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Original article

Creatine-kinase and dialysis patients, a helpful tool for stratifying cardiovascular risk?

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ABSTRACT

Background and aims: Hemodialysis patients have an enhanced risk for cardiovascular events. Cardiac biomarkers provide useful information for stratifying their risk. However the prognosis value of creatine kinase MB isoenzyme (CKMB) has not yet been validated in this population. The aim of the present study is to determine the predictable value of CK-MB in hemodialysis.

Methods: A cohort of 211 hemodialysis patients (58.3% male, median age 73 (60–80) years) were followed for 39 (19–56) months. Cardiac biomarkers including CKMB were recorded at baseline. Factors associated to CKMB and prognosis value of this biomarker was studied.

Results: The median value of CKMB was 1 (1–2) ng/mL with no patient exceeding normal laboratory values. Previous heart disease, diabetes mellitus, peripheral vascular disease and systolic and diastolic dysfunction were associated with higher levels of CKMB. Ninety-four patients (44.5%) cardiovascular events were recorded. CKMB levels ≥ 2 ng/mL was independently associated to cardiovascular events during the follow up after adjusting. Adding CKMB to a model including several variables for predicting cardiovascular events, resulted in 17% improvement in risk discrimination (IDI) with a relative IDI of 9.9% ($p = 0.04$).

Conclusions: CKMB is a good marker for stratifying cardiovascular risk in hemodialysis patients and adds prognosis information to other well known independent predictors for cardiovascular events.

Creatincinasa y pacientes en diálisis, ¿una herramienta útil para estratificar el riesgo cardiovascular?

RESUMEN

Antecedentes y objetivos: Los pacientes en hemodiálisis presentan un riesgo cardiovascular elevado. Los biomarcadores cardiacos otorgan información útil para estratificar dicho riesgo cardiovascular. Sin embargo, el valor pronóstico de la isoenzima MB de la creatincinasa

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CKMB
Hemodiálisis

(CKMB) no ha sido aún validado en esta población. El objetivo del presente trabajo es evaluar el valor predictivo de CKMB en una población en hemodiálisis.

Métodos: Una cohorte de 211 pacientes en hemodiálisis (58,3% varones, con una edad media de 73 [60–80] años) fueron seguidos durante 39 (19–56) meses. Se recogieron basalmente los valores de diferentes biomarcadores cardiacos incluyendo CKMB. Se evaluaron los factores asociados a niveles más elevados de CKMB, así como su valor predictivo independiente.

Resultados: La mediana de CKMB fue de 1 (1–2) ng/mL. Todos los pacientes presentaron valores dentro de los establecidos de referencia en la población normal. Los antecedentes de cardiopatía, diabetes mellitus, enfermedad periférica y la disfunción diastólica y sistólica se asociaron a niveles más elevados de CKMB. Un total de 94 pacientes (44,5%) presentaron un evento cardiovascular. Los niveles de CKMB ≥ 2 ng/mL se asociaron de manera independiente a presentar eventos cardiovasculares durante el seguimiento tras el ajuste para diferentes factores. La adición de CKMB a un modelo predictor con diferentes factores generó una mejoría del 17% en la estimación de la probabilidad de forma lineal (IDI) con un IDI relativo del 9,9% (p = 0,04).

Conclusiones: CKMB es un buen marcador para estratificar el riesgo cardiovascular en los pacientes de hemodiálisis y añade información en cuanto al pronóstico cuando se combina con otros predictores de eventos cardiovasculares.

Introduction

Chronic kidney disease (CKD) is a major cardiovascular risk factor similar to congestive heart failure, and this risk increases with the decline of renal function, being maximum in dialysis.[1,2]

Several strategies have been proposed in order to detect those patients at high risk for developing cardiovascular events and for detecting subclinical alterations to be treated.[3] Current guidelines recommend measuring cardiac biomarkers, specifically troponins and natriuretic peptides, as they are usually increased in our patients.[1,4] If possible, ecocardiography should be performed periodically although recommended intervals vary in function of the guideline. Some studies have found a strong association between cardiac biomarkers, ecocardiographic findings and prognosis.[3,5]

On one hand, serum cardiac biomarkers are increased in virtually all CKD patients especially in dialysis and those who have higher values have poorer prognosis. On the other hand, when these biomarkers are adjusted by ecocardiographic findings (for example, diastolic and systolic dysfunction and left ventricular hypertrophy) they lose their independent prediction value, suggesting their role as observer of cardiac damage, usually subclinically.[5,6] Most importantly, increased cardiac biomarkers seems to be universal with high sensitivity assays, but those with higher values have a better association to postmortem cardiac damage or with coronary lesions demonstrated by angiography.[7,8]

However, and although several authors have proposed different cut-offs for stratifying the cardiovascular risk, lack of agreement has been reached, suggesting that probably those markers must be interpreted as continuous variables.

One important biomarker has not been widely studied in CKD patients until date, creatine kinase MB isoenzyme (CKMB). In general population, its sensitivity in acute coronary syndromes is inferior to troponins. However, due to its small half-life, current guidelines recommend its use for monitoring cardiac damage after revascularization as they present a good correlation with re-infarction.[9,10] Many patients with CKD have been excluded from studies about CKMB due to its difficult interpretation when renal function is impaired. Published series yield controversial data in terms of prevalence of raise serum values and their use in ischemic heart disease. However, it seems to have the same value as prognosis marker in re-infarction in patients with renal impairment.[11,12] The aim of the present study was to analyze the prognosis value of CKMB in a cohort of dialysis patients and also its related factors.

Materials and methods

Patients

A total of 211 patients on hemodialysis in a single center were enrolled in the restrospective study. Stable patients with no cardiovascular events in the 4 weeks before serum determinations were included. During the follow up [39 (19–56) months], patients with changes in hemodialysis parameters, transferred to another center or transplanted were censored. Investigations were in accordance with the Declaration of Helsinki.

Baseline characteristics and measurements

Baseline characteristics were recorded, including age, sex, presence of diabetes mellitus, peripheral vascular disease, previous cardiovascular disease (congestive heart failure determined by echocardiography within the three previous months, myocardial infarction, cerebrovascular disease), dialysis vintage and data regarding the vascular access. Basally, we measured C-reactive protein (CRP), high sensitivity troponin T (hsTnT), CK-MB and N-terminal prohormone of brain