Accession Number 00021607-199711000-00001

Title **Ramipril reduced long-term mortality** after MI.

Source ACP Journal Club. v127:p.57, Nov-Dec, 1997.

Reviewed Source Abstract and Commentary for: Hall AS, Murray GD, Ball SG, on behalf of the AIREX Study Investigators. Follow-up study of patients randomly allocated to **ramipril** or placebo for heart failure after acute myocardial infarction: AIRE Extension (AIREX) Study. Lancet. 1997 May 24;349:1493-7.

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Keywords ACE - angiotensin converting enzyme; ACE inhibitors; ACE level; Acute MI; Acute myocardial infarction; Acute pulmonary edema; AMI - acute myocardial infarction; Angiotensin converting enzyme; Angiotensin I-converting enzyme inhibitors; Angiotensin-converting enzyme inhibition; B-adrenergic blockade; B-blockade; B-blockers; Beta blocker; Biventricular failure; Carboxycathepsin; Cardiac failure; Cardiogenic pulmonary edema; CHF; Chronic heart failure; Congestive failure; Congestive heart failure; Converting enzyme inhibitors; Depressed left ventricular function; Dipeptidyl peptidase A; Heart attack; Heart failure; Kininase A; Kininase II inhibitors; Left heart failure; Left ventricular dysfunction; Left ventricular failure; MI - myocardial infarction; Myocardial failure; Myocardial infarction; Peptidase p; Peptidyl-dipeptidase A; Postoperative MI; Pulmonary edema; Q-wave infarctions; Q-wave myocardial infarction; **Ramipril**; Severe congestive heart failure; Severe heart failure; Systolic dysfunction; Ventricular dysfunction; Wet lung

Abstract

Objective:

To determine the **long-term** survival benefit of **ramipril** for congestive heart failure (CHF) after myocardial infarction (MI).

Design:

Randomized, double-blind, placebo-controlled trial with 3-year follow-up after the end of the

study.

Setting:

30 clinical centers in the United Kingdom.

Patients:

603 patients (mean age 65 y, 75% men) with confirmed MI complicated by CHF defined as left ventricular failure on erect posteroanterior chest radiograph, auscultatory evidence of pulmonary edema, or a third heart sound plus persistent tachycardia. Exclusion criteria were clinical instability, contraindications to angiotensin-converting enzyme (ACE) inhibitors, heart failure of primary valvular or congenital origin, or overt CHF that required ACE inhibitors. Follow-up was > 99% and 100% for death.

Intervention:

Treatment was started 2 to 9 days after MI. 302 patients were allocated to **ramipril**, 1.25 to 2.5 mg twice daily titrated up to 2.5 to 5.0 mg twice daily, and 301 patients were allocated to placebo. Overt CHF was treated with open-label ACE inhibitors. At the end of the 15-month study, patients stopped their double-blind assigned medication and were treated at the discretion of their physicians.

Main outcome measure:

Total **mortality** 3 years after the end of the trial.

Main results:

At discharge from the hospital, 13.7% of patients allocated to **ramipril** and 5.3% of patients allocated to placebo were not taking their assigned medication. 3 years after the end of the study (minimum follow-up of 42 mo, mean 59 mo), 83 deaths (28%) had occurred in the **ramipril** group and 117 deaths (39%) had occurred in the placebo group (P = 0.002) (Table).

Ramipril vs placebo for congestive heart failure*:

Ramipril **EER:**28%

Placebo **CER:**39%

RRR (95% CI):36% (15 to 52)

ARR |EER-CER|:11%

NNT (CI):9 (5 to 26)

Conclusion:

Ramipril reduced long-term mortality in patients with congestive heart failure after myocardial infarction.

Commentary

[beta]-blocker therapy is standard after MI. The original studies showed a short-**term mortality** benefit (1). It was not until the 7-year follow-up of the Norwegian timolol study (2) that this benefit was shown to be maintained over time. The same kind of information is now available on the use of ACE inhibitors in the treatment of patients with CHF after MI.

The Survival and Ventricular (SAVE) (3) and International Study of Infarct Survival (ISIS-4) (4) trials showed that the judicious use of these drugs several days after MI decreased the short-**term mortality** rate. Such studies as the Studies of Left Ventricular Dysfunction (SOLVD) trial (5), which showed the benefit of these drugs in CHF without acute MI, did not reveal a link between the timing of the start of therapy to the onset of congestive symptoms. Combining these 2 ideas would suggest to the clinician that patients with acute MI who developed CHF would benefit from **long-term** treatment.

The study by Hall and colleagues directly addresses this issue by showing an ongoing **mortality** benefit at 42 months when the ACE inhibitors were begun 2 to 9 days after MI. The 11% absolute risk reduction in **mortality** is even more remarkable because any patient who developed CHF during follow-up was permitted to receive an open-label ACE inhibitor. The drug was blindly compared with placebo only during the first 15 months of the study. It is also important to note that the magnitude of the survival benefit did not increase after 24 months, again perhaps because the use of ACE inhibitors was not restricted.

It took several years for ACE inhibitors to be widely used for CHF. Now we have excellent data showing that these agents are highly beneficial in reducing **mortality** in patients with CHF after MI in both the short and **long term**.

References

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Publication Type

Therapeutics.