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Wilhelmsson C, Vedin J A, Wilhelmsen L, Tibblin G & Werkö L. Reduction of sudden deaths after myocardial infarction by treatment with alprenolol. *Lancet* 2:1157-60, 1974.
[Sect. Preventive Cardiol , Medical Dept 1, Sahlgren's Hosp., Univ. Göteborg, Sweden]

The effect of 400 mg alprenolol daily on survival after myocardial infarction was compared to that of placebo in 230 patients discharged alive from the hospital The patients were allocated to four separate risk strata The study was double-blind and the follow-up time was two years After two years, 11 patients in the placebo group and 3 in the actively treated group had died suddenly ($p<0.50$) [The *SCI*® indicates that this paper has been cited in over 385 publications since 1974]

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The nature of the health-care system in Sweden, based on a public hospital service, has encouraged epidemiologic research in various diseases, not least in the area of cardiovascular disease. The Section of Preventive Cardiology of the University of Göteborg has had a major research programme into the pathogenesis and treatment of coronary heart disease. Consequently, by the late 1960s, when the study was planned, we had developed a multidisciplinary research group, an effective post-myocardial-infarction clinic, and an understanding of the role of the beta-adrenoceptors in myocardial infarction. Scientists at Hässle, the local subsidiary of Astra Pharmaceuticals, had developed alprenolol during the 1960s.

With this background, we were able to design and perform a study that provided the first sound evidence that pharmacologic intervention with a beta blocker could prolong survival in patients who had suffered an acute myocardial infarction.

The cause of the high frequency of citation of our article is probably twofold—the plausibility of our results and the subsequent worldwide interest to confirm them, since death from coronary heart disease was increasing in most Western societies at that time.

The credibility arises mainly from the study design—randomised, placebo-controlled, and stratified—common features of today's clinical trials but not so in the early 1970s.

In 1976, the Swedish health authorities approved the prophylactic use of alprenolol after myocardial infarction. Our group has looked further into the trends in mortality in patients who had a first myocardial infarction between 1968 and 1977 in the Göteborg area [1] During this decade, a decrease in mortality after myocardial infarction has been observed independent of age and estimated risk. The mortality at the end of this period was 28 percent lower than at the beginning, while the proportion of patients treated with a beta blocker after an acute myocardial infarction increased from 10 percent to 70 percent. We believe that our initial findings with alprenolol have had a beneficial impact on the health of our community.

More widespread acceptance of the benefit of treating survivors of myocardial infarctions with beta blockers came in the early 1980s with the publication of the Beta-Blocker Heart Attack Trial (BHAT)[2] and Norwegian Timolol studies.[3] Both trials showed extended survival in the actively treated groups. *Lancet*, in an editorial in 1982,[4] pronounced that the case for late intervention (one to three weeks after a myocardial infarction) with certain beta blockers was proved.

After the work with alprenolol in the early 1970s, the group decided to investigate the role of early intervention (within hours) with a beta blocker in patients with symptoms of acute myocardial infarction. These efforts have resulted in the completion of two major studies: the Göteborg Metoprolol Trial[5] and the Metoprolol in Acute Myocardial Infarction (MIAMI) Trial.[6] Together these studies provide firm evidence from some 7,500 patients that early treatment of suspected myocardial infarction patients with metoprolol can be given safely with a view to reduce infarct development and size, severe arrhythmias, reinfarction, and mortality, even during the hospital phase. The studies also show that maintenance treatment will have a sustained benefit on survival and reinfarction rate

We hope that future citation awards will reflect that recent work has also received critical acceptance by our research colleagues and its consequences translated into improved patient care.

1 **MIAMI Trial Research Group.** Metoprolol in acute myocardial infarction (MIAMI) Introductio... *Amer J Cardiol* In press, 1985
2 **β-Blocker Heart Attack Trial Research Group.** A randomized trial of propranolol in patients with acute myocardial infarction I Mortality results *JAMA—J Am Med Assn* 247 1707-14, 1982
3 **Norwegian Multicenter Study Group.** Timolol-induced reduction in mortality and reinfarction in patients surviving acute myocardial infarction *N Engl J Med* 304 801-7, 1981
4 Long-term and short-term beta-blockade after myocardial infarction (Editorial) *Lancet* 2 1159-61, 1982
5 **Hjalmarson A, Elmfeldt D, Herlitz I, Holmberg S, Malek I, Nyberg G, Rydén L, Swedberg K, Vedin A, Waagstein F, Waldenström A, Waldenström J, Wedel H, Wilhelmsen L & Wilhelmsson C.** Effect on mortality of metoprolol in acute myocardial infarction a double-blind randomised trial *Lancet* 2 823-7, 1981
6 **MIAMI Trial Research Group.** Metoprolol in acute myocardial infarction (MIAMI) A randomised placebo-controlled international trial *Eur Heart J* 6 199-226, 1985

