

Revascularization led to less angina and fewer adverse cardiac events than did optimal medical care in angina pectoris in the elderly

In the TIME trial (1), mortality at 6 months showed a trend in favor of medical therapy (4.1% in the medical group vs 8.4% in the invasive-treatment group, $P = 0.15$). This was not noted in the abstract and is downplayed in the text of the report.

Nothing surprising there, but the *ACP Journal Club* abstract (2) repeats the omission and the accompanying commentary concludes that “these data support early angiography and invasive treatment . . .” I submit that they warrant caution and an investigation into why the invasive approach might increase overall mortality.

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References

1. **The TIME Investigators.** Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary-artery disease (TIME): a randomised trial. *Lancet.* 2001;358:951-7.
2. Revascularization led to less angina and fewer adverse cardiac events than did optimal medical care in angina pectoris in the elderly [Abstract]. *ACP J Club.* 2002 Mar-Apr;136:47. Abstract of: The TIME Investigators. Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary-artery disease (TIME): a randomised trial. *Lancet.* 2001;358:951-7.

In response:

As noted by Dr. Walker, there was a tendency toward more deaths in the invasive group, which was not statistically significant but may reflect an early intervention hazard. We have noted this excess mortality in our abstract and addressed this issue in the results as well as in the discussion sections of our paper (1). We would like to emphasize that the TIME study was not intended nor powered as a mortality trial. Rather than mortality, the primary end point of TIME was quality of life (QoL), which was assessed by a standardized questionnaire, and survival without major adverse cardiac events (death, nonfatal myocardial infarction, and rehospitalization for acute coronary syndrome with or without need for revascularization). The study showed a significant improvement in QoL for both the invasive and the optimal medical groups, but the benefit was significantly greater after revascularization. These results were supported by a significantly lower rate of major adverse cardiac events after revascularization, mainly in terms of rehospitalization for acute coronary syndrome.

One reason for the reluctance to do coronary angiography and revascularization in elderly patients is the increased risk associated with such procedures in this population, which usually has a broad risk profile and complex comorbidity. The TIME data confirmed this

risk but showed that with today's techniques the risk is lower than one might expect. Intervention-related mortality was far lower (2.5%) than observed in recent registries (2, 3) and was similar to the mortality of the 1999 Swiss population (4) aged 65 to 79 and ≥ 80 years (2.3% and 11.5%, respectively). Because about half the cardiac deaths in the invasive group occurred in patients who were unwilling to have or unsuitable for revascularization, which resulted in a high mortality rate for that subgroup (9.3% vs 5.5% for revascularized patients), the 6-month mortality rate of 8.4% after intended revascularization was low. Results of 1-year follow-up, which will be presented at the Annual Meeting of the European Society of Cardiology this year, will show whether this early intervention hazard will be outweighed in the long term. As noted in other high-risk patient subsets (5), a mortality benefit of revascularization might be detected only after longer follow-up; the TIME study follow-up is continuing.

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1. **The TIME Investigators.** Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary-artery disease (TIME): a randomised trial. *Lancet.* 2001;358:951-7.
2. **Batchelor WB, Anstrom KJ, Muhlbaier LH, et al.** Contemporary outcome trends in the elderly undergoing percutaneous coronary interventions: results in 7,472 octogenarians. National Cardiovascular Network Collaboration. *J Am Coll Cardiol.* 2000;36:723-30.
3. **Alexander KP, Anstrom KJ, Muhlbaier LH, et al.** Outcomes of cardiac surgery in patients age ≥ 80 years: results from the National Cardiovascular Network. *J Am Coll Cardiol.* 2000;35:731-8.
4. **Bundesamt für Statistik.** Schweizerisches Statistisches Jahrbuch 1999 (Swiss Statistical Yearbook 1999).
5. **Hochman JS, Sleeper LA, White HD, et al.** One-year survival following early revascularization for cardiogenic shock. *JAMA.* 2001;285:190-2.

Commentator's response:

No significant mortality difference existed. The apparent “trend” is probably caused by the short observation period and the fact that most mortalities with surgery occur near the beginning of any observation period. A longer observation period would probably erase any “trend.”

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