Both invasive and optimized medical therapies improved quality of life in angina, but invasive therapy had fewer major adverse cardiac events

Pfisterer M, Buser P, Osswald S, et al. **Outcome of elderly patients with chronic symptomatic coronary artery disease with an invasive vs optimized medical treatment strategy: one-year results of the randomized TIME trial.** JAMA. 2003;289:1117-23.

QUESTION

In older patients with angina, is early invasive therapy better than optimized medical therapy for improving quality of life and preventing major adverse cardiac events (MACEs)?

DESIGN

Randomized (allocation concealed*), {unblinded}†,* controlled trial with 12-month follow-up (Trial of Invasive versus Medical therapy in Elderly patients [TIME]).

SETTING

14 centers in Switzerland.

PATIENTS

301 patients who were ≥ 75 years of age (mean age 80 y, 58% men) and had Canadian Cardiac Society class 2 or higher chronic angina despite treatment with ≥ 2 antianginal drugs, and who survived for the first 6 months after enrollment in the TIME study. Exclusion criteria were acute myocardial infarction (MI) within the previous 10 days, concomitant valvular or other heart disease, predominant congestive heart failure, or no consent for a possible revascularization procedure. Follow-up was 92%.

INTERVENTION

Patients were allocated to an invasive strategy (coronary angiography followed by revascularization [percutaneous coronary intervention or coronary artery bypass graft surgery]) if feasible (n = 153) or optimized medical therapy {an increase in the number or dose of antianginal drugs to reduce pain}† (n = 148).

MAIN OUTCOME MEASURES

Quality of life (assessed by standardized questionnaires [a self-administered questionnaire containing the Short Form 36, the Duke Activity Status Index, the Rose angina questionnaire, and questions about education and social status]) and freedom from MACEs (death, nonfatal MI, or hospitalization for uncontrolled symptoms or the acute coronary syndrome [ACS] with or without the need for revascularization) at 12 months.

MAIN RESULTS

Analysis was by intention to treat. The early invasive therapy and optimized medical therapy groups did not differ for improvement in quality of life. Groups also did not differ for death or nonfatal MI (Table). Patients in the optimized medical therapy group had more MACEs than did those in the invasive therapy group (Table) and had more hospitalizations with or without revascularization (106 vs 28, $P < 0.001$).

CONCLUSION

In older patients with angina, early invasive therapy was as effective as optimized medical therapy for improving quality of life and led to fewer major adverse cardiac events.

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*See Glossary.

†The TIME Investigators. Lancet. 2001;358:951-7.

Invasive therapy vs optimized medical therapy for angina at 12 months‡

Outcomes	Invasive therapy	Optimized medical therapy	RRI (95% CI)	NNH
Death	11.1%	8.1%	37% (–31 to 174)	Not significant
			RRR (CI)	NNT (CI)
Death or nonfatal MI	17%	19.6%	13% (–39 to 46)	Not significant
MACE	25.5%	64.2%	60% (47 to 71)	3 (3 to 4)

‡MI = myocardial infarction; MACE = major adverse cardiac event. Other abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

After 6 months of follow-up, the TIME trial reported that an invasive strategy decreased angina severity, improved quality-of-life indices, and had fewer MACEs than an optimized medical strategy in older patients with stable coronary artery disease (1). The results complemented other trials in younger patients showing greater improvement in quality of life after coronary revascularization for stable angina and superiority of the invasive strategy over medical therapy in ACSs. However, critics argued that the trial was limited in size, the event rates were lower than predicted, medical therapy was not really optimized, and the follow-up was too short.

In the 1-year results of the TIME trial by Pfisterer and colleagues, the significant difference in symptom relief or quality-of-life indices no longer existed. This result may have occurred partly because the crossover to revascularization in the medical group was 46%. In fact, the only difference between the groups was an increased need for hospitalization in the medical group, usually for revascularization. Because no differences existed in death or MI rates, either strategy seems reasonable depending on physician and patient preferences.

The major accomplishment of this trial is that it randomized older patients. This subgroup accounts for one third of the hospitalizations for acute coronary syndromes and one half of all cardiac deaths (2). However, this population has routinely been excluded from previous randomized clinical trials. As a result, this study is an important precedent for future trials. From a clinical standpoint, maximal antiischemic therapy including β-blockers; control of risk factors to target levels; weight control; diet; exercise training; and aspirin, statins, and angiotensin-converting enzyme inhibitors should be used to truly optimize medical therapy.

In older patients with stable angina pectoris, symptom relief and improving quality of life are more important than prolonging life and can usually be accomplished with excellent medical therapy. As with younger patients, the invasive strategy will probably benefit older patients with uncontrollable angina, high-risk noninvasive stress test results, or ACSs.

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References

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