Relationship between serum parathyroid hormone levels and abdominal aortic calcification in patients starting hemodialysis who have never taken calcium tablets, calcitriol, or vitamin D analogs

Jin He, Xiaoyan Sun, Rongjian Nie and Lin Zhao

ABSTRACT

Background: Vascular calcification (VC) and secondary hyperparathyroidism (SHPT) are important causes of the high incidence of cardiovascular events in chronic kidney disease (CKD) patients. The relationship between parathyroid hormone (PTH) and VC is very complex. The aim of this study was to determine the correlation between PTH levels and abdominal aortic calcification (AAC) in patients starting hemodialysis who had not received calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs.

Methods: Seventy-one patients were included. Latero-lateral X-ray lumbar radiography, serum intact PTH (iPTH) levels, and predialysis biochemical parameters were obtained. The degree of AAC was evaluated according to the methods described previously by Kauppila et al.

Results: We found that there was a strong negative correlation between serum PTH and AAC (Spearman’s rho \(-0.76\), \(p < 0.001\)). Receiver operating characteristic (ROC) curve analysis showed that low serum PTH level could predict the presence and extent of AAC (area under the curve values were 0.9013 [\(p < 0.0001\)] and 0.780 [\(p = 0.0041\)], respectively).

Conclusions: Our results indicate that serum PTH level is significantly negatively correlated with AAC within a certain concentration range in patients starting hemodialysis who had not received calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs.

ARTICLE HISTORY

Received 17 June 2022
Revised 10 August 2022
Accepted 11 August 2022

KEYWORDS
Chronic kidney disease; vascular calcification; parathyroid hormone; abdominal aortic calcification

Introduction

The incidence and mortality of cardiovascular disease (CVD) are significantly increased in chronic kidney disease (CKD) patients. Even after stratification by age, sex, race, and presence of diabetes, CVD mortality in end-stage renal disease (ESRD) patients treated by hemodialysis or peritoneal dialysis is 10–20 times higher than that in the general population [1].

Vascular calcification (VC), defined as the inappropriate and pathological deposition of minerals in the form of calcium phosphate salts into the vascular tissues, is a very common complication in CKD patients and is associated with significantly increased all-cause and cardiovascular mortality [2–5]. Secondary hyperparathyroidism (SHPT) is another common complication of CKD that has also been associated with increased cardiovascular mortality and CKD progression, especially in CKD stage 3–5 patients [6–8].

The relationship between VC and parathyroid hormone (PTH) is very complex. A study of 1095 hemodialysis patients (aged 65–88) showed that abdominal aortic calcification (AAC) was more severe in male patients with serum PTH levels within the upper-normal range than in patients with serum PTH levels within the lower-normal range [9]. Another study revealed that in nondialysis CKD stage 2–5 patients with AAC score \(>6\) or pelvic arterial calcification (PAC) score \(>1\) had higher serum PTH [10]. In addition, among patients receiving hemodialysis, serum PTH levels were significantly associated with AAC progression [11]. However, in clinical practice, PTH levels do not match the severity of AAC. The present study examined the relationship between PTH levels and AAC in patients starting hemodialysis who have not received calcium, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs to
determine whether PTH levels are associated with the severity of AAC.

Materials and methods

This study was approved by the Ethics Committee of the Chonggang General Hospital Affiliated with the Chongqing University of Posts and Telecommunications (ethics No.: 2020-SY-04). Written informed consent was obtained from each person at recruitment. Hemodialysis was initiated when the estimated glomerular filtration rate (eGFR) was $<\text{15/min}/\text{1.73 m}^2$ of body surface area and was accompanied by uremic-related symptoms that could not be corrected by drugs (such as nausea and vomiting, hyperkalemia, metabolic acidosis, and heart failure). Patients starting hemodialysis who had not used calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs between August 2020 and May 2022 were initially screened for enrollment in this cross-sectional study. Of the 94 hemodialysis patients, patients with malignancy, diabetes mellitus, systemic hypertension, systemic lupus erythematosus, abdominal aortic aneurysm, acute kidney injury (AKI) or Spearman's correlation (normal distribution) or Spearman's correction (skewed distribution). Receiver operating characteristic (ROC) curves were plotted for serum PTH level and AAC to evaluate the ability of low serum PTH levels to predict the presence and extent of AAC. The area under the curve (AUC) and its 95% confidence interval (CI) were calculated for this ROC curve. A $p$-value of $<0.05$ was considered statistically significant. All computations were performed using SPSS 20.0 software (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0, Armonk, NY).

Results

The clinical characteristics and biochemistry of all patients are shown in Table 1. There were 48 males (67.6%) and 23 females (32.4%). The mean age was 60.23 ± 1.75 years (23–85 years). The cause of ESRD in our patients was diabetes mellitus in 37, glomerulonephritis in 24, systemic hypertension in 9, and autosomal dominant polycystic kidney disease in 1.

The Shapiro–Wilk test showed that serum PTH, AAC, C-reactive protein (CRP), triglycerides, serum creatinine (Scr) and HbA1c skewed distributions, while age, serum calcium, serum phosphorus, blood magnesium, serum urea nitrogen (BUN), systolic blood pressure (SBP), diastolic blood pressure (DBP), hemoglobin (Hb), albumin, and

|
| Table 1. Clinical characteristics and biochemistry of whole cohort ($n = 71$). |
| Age, years (23–85 years) | 60.23 ± 1.75 |
| Male, n (%) | 48 (67.6) |
| Causes of ESRD | |
| Diabetes mellitus | 37 (52.1) |
| Glomerulonephritis | 24 (33.8) |
| Systemic hypertension | 9 (12.7) |
| Autosomal dominant polycystic kidney disease | 1 (1.4) |
| SBP (116–196 mmHg) | 155.10 ± 20.75 |
| DBP (48–108 mmHg) | 83.66 ± 14.31 |
| ACC (score 0–23) | 2.00 (8) |
| iPTH (15.8–594.5 pg/mL) | 176.40 (181.10) |
| BUN (16.37–59.7 mmol/L) | 31.41 ± 9.15 |
| Scr (643–1729 μmol/L) | 892.00 (315.5) |
| Serum magnesium (0.88–2.27 mmol/L) | 0.96 ± 0.15 |
| Serum calcium (0.88–2.27 mmol/L) | 1.79 ± 0.33 |
| Serum phosphorus (0.78–4.15 mmol/L) | 2.05 ± 0.70 |
| Hb (39–116 g/L) | 76.05 ± 16.47 |
| ACC (score 0–23) | 2.00 (8) |
| CRP (1–172 mg/L) | 4 (22) |
| Serum total protein (43.9–80.8 g/L) | 61.91 ± 8.58 |
| Albumin (21.9–48.9 g/L) | 36.39 ± 6.68 |
| ALP (18–154 U/L) | 86.83 ± 36.36 |
| Triglycerides (0.58–5.45 mmol/L) | 1.41 (0.79) |
| Total cholesterol (2.29–6.63 mmol/L) | 3.87 ± 1.05 |
| HDL (0.52–1.89 mmol/L) | 1.06 ± 0.34 |
| LDL (0.93–4.36 mmol/L) | 2.21 ± 0.77 |
| HbA1c (37 diabetes mellitus patients, 6.31–8.45) | 6.57 (0.56) |

ESRD: end-stage renal disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; ACC: abdominal aortic calcification; iPTH: intact parathyroid hormone; BUN: serum urea nitrogen; SCR: serum creatinine; Hb: hemoglobin; CRP: C-reactive protein; ALP: alkaline phosphatase; HDL: high-density lipoprotein; LDL: low-density lipoprotein.
serum total protein (TP), alkaline phosphatase (ALP), serum total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were normally distributed. Because AAC had a skewed distribution and Pearson’s correlation or multiple linear regression analysis was not suitable, Spearman’s rank correlation analysis was employed to analyze the relationship between AAC and other variables.

There was a strong negative correlation between serum PTH and AAC (Spearman’s rho $-0.76$, $p < 0.001$) (Figure 1(A,B); Table 2). Subgroup analysis of patients with diabetes mellitus also suggested that PTH was negatively correlated with AAC (Spearman’s rho $-0.412$, $p = 0.011$) (Figure 1(C,D); Table 3). Receiver-operating characteristic curve analysis (Figures 2 and 3) showed that low serum PTH levels could predict the presence and extent of AAC [AUC values were 0.9013 ($p < 0.0001$) and 0.780 ($p = 0.0041$), respectively]. We also found that there was a moderate negative correlation between Pi and AAC (Spearman’s rho $-0.536$, $p < 0.001$) (Table 2).

To further analyze why there was a negative correlation between serum phosphorus and AAC, the patients were divided into two age groups around the

Figure 1. (A) Representative image of AAC in the low-serum-iPTH group of non-DKD patients. (B) Representative image of AAC in the high-serum-iPTH group of non-DKD patients. (C) Representative image of AAC in the low-serum-iPTH group of DKD patients. (D) Representative image of AAC in the high-serum-iPTH group of DKD patients.
Table 2. Spearman’s rank correlation analysis for the relationship between abdominal aortic calcification scores and baseline characteristics.

| Spearman’s rho | p-Value |
|----------------|---------|
| iPTH (pg/mL)   | −0.760  | <0.001 |
| Age (year)     | 0.730   | <0.001 |
| Serum phosphorus (mmol/L) | −0.536  | <0.001 |
| BUN (mmol/L)   | −0.324  | 0.039  |
| Serum calcium (mmol/L) | 0.223   | 0.160  |
| Serum magnesium (mmol/L) | 0.044   | 0.783  |
| SBP (mmHg)     | −0.056  | 0.728  |
| DBP (mmHg)     | −0.270  | 0.088  |
| Scr (µmol/L)   | −0.144  | 0.369  |
| Hb (g/L)       | 0.089   | 0.581  |
| CRP (mg/L)     | −0.114  | 0.478  |
| Serum total protein (g/L) | −0.290  | 0.066  |
| Albumin (g/L)  | −0.036  | 0.824  |
| ALP (U/L)      | −0.216  | 0.175  |
| Triglycerides (mmol/L) | −0.045  | 0.781  |
| Total cholesterol (mmol/L) | −0.034  | 0.831  |
| HDL (mmol/L)   | 0.002   | 0.999  |
| LDL (mmol/L)   | −0.040  | 0.846  |

ACC: abdominal aortic calcification; iPTH: intact parathyroid hormone; BUN: serum urea nitrogen; SBP: systolic pressure; DBP: diastolic blood pressure; SCR: serum creatinine; Hb: hemoglobin; CRP: C-reactive protein; ALP: alkaline phosphatase; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Table 3. A subgroup analysis of patients with diabetes mellitus for relationship between abdominal aortic calcification scores and baseline characteristics.

| Pearson’s correlation | Spearman’s rho | p-Value |
|-----------------------|----------------|---------|
| AAC                   | iPTH (pg/mL)  | −0.412  | 0.011  |
| AAC                   | Age (year)    | 0.436   | 0.007  |
| AAC                   | Serum phosphorus (mmol/L) | −0.221  | 0.322  |
| AAC                   | Serum calcium (mmol/L) | −0.536  | 0.953  |
| AAC                   | CRP (mg/L)    | −0.058  | 0.798  |
| AAC                   | Triglycerides (mmol/L) | −0.227  | 0.311  |
| AAC                   | HbA1c         | 0.005   | 0.976  |
| AAC                   | Serum magnesium (mmol/L) | 0.124   | 0.581  |
| AAC                   | SBP (mmHg)    | −0.083  | 0.713  |
| AAC                   | DBP (mmHg)    | 0.094   | 0.676  |
| AAC                   | Scr (µmol/L)  | −0.027  | 0.903  |
| AAC                   | BUN (mmol/L)  | 0.071   | 0.754  |
| AAC                   | Hb (g/L)      | 0.158   | 0.483  |
| AAC                   | Serum total protein (g/L) | 0.182   | 0.419  |
| AAC                   | Albumin (g/L) | 0.236   | 0.290  |
| AAC                   | ALP (U/L)     | −0.343  | 0.119  |
| AAC                   | Total cholesterol (mmol/L) | −0.059  | 0.795  |
| AAC                   | HDL (mmol/L)  | −0.150  | 0.505  |
| AAC                   | LDL (mmol/L)  | 0.029   | 0.899  |

ACC: abdominal aortic calcification; iPTH: intact parathyroid hormone; CRP: C-reactive protein; SBP: systolic pressure; DBP: diastolic blood pressure; SCR: serum creatinine; Hb: hemoglobin; ALP: alkaline phosphatase; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Discussion

The present study investigated the correlation between PTH levels and AAC in patients starting hemodialysis who had not received calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs. Our results suggested that lower serum PTH levels were associated with higher AAC scores in this population.

Although the prevalence of VC in CKD patients is higher, the incidence of arterial calcification varies between different sites, and the risk factors for arterial calcification in different locations and their influence on cardiovascular events are also different [13–15].

AAC is an independent risk factor for all-cause mortality or CVD events in non-CKD patients, peritoneal dialysis patients, and hemodialysis patients [16–18]. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines also suggest that a lateral abdominal radiograph can be used to detect the presence or absence of vascular calcification in patients with CKD stage 3–5 to guide the management of chronic kidney disease—mineral and bone disorder (CKD-MBD) [19].

Studies have demonstrated that PTH receptors exist in myocardial cells, vascular smooth muscle cells, and endothelial cells, indicating that inappropriate (excessive or insufficient) secretion of PTH may have adverse effects on the cardiovascular system [20,21]. It has been found that PTH perfusion can lead to intense aortic medial calcification in rats with parathyroidectomy, and this effect has nothing to do with uremia or serum phosphorus levels [22]. Another study also found that cinacalcet could inhibit the calcification of the aorta and heart in 5/6-nephrectomized rats by decreasing serum PTH levels [23]. These results suggest that PTH has a direct pro-calcification effect, at least in animal models of CKD.

Our results showed that the serum phosphorus and serum PTH of patients under 50 years old (20/71) were significantly higher (2.74 mmol/L vs. 1.65 mmol/L, unpaired t-test, p < 0.001; 368.85 pg/mL vs. 173.4 pg/mL, Mann–Whitney U-test, p < 0.001) than those of patients over 50 years old (50/71), and the AAC score was significantly lower in patients under 50 years old (0.08 vs. 6.87, Mann–Whitney U-test, p < 0.001). There was no significant difference in serum calcium between the two groups (1.67 mmol/L vs. 1.89 mmol/L, t-test, p = 0.058) (Table 4).

cutoff of 50 years. The AAC, serum PTH and serum calcium of the two groups had skewed distributions, and the serum phosphorus was normally distributed, so we used the Mann–Whitney U-test and unpaired t-test to compare groups.
between the two or even a negative correlation [13–15,24,25]. One possible explanation for these contradictory conclusions is that the widespread use of calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs affects the natural process of AAC.

Currently, calcium tablets, calcium-containing phosphorus binders, calcitriol, and vitamin D analogs are widely used to treat mineral metabolism abnormalities. The DOPPS study found that up to 52% of participants received vitamin D supplementation; 72.9% of participants used calcium-containing phosphorus binders for the control of hyperphosphatemia [8]. However, improper use of the above drugs may lead to adverse clinical consequences. For example, prolonged and disproportionate consumption of vitamin D supplements may lead to excessive inhibition of PTH and aggravation of vascular calcification [26,27]; and the use of high-dose calcium salts (oral calcium tablets or calcium-based phosphate binders) can easily lead to hypercalcemia, resulting in low serum PTH levels and vascular calcification [28,29]. Therefore, it is difficult to draw reliable conclusions about the association between PTH and AAC in the CKD population taking calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs.

In view of this, in this study, we purposely selected patients starting hemodialysis who had not used calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs as the research subjects. Interestingly, even after eliminating interfering factors such as calcium and vitamin D, PTH and AAC were still significantly negatively correlated. One explanation for
the negative correlation is that lower serum PTH levels lead to adynamic bone disease, and adynamic bone disease will impair the ability of patients to handle and buffer calcium loads and thus put them at higher risk of extraosseous calcifications [30,31]. It should be emphasized that although lower serum PTH levels do contribute to the risk of adynamic bone disease, there is currently no evidence that low PTH alone can represent adynamic bone disease. Another possible explanation for the negative correlation between AAC and PTH is that low serum PTH levels may only be a manifestation of malnutrition, inflammation, or cachexia syndrome (MICS), and malnutrition-inflammation is associated with vascular calcification in uremic patients [32,33]. However, in another study that included 97 hemodialysis patients who were followed up for one year, patients with malnutrition and chronic inflammation (defined as serum albumin <40 g/L and hs-CRP ≥28.57 nmol/L) had significantly higher PTH levels than the control group (241.5 pg/mL vs. 161.8 pg/mL) [11]. Therefore, neither adynamic bone disease nor malnutrition can fully explain why low PTH levels can aggravate AAC. Further studies are needed to elucidate the mechanism of AAC deterioration caused by low PTH levels.

Another surprising finding of the present study is that there was a significant negative correlation between AAC and serum phosphorus. Serum phosphorus plays a very important role in the occurrence and progression of vascular calcification [34]. Subgroup analysis in the MESA study indicated that each 1-mg/dL increment in serum phosphate concentration was associated with a 21%, 33%, 25%, and 62% greater prevalence of coronary artery, thoracic, aortic valve, and mitral valve calcification, respectively [35]. However, other researchers found that there was no significant difference in serum phosphorus levels between the AAC score >6 group and AAC score ≤6 group of hemodialysis patients [10]. A study on a Chinese hemodialysis population (CDCS study) also found that serum phosphorus was a risk factor for coronary artery calcification (CAC), but not a risk factor for AAC [14]. It should be noted that in the above studies, all participants received hemodialysis or peritoneal dialysis, which is effective in removing serum phosphorus, and a large proportion of participants were taking phosphorus binders (64.6% in the CDCS study). Therefore, it cannot be concluded that there is no correlation between serum phosphorus and AAC. In the present study, serum phosphorus was not affected by dialysis, and the patient did not use any form of phosphorus bonding agent, but there was still a significant negative correlation between AAC and serum phosphorus. This finding is consistent with that of Harin Rhee et al. [32], who also found that the prevalence of baseline AAC and its progression in the low-serum-phosphorus group was significantly higher than that in the high-serum-phosphorus group.

Further analysis of patients’ characteristics showed that the serum phosphate of patients under 50 years old was significantly higher than that of patients over 50 years old, but the AAC score was significantly lower in the younger group. We speculate that age may have a greater impact on AAC than serum phosphorus in CKD patients. Indeed, a study of young patients with ESRD who were undergoing dialysis confirmed that there was no significant difference in serum phosphorus between patients with and without CAC [29]. Another study involving 174 Chinese patients also found that age may be the most important factor affecting CAC in maintenance hemodialysis patients, and serum phosphorus had no significant effect on CAC [36].

In our study, the effect of phosphorus on AAC may not have been obvious in young patients. The dietary status of young patients is often better than that of older patients, so they have higher serum phosphorus (without taking phosphate binders); therefore, serum phosphorus may be statistically negatively correlated with AAC, but this does not mean that serum phosphorus has no effect on AAC from a pathophysiological perspective.

There are several limitations to our study. First, the sample size for our study was small. More patients would be necessary to attain adequate power to detect a correlation between serum PTH levels and AAC. Second, we only evaluated the degree of AAC by abdominal radiographs, which are less sensitive and accurate than electron beam computed tomography (EBCT) and multislice CT (MSCT). Due to the relatively high cost and the risk of exposure to high radiation doses, these tests cannot be performed routinely. Third, the serum PTH levels of our observation population were in the range of 15.8–594.5 pg/mL. The correlation between PTH and AAC is not clear in CKD patients with serum PTH levels of 600 pg/mL or higher.

Conclusions

The present study, which is the only study focused on the association between PTH levels and AAC in patients starting hemodialysis who had not taken calcium tablets, calcium-containing phosphorus binders, calcitriol, or vitamin D analogs, demonstrates that PTH levels are significantly negatively correlated with AAC within a
certain concentration range. Inappropriate inhibition of PTH may lead to deterioration of AAC in CKD stage 5 patients.

Ethical approval

All procedures performed on human participants were in accordance with the ethical standards of The Chonggang General Hospital Affiliated with Chongqing University of Posts and Telecommunications and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Each participant signed an informed consent form before entering the study.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

ORCID

Jin He http://orcid.org/0000-0002-5108-4182

References

[1] Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis. 1998;32(5):S112–S119.
[2] Paloian NJ, Giachelli CM. A current understanding of vascular calcification in CKD. Am J Physiol Renal Physiol. 2014;307(8):F891–F900.
[3] Mizobuchi M, Towler D, Slatopolsky E. Vascular calcification: the killer of patients with chronic kidney disease. J Am Soc Nephrol. 2009;20(7):1453–1464.
[4] Russo D, Corrao S, Battaglia Y, et al. Progression of coronary artery calcification and cardiac events in patients with chronic renal disease not receiving dialysis. Kidney Int. 2011;80(1):112–118.
[5] London GM, Guérin AP, Marchais SJ, et al. Arterial media calcification in end-stage renal disease: impact on all-cause and cardiovascular mortality. Nephrol Dial Transplant. 2003;18(9):1731–1740.
[6] Bozic M, Diaz-Tocados JM, Bermudez-Lopez M, et al. Independent effects of secondary hyperparathyroidism and hyperphosphatemia on chronic kidney disease progression and cardiovascular events: an analysis from the NEFRONA cohort. Nephrol Dial Transplant. 2022;37(4):663–672.
[7] Schumock GT, Andress D, Marx SE, et al. Impact of secondary hyperparathyroidism on disease progression, healthcare resource utilization and costs in pre-dialysis CKD patients. Curr Med Res Opin. 2008;24(11):3037–3048.
[8] Tentori F, Blayney MJ, Albert JM, et al. Mortality risk for dialysis patients with different levels of serum calcium, phosphorus, and PTH: the dialysis outcomes and practice patterns study (DOPPS). Am J Kidney Dis. 2008;52(3):519–530.
[9] Buizert PJ, van Schoor NM, Simsek S, et al. PTH: a new target in arteriosclerosis? J Clin Endocrinol Metab. 2013;98(10):E1583–E1590.
[10] Disthabanchong S, Vipattawat K, Phakdeekitcharon B, et al. Abdominal aorta and pelvic artery calcifications on plain radiographs may predict mortality in chronic kidney disease, hemodialysis and renal transplantation. Int Urol Nephrol. 2018;50(2):355–364.
[11] Choi SR, Lee Y-K, Cho AJ, et al. Malnutrition, inflammation, progression of vascular calcification and survival: inter-relationships in hemodialysis patients. PLoS One. 2019;14(5):e0216415.
[12] Kauppila LI, Polak JF, Cupples LA, et al. New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. Atherosclerosis. 1997;132(2):245–250.
[13] Niu Q, Zhao H, Wu B, et al. Study on the prevalence of vascular calcification in different types of arteries and influencing factors in maintenance peritoneal dialysis patients. Blood Purif. 2019;47(1):8–16.
[14] Liu Z-H, Yu X-Q, Yang J-W, et al. Prevalence and risk factors for vascular calcification in Chinese patients receiving dialysis: baseline results from a prospective cohort study. Curr Med Res Opin. 2018;34(8):1491–1500.
[15] Niu Q, Zhao H, Wu B, et al. Abdominal aortic calcification is superior to other arteries calcification in predicting the mortality in peritoneal dialysis patients – a 8years cohort study. BMC Nephrol. 2019;20(1):439.
[16] Golestani R, Tio R, Zeebregts CJ, et al. Abdominal aortic calcification detected by dual X-ray absorptiometry: a strong predictor for cardiovascular events. Ann Med. 2010;42(7):539–545.
[17] Martino F, Di P, Loreto D, et al. Abdominal aortic calcification is an independent predictor of cardiovascular events in peritoneal dialysis patients. Ther Apher Dial. 2013;17(4):448–453.
[18] Zhu X, Cai H, Zhu M, et al. Association of abdominal aortic calcification estimated by plain radiography with outcomes in hemodialysis patients: a six-year follow-up study. Nephrology. 2020;25(7):559–565.
[19] Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD-MBD). Kidney Int Suppl. 2017;7:1–59.
[20] Tomaschitz A, Ritz E, Pieske B, et al. Aldosterone and parathyroid hormone interactions as mediators of metabolic and cardiovascular disease. Metabolism. 2014;63(1):20–31.
[21] Chen H, Han X, Cui Y, et al. Parathyroid hormone fragments: new targets for the diagnosis and treatment of chronic kidney disease-mineral and bone disorder. Biomed Res Int. 2018;2018:9619253.
[22] Neves KR, Graciolli FG, dos Reis LM, et al. Vascular calcification: contribution of parathyroid hormone in renal failure. Kidney Int. 2007;71(12):1262–1270.

[23] Kawata T, Nagano N, Obi M, et al. Cinacalcet suppresses calcification of the aorta and heart in uremic rats. Kidney Int. 2008;74(10):1270–1277.

[24] Fayed A, Elnokeety MM, Attia K, et al. Calcification of abdominal aorta in patients recently starting hemodialysis: a single-center experience from Egypt. Saudi J Kidney Dis Transpl. 2019;30(4):819–824.

[25] Lee SA, Jung M, Lee GW, et al. Low serum intact parathyroid hormone level is an independent risk factor for overall mortality and major adverse cardiac and cerebrovascular events in incident dialysis patients. Osteoporos Int. 2016;27(9):2717–2726.

[26] Razzaque MS. The dualistic role of vitamin D in vascular calcifications. Kidney Int. 2011;79(7):708–714.

[27] Mizobuchi M, Ogata H, Koiwa F, et al. Vitamin D and vascular calcification in chronic kidney disease. Bone. 2009;45(1):S26–S29.

[28] Chertow GM, Burke SK, Raggi P. Sevelamer attenuates the progression of coronary and aortic calcification in hemodialysis patients. Kidney Int. 2002;62(1):245–252.

[29] Goodman WG, Goldin J, Kuizon BD, et al. Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. N Engl J Med. 2000;342(20):1478–1483.

[30] Kurz P, Monier-Faugere MC, Bognar B, et al. Evidence for abnormal calcium homeostasis in patients with adynamic bone disease. Kidney Int. 1994;46(3):855–861.

[31] Andi JBC. Adynamic bone and chronic renal failure: an overview. Am J Med Sci. 2000;320(2):81–84.

[32] Rhee H, Song SH, Kwak IS, et al. Persistently low intact parathyroid hormone levels predict a progression of aortic arch calcification in incident hemodialysis patients. Clin Exp Nephrol. 2012;16(3):433–441.

[33] Avramovski P, Avramovska M, Sotiroski K, et al. Acute-phase proteins as promoters of abdominal aortic calcification in chronic dialysis patients. Saudi J Kidney Dis Transpl. 2019;30(2):376–386.

[34] Shobeiri N, Adams MA, Holden RM. Phosphate: an old bone molecule but new cardiovascular risk factor. Br J Clin Pharmacol. 2014;77(1):39–54.

[35] Adeney KL, Siscovick DS, Ix JH, et al. Association of serum phosphate with vascular and valvular calcification in moderate CKD. J Am Soc Nephrol. 2009;20(2):381–387.

[36] Wen Y, Gan H, Li Z, et al. Safety of low-calcium dialysate and its effects on coronary artery calcification in patients undergoing maintenance hemodialysis. Sci Rep. 2018;8(1):5941.