Myocardial infarction: duration of beta-blocker treatment in people without heart failure

A French observational study found that use of a beta-blocker early after myocardial infarction (MI) (within 48 hours) is associated with a reduction in 30-day mortality in people who do not have heart failure. However, continuing with beta-blockers was not associated with a statistically significant reduction in mortality at 1 year. It also found that stopping beta-blocker treatment in the year after an MI did not appear to affect mortality at 5 years. Despite the limitations of this observational study, the results are consistent with the NICE guideline on myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease, which recommends that people should be offered a beta-blocker as soon as possible after an MI. However, the study adds uncertainty about the optimum duration of beta-blocker treatment after an MI.

Overview and current advice

People who have had an MI benefit from treatment to reduce the risk of further MI or other manifestations of vascular disease (secondary prevention). Since the late 1990s the Myocardial Ischaemia National Audit Project has documented reductions in 30-day mortality resulting from changes in acute treatment of MI and the application of secondary prevention measures.

The NICE guideline myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease recommends that people should be offered a beta-blocker as soon as possible after an MI, when the person is haemodynamically stable. Plans for titrating beta-blockers up to the maximum tolerated or target dose should be communicated — for example, in the discharge summary. The guideline recommends that the beta-blocker should be continued indefinitely in people who have left ventricular systolic dysfunction (LVSD), and that it should be continued for at least 12 months after an MI in people who do not have LVSD or heart failure. For people who have had an MI more than 12 months ago, the guideline advises against starting a beta-blocker, unless the person has LVSD. In this case, the beta-blocker should be offered irrespective of symptoms and, if they have heart failure plus left ventricular dysfunction, they should be managed in line with the NICE guideline on chronic heart failure. The NICE guideline on myocardial infarction also gives recommendations on the use of other medicines after an MI, such as an ACE (angiotensin-converting enzyme) inhibitors, dual antiplatelet therapy (aspirin plus a second antiplatelet agent) and a statin, in addition to lifestyle changes.

The role of using beta-blockers long term in people who have had an MI but do not have heart failure or LVSD is controversial. Also, most of the studies that looked at the effect of beta-blockers after MI...
were carried out when currently used secondary prevention drugs, such as statins, were not available and reperfusion therapy (such as fibrinolysis and primary percutaneous coronary intervention) was not used.

The NICE Pathway on myocardial infarction: secondary prevention brings together all related NICE guidance and associated products on secondary prevention of MI in a set of interactive topic-based diagrams. The Clinical Knowledge Summaries information on myocardial infarction – secondary prevention gives a general overview of prescribing considerations.

New evidence

A multicentre prospective cohort study, carried out in France, looked at the relationship between beta-blocker use and both short-term and long-term mortality after an MI in 2679 people who did not have heart failure or LVSD. Participants were included from 223 intensive care centres if they were aged 18 years or over and were admitted during a one month period (extended another month for people with diabetes) from 1 October 2005 with certain signs and symptoms of MI within 48 hours from the onset of symptoms. People with MI that occurred within 48 hours of a therapeutic procedure and those whose diagnosis was invalidated in favour of another diagnosis were excluded. Data came from the nationwide French registry of Acute ST-elevation and non-ST-elevation Myocardial Infarction (Fast-MI), but were also taken from physicians, patients or their families, discharge letters and other supportive documents. Drug use at follow-up was self-reported by participants, but backed up in many cases by copies of the prescription. The main outcome measures in the study are discussed below.

Beta-blockers in the first 48 hours and 30-day mortality

Of the 3670 people identified, 991 had a history of heart failure before the current episode, or Killip class II or more at admission (class I indicates no heart failure, class II and above indicates heart failure), leaving 2679 people without heart failure or LVSD. Of these, 76.5% (2050) were treated with a beta-blocker during the first 48 hours after admission. Compared with people who were not given beta-blockers, people who received beta-blockers were younger, had a lower risk of death or further MI (assessed by the GRACE score) and had less co-morbidity, but more received a statin, clopidogrel or low molecular weight heparin in the first 48 hours. People taking beta-blockers in the first 48 hours had a statistically significant reduction in 30-day mortality both before and after adjusting the results for confounding factors (unadjusted hazard ratio [HR] 0.26, 95% confidence interval [CI] 0.17 to 0.38, p<0.001; adjusted HR 0.46, 95% CI 0.26 to 0.82, p=0.008). The cause of death was cardiovascular in 89% of people whether receiving beta-blockers or not.

Beta-blockers at discharge and 1-year mortality

Out of 2217 people who were discharged from hospital with no heart failure or LVSD (no history of heart failure or no heart failure during admission and a left ventricular ejection fraction [LVEF] greater than 40%) 80.4% (1783) were treated with beta-blockers at discharge. As seen in the people who were prescribed beta-blockers early in their hospital admission, people prescribed beta-blockers at discharge tended to be younger and have less co-morbidity than those not given beta-blockers. Again, taking a beta-blocker on discharge was associated with a statistically significant reduction in death at 1 year compared with not taking a beta-blocker (unadjusted HR 0.43, 95% CI 0.28 to 0.65, p<0.001), but this was not statistically significant when the results were adjusted for confounding factors (adjusted HR 0.77, 95% CI 0.46 to 1.30, p=0.32).

Beta-blockers continued at 1 year and 5-year mortality

Out of the 1783 people who took beta-blockers at discharge, 78% (1383) were alive at 1 year and details of their prescription were available. Out of these people, 11% (153) had stopped taking beta-blockers. Other secondary prevention drugs were also used less frequently in those who had stopped their beta-blocker. No statistically significant association between taking beta-blockers at one year and
death at 5 years was found before or after the results were adjusted for confounding factors
(unadjusted HR 0.79, 95% CI 0.45 to 1.38, p=0.41; adjusted HR 1.19, 95% CI 0.65 to 2.18, p=0.57)¹.

No differences were found based on the type or dose of beta-blocker used in any of the results. Because trials of beta-blockers were carried out before reperfusion therapy and invasive strategies were available for people with MI, the investigators also looked at 5-year mortality according to continued use of statins at 1 year, to determine whether the results reflected those seen in randomised controlled trials (RCTs) of statins after MI. Out of 1256 people who were given statins and beta-blockers at discharge, 10.8% (136) had stopped taking their statin at 1 year. Continued use of a statin at 1 year was associated with a statistically significant reduction in 5-year mortality compared with stopping a statin both before and after adjusting the results for confounding factors (unadjusted HR 0.32, 95% CI 0.20 to 0.51, p<0.001; adjusted HR 0.42, 95% CI 0.25 to 0.72, p=0.001)¹.

Commentary

Commentary provided by NICE

This observational study¹ suggests that use of a beta-blocker early after MI (within 48 hours) is associated with a reduction in 30-day mortality in people who do not have heart failure. However, taking beta-blockers at discharge does not seem to be associated with a statistically significant reduction in mortality at 1 year. In addition, the results suggest that stopping beta-blocker treatment in the year after an MI does not appear to affect mortality at 5 years. This is in contrast to the increase in 5-year mortality seen when statin treatment is stopped.

An advantage of this study¹ is that it looked at a people in a real-life setting. However, being an observational study it has some limitations. For example, the beneficial effects on 30-day mortality seen with early use of a beta-blocker might be affected by the fact that, in the acute stage, the most severely unwell people might not have been given beta-blockers. Also, there might be a “healthy-user” bias, where people who are more health conscious might also be more likely to adhere to their beta-blocker treatment. Despite this, the increase in mortality at 5 years seen when statin treatment was stopped at 1 year is in contrast to the effects of stopping beta-blockers in the same time frame. This suggests that “healthy-user” bias is less likely to have been an issue on the effects of stopping beta-blockers at 1 year.

The authors used propensity score matching to reduce the likelihood of bias arising from various factors that may have affected the outcomes for patients, such as the use of certain other drugs and medical history, as well as smoking status. The results reported were generally similar when people were matched according to their propensity scores and after various sensitivity analyses¹. However, despite attempts to minimise biases, it is possible that the authors did not fully account for the imbalances, and also that other confounders existed which were not known and, therefore, not adjusted for. Another limitation is that this study was carried out in France, so it is not clear whether these findings will translate to clinical practice in the UK, where patients and their management might have some differences. In addition, the authors highlighted that lack of a formal sample size calculation might have led to underestimation of the effect of beta-blockers, especially during the first year after MI.

In conclusion, the beneficial effects seen in this study¹ from early beta-blocker use and 30-day mortality in people without heart failure or LVSD is consistent with the NICE guideline on myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease, which recommends that people should be offered a beta-blocker as soon as possible after an MI, when they are haemodynamically stable. The lack of a detrimental effect on 5-year mortality from stopping beta-blocker treatment at 1 year in people without heart failure or LVSD suggests that it might be worth considering whether continued beta-blocker treatment needs to be reviewed in these people after a
year. This is consistent with the NICE guideline, which recommends that beta-blocker treatment should be continued indefinitely only in people who have LVSD. (Note, those who have heart failure plus left ventricular dysfunction should be managed in line with the NICE guideline on chronic heart failure.) However, the lack of a statistically significant reduction in mortality seen after a year in people who were discharged on beta-blockers adds uncertainty about the optimum duration of beta-blocker treatment after an MI. Nevertheless, there are limitations to using observational data to guide clinical decision making and more studies are needed to clarify this.

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**References**


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