Carvedilol reduced mortality and morbidity caused by myocardial infarction in patients with left ventricular dysfunction

The CAPRICORN Investigators. **Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial.** Lancet. 2001 May 5;357:1385-90.

QUESTION

In patients with left ventricular dysfunction, does adding carvedilol to the management of myocardial infarction (MI) reduce mortality and nonfatal MI?

DESIGN

Randomized {allocation concealed*}†, blinded (patients, judicial assessors of outcomes, data analysts),* placebo-controlled trial with a mean 1.3-year follow-up.

SETTING

163 centers in 17 countries.

PATIENTS

1959 patients (mean age 63 y, 74% men) participated. Inclusion criteria were age > 18 years; stable and definite MI occurring 3 to 21 days before randomization; left ventricular ejection fraction ≤ 0.40; wall-motion-score index ≤ 1.3; current treatment with angiotensin-converting enzyme (ACE) inhibitors for ≥ 48 hours with a stable dose for ≥ 24 hours; and if the patient was having heart failure, treatment with diuretics and ACE inhibitors. Exclusion criteria included uncontrolled heart failure, unstable angina, and need for intravenous diuretics or inotropes. Follow–up was 100%.

INTERVENTION

975 patients were allocated to carvedilol and 984 to the placebo group. Patients initially received 6.25 mg carvedilol twice daily; the dose was titrated to a maximum of 25 mg twice daily. Treatment was reviewed every 3 months for the first year and every 4 months thereafter until the study ended, at which time medication was withdrawn over 1 to 2 weeks.

MAIN OUTCOME MEASURES

All-cause mortality, cardiovascular mortality, nonfatal MI, and all-cause mortality or nonfatal MI.

MAIN RESULTS

Analysis was by intention to treat. All-cause and cardiovascular mortality and nonfatal MI were lower in the carvedilol group than in the placebo group (Table).

CONCLUSION

Adding carvedilol to the short-term management of myocardial infarction (MI) reduced all-cause and cardiovascular mortality and nonfatal MI in patients with left ventricular dysfunction.

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*See Glossary.

†Information provided by author.

Carvedilol vs placebo in acute management of myocardial infarction (MI) at a mean of 1.3 years‡

Outcomes	Carvedilol	Placebo	RRR (95% CI)	NNT (CI)
All-cause mortality	12%	15%	22% (3 to 38)	30 (16 to 244)
Cardiovascular mortality	11%	14%	24% (4 to 40)	29 (16 to 185)
Nonfatal MI	3%	6%	40% (9 to 60)	44 (24 to 223)
All-cause mortality or nonfatal MI	14%	20%	27% (11 to 40)	20 (12 to 52)

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Determining optimum medical management of patients who have had acute MI has been advancing through a series of randomized controlled trials. Such agents and interventions as aspirin, thrombolytics, β-blockers, ACE inhibitors, and percutaneous transluminal coronary angioplasty have been systematically studied in this setting. Although the current study by the CAPRICORN investigators shows that a clinical benefit existed in patients who were treated with carvedilol after acute MI with left ventricular dysfunction, some of the study's statistical aspects, such as changing the primary end point during the course of the trial, may affect its approval for this indication (1). In fact, enrollment for this trial was impeded in several countries because of the considered-to-be established benefits of β-blocker therapy after acute MI, especially in high-risk patients. For example, most of the mortality benefit of β-blockade in the β-Blocker Heart Attack Trial (BHAT) (2) was seen in the "high-risk" groups, such as patients with heart failure. Similarly, the Survival and Ventricular Enlargement (SAVE) trial data (3) showed that the benefits of β-blockade were seen in addition to ACE inhibitor therapy.

How should this trial alter current management? The intuitive answer is that it should not alter but should strengthen current therapy. A sound therapeutic approach would ensure that all patients with acute MI receive aspirin, some form of immediate revascularization (pharmacologic or nonpharmacologic), and β-blockers. At the time of discharge, all eligible patients should receive ACE inhibitors and a statin in addition to aspirin and β-blockers.

This study highlights the fact that future trials of acute MI cannot ethically withhold β-blocker therapy. Furthermore, the beneficial effects may be a "class effect" and until such trials as the Carvedilol and Metoprolol European Trial (4) are completed, insufficient data exist to choose a particular β-blocker in the clinical setting.

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References

1. **Coats AJ.** CAPRICORN: a story of alpha allocation and beta-blockers in left ventricular dysfunction post-MI. Int J Cardiol. 2001;78:109-13.
2. **Chadda K, Goldstein S, Byington R, Curb JD.** Effect of propranolol after acute myocardial infarction in patients with congestive heart failure. Circulation. 1986;73:503-10.
3. **Vantrimpont P, Rouleau JL, Wun CC, et al.** Additive beneficial effects of beta-blockers to angiotensin-converting enzyme inhibitors in the Survival and Ventricular Enlargement (SAVE) Study. SAVE Investigators. J Am Coll Cardiol. 1997;29:229-36.
4. **Krum H.** Beta-blockers in heart failure. The "new wave" of clinical trials. Drugs. 1999;58:203-10.