J Exp Clin Med 2011;3(2):89–92

Contents lists available at ScienceDirect

Journal of Experimental and Clinical Medicine

journal homepage: http://www.jecm-online.com

ORIGINAL ARTICLE

Comparison of Coronary Artery Calcification in Peritoneal and Hemodialysis Patients

Chi-Ming Lee [1,2*], Pzen-Wen Chen [3], Ting-Kai Leung [1,2], Hung-Jung Wang [1], Ching-Huei Kung [1], Yi-Hsiang Lin [1], Wen-Tien Hsiao [1], Ya-Yen Chen [1]

[1] Department of Diagnostic Radiology, Taipei Medical University Hospital, Taipei, Taiwan
[2] Department of Medicine, Taipei Medical University, Taipei, Taiwan
[3] Department of Nephrology, Taipei Medical University Hospital, Taipei, Taiwan

ARTICLE INFO

Article history:
Received: Dec 21, 2009
Revised: May 28, 2010
Accepted: Dec 30, 2010

KEY WORDS:
64-MDCT;
coronary artery calcification;
hemodialysis;
peritoneal dialysis

Background/Purpose: Cardiovascular disease accounts for more than 50% of deaths among patients with end-stage renal disease, and numerous factors have been proposed that may contribute to this increased risk of death. Coronary artery calcification has been recognized as one of the important risk factors for cardiovascular disease in patients undergoing dialysis. The aim of this study was to compare the coronary artery calcification score (CACS) in peritoneal dialysis (PD) and hemodialysis (HD) patients, and to assess the effect of dialysis during a 12-month period.
Methods: Multidetector computed tomography was performed in 33 chronic dialysis patients (15 PD and 18 HD patients; mean age, 54 years) at Months 1, 6, and 12 during the study period. Blood samples were collected from each patient monthly to measure the serum levels of calcium and phosphorus.
Results: The CACSs were significantly increased at Month 12 versus Month 1 in both PD and HD patients ($p < 0.05$), and no significant differences were found between the two groups ($p = 0.09$). However, the CACS increased during the first half of the study period and then decreased significantly in the second half of the study period. Levels of serum calcium increased during the study period in both the PD and HD groups ($p < 0.05$), but serum phosphorus levels increased only in the HD group ($p < 0.05$). No significant relationship was found between the CACS and calcium–phosphorus product in either group.
Conclusions: Our data suggest that the increase in CACS is not different between the PD and HD patients. Furthermore, the decrease in CACS between Months 7 and 12 suggests that there could be a factor other than the level of the calcium–phosphorus product that accounts for the variation in CACS in both groups.

1. Introduction

Cardiovascular disease accounts for more than 50% of deaths among patients with end-stage renal disease (ESRD),[1] and numerous factors have been proposed that may contribute to this increased risk of death.[2] The coronary artery calcification score (CACS) is considered an index of the severity of atherosclerotic vascular disease, and it has been shown to be associated with cardiovascular events in individuals who have normal renal function.[3–5] However, although a significantly elevated CACS is common and associated with cardiovascular disease in ESRD patients,[6] the predictive value of the CACS in ESRD patients is still under debate.[7] Many studies have shown a correlation between CACS and various laboratory values, such as serum calcium, phosphorus, and the calcium–phosphorus product. Serum phosphorus levels tend to differ between patients undergoing hemodialysis (HD) and peritoneal dialysis (PD). Kim et al[8] reported that CACSs in PD patients are higher than those in HD patients. However, according to our literature review, the differences in CACS between PD and HD patients and the relationship between CACS and other cardiac-related diseases are still multivariate.[9–12] We have undertaken a study to compare CACS and serum calcium and phosphorus levels among patients using these two dialysis methods and to assess the effect of the two types of dialysis treatments on the annual rate of increase in CACS.

2. Subjects and Methods

2.1. Patients

All 46 patients who underwent dialysis from March 2003 to April 2004 in the Dialysis Unit of Taipei Medical University Hospital were initially included in the study. We excluded five patients with severe illnesses, such as liver cirrhosis ($n = 3$), congestive heart failure ($n = 1$), and apparent acute inflammatory symptoms ($n = 1$).

* Corresponding author. Department of Diagnostic Radiology, Taipei Medical University Hospital, 252 Wu Hsing St, Taipei 110, Taiwan.
E-mail: yayen0220@yahoo.com.tw (C.-M. Lee).

1878-3317/$ – see front matter
doi:10.1016/j.jecm.2010.12.012

In addition, five patients dropped out of the study, and three patients died from sepsis and were excluded from the analysis. Thus, a total of 33 maintenance dialysis patients (16 men and 17 women) were included in the study and statistical analysis. Of the 33 patients, 15 underwent PD and 18 underwent HD. The underlying diseases in the patients were Type 2 diabetes mellitus in 21 patients (14 PD and 7 HD), chronic glomerulopathy without Type 2 diabetes mellitus in 10, and uric acid nephropathy in two patients. Eight patients had been treated with phosphate binders (4 in each dialysis group). Five patients (2 HD and 3 PD) received oral calcium or vitamin D supplements during the study. HD patients received dialysis three times per week (dialysis duration: 4 hours) using hollow-fiber dialyzers, such as cellulose triacetate and polysulfone. PD patients were dialyzed (Tenckhoff catheter; Quinton Inc., Seattle, WA) using the Baxter Twin Bag (1500–2500 mL/time, 3–5 times/d, depending on body size) and Baxter Home Choice system (5000–12,000 mL). Each patient gave written informed consent to participate in the study, which was approved by the Institutional Review Board of our hospital.

2.2. Methods

Blood samples were collected in the morning after an overnight fast of at least 12 hours before starting a dialysis session. Calcium (Ca) and phosphorous (P) levels were measured every month during the 1-year study period.

2.3. Assessment of calcium score by 64-row multidetector computed tomography scan

We obtained images at Months 1, 6, and 12 of the study period. All computed tomography (CT) scans were performed using a 64-row multidetector CT (64-MDCT) scanner with a 0.35-second rotation time (Volume Computed Tomography Light Speed CT/I; GE Medical Systems, Milwaukee, WI, USA). The region scanned was from 1 cm below the carina to the apex of the heart. Prospective electrocardiogram (ECG) gating was applied to reduce motion artifacts. All pixels with density greater than 130 Hounsfield units were highlighted in color on the images. The radiologist assigned one of four locations to each calcified plaque: left main artery, left anterior descending artery, left circumflex artery, and right coronary artery. The sum of the scores for each plaque was determined by a single radiologist.

2.4. Statistical analysis

In this study, the data were not normally distributed; therefore, continuous variables were presented as the median (interquartile range), and categorical variables were expressed as number (percentage). For baseline comparisons, the Mann–Whitney *U* test was used to assess differences in age, duration of dialysis, and body mass index between the two groups; for differences in sex, hypertension, diabetes, and smoking and drinking habits, the χ^2 test or Fisher's exact test was used. The differences in CACS and the percent annual changes were measured over a 1-year period to control for a baseline imbalance with respect to the overall duration of dialysis in the two groups using the Friedman test. The percent annual change in CACS was calculated using the formula ([CACS at the 12^{th} month − CACS at the first month]/[CACS at the first month]) × 100, and the Wilcoxon signed-rank test with a Bonferroni-adjusted alpha level, which equaled the former alpha level divided by the number of tests, was used to evaluate whether the variation in CACS for each group was significant. All statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC, USA). Statistical significance was defined as a p value less than 0.05.

3. Results

The baseline characteristics of the 33 subjects are summarized in Table 1. The median ages of the PD and HD patients were 53 years (range, 46–69 years) and 57 years (range, 35–77 years), respectively. The median durations of dialysis of the PD and HD patients were 2 years (range, 0.4–8 years) and 4 years (range, 1–25 years), respectively ($p = 0.04$). However, there were no significant differences in sex, hypertension, diabetes, smoking and drinking habits, lipid profiles, and creatinine levels between the two groups.

To evaluate the difference in CACS between the two groups, the scores were compared over 1 year (Table 2). The CACS increased significantly during the study period in both PD patients (median, 49%; range, 13.0–1665.9%; $p = 0.01$) and HD patients (median,

Table 1 Baseline characteristics in peritoneal dialysis and hemodialysis patients

	Total ($n = 33$)	Peritoneal dialysis ($n = 15$)	Hemodialysis ($n = 18$)	p
Age (yr)	54.0 (11)	53.0 (6)	57.0 (16.5)	NS
Dialysis duration (yr)	3.0 (5.5)	2.0 (2.875)	4.0 (9.125)	<0.05
Body mass index (kg/m^2)	22.6 (3)	22.0 (2.35)	23.0 (2.875)	NS
Males	17 (51.5)	6 (40.0)	11 (61.1)	NS
Cardiac catheter intervention	3 (9.1)	1 (6.7)	2 (1.1)	NS
Cardiac vascular disease family history	21 (63.6)	11 (73.3)	10 (55.6)	NS
Smoking	7 (24.2)	2 (13.3)	5 (29.4)	NS
Drinking	3 (9.1)	0 (0.0)	3 (16.7)	NS
Hypertension	17 (51.5)	9 (60.0)	8 (44.4)	NS
Diabetes	9 (27.3)	5 (33.3)	4 (22.2)	NS
Serum parameters				
Calcium	7.0 (1)	7.0 (0)	6.0 (2)	NS
Phosphorus	6.0 (0)	6.0 (1)	6.0 (0)	NS
Total cholesterol (mg/dL)	213.8 ± 35.7	212.7 ± 34.0	215.2 ± 38.4	NS
Triglyceride (mg/dL)	209.5 ± 21.0	208.9 ± 15.6	209.7 ± 22.5	NS
LDL (mg/dL)	130.2 ± 33.4	128.4 ± 39.4	131.5 ± 36.0	NS
HDL (mg/dL)	49.5 ± 12.0	49.5 ± 12.4	49.6 ± 11.7	NS
Albumin (g/dL)	3.1 ± 1.0	3.1 ± 1.2	3.2 ± 0.8	NS
PTH (pg/mL)	320.0 ± 4.1	323.4 ± 4.4	316.6 ± 3.6	NS
ALP (IU/L)	83.3 ± 2.2	82.8 ± 1.9	83.6 ± 2.8	NS
Creatinine (mg/dL)	9.3 ± 2.6	9.6 ± 2.4	8.9 ± 2.7	NS

Data are presented as n (%), median (interquartile range), or mean ± standard deviation.
NS = not significant; LDL = low-density lipoprotein; HDL = high-density lipoprotein; PTH = parathyroid hormone; ALP = alkaline phosphatase.

Table 2 Coronary artery calcification score of the dialysis patients within 1-year follow-up

	Total ($n = 33$)	Peritoneal dialysis ($n = 15$)	Hemodialysis ($n = 18$)	p
	Median (IQR)	Median (IQR)	Median (IQR)	
1 mo	72.0 (468)	3.0 (823.5)	109.5 (432.75)	NS
6 mo	401.5* (623)	645.5* (1083)	329.5* (491.5)	NS
12 mo	170.0*,† (1032)	76.0*,† (1385.5)	174.5*,† (542.5)	NS
Annual percent change (%)	79.1 (41.5)	49.0 (34.7)	80.4 (40.6)	NS

* Significantly different between the present time point and the first month, $p < 0.0167$; † Significantly different between the present time point and the sixth month, $p < 0.0167$.
IQR = interquartile range; NS = not significant.

80.4%; range, 11.9–1490.0%; $p < 0.001$). However, a significant decrease in CACS was found between 6 and 12 months in both groups ($p < 0.0167$). No statistically significant difference was found in the CACS at the 1-, 6-, or 12-month evaluations, or in the increase over the 1-year period between PD and HD patients (all, $p > 0.05$).

To determine the factors associated with the increased CACS, variations in the levels of serum Ca and P were analyzed. The level of serum Ca increased significantly in the PD and HD patients during the study period ($p < 0.05$, Table 3). However, the level of serum P increased significantly in HD patients only ($p < 0.05$, Table 3). There were no significant differences in the levels of Ca or P between the PD and HD groups for a given measurement.

For further analysis, Pearson's correlation coefficient between the Ca–P product and the CACS was calculated (Figure 1). Despite the nonsignificant correlations (PD group: $\gamma = 0.77$, $p = 0.44$; HD group: $\gamma = 0.74$, $p = 0.47$), the variation of the Ca–P product was almost parallel to the variation of the CACS for both the PD and the HD groups during the first 6 months. Between 6 and 12 months, the CACS decreased in both groups, although the Ca–P product continued to increase.

In addition, there were no significant differences in lipid profile (total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein); albumin; parathyroid hormone (PTH); alkaline phosphatase (ALP); or creatinine levels between the two groups (all, $p > 0.05$, data not shown).

4. Discussion

Patients on dialysis have an annual cardiovascular mortality rate significantly higher than that of the general population.[9] As many as one-third of the dialysis patients admitted to the hospital suffer from cardiovascular disease, and most of the dialysis patients die from cardiovascular complications.[10,11] Renal failure patients on dialysis are at increased risk of developing calcifications of the coronary arteries, which may contribute to the increased cardiovascular mortality observed in this population.[12] Thus, many researchers have explored the relationship between the CACS and coronary artery disease in dialysis patients, and correlations of CACS with abnormal coronary angiography, number of diseased vessels, and atherosclerosis have been reported.[13–15]

Electron-beam computed tomography scanning has been used for more than 10 years and is considered the gold standard for the determination of CACS.[16] However, electron-beam computed tomography is not readily available in every hospital.[8] We used a new noninvasive approach, 64-MDCT, for the assessment of coronary calcifications.[17] This method provides noninvasive imaging, complete coverage of the heart, and enables ECG-gated scanning to decrease major motion artifacts. Moreover, 64-MDCT readily depicts the proximal course of the coronary arteries and enables the assessment of the luminal diameter.[18]

The high CACSs in the dialysis patients found in our investigation are consistent with those of previous studies.[19–21] Although the CACS increased significantly in all patients between the beginning and end of the study, we observed no significant difference in CACS between the two dialysis methods at any time point. A previous study[8] determined CACSs in PD and HD patients and reported a score of 211.8 ± 325.5 in HD patients and 655.7 ± 1009.8 in PD patients. Although the score was higher in the PD group, the difference was not statistically significant. Block et al[22] have discussed that a decrease in renal clearance leads to hyperparathyroidism, which can lead to calcifications of internal organs by increasing the Ca–P product. Indeed, some studies have found a significant correlation between coronary artery calcification and Ca–P balance.[6] However, other researchers have found no relationship of the CACS with the Ca–P product.[23]

Both Ca and P levels increased throughout the study period in HD patients, but only Ca levels increased in PD patients. Thus, our data suggest that the Ca level might be related to the increasing CACS in PD patients, although both Ca and P levels may be related to

Table 3 Serum levels of calcium and phosphorus of peritoneal dialysis and hemodialysis patients within 1-year follow-up

	Total ($n = 33$)	Peritoneal dialysis ($n = 15$)	Hemodialysis ($n = 18$)	p
	Median (IQR)	Median (IQR)	Median (IQR)	
Calcium				
1 mo	7.0 (1)	7.0 (0)	6.0 (2)	NS
6 mo	7.0* (1)	8.0* (1)	7.0* (0.8)	NS
12 mo	8.0*,† (2)	10.0*,† (0)	8.0*,† (0)	NS
Annual percent change (%)	38.6 (32.1)	44.9 (25.0)	33.6 (39.0)	NS
Phosphorus				
1 mo	6.0 (0)	6.0 (1)	6.0 (0)	NS
6 mo	7.0 (1)	6.0 (1)	7.0* (1)	NS
12 mo	7.0* (1)	6.0 (1)	7.0*,† (1)	NS
Annual percent change (%)	12.7 (16.7)	4.9 (16.7)	19.3 (14.3)	NS

* Significantly different between the present time point and the first month, $p < 0.0167$; † Significantly different between the present time point and the sixth month, $p < 0.0167$.
IQR = interquartile range; NS = not significant.

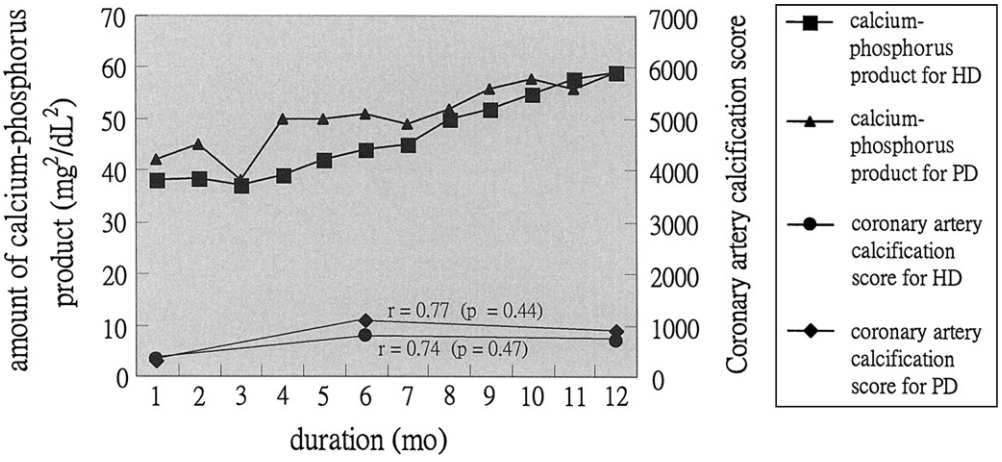

Figure 1 Variations in coronary artery calcification score and levels of serum calcium−phosphorus product during 1 year. HD = hemodialysis; PD = peritoneal dialysis.

the increasing CACS in HD patients. The Ca−P product was not significantly correlated with the CACS.

Our data do not provide an explanation for the decrease in CACS between Months 7 and 12. The high variation between individuals may have contributed to this finding. Alternatively, there could be another factor, rather than the Ca−P product, that accounts for the variation of CACS in both groups.

No significant differences were observed in the levels of several other analytes that might account for the changes in CACS, including lipid profile and creatinine, which could act as a marker of renal function. Although the duration of dialysis was significantly different between the two groups, there was no significant difference between the groups in renal function (creatinine level) or CACS (either absolute value or % change). Therefore, we hypothesize that the difference in duration of dialysis may not be the only factor influencing the increase in CACS in this study, and the effect of duration of dialysis on the CACS is multifactorial and requires further study.

This study is limited by the small number of patients and by the fact that some inflammatory markers, such as transforming growth factor beta and other cytokines, are not routinely studied in our institution and could not be included in this analysis. Future studies involving a greater number of patients and measuring additional factors, such as systemic inflammatory markers and protein intake, should be carried out to understand the differences in CACS between PD and HD patients.

References

1. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis* 1998;**32**:S112−9.
2. Oda H, Keane WF. Lipid abnormalities in end-stage renal disease. *Nephrol Dial Transplant* 1998;**13**:45−9.
3. Raggi P, Callister TQ, Cooil B, He ZX, Lippolis NJ, Russo DJ. Identification of patients at increased risk of first unheralded acute myocardial infarction by electron beam computed tomography. *Circulation* 2000;**101**:850−5.
4. Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD. Prediction of coronary events with electron beam computed tomography. *J Am Coll Cardiol* 2000;**36**: 1253−60.
5. Wong ND, Hsu JC, Detrano RC, Diamond G, Eisenberg HJ, Gardin JM. Coronary artery calcium evaluation by electron beam computed tomography and its relation to new cardiovascular events. *Am J Cardiol* 2000;**86**:495−8.
6. Raggi P, Boulay A, Chasan-Taber S, Amin N, Dillon M, Burke SK, Chertow GM. Cardiac calcification in adult hemodialysis patients. A link between end-stage renal disease and cardiovascular disease? *J Am Coll Cardiol* 2002;**39**:695−701.
7. Fujimoto N, Iseki K, Tokuyama K, Tamashiro M, Takishita S. Significance of coronary artery calcification score (CACS) for the detection of coronary artery disease (CAD) in chronic dialysis patients. *Clin Chim Acta* 2006;**367**:98−102.
8. Kim CD, Cho JH, Choi HJ, Jang MH. Coronary artery calcium scores using electron beam CT in patients with chronic renal failure. *J Korean Med Sci* 2005;**20**: 994−9.
9. Collins AJ, Hao W, Xia H, Ebben JP, Everson SE. Mortality risks of peritoneal dialysis and hemodialysis. *Am J Kidney Dis* 1999;**34**:1065−74.
10. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE. Hypoalbuminemia, cardiac morbidity, and mortality in end-stage renal disease. *J Am Soc Nephrol* 1996;**7**:728−36.
11. Lindner A, Charra B, Sherrard DJ, Scribner BH. Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med* 1974;**290**:697−701.
12. Ribeiro S, Ramos A, Brandao A, Rebelo JR. Cardiac valve calcification in hemodialysis patients: role of calcium-phosphate metabolism. *Nephrol Dial Transplant* 1998;**13**:2037−40.
13. Haydar AA, Hujairi NM, Covic AA, Pereira D, Rubens M, Goldsmith DJ. Coronary artery calcification is related to coronary atherosclerosis in chronic renal disease patients: a study comparing EBCT-generated coronary artery calcium scores and coronary angiography. *Nephrol Dial Transplant* 2004;**19**:2307−12.
14. Yildiz A, Tepe S, Oflaz H, Yazici H, Pusuroglu H, Besler M. Carotid atherosclerosis is a predictor of coronary calcification in chronic haemodialysis patients. *Nephrol Dial Transplant* 2004;**19**:885−91.
15. Krasniak A, Drozdz M, Pasowicz M, Chmiel G, Michalek M, Szumilak D. Factors involved in vascular calcification and atherosclerosis in maintenance haemodialysis patients. *Nephrol Dial Transplant* 2007;**22**:515−21.
16. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990;**15**:827−32.
17. Thilo C, Standl E, Knez A, Reiser M, Steinbeck G, Haberl R. Coronary calcification in long term type 1 diabetic patients—a study with multislice spiral computed tomography. *Exp Clin Endocrinol Diabetes* 2004;**112**:561−5.
18. Karaca M, Kirimaz A. The value of 64-slice computed tomography in a patient with an anomalous and atherosclerotic coronary artery. *Int J Cardiovasc Imaging* 2006;**25**:15−8.
19. U.S. Renal Data System. *USRDS 1992 Annual Data Report*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 1992.
20. Sesso R, Belasco AG. Late diagnosis of chronic renal failure and mortality on maintenance dialysis. *Nephrol Dial Transplant* 1996;**11**:2417−20.
21. Goodman WG, Goldin J, Kuizon BD. Coronary artery calcification in young adults with end-stage renal disease who are undergoing dialysis. *N Engl J Med* 2000;**342**:1478−83.
22. Block GA, Hullbert-Shearon TE, Levin NW, Port FK. Association of serum phosphorus and calcium × phosphate product with mortality risk in chronic hemodialysis patients: a national study. *Am J Kidney Dis* 1998;**31**:607−17.
23. Nitta K, Akiba T, Suzuki K, Uchida K, Ogawa T, Majima K. Assessment of coronary artery calcification in hemodialysis patients using multi-detector spiral CT scan. *Hypertens Res* 2004;**27**:527−33.