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Pharmacologic Management of Heart Failure and Left Ventricular Systolic Dysfunction: Effect in Female, Black, and Diabetic Patients, and Cost-Effectiveness

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

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Structured Abstract

Objectives. This evidence-based report had two objectives. The first objective was to assess whether angiotensin-converting enzyme inhibitors (ACE inhibitors) and beta-adrenergic blocking agents (beta-blockers) are effective in patients with left ventricular systolic heart failure and whether this effectiveness differs in the following subpopulations: men, women, blacks, whites, diabetics, and nondiabetics. The second objective was to assess the cost-effectiveness of both treatment of and screening for left ventricular systolic dysfunction.

Search Strategy. We conducted a thorough computerized library search and retrieved all articles that pertained to the twelve largest placebo-controlled studies on ACE inhibitors and beta-blockers. We also contacted leading experts in cardiology for unpublished data, contacted the authors of the clinical trials for patient-level data, and obtained patient-level data from the FDA.

Selection Criteria. We selected the twelve largest randomized placebo-controlled trials of ACE inhibitors and beta-blockers.

Data Collection and Analysis. We retrieved data through published articles or patient-level data files. For each, we estimated the mortality relative risk and hazard ratio for the subgroups of interest. For example, the relative risk of mortality for women is equal to the risk of dying for women who received the drug divided by the risk of dying for women who received a placebo. We pooled these statistics across studies. We then assessed whether these risks differed statistically via a ratio statistic. For example, to assess the relative effect of the drug on the relative risk of mortality for women as compared to men, we divided the relative risk in women by the relative risk in men to produce a ratio of relative risks. We pooled these statistics and tested whether the pooled ratio estimate was significantly different from 1.

In order to assess the cost-effectiveness of screening for and treating asymptomatic left ventricular dysfunction, we created a decision model. We modeled lifetime health and economic outcomes for a hypothetical cohort of 55-year-old asymptomatic patients with ejection fraction of 35% or less but no history of heart failure (HF), using two treatment strategies and six screening strategies.

Main Results. We found evidence, with two exceptions, that treatment with ACE inhibitors or beta-blockers reduces all-cause mortality in male, female, black, white, diabetic, and nondiabetic patients. The two exceptions were the use of ACE inhibitors in women and the use of beta-blockers in black patients. Regarding the former, we found clear evidence that treating women with symptomatic heart failure with ACE inhibitors was beneficial. However, the available evidence do not support a beneficial effect in women with asymptomatic left ventricular systolic dysfunction. Regarding black patients, treatment with the beta-blocker bucindolol was associated with a nonstatistically significant increase in all-cause mortality, while treatment with other beta-blockers was associated with a nonstatistically significant reduction in mortality of similar magnitude to the statistically significant reductions observed in white patients.

In our cost-effectiveness analyses, we found that treatment of asymptomatic left ventricular dysfunction with ACE inhibitors was very cost-effective under virtually all assumptions, with typical costs per quality-adjusted life-year gained of between $5,000 and $10,000. Additional

analysis showed that screening with B-type natriuretic peptide followed by echocardiography in a cohort of asymptomatic 55-year-old individuals was also cost-effective, compared with the costs of other therapies currently considered standard medical care. The number needed to screen in order to gain one year of additional life was 77. These results were only modestly sensitive to cost and were most sensitive to the prevalence of asymptomatic decreased left ventricular ejection fraction. When the prevalence falls below about 1%, a strategy of screening becomes less cost-effective than commonly accepted thresholds for cost-effective care.

Conclusions. ACE inhibitors and beta-blockers reduce mortality in a broad range of patients with left ventricular systolic dysfunction, including men and women, blacks and whites, and diabetics and nondiabetics. However, the value of ACE inhibitors in women with asymptomatic left ventricular systolic dysfunction is uncertain, and additional study is needed. In addition, based on data from a single study, the beta-blocker bucindolol may be associated with increased mortality in blacks, whereas other beta-blockers provide similar benefits in blacks and whites.

Treatment of asymptomatic left ventricular dysfunction with ACE inhibitors is very cost-effective. In addition, screening for asymptomatic left ventricular dysfunction with B-type natriuretic peptide followed by echocardiography is cost-effective in populations where the prevalence of this condition is 1% or greater.

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