

Predictive cardiovascular risk factors in patients with chronic kidney disease (CKD)

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Predictive cardiovascular risk factors in patients with chronic kidney disease (CKD).

Background. Traditional cardiovascular risk factors and uremia-related specific factors have been identified in patients with CKD, explaining the highest risk for morbidity and mortality from cardiovascular disease. The aim of this study was to analyze the predictive power of several cardiovascular risk factors and markers in a population of stable patients with moderate CKD.

Methods. One hundred twenty-eight (78 M, 50 F) outpatients with estimated glomerular filtration rate (GFR) <60 mL/min were included in the study. Medical records about cardiovascular factors were recorded. Analytical parameters and cardiac markers were analyzed. The patients were prospectively followed, and the end points were fatal and nonfatal cardiovascular events.

Results. After a mean follow-up of 22.3 months, 27 patients had a cardiovascular event. The patients who suffered a cardiovascular event were older ($P = 0.002$), with more anemia ($P = 0.014$), higher pulse pressure ($P = 0.011$), and cTnT levels ($P = 0.000$). In addition, they had more prevalence of LVH ($P = 0.001$), diabetes ($P = 0.013$), previous coronary heart disease ($P = 0.008$), chronic heart failure ($P = 0.000$), vascular peripheral disease ($P = 0.006$), and had also a higher score of 10-year coronary heart disease predicted risk ($P = 0.006$). Age [hazard ratio (HR) 1.07, $P = 0.02$], previous coronary artery disease (HR 4.08, $P = 0.0012$), and cTnT levels (HR 1.64, $P = 0.0000$) independently predicted cardiovascular events on multivariate Cox analysis.

Conclusion. In stable patients with CKD, age and previous coronary artery disease were the traditional cardiovascular risk factors more predictive for cardiovascular events. Cardiac troponin T is a powerful marker of cardiovascular events in CKD patients.

Patients with chronic kidney disease (CKD) are at significantly increased risk for both morbidity and mortality from cardiovascular disease (CVD) [1, 2]. Traditional risk factors, described primarily in the Framingham population, include, among others, hypertension, smoking, diabetes, dyslipidemia, left ventricular

hypertrophy, and male sex. Although patients with CKD have a high prevalence of many of these traditional risk factors, they also are exposed to nontraditional, or uremia-related, risk factors (anemia, altered calcium-phosphorus metabolism, inflammation, oxidative stress, and others) that increase in prevalence as kidney function declines [3]. At the actual moment, several cardiovascular markers have been identified in CKD patients (e.g., C-reactive protein, carotid intima-media thickness, asymmetric-dimethylarginine) [4, 5].

Several studies have shown that even moderate CKD is associated with higher mortality rates from CVD; however, only a few epidemiologic studies are available about the predictive factors and markers of cardiovascular events in patients with moderate CKD.

The aim of this study was to analyze which factors and other parameters are predictive of cardiovascular events in a group of stable patients with moderate CKD.

METHODS

In this cross-sectional study, we included 128 consecutive outpatients with estimated glomerular filtration rate (GFR) <60 mL/min who attended in a nephrology clinic from January to May 2002. The exclusion criteria were any cardiovascular events occurring within a period of 3 months before the start of the study. The medical records of each patient were examined by a nephrologist.

Prevalent diseases, weight and height, body mass index (BMI), blood pressure, lifestyle habits, and use of antihypertensive and lipid-lowering drugs were recorded.

Cardiovascular risk factors and markers evaluated were: age, gender, renal function, pulse pressure, anemia, dyslipidemia, disturbances of calcium and phosphate metabolism, albuminuria, serum albumin, cardiac troponin T levels, and left ventricular hypertrophy (LVH).

Clinical cardiovascular disease was considered if the patient had a myocardial infarction, coronary revascularization (by coronary artery bypass graft or percutaneous transluminal coronary angioplasty), or angina pectoris. Congestive heart failure (CHF) was diagnosed by x-ray

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examination (pulmonary edema) and echocardiogram with left ventricular dysfunction. This diagnosis was considered because the patients were symptomatic and in New York Heart Association (NYHA) class II-IV with a left ventricular ejection fraction $\leq 45\%$. Cerebrovascular disease was established if the patient had a history of transient ischemic attacks, whenever stroke could be verified by computer tomography or carotid artery stenosis $>70\%$ could be verified by Doppler ultrasound. Peripheral vascular disease (PVD) was diagnosed by intermittent claudication, stenosis of the major arteries of the lower limbs proven angiographically or sonographically, and the presence of ulcers caused by atherosclerotic disease or by surgery was used for diagnosis. Hypertension was associated with the use of antihypertensive drugs or with a blood pressure $\geq 140/90$ mm Hg.

All patients were examined by electrocardiography. We chose electrocardiogram (ECG) criteria for LVH diagnosis. LVH was established by mean of a Sokolow-Lyon voltage >35 mm, and a product of QRS duration and Cornell voltage >2440 mm \times ms (adjusted to 8 mm in female patients).

The 10-year absolute risk of developing coronary heart disease (CHD) was derived from following the risk-prediction algorithm of the Framingham model, and by using a point score sheet. The risk prediction for CHD was based on categorical variables such as age, sex, blood pressure, smoking history, total and high-density lipoprotein (HDL) cholesterol, and diabetes history [6].

Analytical methods

Routine clinical and biochemical variables were measured by standardized methods on autoanalyzers. cTnT was determined on sera using the ELECSYS system with cTnT stat cardiac T reagents (both from Roche Diagnostics, Mannheim, IN, USA). In this third-generation immunoassay, the capture and detection antibodies show no cross-reactivity with skeletal cTnT. This assay is an electrochemiluminescence immunoassay, or ECLIA. Its detection limit is 0.01 ng/mL, and 0.1 ng/mL is recommended as clinical threshold, and above this level damage to the myocardium can be assumed to have occurred.

To measure renal function, estimated glomerular filtration rate (GFR) using the Cockcroft-Gault formula was used.

Blinding

The laboratory researcher was unaware of the baseline clinical status of the patients. The clinical data, including baseline and outcome status of the patient, were recorded by the clinicians, who were unaware of the laboratory results. The blinding was realized by keeping the patient's clinical data files apart from the laboratory results files until the study was completed.

Follow-up

After the initial assessment, patients were followed-up for an average of 22.3 months (range 8 to 30 months). End points were first fatal and nonfatal cardiovascular events. Outcome was recorded by the nephrologists, who were unaware of the results of the laboratory until the final study. This information always included study and hospitalization records. All cardiovascular events were verified by clinicians not involved in the study, and all patients were admitted to the hospital during cardiac events. The patients who started with hemodialysis were censored for outcome cardiovascular events.

Cardiovascular events were sudden death, acute myocardial infarction based on the Consensus Document of the Joint ESC/ACC Committee for redefinition of myocardial infarction [7], newly observed unstable angina pectoris, requirement for coronary bypass surgery or angioplasty, CHF, severe arrhythmia documented by ECG, stroke, and stenosis of the major arteries of the lower limbs proven angiographically or sonographically.

Statistical analysis

Values were expressed as mean \pm SD or median (interquartile range). Kolmogorov-Smirnov test was used for analyzing the normality of the distribution of the parameters. We assessed baseline differences between patients who suffered a cardiovascular event and those who did not using the chi-square test and *t* test for univariate analysis for normally distributed variables, and Mann-Whitney *U* test for skewed variables.

The prognostic power of different factors for cardiovascular events was analyzed by introducing into the models all covariates related ($P < 0.1$) to cardiovascular events. Hazard ratios and their 95% confidence intervals (CI) were calculated using estimated regression coefficients (B) and their standard errors (SE) in the Cox regression multivariate analysis. Analyses were performed using SPSS, Inc. statistical software (Chicago, IL, USA).

RESULTS

One hundred and twenty-eight patients (78 male, 50 female) with a median age of 70 years (58.2–81.7) and mean of GFR of 34.8 ± 13.6 mL/min were studied.

Demographic and cardiovascular characteristics of the patients are shown in Table 1. Five patients were lost to follow-up, and 5 patients were included in hemodialysis. Seven patients died, 4 of them from cardiovascular causes, 2 from tumoral causes, and another from a casual accident. Cardiac events developed in 27 patients, including 4 who died from a cardiovascular cause. The cardiovascular events were: 2 sudden deaths, 5 myocardial infarctions, 3 cases of angina pectoris, 1 stroke, 2 complete atrioventricular blocks, 5 thromboses of major artery of the

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