

# Women responded to an early invasive strategy as well as men in the acute coronary syndrome

Glaser R, Herrmann HC, Murphy SA, et al. **Benefit of an early invasive management strategy in women with acute coronary syndromes.** JAMA. 2002;288:3124-9.

## QUESTION

In patients with the acute coronary syndrome (ACS), do sex differences exist in the response to an early invasive strategy compared with a conservative strategy?

## DESIGN

Sex-based subgroup analysis of a {randomized (allocation concealed\*), blinded (outcome assessors),\* controlled trial with 6-month follow-up (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy—Thrombolysis in Myocardial Infarction 18 [TACTICS-TIMI 18])}†.

## SETTING

169 centers in 9 countries in North America and Europe.

## PATIENTS

2220 patients (757 women, mean age 64 y; 1463 men, mean age 61 y) who had an episode of unstable angina in the previous 24 hours; were candidates for coronary revascularization; and had  $\geq 1$  of ST-segment depression, transient ST-segment elevation, or T-wave inversion in  $\geq 2$  leads; increased cardiac biomarker levels; or history of coronary disease. All patients were included in the analysis.

## INTERVENTION

Patients were allocated to an early invasive strategy (coronary angiography at 4 to 48 h after randomization and revascularization when appropriate) ( $n = 395$  women and 719 men) or a conservative strategy (medical treatment and coronary angiography and appropriate revascularization only if specified criteria were met) ( $n = 362$  women and 744 men).

## MAIN OUTCOME MEASURES

A primary composite endpoint of death, myocardial infarction (MI), and rehospitalization for ACS at 6 months. Multivariable logistic regression was done to determine the effect of sex on the combined endpoint.

## MAIN RESULTS

Statistically significant differences existed between women and men at baseline: Women were older, more likely to have hypertension, less likely to have previous cardiac disease, and less likely to present with elevated troponin T levels ( $P < 0.001$ ). Men

and women did not differ for distribution of TIMI risk scores. The composite endpoint was lower in men who received the invasive strategy than in those who received the conservative strategy; the rate was also lower in women receiving the invasive strategy, but the difference did not reach statistical significance (Table). However, multivariable analysis showed that sex was not an independent risk factor for treatment outcome ( $P = 0.60$  for interaction).

## CONCLUSION

In patients with the acute coronary syndrome, women responded to an early invasive strategy as well as men.

Source of funding: No external funding.

For correspondence: Dr. H.C. Herrmann, Hospital of the University of Pennsylvania, Philadelphia, PA, USA. E-mail howard.herrmann@uphs.upenn.edu. ■

\*See Glossary.

†Cannon CP, Weintraub WS, Demopoulos LA, et al. N Engl J Med. 2001;344:1879-87.

## Invasive vs conservative strategy for the acute coronary syndrome at 6 months‡

Outcome	Group	Invasive	Conservative	Odds ratio (95% CI) <sup>§</sup>	RRR (CI)	NNT (CI)
Composite endpoint	Women	17.0%	19.6%	0.72 (0.47 to 1.11)	24% (-8.7 to 48)	Not significant
	Men	15.3%	19.4%	0.64 (0.47 to 0.88)	31% (9.9 to 48)	

‡Composite endpoint = death, myocardial infarction, and rehospitalization. Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

§Adjusted for baseline differences.

## COMMENTARY

The study by Glaser and colleagues provides some support that an early invasive strategy in ACS without ST elevation has similar efficacy in men and women. This is a subgroup analysis comparing men and women in the TACTICS-TIMI 18 study. Apparent benefit existed in both groups without evidence of a sex interaction. This finding is at odds with other subgroup analyses from the FRISC II and RITA 3 trials, both of which compared an early invasive strategy with a conservative strategy in ACS (1, 2). In FRISC II ( $n = 749$  women), the rates of death or MI after 1 year were 15.8% for the noninvasive group and 9.6% for the invasive group in men and 10.5% and 12.4% in women, respectively. In RITA 3 ( $n = 682$  women), the results were 10.1% and 7.0% in men and 5.1% and 8.6% in women. A true sex-based interaction may exist with respect to early invasive procedures, but these and previous analyses have not established this beyond reasonable doubt because of the limitations of subgroup analyses.

The meta-analysis of glycoprotein IIb/IIIa agents in ACS has also raised the issue of a possible sex interaction (3). We know that the women are older and generally sicker than men in clinical trials. They have different coronary anatomy, and it is possible that they respond

differently to invasive procedures. Methodologic differences may also exist in the outcome definitions between the TACTICS, FRISC, and RITA trials. TACTICS relies more heavily on elevation of CKMB or troponin, whereas the others use more conventional definitions including electrocardiographic changes and elevation of biomarkers to define MI. The true result cannot be inferred from available data, although the consistency of FRISC II and RITA 3 results raises concerns that women somehow react poorly to early coronary intervention in ACS. The OASIS group is planning a study of 1600 women randomized to invasive or conservative management in ACS to determine if a benefit exists from an invasive approach. This and other randomized trials are needed to find out if women benefit from early revascularization in ACS.

Marcus D. Flather, MBBS, FRCP  
Umair Mallick, MD  
Royal Brompton Hospital  
London, England, UK

## References

- Wallentin L, Lagerqvist B, Husted S, et al. Lancet. 2000;356:9-16.
- Fox KA, Poole-Wilson PA, Henderson RA, et al. Lancet. 2002;360:743-51.
- Boersma E, Harrington RA, Moliterno DJ, et al. Lancet. 2002;359:189-98.