

Revascularization versus Medical Therapy for Elderly Chronic Angina Patients

Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary-artery disease (TIME): a randomized trial. The TIME Investigators. Lancet 2001;358:951-7.

Study Overview

Objective. To determine if adults older than age 75 with chronic anginal chest pain despite at least 2 antianginal drugs had better quality of life or cardiac outcomes with intensified medical therapy or early revascularization.

Design. Randomized controlled multicenter trial. Analysis was by intention-to-treat.

Setting and participants. 305 participants enrolled at several Swiss centers. Participants were at least 75 years old with Canadian Cardiac Society class II angina despite at least 2 antianginal medications. Potential participants were excluded for myocardial infarction (MI) in the past 10 days; valvular heart disease, congestive heart failure, or other heart disease; life-limiting noncardiac disease; unwillingness to undergo revascularization; inability to be revascularized; or inability to further increase medical therapy.

Intervention. Participants were assigned to either the control group, to optimal medical therapy (which consisted of increasing the number or dose of antianginal medications), or to initial invasive treatment, consisting of cardiac catheterization followed by coronary artery bypass graft surgery (CABG) or percutaneous coronary intervention (PCI) if appropriate.

Main outcome measures. Primary endpoints were quality of life (QOL) assessed by questionnaires using previously developed general and disease specific measures (the SF-36, Duke activity score index, and the Rose questionnaire of angina), and the composite endpoint of death, nonfatal MI, or hospitalization for increasing or unstable angina. Endpoints were assessed at 6 months.

Main results. 2 participants from each arm were not included in the analysis (3 because of MI within 10 days of randomization and 1 due to withdrawal of consent). Of 153 patients in the invasive arm, 96% had catheterization, 52% had PCI, 20% had CABG, and 28% received medical

therapy because attending physicians did not think revascularization was possible. Only 4 participants (< 3%) who underwent catheterization did not receive the assigned revascularization.

The composite cardiac endpoint was reached in 65% of the medical therapy group and 26% of the invasive group ($P < 0.001$). The magnitude of the difference between the groups was driven by the high number of hospital admissions in the medical therapy group (49% versus 10%). 37% of the medical therapy group received revascularization after presenting with worsening or unstable symptoms during the 6-month follow-up. There was a nonsignificant increase in deaths in the invasive group (8.5% versus 4.1%); however, most of the deaths in this group occurred in participants who were not revascularized. 3 deaths in the invasive group and 1 in the medical therapy group were intervention-related. In each group there were 3 intervention-related MIs. QOL at 6 months improved in both groups. There were statistically significant improvements in several QOL measures in the invasive group. The invasive group did not appear worse by any QOL measure. When the invasive group was compared to those in the medical therapy group who did not undergo revascularization, the improvement seen in the intervention group was larger and statistically significant by all measures.

Conclusion. As compared to intensified antianginal therapy, revascularization led to greater improvements in QOL and a reduction in the combined endpoints of death, nonfatal MI, or hospitalization for anginal symptoms in an elderly population with chronic angina.

Commentary

This study demonstrates that in an elderly population (mean age, 80 years), an invasive strategy can perform better than medical therapy despite the fact that procedural complication rates are generally higher in this age-group as compared with younger patients. Even when medical therapy was assigned, almost 40% of participants ended up requiring revascularization within 6 months. In the intention-to-treat analy-

sis, QOL was slightly better in the intervention group. The size of this difference may have been decreased by the members of the medical therapy group who underwent revascularization. Improving QOL is an important goal in persons in this age-group; since improved QOL was achieved without an increase in major adverse events, strong consideration should be given to an invasive approach.

Still, there are reasons not to universally adopt an invasive strategy in this age-group. An important difference in early death could not be determined or excluded due to the limited size of this study. Data concerning the rate of stroke also would be valuable, especially considering the number of participants in the invasive group who underwent CABG. In addition, only about one quarter of participants were treated with lipid-lowering therapy or an angiotensin-converting enzyme inhibitor on entry to the study. The number of participants who began these drugs during the study period is not given. These drugs have been shown to decrease major cardiac events in groups of younger participants [1,2], and outcomes in the medical group may have been improved if these drugs were added.

Applications for Clinical Practice

When chronic angina cannot be controlled easily, clinicians should not avoid angiographic evaluation in the willing patient merely because of advanced age. In centers with comparably low complication rates for elderly patients undergoing PCI or CABG, revascularization offers the potential to improve QOL and decrease hospitalizations. Long-term follow-up of this study cohort will further elucidate the issue.

—Review by Stephen D. Persell, MD

References

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2. Pitt B, Waters D, Brown WV, et al. Aggressive lipid-lowering therapy compared with angioplasty in stable coronary artery disease. Atorvastatin Versus Revascularization Treatment Investigators. *N Engl J Med* 1999;341:70–6.

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