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Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers in Myocardial Infarction Patients With Renal Dysfunction

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ABSTRACT

BACKGROUND There is no consensus whether angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor blocker (ARB) should be used for secondary prevention in all or in only high-risk patients after an acute myocardial infarction (AMI).

OBJECTIVES This study sought to investigate whether ACEI/ARB treatment after AMI is associated with better outcomes across different risk profiles, including the entire spectrum of estimated glomerular filtration rates.

METHODS This study evaluated discharge and continuous follow-up data on ACEI/ARB use among AMI survivors (2006 to 2009) included in a large Swedish registry. The association between ACEI/ARB treatment and outcomes (mortality, myocardial infarction, stroke, and acute kidney injury [AKI]) was studied using Cox proportional hazards models (intention-to-treat and as treated).

RESULTS In total, 45,697 patients (71%) were treated with ACEI/ARB. The 3-year mortality was 19.8% (17.4% of ACEI/ARB users and 25.4% of nonusers). In adjusted analysis, significantly better survival was observed for patients treated with ACEI/ARB (3-year hazard ratio: 0.80; 95% confidence interval: 0.77 to 0.83). The survival benefit was consistent through all kidney function strata, including dialysis patients. Overall, those treated with ACEI/ARB also had lower 3-year risk for myocardial infarction (hazard ratio: 0.91; 95% confidence interval: 0.87 to 0.95), whereas treatment had no significant effect on stroke risk. The crude risk for AKI was in general low (2.5% and 2.0% for treated and nontreated, respectively) and similar across estimated glomerular filtration rate categories but was significantly higher with ACEI/ARB treatment. However, the composite outcome of AKI and mortality favored ACEI/ARB treatment.

CONCLUSIONS Treatment with ACEI/ARB after AMI was associated with improved long-term survival, regardless of underlying renal function, and was accompanied by low rates of adverse renal events. (J Am Coll Cardiol 2016;67:1687–97)

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ABBREVIATIONS AND ACRONYMS

ACEI = angiotensin-converting enzyme inhibitor

AKI = acute kidney injury

ARB = angiotensin receptor blocker

CI = confidence interval

CKD = chronic kidney disease

eGFR = estimated glomerular filtration rate

HR = hazard ratio

LVSD = left ventricular systolic dysfunction

Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) should be considered for secondary prevention after an acute myocardial infarction (AMI) (1,2). ACEI use was first shown to reduce short- and long-term mortality in patients with myocardial infarction (MI) and heart failure (HF) or left ventricular systolic dysfunction (LVSD) (3–6). Subsequently, 2 trials showed noninferiority for ARBs compared with ACEIs in MI patients with evidence of HF for improving survival with better tolerability (7,8). However, there is still no clear evidence as to whether ACEI/ARB should be used in all MI patients without HF or LVSD (1,9).

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Chronic kidney disease (CKD) is an important risk factor for cardiovascular disease (10); the cardiovascular risk increases even with slightly decreased estimated glomerular filtration rate (eGFR) and becomes 8-fold higher in patients with severe renal dysfunction (11). Patients with CKD also have worse outcomes after an acute cardiovascular event compared with patients with normal renal function (12,13). Even though patients with low eGFR are considered a high-risk group, the evidence for treating these patients with ACEI/ARB after MI is almost nonexistent as they were excluded from most trials (4–6,14,15). Importantly, ACEI or ARB use can also potentially result in acute kidney injury (AKI) and hyperkalemia, adverse events believed to be more common in CKD patients, perhaps discouraging clinicians from treating these patients with these agents. However, a recent observational study among U.S. veterans with CKD showed that use of an ACEI or ARB for any indication was associated with a 19% lower all-cause mortality (16). We aimed to investigate current use of ACEI and ARB therapy after MI to assess long-term outcomes associated with their use in routine clinical practice across different risk profiles, including the entire spectrum of estimated glomerular function.

METHODS

We analyzed consecutive MI patients admitted to Swedish coronary care units and entered in the nationwide SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry (17). The registry includes patients with symptoms suggestive of acute coronary syndromes admitted to a coronary care unit or other specialized facility, covering all Swedish hospitals (n = 72) where treatment for acute cardiac diseases is provided. Patients were included if they were admitted for an AMI between 2006 and 2009, were alive at discharge, and had a registered measurement of serum creatinine on admission (Online Figure 1). Only the first MI during this time period was considered. Patients were followed until the end of 2010. On admission, patients received written information about SWEDEHEART and other quality-of-care registries; patients are permitted to deny participation in the registry, although few exercise this right. According to Swedish law, written consent is not required because quality control is an inherent element of hospital health care. The regional ethics committee of Stockholm approved the study protocol.

Comorbidities were obtained from the SWEDEHEART registry form and supplemented with data from the National Patient Register that included diagnoses on the basis of International Classification of Diseases codes for all patients hospitalized in Sweden from 1987 and onward. History of diabetes mellitus was further confirmed with active dispensation of oral antidiabetic agents and insulin as registered in the Swedish Registry of Dispensed Drugs (18). Information on patient presentation at admission, hospital course variables, and medications at admission and discharge were also obtained from the SWEDEHEART registry.

RENAL FUNCTION ASSESSMENT. Patient eGFR was calculated from the creatinine level on admission using the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) (19). The majority of creatinine assessments were performed by either enzymatic or corrected Jaffe method (alkaline picrate reaction), both of which are traceable to isotope dilution mass spectrometry standards. Creatinine measurements performed with nonstandardized methods were reduced by 5% prior to being entered into the CKD-EPI equation (20). Renal function was classified into categories of eGFR using the current International Society of Nephrology Kidney Disease Improving Global Outcomes definition (21). Because data on albuminuria were missing, any eGFR ≥60 ml/min/1.73 m^2 could not define CKD stage 1 or 2. Thus, we referred to the categories as eGFR strata. The Swedish Renal Registry (22) was used to identify individuals undergoing dialysis treatment and having a functioning kidney transplant.

ASCERTAINMENT OF EXPOSURES. ACEI or ARB use was recorded in the SWEDEHEART protocol and in the Registry of Dispensed Drugs, the latter of which contains all pharmacy-drug dispensations in the country linked to each citizen's unique personal