Body Mass Index, Left Ventricular Mass Index and Cardiovascular Events in Chronic Kidney Disease

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ABSTRACT

Background: Obesity and left ventricular hypertrophy are prevalent in chronic kidney disease (CKD), but the association of body mass index (BMI) and left ventricular mass index (LVMI) with cardiovascular outcomes in patients with CKD is unclear. This study was designed to assess whether the combination of BMI and LVMI is independently associated with cardiovascular events in patients with CKD stages 3-5.

Methods: From the outpatient department, 523 patients with CKD who received echocardiographic examination were enrolled. The patients under study were classified into 4 groups according to sex-specific median BMIs and LVMIs. Cardiovascular events were defined as cardiovascular death, hospitalization for unstable angina, nonfatal myocardial infarction, sustained ventricular arrhythmia, hospitalization for congestive heart failure, transient ischemia attack and stroke. The relative cardiovascular event risk was analyzed using Cox-regression methods.

Results: The patients were stratified into 4 groups according to sex-specific median BMIs (men: 25.2 kg/m^2; women: 24.9 kg/m^2) and LVMIs (men: 140.1 g/m^2; women: 131.6 g/m^2). A combination of low BMI and high LVMI (versus the combination of high BMI and low LVMI) was significantly associated with cardiovascular events in an unadjusted model (hazard ratio [HR] = 3.178; 95% confidence interval [CI]: 1.645-6.140; $P < 0.001$) and in a multivariable model after adjustment for demographic, clinical and biochemical characteristics and medications (HR = 3.553; 95% CI: 1.494-8.450; $P = 0.004$).

Conclusions: The findings showed that the combination of low BMI and high LVMI was associated with adverse cardiovascular events in patients with CKD stages 3–5.

Key Indexing Terms: Cardiovascular events; Chronic kidney disease; Body mass index; Left ventricular mass index. **[Am J Med Sci 2016;351(1):91–96.]**

INTRODUCTION

Obesity has reached epidemic proportions in the developed world[1] and has increased the risk of cardiovascular disease–related mortality in the general population.[2,3] In contrast to the general population, obesity appears to be associated with better survival in patients undergoing hemodialysis.[4] However, published data on the relationship between obesity and cardiovascular morbidity and mortality in chronic kidney disease (CKD) are limited and inconsistent. Among studies related to obesity and mortality, one study reported that high body mass index (BMI) was associated with an increased risk of coronary artery disease,[5] another study failed to identify BMI as a prognostic factor,[6] whereas a third study suggested that a reverse association exists between obesity and mortality in patients with CKD.[7,8] Thus, the status of obesity as a risk factor for adverse cardiovascular events in patients with CKD remains controversial.

An increased BMI was affected by or linked to various risk factors for left ventricular hypertrophy (LVH), such as obesity, insulin resistance, metabolic syndrome and hypertension.[9–11] Rider et al[10] positively associated BMI with LVH detected using echocardiography. LVH was also frequently encountered in patients with CKD because of pressure and volume overload.[12,13] Furthermore, recent study involving patients with CKD stages 3-5 demonstrated that an increased left ventricular mass index (LVMI) was independently associated with adverse cardiovascular outcomes.[14]

CKD is an increasing worldwide public health problem associated with increased morbidity and mortality. Cardiovascular disease is the leading cause of morbidity and mortality in patients with CKD.[15,16] No studies have evaluated the association between the combination of BMI and LVMI and cardiovascular outcome in patients with CKD. Therefore, the aim of this study was to assess whether the combination of BMI and LVMI is associated with cardiovascular events in patients with CKD stages 3–5.

STUDY PATIENTS AND METHODS

Study Patients and Design

This study was conducted in a regional hospital in Southern Taiwan. The study consecutively recruited 523 patients with CKD stages 3–5, who had underwent predialysis, according to the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines,[17] from January 2007-May 2010. The study classified patients with evidence of kidney damage lasting longer than 3 months into CKD stages 3a, 3b, 4 and 5, based on estimated glomerular filtration rates (eGFRs) of 45–59, 30–44, 15–29 and <15 mL/min/1.73 m^2, respectively. The study patients were followed-up regularly at the Outpatient Department of Internal Medicine. They were selected to participate in this study if they agreed to receive echocardiographic examination. A total of 3 patients refused echocardiographic examinations because of personal reasons. A total of 10 patients with significant mitral and aortic valve diseases and 5 other patients with inadequate image visualization were also excluded. Finally, 505 patients were included. The protocol was approved by the Institutional Review Board and enrolled patients gave written, informed consents.

Evaluation of Cardiac Structure and Function

The echocardiographic examination was performed by an experienced cardiologist using a VIVID 7 (General Electric Medical Systems, Horten, Norway), with the participant respiring quietly in the left decubitus position. The cardiologist was blinded to the other data. Two-dimensional and 2-dimensionally–guided M-mode images were recorded in the standardized views. The echocardiographic measurements included the left ventricular internal diameter in diastole (LVIDd), left ventricular posterior wall thickness in diastole (LVPWTd), interventricular septal wall thickness in diastole (IVSTd), E-wave deceleration time, transmitral E-wave velocity and transmitral A-wave velocity. The left ventricular ejection fraction was measured using the modified Simpson's method. Impaired left ventricular systolic function was defined as left ventricular ejection fraction $<50\%$. The left ventricular relative wall thickness was calculated as the ratio of $2 \times$ LVPWTd/LVIDd. The left ventricular mass (LVM) was calculated using Devereux-modified method (ie, LVM $= 1.04 \times$ [(IVSTd + LVIDd + LVPWTd)^3 – LVIDd^3] – 13.6 g).[18] The LVMI was calculated by dividing the LVM by the body surface area. LVH was defined as LVMI >125 g/m^2 in men and >110 g/m^2 in women.[19]

Collection of Demographic, Medical and Laboratory Data

Demographic and medical data including age, sex, smoking history (ever versus never) and comorbid conditions were obtained from medical records or patient interviews. The patients under study were defined as having diabetes mellitus (DM) if the fasting blood glucose level was >126 mg/dL or if hypoglycemic agents were used to control blood glucose levels. Similarly, patients were considered as having hypertension if the systolic blood pressure was ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, or if antihypertensive drugs were prescribed. Coronary artery disease was defined as a history of typical angina with a positive result for stress test, angiographically documented coronary artery disease, history of myocardial infarction or history of coronary artery bypass surgery or angioplasty. The BMI was calculated as the ratio of the weight in kilograms divided by the square of the height in meters. Laboratory data were measured from fasting blood samples by using an autoanalyzer (Roche Diagnostics GmbH, D-68298 Mannheim COBAS Integra 400). Serum creatinine was measured using the compensated Jaffé (kinetic alkaline picrate) method in a Roche/Integra 400 Analyzer (Roche Diagnostics, Mannheim, Germany) with a traceable calibrator to perform isotope-dilution mass spectrometry.[20] The eGFR was calculated using the 4-variable equation in the Modification of Diet in Renal Disease study.[21] Proteinuria was examined using dipsticks (Hema-Combistix, Bayer Diagnostics). A test result of 1+ or higher was defined as positive. Blood and urine samples were obtained within 1 month of enrollment. In addition, data related to angiotensin converting enzyme inhibitors (ACEIs) and angiotensin II receptor blocker (ARB) use during the study period were obtained from medical records.

Definition of Cardiovascular Events

Cardiovascular events were defined as cardiovascular death, hospitalization for unstable angina, nonfatal myocardial infarction, sustained ventricular arrhythmia, hospitalization for congestive heart failure, transient ischemia attack and stroke. Cardiovascular events were ascertained and adjudicated by 2 cardiologists with disagreement resolved by adjudication from a third cardiologist from the hospital course and medical records. The patients were followed-up until either the first episode of cardiovascular events or until February 2011.

Statistical Analysis

Statistical analysis was performed using SPSS 17.0 for Windows (SPSS Inc, Chicago, USA). Data were expressed as percentages or mean $\pm$ standard deviation. Multiple comparisons among the study groups were performed using one-way analysis of variance followed by a Boneferroni-adjusted post hoc test. A Cox proportional hazards model was used to model the covariates of the risk factors and the time required for the cardiovascular events to occur. The association of the study groups with cardiovascular events was assessed using a modified stepwise procedure in a 2-step model. The first model consisted of age,