Association of severity of conjunctival and corneal calcification with all-cause 1-year mortality in maintenance haemodialysis patients

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Abstract

Background. Conjunctival and corneal calcification (CCC) is the most common form of metastatic calcification in patients with chronic renal failure. The aim of this study is to investigate if severity of CCC correlates with vascular calcification and mortality in maintenance haemodialysis (MHD) patients.

Methods. One hundred and nine MHD patients were recruited. CCC was evaluated by external eye photographs, and was graded and scored according to modified Porter and Crombie classification system described by Tokuyama et al. Chest X-ray examination was used to evaluate aortic arch calcification. Geographic, haematological, biochemical and dialysis-related data were obtained. The patients were analysed for traditional and non-traditional risk factors for cardiovascular disease stratified by severity of CCC. All patients were followed up for 1 year to investigate the risks for mortality.

Results. Forty-three, 35 and 31 patients had mild (scores ≤ 4), moderate and severe (scores ≥ 9) CCC at baseline, respectively. With trend estimation, patients with severe CCC had a significantly higher percentage of severe aortic arch calcification. Multiple linear regression analysis showed that hypertension, haemodialysis duration and corrected calcium level were associated with scores of CCC in MHD patients. Moreover, age, corrected calcium-phosphate level, and moderate and severe CCC were associated with grades of aortic arch calcification. At 1-year follow-up, 11 of 109 (10.1%) patients had died. Multivariate Cox proportional hazards model showed that age, corrected calcium and severe CCC were significant risk factors for all-cause 1-year mortality in MHD patients. Each increment of one score of CCC is associated with a 26.4% increased risk for all-cause mortality.

Conclusions. Severity of CCC, which is easily obtained at bedside, acts as an independent predictor for all-cause 1-year mortality in MHD patients.

Introduction

The United States Renal Data System reports a 25% annual mortality rate for maintenance haemodialysis (MHD) patients, and that nearly 50% of all reported MHD patient deaths are due to cardiovascular disease (CVD) [1]. Traditional risk factors for CVD (such as hypertension, age, smoking, diabetes and abnormal lipid metabolism) are common in MHD patients, but these factors do not fully explain the high prevalence of CVD in these patients [2,3]. Recent studies have pointed to non-traditional risk factors such as malnutrition, inflammation and disturbances in mineral metabolism, which may cause progressive atherosclerosis, as important determinants of the high cardiovascular morbidity and mortality rates in MHD patients [3–9].

The most common long-term ocular change in MHD patients is conjunctival and corneal calcification (CCC) [10–15]. These calcific deposits have been shown histologically to be calcium phosphate. Precipitation of calcium salts is assumed to occur when serum concentrations of calcium and phosphate exceed solubility [14,16]. Recently, Seyahi et al. linked CCC, a form of metastatic calcification in dialysis patients, to vascular calcification [15]. Whether the severity of CCC correlates with mortality has yet to be elucidated.

Here, we conducted a cross-sectional, 1-year longitudinal study to investigate the relationship between traditional and non-traditional risk factors for CVD in MHD patients, stratified by severity of CCC, and determine whether CCC poses a mortality risk for these patients.

Materials and methods

Patients

One hundred and nine MHD patients were recruited for this 1-year longitudinal observational study from two branches of Chang Gung Memorial...
Hospital (CGMH) in Taipei and Linkou. Excluded were those with malignancies or active infectious diseases, those who had been hospitalized or underwent surgery or kidney transplantation in the previous 3 months, and those who had been on haemodialysis for less than 6 months. All patients underwent 4 h of haemodialysis, three times per week. Haemodialysis was performed with single-use hollow-fibre dialysers equipped with modified cellulose-based polyamide or polysulphone membranes. The dialysate used was a standard ionic composition with bicarbonate-based buffer. Presence of CVD, including cerebrovascular disease, coronary artery disease, congestive heart failure and peripheral vascular diseases, was recorded. Patients with hypertension were defined as those with the presence of at least two blood pressure measurements >140/90 mmHg or taking anti-hypertensive drugs regularly to control their blood pressure. Any history of use of tobacco or drugs, such as statins or aspirin, which could influence inflammation, was also recorded. This clinical study followed the Declaration of Helsinki and was approved by the Medical Ethics Committee of CGMH, Taipei, Taiwan. All subjects provided signed informed consent before being included in the study.

Classification of conjunctival and corneal calcification
Slit-lamp and dilated fundus examinations were performed on patients who met the inclusion criteria. Patients with chronic inflammatory ocular diseases such as uveitis and interstitial keratitis, previous ocular trauma, or intraocular silicon oil were excluded, as were those exposed to chemicals such as mercurial vapour or eye drops containing phosphate. External eye photographs were taken and graded by an ophthalmologist (CCH) masked to the medical condition of patients. Calcification was graded according to Porter and Crombie classification [14,17]: grade 0 indicates normal with no deposits in the conjunctiva or cornea; grade 1 indicates conjunctival calcium deposits only; grade 2 indicates irregular corneal deposits and conjunctival deposits; grade 3 indicates single line of corneal deposits and conjunctival deposits; grade 4 indicates increased corneal deposits, often as two lines, and conjunctival deposits; and grade 5 indicates extensive corneal deposits, often as three lines, and conjunctival deposits (Figure 1). Calcification was scored as the method described by Tokuyama et al. [14], i.e. the nasal and temporal regions of both corneas were evaluated, and a total calcification score ranging from 0 to 20 was obtained by adding scores for each regions. To calculate intraobserver variability, the same ophthalmologist re-evaluated 69 randomly selected photographs 3 months after the first evaluation. Sixty-seven of the samples were reclassified correctly (κ = 0.96). For comparison, we stratified patients into three equal groups: mild (n = 43, scores 0–4), moderate (n = 35, scores 5–8), and severe calcification grade (n = 31, scores 9–20). All patients were followed up for 1 year, with mortality as the primary end point.

Grading of aortic arch calcification
Chest X-ray examination was used to assess the presence of vascular calcification. An experienced radiologist (CSY), who was blinded to the laboratory and ocular data of the patients, evaluated all radiographic films. The grading of aortic arch calcification was modified from the categorization proposed in a previous report [18] and was divided into four grades as follows: grade 0 indicates no calcification in the aortic arch; grade 1 indicates linear or curvilinear calcification in aortic arch, and the length of calcification <1 cm and the thickness of calcification <1 mm; grade 2 indicates the length of calcification ≥1 cm and the thick-
ness of calcification <1 mm or the length of calcification <1 cm, but the thickness of calcification ≥1 mm; and grade 3 indicates the length of calcification ≥1 cm, and the thickness of calcification is ≥1 mm (Figure 2).

Grade 3 aortic arch calcification was defined as severe calcification.

Laboratory, nutritional and inflammatory parameters
Blood specimens were collected within a few days of clinical examination during stable haemodialysis sessions to minimize the effect of any acute event. Blood was drawn from the arterial end of the vascular access immediately before mid-week haemodialysis, centrifuged, and then stored at −70°C until used in assays. Serum levels of albumin, blood urea nitrogen and creatinine, transferrin saturation, and normalize protein catabolic rate (nPCR) were measured and used as nutritional markers. High sensitivity C-reactive protein (hsCRP), used as an inflammatory marker, was analysed by immunonephelometry (Nanopia CRP; Daiichi, Inc., Tokyo, Japan). The lowest detection limit was <0.15 mg/L. All other data were obtained with standard laboratory procedures using an automatic analyser (Hitachi 705, Boehringer Ingelheim GmbH, Ingelheim, Germany). nPCR was calculated using validated equations, and normalized to body weight [4]. Dialysis clearance of urea was expressed as Kt/Vurea, as reported by Daugirdas [5]. Serum levels of calcium, phosphate and intact parathyroid hormone (PTH) were also measured, and the corrected serum calcium level was calculated as: calcium (mg/dL) + [0.8 [4.0 – albumin (g/dL)].

Definition of malnutrition and inflammation
The presence of inflammation was defined as hsCRP >3 mg/dL, a level correlated with increased risk of cardiovascular disease in the general population [19]. Serum albumin level <3.6 g/dL was defined as malnutrition, a level representing the 10th percentile of the Third National Health and Nutrition Examination Survey [20].

Statistical analysis
Continuous variables were expressed as means with the standard deviation for number of observations, and categorical variables were expressed as numbers with percentages in brackets. Non-normal distribution data were presented as median (minimum and maximum). All data were routinely tested for normality of distribution and equality of standard deviation before analysis. As PTH and hsCRP data were not normally distributed, these data were log-transformed before being entered into the regression model. Comparisons of variables by severity of CCC were performed using trend estimation. To identify factors associated with CCC or aortic arch calcification, all significant variables assessed by using simple linear regression were entered into backward stepwise procedures. An initial univariate Cox regression analysis was performed to compare the frequency of potential risk factors associated with all-cause 1-year mortality. Similarly, to control for confounding factors, a multivariate Cox regression analysis was performed to analyse the significant factors on univariate analysis that met
Severity of conjunctival and corneal calcification and mortality

Table 1. Baseline characteristics of MHD patients, as stratified according to tertiles of conjunctival and corneal calcification (n = 109)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mild calcification (score 0–4; n = 43)</th>
<th>Moderate calcification (score 5–8; n = 35)</th>
<th>Severe calcification (score 9–20; n = 31)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
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<tr>
<td>Age (year)</td>
<td>56.4 ± 15.7</td>
<td>56.9 ± 10.8</td>
<td>58.0 ± 9.4</td>
<td>0.586</td>
</tr>
<tr>
<td>Female sex</td>
<td>18 (41.9)</td>
<td>18 (51.4)</td>
<td>16 (51.6)</td>
<td>0.368</td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.2 ± 3.3</td>
<td>22.1 ± 2.6</td>
<td>21.4 ± 3.1</td>
<td>0.420</td>
</tr>
<tr>
<td>Smoking</td>
<td>10 (23.3)</td>
<td>6 (17.1)</td>
<td>4 (12.9)</td>
<td>0.241</td>
</tr>
<tr>
<td>Previous cardiovascular disease</td>
<td>2 (4.7)</td>
<td>1 (2.9)</td>
<td>4 (12.9)</td>
<td>0.269</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7 (16.3)</td>
<td>2 (5.7)</td>
<td>5 (16.1)</td>
<td>0.834</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (23.3)</td>
<td>13 (37.1)</td>
<td>15 (48.4)</td>
<td>0.020</td>
</tr>
<tr>
<td>Grade 3 aortic calcification</td>
<td>7 (16.3)</td>
<td>16 (45.7)</td>
<td>14 (45.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dialysis-related data</td>
<td></td>
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<tr>
<td>Haemodialysis duration (years)</td>
<td>4.8 ± 5.0</td>
<td>8.1 ± 6.1</td>
<td>13.4 ± 6.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use of fistula</td>
<td>36 (83.7)</td>
<td>25 (71.4)</td>
<td>28 (80.0)</td>
<td>0.613</td>
</tr>
<tr>
<td>Use of BCM dialyser</td>
<td>29 (67.4)</td>
<td>26 (74.3)</td>
<td>26 (83.9)</td>
<td>0.102</td>
</tr>
<tr>
<td>Erythropoietin (U/kg/week)</td>
<td>75.3 ± 42.3</td>
<td>62.8 ± 43.8</td>
<td>67.3 ± 48.3</td>
<td>0.342</td>
</tr>
<tr>
<td>Kt/Vurea (Daugirdas)</td>
<td>1.74 ± 0.33</td>
<td>1.81 ± 0.34</td>
<td>1.89 ± 0.31</td>
<td>0.091</td>
</tr>
<tr>
<td>nPCR (g/kg/day)</td>
<td>1.17 ± 0.29</td>
<td>1.24 ± 0.26</td>
<td>1.32 ± 0.41</td>
<td>0.057</td>
</tr>
<tr>
<td>Biochemical data</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>White blood cell (×10^3/μL)</td>
<td>6.73 ± 1.94</td>
<td>5.77 ± 1.70</td>
<td>6.41 ± 2.21</td>
<td>0.418</td>
</tr>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>10.7 ± 1.3</td>
<td>10.5 ± 1.5</td>
<td>10.5 ± 1.4</td>
<td>0.449</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.03 ± 0.28</td>
<td>3.87 ± 0.27</td>
<td>3.82 ± 0.35</td>
<td>0.003</td>
</tr>
<tr>
<td>Malnutrition (albumin &lt;3.6 g/dL)</td>
<td>3 (7)</td>
<td>2 (5.7)</td>
<td>6 (16.9)</td>
<td>0.155</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>11.2 ± 2.4</td>
<td>10.7 ± 2.2</td>
<td>10.6 ± 2.3</td>
<td>0.326</td>
</tr>
<tr>
<td>Ferritin (μg/L)</td>
<td>337.7 ± 285.0</td>
<td>313.7 ± 271.9</td>
<td>288.5 ± 190.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Corrected calcium (mg/dL)</td>
<td>9.6 ± 0.8</td>
<td>10.3 ± 1.1</td>
<td>10.7 ± 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phosphate (mg/dL)</td>
<td>4.4 ± 1.1</td>
<td>4.4 ± 1.3</td>
<td>4.8 ± 1.1</td>
<td>0.114</td>
</tr>
<tr>
<td>Corrected × phosphate (mg^2/dL^2)</td>
<td>42.1 ± 11.7</td>
<td>46.0 ± 15.4</td>
<td>51.8 ± 13.4</td>
<td>&lt;0.001</td>
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<tr>
<td>Cardiovascular risks</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>174.3 ± 34.3</td>
<td>178.4 ± 39.8</td>
<td>172.5 ± 35.1</td>
<td>0.878</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>171.0 ± 102.0</td>
<td>177.6 ± 149.5</td>
<td>132.0 ± 50.3</td>
<td>0.178</td>
</tr>
<tr>
<td>hsCRP (mg/L)</td>
<td>3.70 (0.25–44.3)</td>
<td>3.34 (0.46–73.18)</td>
<td>4.26 (0.36–51.95)</td>
<td>0.221</td>
</tr>
<tr>
<td>Inflammation (hsCRP &gt; 3.0 mg/L)</td>
<td>25 (58.1)</td>
<td>18 (51.4)</td>
<td>19 (61.3)</td>
<td>0.874</td>
</tr>
</tbody>
</table>

P < 0.05 is a significant trend among three study groups. Non-normal distribution data were presented as median (minimum and maximum). Data were measured by Mann–Whitney U-tests. BCM, biocompatible membrane; nPCR, normalized protein catabolic rate; hsCRP, high sensitivity C-reactive protein.

Results

Characteristics of the study population

A total of 109 patients (57 males and 52 females) with a mean HD duration of 8.3 ± 6.8 years were enrolled for analysis. Clinical characteristics—including age, sex, body mass index, and biological and haematological data—are listed in Table 1. Mean patient age was 57.0 ± 12.5 years (range, 28–87 years). After analysis, the three calcification groups did not differ in age, sex, history of cardiovascular disease, incidence of smoking or diabetes mellitus, use of fistula or biocompatible membrane (BCM) dialyser, erythropoietin, Kt/Vurea, nPCR, haemoglobin, creatinine, transferrin saturation, ferritin, corrected calcium, intact parathyroid hormone, cholesterol, triglyceride, hsCRP levels, or percentage of malnutrition and inflammation (all P > 0.05). However, those with severe calcification tended to have hypertension, higher frequency of grade 3 aortic arch calcification, longer duration of HD therapy, higher corrected serum calcium and calcium-phosphate levels, and lower serum albumin than the other two groups (Table 1).

Variables associated with scores of conjunctival and corneal calcification in MHD patients

Simple linear regression analysis demonstrated that HD duration, hypertension, albumin, using BCM dialysers, corrected calcium, phosphate, calcium phosphate, log intact parathyroid hormone and grading of aortic arch calcification were potential determinants associated with scores of CCC (all P < 0.05). Backward stepwise multiple linear regression analysis showed that HD duration (P < 0.001), hypertension (P = 0.001) and corrected calcium level (P < 0.001) were associated with scores of CCC in MHD patients (Table 2).

Variables associated with grading of aortic arch calcification in MHD patients

Simple linear regression analysis demonstrated that age, HD duration, albumin, corrected calcium, corrected calcium-phosphate level, and moderate and severe CCC were...
potential determinants associated with grading of aortic arch calcification (all \( P < 0.01 \)). With backward stepwise multiple linear regression analysis, only age \( (P < 0.001) \), corrected calcium and phosphate level \( (P < 0.001) \), and moderate and severe CCC \( (P = 0.003) \) were associated with grading of aortic arch calcification in MHD patients (Table 3).

**Cox regression multivariate analysis for 1-year mortality in MHD patients**

At the end of the 1-year observation period, 11 of 109 (11.1%) patients had died: 2 of 43 (4.7%) with mild CCC, 1 of 35 (2.9%) with moderate calcification and 8 of 31 (25.8%) with severe calcification. Of these, five (5/11, 45.5%) died of CVD, four (4/11, 36.4%) of infection and two (2/11, 18.2%) of malignancies.

Univariate Cox proportional hazards models showed that age, albumin, creatinine, corrected calcium and severe CCC were potential predictors of patient mortality. To confirm the independent predictive power of patient mortality, the above data were entered into a multivariate Cox proportional hazards model using the conditional forward stepwise method \( (P > 0.05 \) removed). However, the dialysis vintage of patients with severe CCC was significantly much longer than that of the patients with moderate and mild calcification. As the duration on dialysis may have contributed to the severe calcification and dialysis vintage to be directly related to all cause mortality, we entered the dialysis vintage to the final model of multivariate. Cox regression analysis adjusted the possible bias resulting from the different dialysis duration among the three study groups. In the final multivariate model, age \( (\text{hazard ratio} \ 1.083; 95\% \ CI \ 1.003–1.169; P = 0.041) \), corrected calcium \( (\text{hazard ratio} \ 3.467; 95\% \ CI \ 1.320–9.104; P = 0.012) \) and, if mild CCC as the reference, severe CCC \( (\text{hazard ratio} \ 10.526; 95\% \ CI \ 1.580–71.429; P = 0.005) \) were significant risk factors for all-cause 1-year mortality in MHD patients (Table not shown). Similarly, after adjustment for potential related variables, score of CCC \( (\text{hazard ratio} \ 1.264; 95\% \ CI \ 1.034–1.545; P = 0.022) \) is a significant risk factor for all-cause 1-year mortality in MHD patients. Each increment of one score of CCC is associated with an increased 26.4% of risk for all-cause mortality (Table 4). The Kaplan–Meier survival analysis for all MHD patients showed that patients with severe CCC had a higher mortality than those with moderate and mild CCC (log-rank test, chi-square \( = 11.95, P = 0.003 \), Figure 3).

**Discussion**

In this study, grading of aortic arch calcification was significantly associated with moderate and severe CCC. In
addition, severe CCC was a predictor of all-cause 1-year mortality in MHD patients, after adjusting for other significant factors. This finding suggests the need to monitor CCC in MHD patients.

The physiological cause of interpalpebral CCC, the most common form of metastatic calcification in patients with chronic renal failure [21], is unknown. A relatively alkaline environment secondary to the loss of carbon dioxide from the exposed interpalpebral fissure and high serum concentrations of calcium and phosphate exceeding in vivo solubility are thought to result in calcification in these regions [10–13]. In this study, grade of CCC was correlated with corrected HD duration, calcium level and hypertension. As with previous reports of cardiovascular calcification in MHD patients, severity of cardiovascular calcification was associated with HD duration [22], as was the degree of CCC [14,15,17,23]. However, consensus has not been reached on the relationship between severity of CCC and serum calcium, phosphate and calcium-phosphate concentrations in previous studies [14,15,17,23–25]. Results may differ because blood levels of calcium and phosphate fluctuate over time, while ocular calcification is slowly progressive and the long-term effect of derangement in mineral metabolism. As for hypertension, as far as we are aware, no previous reports have ever studied the relationship between hypertension and CCC. Hypertension is very common in patients with chronic kidney disease, and arterial stiffness plays a major role in the genesis of systolic hypertension [26–28]. CCC is thought to result from derangements in mineral metabolism, which is one of the risk factors for arterial stiffness [8] (this will be described in detail in the next paragraph). Thus, the relationship between hypertension and CCC could be explained by arterial stiffness, but it requires further study.

The novel finding of the present study was that severe CCC is an independent and significant risk factor for all-cause 1-year mortality in MHD patients. CVD is the leading cause of mortality in patients with chronic kidney disease [29]. Vascular calcification, in the form of calcium phosphate deposits, is a common feature of multiple types of arteriosclerosis, and is associated with the extremely high rates of cardiovascular and all-cause mortality found in the chronic kidney disease population [8,29–31]. In dialysis patients, hyperphosphataemia, hypercalcaemia and elevated calcium-phosphate product may cause or exacerbate vascular calcification [6,8,32,33]. Derangements in calcium and phosphate metabolism could be the source for CCC, as previously mentioned. Furthermore, we found that grading of aortic arch calcification was significantly associated with moderate and severe CCC. Seyahi et al. also evaluated the presence of vascular calcification by using plain X-ray films in 63 peritoneal and haemodialysis patients and found that those with greater CCC were
more likely to also have vascular calcification. Thus, the severity of CCC may reflect the presence and severity of vascular calcification, and predict 1-year mortality in MHD patients.

Recent evidence shows that chronic inflammation, common in MHD patients, may cause protein–energy cachexia and progressive atherosclerosis [4,5,9]. Malnutrition and inflammation have been identified as factors in the poor short-term survival of MHD patients [9]. Recent coinage of the term ‘malnutrition–inflammation complex syndrome’ or ‘malnutrition–inflammation–atherosclerosis syndrome’ emphasizes the strong association of malnutrition and inflammation with atherosclerotic cardiovascular disease and the high morbidity and mortality seen in MHD patients [9,34,35]. The relationship between CCC and inflammation/malnutrition was not investigated previously except for one study by Seyahi et al. that showed no association between CRP level and CCC [15], similar to our result. In this population, an association between the parameters used to evaluate malnutrition and inflammation with CCC was not found.

The finding that severe CCC can predict short-term mortality in MHD patients is important for two reasons. Firstly, CCC is easily detectable at bedside. In this study, CCC was graded by photographs for the sake of objectivity. However, CCC is easy to check with a portable slit lamp during routine HD. Although vascular calcification correlates well with clinical outcome, these values need to include more complete clinical observations and examinations. CCC may provide useful information on the status of vascular calcification in MHD patients. Secondly, they may serve as indications to treat disorders of mineral metabolism, which are potentially modifiable, to retard progression of calcification. Recent clinical trials have shown that patients receiving the non-calcium-containing phosphate binder sevelamer have little or no progression in coronary artery and aorta calcification when compared with those treated with a calcium-containing phosphate binders, when serum phosphate levels were equivalently controlled in both groups [36–38]. Improved survival after treatment with sevelamer instead of calcium-containing phosphate binder was also reported [39,40]. The potential benefit of sevelamer on survival in MHD patients with high grades of CCC warrants further investigation. Raggi et al. found an arrest or regression in total cardiac valvular and vascular calcification in sevelamer-treated patients [41]. Porter and Cram have shown that most patients (7/11) receiving kidney transplants had gradual regression of CCC when calcium and phosphate levels were normalized [17]. Further studies are needed to determine whether CCC regresses when mineral metabolism levels are brought within the normal range. If so, it would be a useful marker to monitor vascular calcification and the effect of treatment.

There are several limitations to this study. Although this study suggests that CCC relates increased risk of mortality in MHD patients, causality has not been established. Whether correction of disturbances in mineral metabolism in these patients would improve mortality needs further evaluation. Additionally, the presence of vascular calcification was evaluated by plain chest X-ray films. Although there were some reports using plain radiography in detection of vascular calcification [15,22,42], further investigation using more sensitive methods to detect and quantify vascular calcification, such as electron beam and helical computed tomography, to confirm our result may be needed. Other limitations of this study are its relatively small sample size, sparse outcomes and limited follow-up.

In conclusion, vascular calcification is strongly associated with CCC. This study is the first to show that severity of CCC is an independent predictor for all-cause 1-year mortality in MHD patients. A simple bedside test to evaluate CCC may be an inexpensive and non-invasive method that allows the identification of patients with higher mortality risk. This information can be used to guide the management of MHD patients.

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Conflict of interest statement. None declared.

References

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