Kidney Res Clin Pract 33 (2014) 95–102

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Original Article

The association between mortality and abdominal aortic calcification and relation between its progression and serum calcium concentration in chronic hemodialysis patients

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Article history:
Received 5 October 2013
Received in revised form
17 April 2014
Accepted 18 April 2014
Available online 13 June 2014

Keywords:
Abdominal aorta
End-stage renal disease
Hemodialysis
Mortality
Vascular calcification

Abstract

Background: The composite summary score (range, 0–24) of abdominal aortic calcification (AAC) devised by Kauppila et al is a simple method of assessing AAC severity. However, few studies have been conducted to determine an optimal AAC cutoff score for the prediction of mortality or to investigate the relation between mineral metabolism and AAC progression using the scoring system.

Methods: The medical records of 112 patients on hemodialysis who had undergone simple lateral lumbar radiography every 6 months from August 2009 were reviewed. Patients were followed until November 2012, and the relationship between the degree of AAC at baseline and mortality was evaluated. In addition, the relationship between the progression of AAC and serum concentrations of calcium and phosphate was evaluated in the 75 patients who were successfully followed until November 2012.

Results: The mean AAC score at baseline was 5.5 ± 4.8, and the cutoff calcification score for the prediction of mortality was 7.75 (sensitivity=61%, specificity=81%). Patients were allocated to Group A (baseline total calcification score ≤ 8.0, $n=85$) or Group B (baseline total calcification score > 8.0, $n=27$), and multivariate analysis showed that Group B was an independent risk factor of all-cause mortality and cardiovascular events. Of the 75 patients successfully followed, 51 showed AAC progression (Group 1) and 24 showed no change or improvement (Group 2). Group 1 was found to have significantly higher mean serum corrected calcium levels during the 2nd year and 3rd year of follow-up than Group 2. Furthermore, repeated-measures analysis of variance showed higher monthly corrected calcium concentrations ($P=0.099$) and mean corrected calcium levels during the 1st year, 2nd year, and 3rd year of follow-up ($P=0.062$) in Group 1, but without statistical significance. The cutoff values of mean corrected calcium of the 2nd year and 3rd year for the prediction of AAC progression during follow-up years were 8.96 mg/dL and 9.45 mg/dL, respectively. Serum phosphate levels and corrected calcium × phosphate values were similar in Groups 1 and 2.

Conclusion: Patients with an AAC score of > 8 at baseline seem to be at higher risk of mortality during follow-up. Of the serum variables examined, such as corrected calcium, phosphate, and corrected calcium × phosphate, corrected calcium was

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http://dx.doi.org/10.1016/j.krcp.2014.04.003

found to be marginally associated with AAC progression. However, a larger-scale prospective study is required to confirm our findings.

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Introduction

Arterial calcification, including aortic calcification, is highly prevalent in end-stage renal disease (ESRD) patients, and the extent of arterial calcification has been shown to be predictive of subsequent cardiovascular disease (CVD) and mortality in these patients [1–5].

Animal experiments suggest that disturbances in mineral metabolism play a major role in the initiation and progression of medial wall calcification [6,7]. Human studies have shown that, in addition to traditional risk factors, several clinical factors—such as hypercalcemia, hyperphosphatemia, elevated calcium (Ca) × phosphate (P) product, hyperparathyroidism, chronic inflammation, Ca overload (induced by the use of Ca-based P binders and vitamin D analogues), higher dialysate Ca concentration, adynamic bone disease, and old age—are associated with the progression of arterial calcification in ESRD patients on dialysis [1,8–11].

Hyperphosphatemia is being increasingly recognized as a major stimulus of vascular calcification [12]; however, studies have produced inconsistent results about associations between hyperphosphatemia and the extent and progression of vascular calcification [2]. Furthermore, in one report, it was suggested that arterial calcification may be a bystander, rather than the cause of changes in cardiac structure and function [13,14]. In addition, patients without evidence of arterial calcification at presentation are unlikely to develop arterial calcification *de novo*, at least in the short term [15,16].

The composite summary score (range 0–24) of abdominal aortic calcification (AAC) devised by Kauppila et al [17] provides a simple, low-cost means of assessing subclinical vascular disease, and has been shown to be highly predictive of subsequent cardiovascular morbidity and mortality in the general population and hemodialysis (HD) patients [4,5,18]. However, few studies have sought to determine optimal AAC score cutoff values for the prediction of mortality or the relation between mineral metabolism and AAC progression using the scoring system.

Accordingly, the aims of this study were to evaluate the relationship between baseline AAC score and mortality and to identify an optimum AAC cutoff score for the prediction of mortality in ESRD patients on HD. In addition, the serum levels of Ca, P, and Ca × P products were monitored during follow-up, and their relationships with AAC progression were analyzed.

Methods

Participants

This retrospective study was performed on ESRD patients on HD who had been followed up at the outpatient HD clinic of Inha University Hospital (Incheon, Republic of Korea). A total of 112 ESRD patients on HD at study commencement in September 2009 were included. Patients were followed up until death, kidney transplantation, transfer to other hospital, or until November 2011. Demographic, clinical, and biochemical data were collected from medical records. Comorbidities were assessed using modified Charlson comorbidity index (CCI) score [19,20].

HD was performed for 4 hours per session, three times per week, using a polysulfone dialyzer (F6HPS; Fresenius Medical Care, Bad Homburg, Germany) and a Fresenius Medical Care 5008 machine. Dialyzers were not reused. Dialysate concentrations of sodium, potassium, bicarbonate and calcium were 138 mEq/L, 2.5 mEq/L, 30 mEq/L, and 3.5 mEq/L, respectively, for nondiabetics, and 140 mEq/L, 2.0 mEq/L, 25 mEq/L, and 2.5 mEq/L, respectively, for diabetics. Blood flow rates were between 250 mL/minute and 300 mL/minute, depending on arteriovenous fistula status. The dialysate flow rate was 500 mL/min and Kt/Vurea was calculated using the Daugirdas second-generation equation [21].

The study protocol was approved by the Institutional Review Board of Inha University Hospital and complied with the Declaration of Helsinki. Written consent forms were not required because of the retrospective nature of the study. All data used were obtained routinely for patient management purposes.

Evaluation of abdominal aortic calcification

Between September 2009 and November 2011, radiographs of the left lumbar spine were acquired in the standing position every 6 months. The severity of AAC was graded using the scoring system devised by Kauppila et al [17].

Calcific deposits in the abdominal aorta adjacent to each lumbar vertebra from the first lumbar vertebrae to the fourth lumbar vertebrae were assessed separately at baseline for the anterior and posterior aortic walls. Lesions were graded as follows: 0, no aortic calcific deposits; 1, small scattered calcific deposits occupying less than one-third of the longitudinal wall of the aorta; 2, calcific deposits occupying one-third or more, but less than two-thirds of the longitudinal wall of the aorta; and 3, calcific deposits occupying two-thirds or more of the longitudinal wall of the aorta. Individual level-specific severity scores were summarized to yield anterior wall (ScAnt; range 0–12), posterior wall (ScPost; range 0–12), and sum (ScSum; range 0–24) AAC scores.

AAC scoring was performed using radiographs taken at baseline and after 3 years by three physicians (HYK, OHL, and MJK) who were completely unaware of the patient data. Prior to scoring, the three assessors were trained by a radiologist on how to perform the scoring until similar scores were achieved. When the scores of the three assessors differed, mean scores were used.

To decide whether AAC had progressed over the 3-year study period, the three assessors compared baseline and final X radiographs. Progression of AAC was defined as the occurrence of new calcifications or as enlargements of the calcified area present at baseline. Patients were assigned to Group 1 (exhibit progression; $n=51$) or Group 2 (showed no change or an improvement; $n=24$) based on the assessors' opinions.

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