

Underuse of β -Blockers in Cardiovascular Medicine

Based on a presentation by Stephen S. Gottlieb, MD

Presentation Summary

Clinical trials have conclusively demonstrated that long-term administration of β -adrenergic blockers following myocardial infarction (MI) improves survival. Yet physicians in general prescribe β -blockers for fewer than one third of patients, and cardiologists in particular for less than 50% of their patients with MI. A recent analysis of data from the Cooperative Cardiovascular Project evaluated the relationship between β -blocker treatment and outcomes in more than 200,000 patients hospitalized for myocardial infarction. Con-

firming earlier estimates, the analysis showed 34% of patients were prescribed β -blockers at the time of discharge from the hospital. β -blocker therapy was associated with a 40% reduction in mortality, a benefit that extended across a variety of patient subgroups, including older patients and patients with diabetes and those with non-Q-wave infarctions, chronic obstructive pulmonary disease, or low left ventricular ejection fraction. The findings strongly demonstrated that β -blockers are underused for patients with MI.

Data from large, randomized clinical trials have consistently shown that treatment with a β -blocker reduces risk or recurrence after myocardial infarction (MI). One widely cited meta-analysis of clinical trial data showed a 20% average reduction in mortality among MI patients treated with β -blockers, compared with those treated with placebo.¹ Despite the abundance of evidence of a substantial clinical benefit, β -blockers remain significantly underused. Only about a third of post-MI patients receive β -blockers, a figure comparable to that of calcium-channel blocker use for which data are less supportive.²

The benefits of β -blocker use span a wide spectrum of patient subgroups. However, the data from clinical trials have made it clear that the patients at highest risk derive the most benefit, which should come as no great surprise. Nonetheless, a number of large subgroups of high-risk patients exist for whom β -blockers are often considered contraindicated, such as elderly patients and those with diabetes. To be sure, higher-risk patients, such as those with diabetes, have worse outcomes than lower-risk patients, but the outcomes are improved by β -blocker therapy.³

Perceived contraindications to β -blocker treatment have evolved and

persisted despite a background of limited clinical data. In general, data from randomized clinical trials have shown that patient subgroups that have high mortality from use (ie, sicker patients) derive considerable benefit from β -blocker therapy. The few negative studies had low mortality among subjects taking placebo.

Medicare Population and β -Blockers

The Cooperative Cardiovascular Project (CCP) provided an opportunity to evaluate a variety of issues related to β -blocker use, including contraindications. The CCP database documents the care provided to more than 200,000 Medicare patients following MI.⁴

The CCP database includes all acute-care hospital claims submitted to the Health Care Financing Administration for Medicare patients with a primary diagnosis of acute MI. Each state participating conducted the study for a 9-month period in 1994 and 1995.

The CCP database contains a wealth of information about each patient. Because the database includes Medicare patients, the study's ability to document every death and cause of death is quite extensive. However, the depth of information goes well beyond mortality. In our investigation, for example, more than 95% had serum creatinine measurements in their records. Ejection fraction was documented in 134,000 of the patients.

The database contains more than 400 different variables, including demographics, clinical status, treatment, and outcome. The large number of patients and the detailed information in the CCP database allowed an extensive analysis of the impact of β -blocker therapy on high-risk patients. Such a detailed analysis had not been performed previously. The analysis covered a wide range of variables, from demographics to treatment decisions and issues to a wide range of physiologic parameters.

Overall, about a third of patients had a β -blocker prescription at the time of hospital discharge. This finding was consistent with those from earlier studies, suggesting the emerging data on the benefits of β -blocker therapy have yet to have a major impact on clinical practice in the United States. Use of β -blockers was lower among the very elderly, African Americans, and patients judged to be the sickest on the basis of their Acute Physiology and Chronic Health Evaluation (APACHE II) and Killip scores.

Despite the overall low use of β -blockers, the CCP data confirmed previously reported evidence of a substantial benefit from β -blocker therapy in post-MI patients. Overall, treatment with a β -blocker was associated with a 40% reduction in mortality in patients who had MI uncomplicated by other conditions.

A primary hypothesis underlying the analysis was that sicker, higher-risk patients would be less likely to receive β -blockers. The CCP data supported that hypothesis. For example, almost 37% of patients younger than 75 years were discharged with a prescription for a β -blocker, compared with 26.7% of patients ages 85 years and older. Despite the age-related disparity in prescriptions for β -blockers, the analysis showed that age did not predict whether a patient would benefit from β -blocker therapy. A comparison of survival in patients who did or did not receive a β -blocker showed that patients ages 70 years and older benefited, as did those patients who were younger than 70 years. Patients 80 years and older had a 32% reduction in mortality when given a β -blocker.

Lower ejection fraction was associated with lower use of β -blockers. Less than 15% of patients who had an ejection fraction of less than 20% were prescribed β -blockers at discharge, compared with 41% of patients who had a normal ejection fraction. However, it should be noted that the

41% use rate for patients with a normal ejection fraction is inappropriately low. Equally notable, patients with the lowest ejection fractions on admission derived the greatest benefit in terms of risk reduction (an adjusted reduction in absolute risk of 11%) when treated with a β -blocker, as compared with patients who did not receive β -blockers.

Chronic obstructive pulmonary disease (COPD) offers another example of how high-risk patients benefit from β -blocker therapy. The presence of COPD often has been considered a contraindication to β -blocker use. In the CCP, patients with COPD had an 11% reduction in absolute risk (40% reduction in relative risk) when treated with a β -blocker, when compared with MI patients who had a history of COPD and did not receive β -blockers. Despite the clear benefit, only 22% of patients with COPD were prescribed β -blockers at discharge.

The benefit was similar for patients with diabetes, who had an absolute risk reduction of almost 10% and a 36% reduction in relative risk when treated with a β -blocker. About 30% of patients with diabetes (type 1 and type 2) were prescribed β -blockers at discharge. Perhaps swayed by the knowledge that β -blockers can worsen or mask hypoglycemia, physicians have been reluctant to prescribe β -blockers for their patients with diabetes. However, our results confirmed those of previous investigations that documented a substantial benefit among patients with diabetes who received β -blockers after MI.

Other high-risk subgroups also derived substantial benefits from β -blocker therapy: a reduction in relative risk was noted for patients with prior MI (33%), history of congestive heart failure (40%), elevated serum creatinine levels (35%), heart rate exceeding 100 bpm (35%), and in African-American patients (28%). The benefits of β -blocker therapy occurred irrespective of other treatment during

hospitalization, including bypass surgery (40%), coronary angioplasty (40%), thrombolytic therapy (40%), calcium-channel blockers (30%), angiotensin-converting enzyme (ACE) inhibitors (40%), and aspirin (40%).

The CCP data also provided evidence of a beneficial effect in another large patient population sometimes

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thought not to benefit from β -blockers: patients with Q-wave infarctions. In our analysis patients with Q-wave infarcts derived a 40% benefit from β -blocker therapy, identical to the benefit observed in patients with non-Q-wave infarcts.

In a retrospective analysis investigators cannot control for every possible influence on outcome. Nonetheless, the 40% overall reduction in relative risk for patients with Q-wave infarcts provides considerable leeway for determining the true risk reduction. The data make a compelling argument that β -blockers benefit a wide spectrum of patient subgroups, including patients who would be considered at high risk by virtually any clinical criteria.

Some of the most compelling evidence came from analyses that took into account other therapies patients received during hospitalization, including bypass surgery, angioplasty, thrombolytic therapy, and ACE inhibitors. All of these interventions have been shown to improve outcome. Yet, the addition of a β -blocker to those interventions led to further improvement.

Not surprisingly, in this CCP investigation high-risk patients still had the

worst outcomes. However, the point to keep in mind is that high-risk patients derived the same degree of benefit from β -blocker therapy as did those patients whose baseline characteristics placed them at lower risk. These new data suggest β -blockers, which have been around for decades, have remarkable therapeutic capabilities.

... DISCUSSION ...

Dr. Packer: I think these data effectively dispel many of the myths about use of β -blockers, especially in high-risk patients, many of which account for the underutilization of β -blockers in clinical practice. Do you have any insights into the reasons behind the underutilization? Is it still driven largely by fear or lack of information about benefits or both?

Dr. Gottlieb: If you look at the β -blocker literature you will see that these findings are very consistent with what has been reported previously. The literature is consistent in showing that high-risk patients benefit from β -blocker therapy. However, various clinical guidelines suggest that high-risk subgroups don't benefit. In reality, there are not a lot of data on many of the subgroups we studied, so I can't condemn people for believing that those patient groups won't benefit. I think everyone knows that post-MI [myocardial infarction] patients benefit from β -blockers, but when you get to subgroup analysis, you see evidence that physicians consider β -blockers to be good for everyone else

but not "this" patient. Our data really support that. The fact remains that sicker patients were less likely to get β -blockers, but the data do not support that.

Dr. Packer: Are there any data to indicate whether cardiologists use β -blockers more appropriately than primary care physicians do?

Dr. Gottlieb: There are good data to indicate that physicians with the most knowledge clearly use β -blockade more often, so cardiologists are more likely to use it than internists, who are more likely to use it than family practitioners. I think that the data also indicate pretty clearly that the knowledge about the use and benefits of β -blocker therapy is not widely disseminated among physicians.

... REFERENCES ...

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