were < 65 years of age and 962 (43%) were ≥ 65 years of age. Fewer patients who were ≥ 65 years of age and who received an early invasive strategy died or had a nonfatal MI than did those who received an early conservative strategy (Table). The early invasive and early conservative strategies did not differ for death or nonfatal MI in patients < 65 years of age (Table). The groups

did not differ for death in patients < 65 years of age (odds ratio [OR] 1.02, 95% CI 0.44 to 2.37) or ≥ 65 years of age (OR 0.88, CI 0.51 to 1.53). Bleeding complications increased with increasing age in both invasive and conservative treatment groups but occurred more frequently in patients who were ≥ 75 years of age who were managed invasively (16.6% vs 6.5%, $P = 0.009$).

CONCLUSIONS

In patients with unstable angina and non-ST-segment elevation myocardial infarction (MI), an early invasive strategy was more effective than an early conservative strategy for reducing death or MI in patients ≥ 65 years of age, but not in patients < 65 years of age. The early invasive strategy did not reduce death in either age group.

*See Glossary.

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Early invasive strategy vs early conservative strategy for unstable angina and non-ST-segment elevation myocardial infarction (MI) at 6 months†

Outcome	Age group	Invasive	Conservative	RRR (95% CI)	NNT (CI)
Death or MI	Age < 65 y	6.1%	6.5%	5.5% (–44 to 38)	Not significant
	Age ≥ 65 y	8.8%	13.6%	36% (7 to 55)	21 (12 to 117)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The study by Bach and colleagues is a prespecified subgroup analysis from the TACTICS-TIMI 18 trial that randomized patients with non-ST-elevation acute coronary syndromes to an early invasive or an early conservative management strategy. Compared with younger patients (age < 65 y), those ≥ 65 years of age were more often women and more likely to have diabetes, a history of heart failure, elevated troponin levels, ST-segment electrocardiographic changes, or higher TIMI risk scores.

Older patients had a higher risk for death or MI at 6 months, and these risks were substantially lowered with the invasive strategy. In contrast, the invasive strategy was associated with a nonsignificant risk reduction in younger patients with lower risk. Despite greater therapeutic benefit and cost-effectiveness in the elderly, the clinical paradox is that use of invasive cardiac procedures in every registry study declines as patients get older.

Risk for bleeding may be the most common reason for not pursuing an invasive strategy in the elderly. This study showed higher rates of major bleeding and blood transfusion but not stroke in older patients (especially those > 75 y of age). However, the unfractionated heparin

doses were higher than currently recommended and not weight-adjusted, and tirofiban was infused for more hours than in current practice. Lower bleeding rates would be expected with weight-adjusted unfractionated heparin dosing. Also, earlier performance of cardiac catheterization would decrease the infusion times for both unfractionated heparin and glycoprotein IIb/IIIa inhibitors, potentially further decreasing bleeding risk.

Previous analyses from this trial suggested that the invasive strategy was beneficial in patients with elevated troponin levels or high TIMI risk scores, but not for those with normal biomarker levels or low TIMI risk scores. Thus, simple clinical variables exist that can help clinicians selectively choose an invasive strategy. In high-risk patients including the elderly, ischemic complications can be decreased with earlier coronary angiography; and bleeding complications can be decreased with lower, weight-adjusted doses of antithrombotic therapy and shorter infusion times.

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