Clinical Investigations

Addition of Angiotensin-Converting Enzyme Inhibitors to Beta-Blockers Has a Distinct Effect on Hispanics Compared With African Americans and Whites With Heart Failure and Reduced Ejection Fraction: A Propensity Score–Matching Study

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ABSTRACT

Background: There are currently no data on the efficacy of angiotensin-converting enzyme inhibitors (ACEis) in Hispanic patients with heart failure (HF) and reduced ejection fraction (HFrEF). We aimed to investigate the effect of adding ACEis to beta-blockers on mortality and hospitalization for HF exacerbation in patients with HFrEF stratified by race/ethnicity.

Methods and Results: From Montefiore Medical Center's 3 large hospitals, 618 consecutive patients with HFrEF (left ventricular ejection fraction [LVEF] <35%) who were on a beta-blocker were retrospectively identified. Patients were divided into 2 groups based on whether or not they were on an ACEi for 24 consecutive months. Propensity score matching including all baseline characteristics was performed and patients were then categorized into 3 groups: African Americans, Hispanics, and Whites/Caucasians. We evaluated 2-year all-cause mortality and 2-year hospitalization for HF exacerbation. Of 618 patients, 66% were categorized as ACEi and 34% as no-ACEi. Four hundred twenty-seven patients were matched 2:1 between the ACEi and no-ACEi groups. After matching, overall 2-year mortality and hospitalization rates were similar between ACEi and no-ACEi (12.4% vs 17.8%, hazard ratio [HR] 0.66, 95% confidence interval [CI] 0.38–1.16; $P = .14$; and 8.1% vs 9.5%, HR 0.84, 95% CI 0.44–1.60; $P = .6$; respectively). After stratifying patients based on race/ethnicity, ACEi demonstrated a lower 2-year mortality compared with no-ACEi in Hispanics (9.8% vs 28.4%, HR 0.33, 95% CI 0.13–0.87; $P = .018$) but not in African Americans (17.0% vs 11.8%, HR 0.94, 95% CI 0.34–2.65; $P = .91$) or Whites (9.2% vs 10.3%, HR 0.89, 95% CI 0.29–2.74; $P = .83$). Two-year hospitalization was not different between ACEi and no-ACEi in Hispanics, African Americans, or Whites (all P = NS). In multivariate analysis, ACEi therapy was an independent predictor of lower 2-year mortality (HR 0.33, 95% CI 0.12–0.89; $P = .028$) in Hispanics only.

Conclusions: In this retrospective propensity-matched study of patients with HFrEF who were on a beta-blocker, ACEi therapy was associated with greater mortality reduction in Hispanic patients compared with African Americans and Whites. These findings need to be confirmed in large national studies that include a significant fraction of Hispanic patients. (*J Cardiac Fail 2015;21:448–456*)

Key Words: Angiotensin-converting enzyme inhibitor, heart failure, beta-blocker, mortality, race and ethnicity.

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Along with beta-blockers and mineralocorticoid receptor antagonists, angiotensin-converting enzyme inhibitors (ACEis) are considered to be neurohormonal antagonists and now a part of the modern disease-modifying therapy for heart failure (HF) with reduced ejection fraction (HFrEF).[1,2] Multiple placebo-controlled randomized clinical trials and meta-analyses have demonstrated that ACEis decrease mortality and improve symptoms, exercise tolerance, and quality of life in patients with HFrEF,[3−8] and therefore the use of ACEi has dramatically increased.[1]

There is currently a paucity of data regarding the influence of race/ethnicity on the efficacy of ACEi, with studies showing conflicting results; some demonstrate differences between Blacks (African Americans) and Whites (non−African Americans) with a lower efficacy in the African-American population,[9,10] whereas others report a similar efficacy of ACEi in African Americans and Whites.[11,12] Some have attributed the observed difference to an overall higher mortality of African Americans with HF compared with Whites.[13] Nevertheless, current guidelines support the use of ACEi in all races/ethnicities with no specific recommendations regarding changes in management based on race/ethnicity.[1,2]

Hispanics are the fastest growing racial/ethnic group in the United States, composing 17% of the total population[14]; they are expected to make up 30% of the total US population by 2050.[15] Although there are several studies comparing the efficacy of ACEi in African American and White patients with HFrEF,[10−13] none of those reports have separated Hispanics from non-Hispanic Whites and non-Hispanic Blacks. Therefore, there are currently no data regarding the efficacy of ACEi in Hispanic patients with HF. The aim of the present study was to investigate the effect of ACEi on mortality and hospitalization for HF exacerbation in patients with HFrEF treated with a beta-blocker stratified by race/ethnicity.

Methods

Study Setting and Population

From January 2002 to January 2012, we identified 618 patients with HFrEF who had their self-identified race/ethnicity documented, were ≥18 years old, and were on a beta-blocker. Patients were admitted to (or seen in the outpatient clinics of) Montefiore Medical Center's 3 large urban academic tertiary care centers in Bronx, New York. Patients were identified from the Montefiore Medical Center's Clinical Information System (Emerging Health Information Technology, Yonkers, New York) with the use of the Clinical Looking Glass, a proprietary query tool and software application that allows clinicians and researchers to identify populations of interest from the Montefiore Medical Centers' database and to gather information about the demographics, clinical, and outcome data.[16−20] The database is combined monthly with the Social Security Death Registry, which allows extraction of mortality data. Hospitalization data were obtained from the Montefiore Medical Center patient database. This retrospective multicenter study was approved by the Institutional Review Board of Albert Einstein College of Medicine of Yeshiva University (protocol 13-03-090).

Study Design

The diagnostic criterion to establish HFrEF was an LVEF <35% as determined by transthoracic echocardiography. To be included in the study, patients were required to have been started on a prescription for a beta-blocker within 60 days from the diagnosis of HF (or documentation of LVEF <35%) and to have subsequently continued that medication for 24 consecutive months without an interruption. Patients' self-identified race/ethnicity was determined in our database and categorized into 3 groups: 1) African Americans/Blacks (non-White and non-Hispanic Blacks), 2) Hispanics, 3) Whites/Caucasians (non−African-American and non-Hispanic Whites). The study population was divided into 2 groups based on whether or not they were being treated with an ACEi (ACEi group and no-ACEi group). To be included in the ACEi group, ACEi therapy must have been started within 60 days of diagnosis of HF and subsequently continued for 24 consecutive months without interruption. All patients who were being treated with hydralazine, a nitrate, or an angiotensin receptor blocker during the 2-year follow-up, even briefly, and patients who had a transient cessation of ACEi therapy were excluded from the study. Patients included in the no-ACEi group did not receive any ACEi during the sutdy period, even briefly.

Echocardiographic Data

Transthoracic 2-dimensional Doppler echocardiography was performed with the use of a commercially available Philips ultrasound system (Sonos 5500, Sonos 7500, or IE-33) and analyzed with the use of an Xcelera workstation (Philips, Andover, Massachusetts). Left ventricular end-diastolic and end-systolic volumes were measured by means of the biplane Simpson method from the apical 2- and 4-chamber views, and LVEF was calculated from the measured end-diastolic and end-systolic volumes.

Clinical Outcomes

At the time of analysis, 2-year follow-up was available for all patients. The clinical outcomes in this study were 2-year all-cause mortality as well as 2-year hospitalization with a diagnosis of acute congestive HF exacerbation. Hospitalization was defined as the 1st hospital admission with a diagnosis of acute congestive HF exacerbation, and any further hospitalization of the same patient was not counted as a hospitalization.

Statistical Analysis

Continuous variables were not normally distributed and therefore are expressed as median and interquartile range, and differences were compared with the use of the Mann-Whitney or Kruskal-Wallis test as appropriate. Categoric variables are expressed as counts and percentages, and differences were assessed by the χ^2 test. We performed 2:1 propensity score matching on the treatment variable (ACEi vs no-ACEi) without replacement with the use of calipers of width equal to 0.2 SD of the logit of the estimated propensity score. Propensity score calculation included age, sex, LVEF, presence of an implantable cardioverter defibrillator, New York Heart Association (NYHA) functional class III or IV, history of hypertension (HTN), diabetes, myocardial infarction, atrial fibrillation, chronic kidney disease (creatinine ≥1.5 mg/dL used as a surrogate), and use of aspirin, clopidogrel, statin, and calcium