

An early invasive strategy improved long-term freedom from major adverse cardiac events in older patients with angina

Pfisterer M. Long-term outcome in elderly patients with chronic angina managed invasively versus by optimized medical therapy: four-year follow-up of the randomized Trial of Invasive versus Medical therapy in Elderly patients (TIME). *Circulation*. 2004;110:1213-8.

QUESTION

In older patients with angina, is early invasive therapy (EIT) better than optimized medical therapy (OMT) for improving long-term survival, freedom from major adverse cardiac events (MACEs), and quality of life (QOL)?

METHODS

Design: Randomized controlled trial (Trial of Invasive versus Medical therapy in Elderly patients [TIME]).

Allocation: Concealed.*

Blinding: Unblinded.*

Follow-up period: Median 4.1 years.

Setting: 14 hospitals in Switzerland.

Patients: 276 patients who survived for the first 12 months after enrollment in the TIME study of 301 who were ≥ 75 years of age (mean age 80 y, 58% men) and had Canadian Cardiovascular Society class 2 angina or higher despite treatment with ≥ 2 antiangina drugs.

Intervention: EIT (coronary angiography followed by revascularization [percutaneous coronary intervention or coronary artery bypass graft surgery]) if feasible ($n = 153$) or OMT (an increase in the number or dose of antiangina drugs to reduce pain) ($n = 148$).

Outcomes: All-cause mortality, MACE including cardiac deaths and hospitalizations

for cardiac causes (i.e., nonfatal infarctions and late revascularization), angina severity, QOL, and antiangina drug use.

Patient follow-up: 100% for survival and 92% for QOL (intention-to-treat analysis).

MAIN RESULTS

The rates of cardiac rehospitalizations and overall nonfatal cardiac events (including nonfatal myocardial infarctions and cardiac rehospitalizations) were lower in the EIT group than in the OMT group (Table). The rate of freedom from MACE was greater in the EIT group than in the OMT group (Table). The mean number of antiangina drugs used per person was greater in the OMT group than in the EIT group throughout follow-up ($P < 0.05$). Groups did not

differ for all-cause mortality (29.4% vs 27%), cardiac mortality (21% vs 22%), nonfatal infarction (12% vs 12%), or angina severity and quality of life (P values > 0.05).

CONCLUSIONS

In older patients with angina, early invasive therapy was more effective than optimized medical therapy for improving freedom from major adverse cardiac events. However, the groups did not differ for long-term survival or quality of life.

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*See Glossary.

Early invasive therapy (EIT) vs optimized medical therapy (OMT) for angina at median 4.1 years†

Outcomes	EIT	OMT	RRR (95% CI)	NNT (CI)
Cardiac rehospitalizations	12%	45%	73% (57 to 83)	4 (3 to 5)
Overall nonfatal cardiac events	37%	68%	45% (32 to 57)	4 (3 to 6)
RBI (CI)				
Freedom from MACE	39%	20%	93% (34 to 183)	6 (4 to 12)

†MACE = major adverse cardiac event. Other abbreviations defined in Glossary; RRR, RBI, NNT, and CI calculated from data in article.

COMMENTARY

The main findings in the study by Pfisterer and colleagues are that elderly patients selected for revascularization do well, whether they receive the procedure initially or after “failure” of OMT. The conclusion would suggest that symptomatic patients with angina should be offered revascularization early on, because the outcome is good and many patients wind up requiring revascularization later.

At first glance, the study also seems to support watchful waiting, because death and myocardial infarction did not differ. However, patients who received revascularization within the first year, either because of randomization to the early-intervention group or because of ongoing symptoms, had better survival than patients managed medically. Revascularization within the first year was an independent predictor of survival in a multivariate analysis. This finding suggests that revascularization may be better not only for symptom control—preventing myocardial infarction and hospitalization—but survival as well. The fact that drug-eluting stents were not available for this trial suggests that the benefits of revascularization may be understated.

One important caveat is that patients with such comorbid conditions as cancer, substantial renal dysfunction, and cognitive impairment were excluded. Study patients were thus selected for their suitability for catheterization, a criterion that is not fulfilled by all older patients. However, we should modify our concepts of who is suitable for intervention based on studies like TIME. Such studies should help us recognize that although adverse outcomes associated with catheterization and revascularization procedures occur more frequently in older patients than in younger ones, these disadvantages may be outweighed by repeated hospitalizations and events, even death, in conservatively managed patients.

The standard of care for older patients continues to evolve: Consider chronological age less and quality of life and concomitant factors (e.g., renal failure and patients’ choices) more.

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