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Research paper

Comparison of CT acquired cardiac valvular calcification scores in hemodialysis and peritoneal dialysis patients undergoing open heart surgery☆

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ABSTRACT

Study objective: Data is scarce regarding which dialysis modality portends more severe cardiac valvular calcification (CVC). Our aim was to compare the degree of CVC in hemodialysis (HD) and peritoneal dialysis (PD) patient cohorts prior to open heart surgery (OHS) using a CT calcium score.
Design, setting, and participants: Dialysis patients who underwent OHS at our institution from 2009 to 2019 and who had pre-surgical cardiac CT were included in our study. We obtained duration of dialysis modality prior to their surgical date. There were two study cohorts to evaluate outcomes of interest: mitral and aortic calcification. CVC was assessed using the Agatston score. Logistic regression was performed to test for the association of PD and HD cumulative dialysis duration with presence of CVC.
Results: A total of 214 and 166 patients met inclusion for the mitral and aortic strata, respectively. Age, female sex, and BMI were associated with higher odds of presence of mitral calcification. Age and BMI were associated with higher odds of presence of aortic calcification, while female sex was associated with lower odds in the aortic strata. Cumulative years on PD and cumulative years on HD were not significantly associated with presence of CVC in either cohort.
Conclusion: Presence of mitral and aortic calcification for patients undergoing OHS was not significantly associated with cumulative length of PD or HD after adjusting for age, gender, and BMI suggesting that there may be more factors at play in the progression of CVC in end stage renal disease patients than what was previously established.

1. Introduction

Cardiovascular disease is the leading cause of mortality in both intermittent hemodialysis (HD) and peritoneal dialysis (PD) populations [1]. These patients often suffer from downstream complications including vascular or tissue calcification after years of therapy, which has been noted to increase cardiovascular mortality up to 100-fold higher than in the general, age-matched population [2]. The prognostic role of valvular calcification in chronic dialysis patient is well recognized and has even been equated by some authors to that of atherosclerotic vascular disease [3]. Several factors have been identified as independent risk factors for cardiac valvular calcification (CVC). Those include age, inflammatory conditions, loss of calcification inhibitors, and dysregulated bone mineral metabolism [4,5], in particular elevated phosphate levels [6]. However, the data is lacking on which dialysis population portends more severe CVC. While the complications

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of hyperphosphatemia have been linked to increased CVC and mortality in the HD population, this association is less established among PD patients [7–9]. PD patients have lower phosphate levels [10], and so theoretically, they could be expected to have less calcification. To this day, there is scarcity of data comparing the degree of CVC between dialysis modalities, as most research has been dedicated to comparing the level of coronary artery calcification (CAC). We aimed to compare the degree of aortic valve and mitral annulus calcification in HD and PD patients who underwent open heart surgery (OHS) using a computed CT score.

2. Materials and methods

We used our institution's cardiothoracic surgery database and identified patients that had dialysis prior to heart surgery. We included records from October 2009 to October 2019. We included the first surgical record per patient for patients undergoing isolated coronary artery bypass graft (CABG), or CABG+valve surgery (repair or replacement), or valve-only surgery (repair or replacement). Only patients receiving dialysis for end stage renal disease (ESRD) were included in our study. Patients with congenital heart disease and those lacking information on the length of dialysis were excluded.

We had two different study cohorts to evaluate each of the outcomes of interest: mitral and aortic calcification. To evaluate mitral calcification, we excluded any patients who previously underwent mitral valve surgery, such as those with a history of mitral valve repair or replacement. To evaluate aortic calcification, we excluded any patients who previously underwent aortic valve surgery, such as those with a history of aortic valve repair or replacement. Patients were included in both cohorts if they met criteria for both, and in one cohort if they met criteria for only one. Patients missing data to calculate a calcification score for their respective strata were excluded from the strata (Fig. 1). This study was approved by the Institutional Review Board of the Cleveland Clinic Foundation and was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

We obtained cumulative length of PD and HD at the time of surgery from the United States Renal Data System (USRDS) prescription history and supplemented the data with chart review. We categorized patients based on their history of prior dialysis as: prior PD only, prior HD only, or both prior PD and HD.

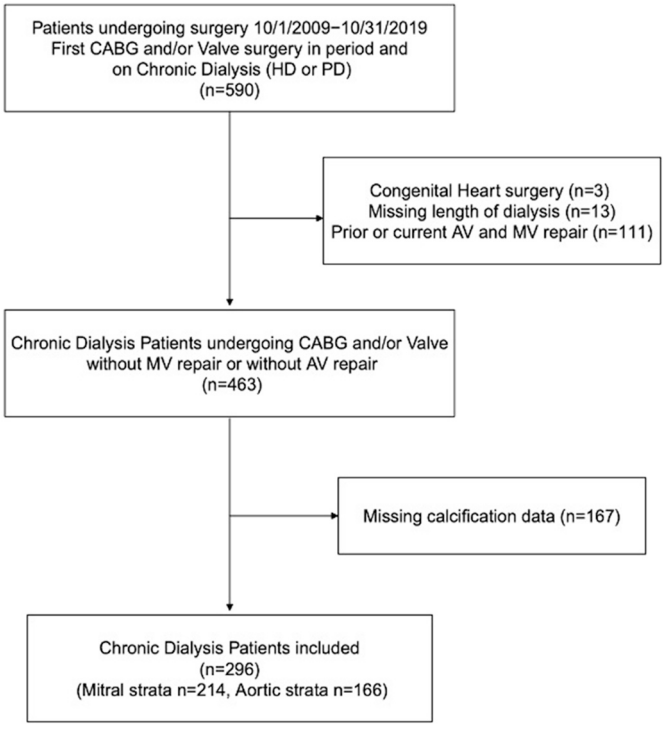

Fig. 1. Flow chart for patient selection; CABG, coronary artery bypass graft; HD, hemodialysis; PD, peritoneal dialysis; AV, aortic valve; MV, mitral valve.

Our study outcomes were mitral and aortic calcification scores. We obtained calcification scores prior to the surgical interventions through chart review. The Agatston score was used to quantify calcification on mitral and aortic valves. The score was automatically calculated by the software on a manually defined volume of interest. CT reading and calcium scoring were done using TeraRecon Aquarius iNtuition (TeraRecon Headquarters, Durham, NC). In addition to evaluating continuous calcification scores, we evaluated calcification present (above 0) vs. absent. The calcification scores were calculated using cardiac CT in end-systole and imaging review was done by an expert cardiac imaging CT reader from our institution.

For each study strata, we compared patient characteristics by prior PD only, prior HD only, and prior PD and HD using Chi-square and Kruskal-Wallis tests for categorical and continuous variables, respectively. We summarized and compared calcification scores across the different dialysis modalities using Kruskal-Wallis tests. We categorized calcification scores into presence of any calcification (>0) vs. no calcification, and used logistic regression analysis to evaluate the association between cumulative years on each dialysis modality and presence of calcification while adjusting for age, sex, BMI, and serum calcium. We had phosphorus values on a subset of the study patients and as a sensitivity analysis, we evaluated a similar model adjusting for the calcium phosphorus product instead of solely the serum calcium.

3. Results

A total of 296 patients met inclusion criteria for at least one of the strata in our study. Of those, 214 met inclusion for the mitral strata, and 166 met criteria for the aortic strata.

Of the 214 patients included in the mitral strata, 16 had only prior PD, 166 had only prior HD, and 32 had prior PD and HD. The median age of patients was 65.5 and 68 % were male. Table 1 shows patient characteristics for each group. The median number of years on PD was 2.1 and 1.7 respectively for those in the PD only group vs. PD and HD group. The median number of years on HD was 2.8 and 1.8 respectively for those in the HD only group vs. PD and HD group.

The median mitral calcification score was 0 for those that had only prior PD or only prior HD, and 137.3 for those with history of both PD and HD ($P = 0.38$). The proportion of patients with presence of mitral calcification (>0) was 43.8 %, 44.0 %, and 53.1 % respectively for those in the PD only group, HD only group, and combined PD and HD group ($P = 0.63$).

In the logistic regression model, age, female sex, and BMI were associated with higher odds of presence of mitral calcification (Table 3). Cumulative years on PD and cumulative years on HD were not significantly associated with presence of mitral calcification. The odds ratio per 1 year of PD was 1.23 (95 % CI: 0.95, 1.58) and 1.05 per 1 year of HD (95 % CI: 0.97, 1.13) shown in Fig. 2. There were 147 of 214 patients in the mitral strata who had phosphorus values and were included in the sensitivity analysis. The model from the sensitivity analysis that adjusted for calcium-phosphorus product produced similar results, but sex was not significantly associated with presence of mitral calcification.

Of the 166 patients included in the aortic strata, 20 had only prior PD, 115 had only prior HD, and 31 had prior PD and HD. The median age of patients was 62 and 56 % were male. Table 2 shows patient characteristics for each group. The median number of years on PD was 2.1 and 1.1 respectively for those in the PD only group vs. PD and HD group. The median number of years on HD was 2.6 and 1.7 respectively for those in the HD only group vs. PD and HD group.

The median aortic calcification score was 92.6, 0, and 7.6 respectively for those that had only prior PD, only prior HD, and for those with history of both ($P = 0.29$). The proportion of patients with presence of

Table 1
Descriptive statistics by prior PD/HD at surgery (Mitral strata).

Factor	Overall (N = 214)	Prior PD only (N = 16)	Prior HD only (N = 166)	Prior PD and HD (N = 32)	P-value
Age	65.5 [57.0,73.0]	63.5 [48.0,75.0]	67.0 [58.0,74.0]	63.0 [51.5,68.5]	0.063[b]
Gender					0.80[c]
Female	69 (32.2)	4 (25.0)	54 (32.5)	11 (34.4)	
Male	145 (67.8)	12 (75.0)	112 (67.5)	21 (65.6)	
Race					0.35[d]
American Indian	2 (0.93)	0 (0.0)	2 (1.2)	0 (0.0)	
Black	65 (30.4)	1 (6.3)	53 (31.9)	11 (34.4)	
Hawaiian	1 (0.47)	0 (0.0)	1 (0.60)	0 (0.0)	
Multiracial	9 (4.2)	0 (0.0)	9 (5.4)	0 (0.0)	
Unknown	1 (0.47)	0 (0.0)	1 (0.60)	0 (0.0)	
White	136 (63.6)	15 (93.8)	100 (60.2)	21 (65.6)	
BMI	27.4 [24.4,31.2]	29.0 [26.2,31.2]	26.9 [23.7,31.2]	28.1 [26.1,31.2]	0.18[b]
Calcium mg/dl	9.0 [8.5,9.5]	8.8 [8.2,9.1]	9.1 [8.5,9.5]	8.9 [8.5,9.8]	0.19[b]
PTH pg/ml	232.0 [123.0,345.0]	234.0 [130.0,431.0]	230.0 [120.0,335.0]	322.0 [124.0,380.0]	0.80[b]
Phosphorus mg/dl	4.0 [3.0,5.0]	5.5 [4.7,6.7]	3.8 [2.9,4.7]	4.6 [4.2,5.6]	<0.001[b]
Calcium phosphorus product	35.8 [27.4,46.0]	46.0 [41.4,59.6]	33.2 [26.3,44.0]	42.7 [37.3,57.1]	<0.001[b]
Hypertension	201 (93.9)	15 (93.8)	155 (93.4)	31 (96.9)	0.88[d]
Diabetes	138 (64.5)	11 (68.8)	107 (64.5)	20 (62.5)	0.91[c]
Heart failure	151 (70.6)	8 (50.0)	124 (74.7)	19 (59.4)	0.038[c]
Dyslipidemia	181 (84.6)	15 (93.8)	137 (82.5)	29 (90.6)	0.38[d]
Chronic lung disease	93 (43.5)	7 (43.8)	74 (44.6)	12 (37.5)	0.76[c]
Cerebrovascular disease	59 (28.8)	3 (18.8)	49 (30.8)	7 (23.3)	0.46[c]
Stroke	34 (16.2)	1 (6.7)	31 (19.0)	2 (6.3)	0.12[c]
Smoking history	137 (64.3)	11 (68.8)	104 (63.0)	22 (68.8)	0.77[c]
Phosphate binder in prior year	174 (81.3)	13 (81.3)	131 (78.9)	30 (93.8)	0.14[c]
Years on PD	1.8 [0.83,2.7]	2.1 [0.84,3.7]	–	1.7 [0.83,2.6]	0.53[b]
Years on HD	2.7 [0.86,5.0]	–	2.8 [1.01,4.8]	1.8 [0.36,8.7]	0.92[b]
Surgery procedure					0.035[c]
CABG	73 (34.1)	9 (56.3)	48 (28.9)	16 (50.0)	
CABG and valve	40 (18.7)	3 (18.8)	31 (18.7)	6 (18.8)	
Valve	101 (47.2)	4 (25.0)	87 (52.4)	10 (31.3)	

Values presented as Median [P25, P75] or N (column %) unless otherwise stated. *p*-Values: b = Kruskal-Wallis test, c = Pearson's chi-square test, d = Fisher's Exact test. BMI, body mass index; PTH, parathyroid related hormone; CABG, coronary artery bypass graft.

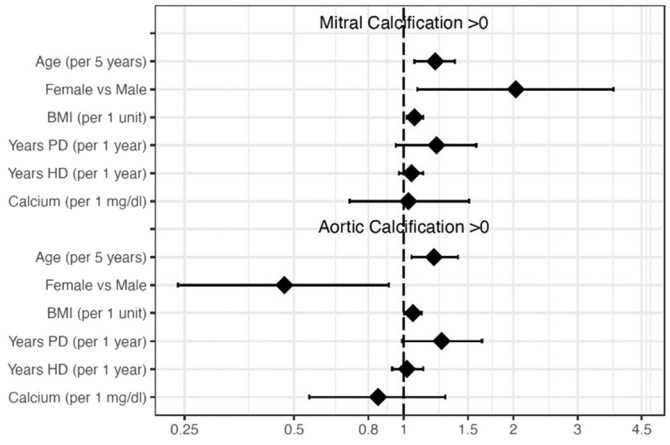

Fig. 2. Adjusted odds ratios for presence of calcification in mitral and aortic strata. PD, peritoneal dialysis; HD, hemodialysis.

aortic calcification (>0) was 60.0 %, 45.2 %, 51.6 % respectively for those in the PD only group, HD only group, and combined PD and HD group ($P = 0.43$).

In the logistic regression model, age and BMI were associated with higher odds of presence of aortic calcification, while female sex was associated with lower odds (Table 4). Cumulative years on PD and cumulative years on HD were not significantly associated with presence of aortic calcification. The odds ratio per 1 year of PD was 1.27 (95 % CI: 0.99, 1.64) and 1.02 per 1 year of HD (95 % CI: 0.93, 1.13). There were 134 of 166 patients in the aortic strata who had phosphorus values and were included in the sensitivity analysis (Fig. 2). The model from the sensitivity analysis that adjusted for calcium phosphorus product produced similar parameter estimates but no variables were significantly associated with presence of aortic calcification.

4. Discussion

Our study investigated whether valvular calcification is worse in one dialysis modality over the other. The results of our study show that the degree of CVC in the aortic and mitral valves did not differ between dialysis modalities based on cumulative dialysis years on either PD or HD, nor did it differ if patients had years on both modalities as opposed to just one modality.

In the general population, the prevalence of CVC is up to five times higher in dialysis patients than in those not on dialysis, ranging between 32 and 47 % in PD patients and 19–84 % in HD patients [11–14]. PD patients are expected to maintain more optimal bone mineral disease profiles. This is due in part to fewer hemodynamic changes and less hyperdynamic circulation, but also because many of these patients retain residual renal function (RRF), and thus the ability to clear small solutes, maintain fluid balance, and control phosphorus levels [15]. To this point, some studies have illustrated an inverse relationship between the maintenance of renal function and decreased vascular/valvular calcification [16,17]. Given this information, it would be expected that PD patients, with their increased residual renal function compared to HD counterparts, might therefore manifest significantly less CVC over years on this modality. However, our findings did not support this hypothesis. When adjusting for covariates in our logistic regression model, we did not see a difference in calcium levels or calcium phosphate product in either the mitral or aortic strata. Rather, our descriptive data surprisingly showed a trend toward higher phosphorus and calcium phosphate product in patients who only received PD as opposed to HD or a combination of HD and PD. Various reasons can account for this unexpected trend. First, PD patients have been shown to have a higher degree of

Table 2
Descriptive statistics by prior PD/HD at surgery (Aortic strata).

Factor	Overall (N = 166)	Prior PD only (N = 20)	Prior HD only (N = 115)	Prior PD and HD (N = 31)	P-value
Age	62.0 [51.0,70.0]	65.5 [56.0,73.5]	62.0 [53.0,71.0]	57.0 [48.0,65.0]	0.019[b]
Gender					0.48[c]
Female	73 (44.0)	10 (50.0)	47 (40.9)	16 (51.6)	
Male	93 (56.0)	10 (50.0)	68 (59.1)	15 (48.4)	
Race					0.77[d]
Asian	1 (0.60)	0 (0.0)	1 (0.87)	0 (0.0)	
Black	60 (36.1)	6 (30.0)	44 (38.3)	10 (32.3)	
Multiracial	5 (3.0)	0 (0.0)	5 (4.3)	0 (0.0)	
White	100 (60.2)	14 (70.0)	65 (56.5)	21 (67.7)	
BMI	27.6 [23.8,30.6]	28.1 [24.0,29.5]	27.7 [24.1,33.1]	27.0 [22.4,29.9]	0.60[b]
Calcium mg/dl	8.9 [8.4,9.4]	8.9 [8.3,9.4]	9.0 [8.4,9.4]	8.8 [8.5,9.5]	0.99[b]
PTH pg/ml	234.0 [126.0,377.2]	332.5 [173.0,514.0]	230.0 [120.0,308.0]	349.6 [124.0,1955.0]	0.30[b]
Phosphorus mg/dl	3.9 [3.1,5.2]	5.3 [4.7,8.1]	3.6 [2.8,4.5]	4.8 [3.8,6.5]	<0.001[b]
Calcium phosphorus product	34.8 [27.0,45.8]	46.8 [41.2,71.2]	32.2 [24.2,39.5]	42.7 [34.7,61.8]	<0.001[b]
Hypertension	151 (91.0)	18 (90.0)	103 (89.6)	30 (96.8)	0.53[d]
Diabetes	108 (65.1)	13 (65.0)	78 (67.8)	17 (54.8)	0.40[c]
Heart failure	120 (72.3)	11 (55.0)	89 (77.4)	20 (64.5)	0.067[c]
Dyslipidemia	139 (83.7)	20 (100.0)	91 (79.1)	28 (90.3)	0.036[c]
Chronic lung disease	67 (40.6)	7 (35.0)	48 (42.1)	12 (38.7)	0.81[c]
Cerebrovascular disease	51 (32.5)	5 (25.0)	38 (34.9)	8 (28.6)	0.61[c]
Stroke	40 (24.7)	3 (15.8)	29 (25.9)	8 (25.8)	0.63[c]
Smoking history	106 (65.8)	14 (73.7)	73 (65.2)	19 (63.3)	0.73[c]
Phosphate binder in prior year	135 (81.3)	17 (85.0)	92 (80.0)	26 (83.9)	0.80[c]
Years on PD	1.6 [0.77,2.8]	2.1 [0.98,4.5]	–	1.10 [0.73,2.5]	0.13[b]
Years on HD	2.5 [0.92,5.1]	–	2.6 [0.97,5.2]	1.7 [0.27,5.0]	0.36[b]
Surgery procedure					0.86[c]
CABG	71 (42.8)	9 (45.0)	47 (40.9)	15 (48.4)	
CABG and valve	41 (24.7)	6 (30.0)	28 (24.3)	7 (22.6)	
Valve	54 (32.5)	5 (25.0)	40 (34.8)	9 (29.0)	

Values presented as Median [P25, P75] or N (column %) unless otherwise stated. p-values: b = Kruskal-Wallis test, c = Pearson's chi-square test, d = Fisher's Exact test. BMI, body mass index; PTH, parathyroid related hormone; CABG, coronary artery bypass graft.

overall phosphorus exposure. For instance, in a study by Evenepoel et al. [18], a validated mathematical model was used to calculate time-averaged-concentration of phosphorus between HD and PD patients rather than relying on a single phosphorus measurement, and noted that PD patients had a higher degree of overall phosphorus exposure. This was attributed to inferior phosphorus clearance in the PD population, and challenged commonly held convictions [18]. Second, the introduction of convective therapies and use of HD membranes with higher efficiency and permeability could optimize phosphate removal compared to the lower efficiency therapy of PD [11]. Third, the loss of RRF has been linked to increased inflammation and calcium phosphate product, contributing to a higher burden of calcification [19]; however, we did not have data regarding the RRF of our patient sample.

Data on the direct comparison of CVC in PD and HD populations is scarce. To our knowledge, only one study directly compared CVC in the two adult populations, reporting a lower prevalence of CVC in PD as opposed to HD patients, which was hypothesized as being due to the presence of RRF contributing to tighter phosphate control and removal of uremic toxins in PD patients [8,11,16,17]. Despite the lack of data on direct CVC comparisons, our study results are in line with much of what has been published when comparing the dialysis populations in CAC. Jansz et al. [20] reported that PD patients did not develop less CAC compared to HD patients, despite the fact that HD patients had a 6-month longer median time on dialysis than their PD counterparts. Kim et al [21] showed similar findings, with no difference in CAC score between PD and HD patients. In contrast, Srivaths et al [22] reported a higher incidence of CAC in patients on HD compared to PD, a finding that was attributed to better control of mineral imbalance; however, this

Table 3
Logistic regression model of presence of mitral calcification.

Model 1 (N = 214)	OR (95%CI)	Model 2 sensitivity analysis (N = 147)	OR (95%CI)
Age (per 5 years)	1.22 (1.07, 1.38)	Age (per 5 years)	1.21 (1.03, 1.41)
Female vs male	2.03 (1.09, 3.76)	Female vs male	1.92 (0.88, 4.19)
BMI (per 1 unit)	1.07 (1.02, 1.13)	BMI (per 1 unit)	1.12 (1.05, 1.20)
Years PD (per 1 year)	1.23 (0.95, 1.58)	Years PD (per 1 year)	1.15 (0.81, 1.63)
Years HD (per 1 year)	1.05 (0.97, 1.13)	Years HD (per 1 year)	1.04 (0.95, 1.14)
Calcium (per 1 mg/dl)	1.03 (0.71, 1.51)	Calcium × phosphorus	1.01 (0.99, 1.04)

Table 4
Logistic regression model of presence of aortic calcification.

Model 1 (N = 166)	OR (95%CI)	Model 2 sensitivity analysis (N = 134)	OR (95%CI)
Age (per 5 years)	1.21 (1.05, 1.41)	Age (per 5 years)	1.21 (1.02, 1.43)
Female vs male	0.47 (0.24, 0.91)	Female vs male	0.44 (0.20, 0.94)
BMI (per 1 unit)	1.06 (1.002, 1.12)	BMI (per 1 unit)	1.07 (1.004, 1.13)
Years PD (per 1 year)	1.27 (0.99, 1.64)	Years PD (per 1 year)	1.12 (0.77, 1.63)
Years HD (per 1 year)	1.02 (0.93, 1.13)	Years HD (per 1 year)	1.03 (0.93, 1.15)

study was carried out on a pediatric population.

Our study showed that age was associated with higher odds of presence of mitral and aortic calcification. This is not surprising as it is well established that the prevalence of CVC increases with age, after years of lipid accumulation, chronic inflammation and endothelial dysfunction [23,24]. While our study showed an association between female sex and increased mitral calcification, several studies have shown a higher prevalence of CVC among males [25]. Some have hypothesized that the sexes differ by way of pathogenesis and extracellular matrix remodeling. Others attribute the difference to hormonal variability such that there is a clear role for androgens in the promotion of calcific nodule and reactive oxygen species formation [26]. In an in-depth review on whether chronic kidney disease modifies vascular calcification risk, heterogeneous conclusions were found such that some large scale studies yielded neutral results with a few noting higher vascular calcification risk in females, similar to our study [27]. Interestingly, our results for the prevalence of mitral and aortic calcification are concordant of those published in patients without ESRD. Repeated studies have demonstrated that men have a greater degree of aortic valve calcification as well as faster rates of calcification progression along the valve leaflets [23,28]. On the other hand, women have shown an enhanced predisposition toward mitral annular calcification compared to men, which was corroborated by our study [29,30]. While the molecular mechanisms have not been distinctly identified, such findings suggest a gender-related pathophysiologic process responsible for calcification at certain sites. Clearly, there are many factors unaccounted for that modulate the deposition of calcium between sexes. Whether dialysis modality has an impact on the accumulation of valvular calcification is unknown and cannot be determined by the results of our study, though there may be insights to be gained from future studies.

Our results require cautious interpretation as the size of our cohorts was small, especially that of the PD population. The number of years on PD was also limited and could have influenced our outcomes. PD patients had higher rates of smoking and diabetes, though not significant, which could have played a role in the progression of valvular calcification. These results also could have been explained by a potentially lower degree of compliance exhibited by peritoneal dialysis patients in the face of more demanding daily regimens [31]. The degree of calcification was analyzed as presence vs. absence because there were not enough patients to stratify their scores into mild, moderate, and severe. Therefore, we opted to focus on the prevalence of CVC. It is also important to note that these patients may have had differing lengths of pre-existing chronic kidney disease, which may have in part contributed to the degree of CVC beyond that of solely the period the patients were on dialysis. Seeing as the patients presented to our institution at different points in their disease process, the length of baseline CKD could not be quantified prior to dialysis commencement. Generalizations to a wider cardiac population (e.g. congenital heart disease, those lacking information of dialysis length) should be made with caution. Last, it is important to note that patients who undergo OHS typically tend to have lower degrees of valvular calcification.

Our study is unique in that there are few studies that directly compared cardiac valvular calcification, rather than coronary artery calcification, in HD and PD populations using CT scoring. Further, both groups were comparable in their baseline characteristics and risk factors, as this study only included dialysis patients who had progressed to the point of requiring cardiothoracic intervention.

5. Conclusion

It appears that the severity of valvular calcification may not be worse in the hemodialysis patient population, and that there may be more factors at play in the progression of valvular calcification in end stage renal disease patients than what was previously thought. Future studies with larger populations should be designed to investigate whether a specific dialysis modality predicts a higher burden of valvular calcification, and whether this leads to worse outcomes after open heart surgery.

Abbreviations

CVC	cardiac valvular calcification
HD	hemodialysis
PD	peritoneal dialysis
OHS	open heart surgery
CAC	coronary artery calcification
CABG	coronary artery bypass graft
ESRD	end stage renal disease

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None.

CRediT authorship contribution statement

Conceptualization: C Kanaan, H Layoun, S Harb, G Nakhoul; Data Curation: C Kanaan, H Layoun, N Kondoleon, R Fadel, S Mirzai; Formal Analysis: S Arrigain, J Schold, H Layoun; Roles/Writing: C Kanaan, H Layoun, S Arrigain, S Harb, G Nakhoul; Manuscript Review: All authors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

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References

[1] S. Genovesi, L. Porcu, M.C. Luise, H. Riva, E. Nava, G. Contaldo, A. Stella, C. Pozzi, P. Ondei, C. Minoretti, M. Gallieni, G. Pontoriero, F. Conte, V. Torri, S. Bertoli, A. Vincenti, Sudden death in end stage renal disease: comparing hemodialysis versus peritoneal dialysis, Blood Purif. 44 (1) (2017).
[2] A.S. Go, G.M. Chertow, D. Fan, C.E. McCulloch, Hsu C. Yuan, Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization, N. Engl. J. Med. 351 (13) (2004).
[3] A.Y.M. Wang, M. Wang, J. Woo, Lam CWK, Li PKT, Lui S. Fai, J.E. Sanderson, Cardiac valve calcification as an important predictor for all-cause mortality and cardiovascular mortality in long-term peritoneal dialysis patients: a prospective study, J Am Soc Nephrol 14 (1) (2003).
[4] M. Ketteler, R. Westenfeld, G. Schlieper, V. Brandenburg, Pathogenesis of vascular calcification in dialysis patients, Clin. Exp. Nephrol. 9 (4) (2005).
[5] S.M. Moe, M. Reslerova, M. Ketteler, K. O'Neill, D. Duan, J. Koczman, R. Westenfeld, W. Jahnen-Dechent, N.X. Chen, Role of calcification inhibitors in the pathogenesis of vascular calcification in chronic kidney disease (CKD), Kidney Int. 67 (6) (2005).
[6] M.G. Vervloet, S. Sezer, Z.A. Massy, L. Johansson, M. Cozzolino, D. Fouque, The role of phosphate in kidney disease, Nat. Rev. Nephrol. 13 (1) (2017).
[7] G.A. Block, T.E. Hulbert-Shearon, N.W. Levin, F.K. Port, Association of serum phosphorus and calcium x phosphate product with mortality risk in chronic hemodialysis patients: a national study, Am. J. Kidney Dis. 31 (4) (1998).
[8] M. Rroji, S. Seferi, M. Cafka, E. Petrela, E. Likaj, M. Barbullushi, N. Thereska, G. Spasovski, Is residual renal function and better phosphate control in peritoneal dialysis an answer for the lower prevalence of valve calcification compared to hemodialysis patients? Int. Urol. Nephrol. 46 (1) (2014).
[9] A.Y.M. Wang, K.N. Lai, The importance of residual renal function in dialysis patients, Kidney Int. 69 (10) (2006).
[10] M. Noordzij, J.C. Korevaar, W.J. Bos, E.W. Boeschoten, F.W. Dekker, P.M. Bossuyt, R.T. Krediet, Mineral metabolism and cardiovascular morbidity and mortality risk: peritoneal dialysis patients compared with haemodialysis patients, Nephrol. Dial. Transplant. 21 (9) (2006).
[11] S. Ribeiro, A. Ramos, A. Brandão, J.R. Rebelo, A. Guerra, C. Resina, A. Vila-Lobos, F. Carvalho, F. Remédio, F. Ribeiro, Cardiac valve calcification in haemodialysis patients: role of calcium-phosphate metabolism, Nephrol. Dial. Transplant. 13 (8) (1998).
[12] A.Y.M. Wang, J. Woo, M. Wang, M.M.M. Sea, R. Ip, P.K.T. Li, Siu Fai Lui, J. E. Sanderson, Association of inflammation and malnutrition with cardiac valve

calcification in continuous ambulatory peritoneal dialysis patients, J Am Soc Nephrol 12 (9) (2001).
[13] J. Huting, Mitral valve calcification as an index of left ventricular dysfunction in patients with end-stage renal disease on peritoneal dialysis, Chest 105 (2) (1994).
[14] A.Y.M. Wang, Vascular and valvular calcification in chronic peritoneal dialysis patients, Int. J. Nephrol. 2011 (2011).
[15] K. Iseri, A.R. Qureshi, J. Ripsweden, O. Heimbürger, P. Barany, I.B. Bergström, P. Stenvinkel, T.B. Brismar, B. Lindholm, Sparing effect of peritoneal dialysis vs hemodialysis on BMD changes and its impact on mortality, J. Bone Miner. Metab. 39 (2) (2021).
[16] J. Perl, J.M. Bargman, The importance of residual kidney function for patients on dialysis: a critical review, Am. J. Kidney Dis. 53 (6) (2009).
[17] A.Y.M. Wang, J. Woo, M. Wang, M.M.M. Sea, J.E. Sanderson, S.F. Lui, P.K.T. Li, Important differentiation of factors that predict outcome in peritoneal dialysis patients with different degrees of residual renal function, Nephrol. Dial. Transplant. 20 (2) (2005).
[18] P. Evenepoel, B.K.I. Meijers, B. Bammens, L. Viaene, K. Claes, B. Sprangers, M. Naesens, T. Hoekstra, G. Schlieper, D. Vanderschueren, D. Kuypers, Phosphorus metabolism in peritoneal dialysis- and haemodialysis-treated patients, Nephrol. Dial. Transplant. 31 (9) (2016).
[19] A.Y.M. Wang, C.W.K. Lam, M. Wang, I.H.S. Chan, S.F. Lui, J.E. Sanderson, Is valvular calcification a part of the missing link between residual kidney function and cardiac hypertrophy in peritoneal dialysis patients? Clin. J. Am. Soc. Nephrol. 4 (10) (2009).
[20] T.T. Jansz, F.E. Van Reekum, A. Özyilmaz, P.A. De Jong, F.T.J. Boereboom, T. Hoekstra, M.C. Verhaar, B.C. Van Jaarsveld, Coronary artery calcification in hemodialysis and peritoneal dialysis, Am. J. Nephrol. 48 (5) (2018).
[21] C.D. Kim, J.H. Cho, H.J. Choi, M.H. Jang, H.M. Kwon, J.C. Kim, S.H. Park, J. M. Lee, D.K. Cho, Y.L. Kim, Coronary-artery calcium scores using electron beam CT in patients with chronic renal failure, J. Korean Med. Sci. 20 (6) (2005).
[22] P. Srivaths, R. Krishnamurthy, L. Brunner, B. Logan, M. Bennett, Q. Ma, R. VanDeVoorde, S.L. Goldstein, Cardiac calcifications are more prevalent in children receiving hemodialysis than peritoneal dialysis, Clin. Nephrol. 81 (4) (2014).
[23] V.I. Summerhill, D. Moschetta, A.N. Orekhov, P. Poggio, V.A. Myasoedova, Sex-specific features of calcific aortic valve disease, Int. J. Mol. Sci. 21 (16) (2020).
[24] B.F. Stewart, D. Siscovick, B.K. Lind, J.M. Gardin, J.S. Gottdiener, V.E. Smith, D. W. Kitzman, C.M. Otto, Clinical factors associated with calcific aortic valve disease, J. Am. Coll. Cardiol. 29 (3) (1997).
[25] A.M. Porras, C.M. McCoy, K.S. Masters, Calcific aortic valve disease: a Battle of the sexes, Circ. Res. 120 (4) (2017).
[26] A.Z. Chignalia, M.A. Oliveira, V. Debbas, R.O. Dull, F.R.M. Laurindo, R.M. Touyz, M.H.C. Carvalho, Z.B. Fortes, R.C. Tostes, Testosterone induces leucocyte migration by NADPH oxidase-driven ROS- and COX2-dependent mechanisms, Clin. Sci. 129 (1) (2015).
[27] P.Y. Wu, S.Y. Lee, K.V. Chang, Chao C. Ter, J.W. Huang, Gender-related differences in chronic kidney disease-associated vascular calcification risk and potential risk mediators: a scoping review, Healthc 9 (8) (2021).
[28] F.E.C.M. Peeters, M.K. Doris, T.R.G. Cartlidge, J. Kwiecinski, T.A. Pawade, W.S. A. Jenkins, B.L.J.H. Kietselaer, H.J.G.M. Crijns, D.E. Newby, M.R. Dweck, Sex differences in valve-calcification activity and calcification progression in aortic stenosis, JACC Cardiovasc. Imaging 13 (9) (2020) 2045–2046.
[29] S. Elmariah, M.J. Budoff, J.A.C. Delaney, Y. Hamirani, J. Eng, V. Fuster, R. A. Kronmal, J.L. Halperin, K.D. O'Brien, Risk factors associated with the incidence and progression of mitral annulus calcification: the multi-ethnic study of atherosclerosis, Am. Heart J. 166 (5) (2013) 904.
[30] A. Boon, E. Cheriex, J. Lodder, F. Kessels, Cardiac valve calcification: characteristics of patients with calcification of the mitral annulus or aortic valve, Heart 78 (5) (1997) 472–474.
[31] K. Griva, A.Y. Lai, H.A. Lim, Z. Yu, M.W.Y. Foo, S.P. Newman, Non-adherence in patients on peritoneal dialysis: a systematic review, PLoS One 9 (2) (2014).