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Research Article

Clinical determinants and prognostic significance of the electrocardiographic strain pattern in chronic kidney disease patients

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Abstract

The electrocardiographic (ECG) strain pattern (Strain) is a marker of left ventricular hypertrophy (LVH) severity that provides additional prognostic information beyond echocardiography (ECHO) in the community level. We sought to evaluate its clinical determinants and prognostic usefulness in chronic kidney disease (CKD) patients. We evaluated 284 non-dialysis-dependent patients with CKD stages 3 to 5 (mean age, 61 years [interquartile range, 53–67 years]; 62% men). Patients were followed for 23 months (range, 13–32 months) for cardiovascular (CV) events and/or death. Strain patients (n = 37; 13%) were using more antihypertensive drugs, had higher prevalence of peripheral vascular disease and smoking, and higher levels of C-reactive protein, cardiac troponin, and brain natriuretic peptide (BNP). The independent predictors of Strain were: left ventricular mass index (LVMI), BNP, and smoking. During follow-up, there were 44 cardiovascular events (fatal and non-fatal) and 22 non-CV deaths; and Strain was associated with a worse prognosis independently of LVMI. Adding Strain to a prognostic model of LVMI improved in 15% the risk discrimination for the composite endpoint and in 12% for the CV events. Strain associates with CV risk factors and adds prognostic information over and above that of ECHO-assessed LVMI. Its routine screening may allow early identification of high risk CKD patients. J Am Soc Hypertens 2014;8(5):312–320.

Keywords: Coronary artery disease; inflammation; myocardial ischemia; uremia.

Introduction

Chronic kidney disease (CKD) patients have a remarkably high prevalence of cardiovascular disease (CVD)[1]; and among the different clinical presentations of CVD in CKD, left ventricular hypertrophy (LVH) is probably the most frequent.[2–5] Some conditions that accompany CKD

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such as hypertension, obesity, fluid overload, inflammation, and albuminuria are incrementally more prevalent across increases in left ventricular mass.[6] Echocardiography (ECHO) is the preferred method for LVH identification; and although electrocardiography (ECG) is considered to be a helpful complementary diagnostic tool, recent evidence suggests inaccuracy of routine ECG for LVH diagnosis in CKD patients.[6,7]

The electrocardiographic strain pattern (Strain) of ST depression and T-wave inversion on the ECG is an established marker of the presence and severity of LVH.[8] Among the various readily-available ECG criteria for LVH diagnosis, Strain has emerged as the strongest predictor of adverse outcomes.[9–11] Interestingly, this pattern has shown to provide additional prognostic information beyond that derived from ECHO-based assessment of LVH at a community level.[8] Presently, and to the best of our knowledge, there is no study evaluating phenotype characteristics and prognosis associated to Strain in a population with CKD patients. In this study, we aimed to evaluate the prevalence, clinical correlates and prognostic significance of Strain in a cohort of CKD stage 3 to 5 patients.

Methods

Patients and Study Design

The present study is an ancillary analysis of the Malnutrition, Inflammation, and Vascular Calcification (MIVC) cohort. MIVC is composed of 300 consecutive patients with CKD stages 3 to 5 prior to initiation of dialysis recruited at the outpatient clinic of the Hypertension and Nephrology Division at Dante Pazzanese Institute of Cardiology in Sao Paulo, Brazil.[6,12] The aim of MIVC was to evaluate the association between traditional, novel, and uremic risk factors with cardiovascular and general morbimortality in this population. Recruitment took place between March 2010 and March 2013. Exclusion criteria were age below 18 and above 80 years, clinical signs of acute infection during the month preceding the inclusion, active cancer or liver disease at the time of evaluation, previous diagnosis of immunological diseases, and unwillingness to participate in the study. The presence of CKD was confirmed by glomerular filtration rate (GFR <60 mL/min/1.73 m^2) based on 24-hour urinary creatinine clearance. A single physician (ACC) performed a complete chart review and interviewed each patient regarding their comorbidity history, smoking habits, and drug prescription. Prescribed drugs were recorded, and the following were grouped as antihypertensive medication and added to a score: angiotensin-converting enzyme inhibitors and/or angiotensin II receptor blockers, calcium channel blockers, beta-blockers and diuretics, and other classes (nitrates, alpha-blockers, centrally acting sympatholytics). For the purpose of the present study, we excluded patients with complete left bundle branch block or atrial fibrillation that prevented correct evaluation of the strain pattern presence on ECG ($n = 16$). Thus, we here included 284 non-dialysis-dependent (NDD) patients with CKD stages 3 to 5. Their median age was 61 years (interquartile range, 53–67 years); 62% were men and 57% were smokers (ie, current and former story of smoking).

Follow-Up Data

The patients were followed from the day of inclusion until a cardiovascular (CV) event or death, whichever occurred first. CV events were defined as fatal and nonfatal acute myocardial infarctions (AMIs), sudden cardiac death, unstable angina, fatal and nonfatal stroke, transient ischemic attacks (TIA), and deaths from aortic or peripheral arterial disease. Endpoints were ascertained from medical records, death certificates, and interviews with attending physicians and patient families. CV events were computed only when the patients were admitted at a hospital and had a length of stay of at least 24 hours with the realization of confirmatory exams. There was no loss of follow-up of any patient. The Ethics Committee at Dante Pazzanese Institute of Cardiology approved the study, and informed consent was obtained from each patient.

Anthropometry, Body Composition, Blood Pressure, and Comorbidities

Anthropometric parameters included body weight, height, body mass index (BMI; body weight divided by squared height) and waist circumference (at midway between the lowest lateral border of the ribs and the uppermost lateral iliac crest). Blood pressure (BP) measurements were performed in the upper arm with digital sphygmomanometer (HEM-705CP; Omron Healthcare, Inc, IL, USA). The measurements were repeated three times, according to the recommendations of the JNC-7 report,[13] and the mean of the two last measurements was used. History of comorbidities were calculated by the Charlson comorbidity index,[14] which assigns 1 point for history of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease (transient ischemic attack or cerebrovascular accident with minor or no residua), dementia, chronic pulmonary disease, connective tissue disorder, peptic ulcer disease, mild liver disease, and diabetes without end-organ damage; 2 points are assigned for hemiplegia, moderate to severe renal disease, diabetes with end-organ damage, tumor without metastases, leukemia, lymphoma, and myeloma; 3 points are assigned for moderate or severe liver disease; and 6 points are assigned for metastatic solid tumor or acquired immune deficiency syndrome (AIDS). For every decade over 40 years of age, 1 point is added to the score. For the purposes of the present study, all patients received 2 for the presence of renal