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Original Research Article

Prevalence of carotid artery calcification on the panoramic radiographs of turkish hemodialysis patients and its relationship with traditional atherogenic risk factors: a research article

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Abstract

The aim of this retrospective study is to determine the presence of carotid artery calcifications (CAC) detected on panoramic radiographs in hemodialysis patients and relationship between and traditional risk factors evaluated. This study was designed as a retrospective study evaluating totally 143 patients (92 hemodialysis, 51 controlsubjects) who presented to, the department of Oral and Maxillofacial Radiology for routine examination. The subjects were assessed for the presence of traditional risk factors and the possible association to CAC. Statistical analysis was done using Chi-square test. P<0.05 was considered to be statistically significant. Carotid artery calcification (CAC) was observed in 28 (30.4%) of 92 patients in hemodialysis group and 6 (11.8%) of 51 patients in the control group (*P*=0.012). Diabetes, hypertension, hyperlipidemia, age, parathyroidectomy, and longer hemodialysis duration were significantly (*P*<0.05) related to the presence of CAC while gender, and smoking were not significantly (*P*>0.05) related to CAC. No statistically significant differences were observed between males and females (*P*=0.07). The prevalence of CAC is higher in hemodialysis patients compared to general population. The increased age, type 2 diabetes, hypertension, hyperlipidemia, and parathyroidectomy are associated with a high CAC prevalence.

Keywords: Carotid artery calcification, hemodialysis, panoramic radiography, traditional risk factors

INTRODUCTION

Atherosclerosis is a disease of the large and medium caliber arteries characterized by the deposition of lipids and inflammatory cells (atheroma plaque) on its wall. Chronic kidney disease (CKD) is associated with increased incidence of accelerated atherosclerosis, coronary artery disease, stroke and peripheral artery disease. The most important cause of mortality in CKD is cardiovascular disease (Jaradad and Molitoris, 2002). Besides traditional risk factors (smoking, hypertension, hyperlipidemia, diabetesmellitus, obesity, family history of cardiovascular disease etc.), CKD specific factors including anemia, hyperphosphatemia, abnormal mineral metabolism, hypervolemia, uremic toxins and vascular calcification also play an important role in CKD (Chen and Moe, 2012).

Vascular calcification (VC) is an important complication of CKD (Ketteler and Biggar, 2009). VC is frequently observed and is an important determinant of

Figure 1A. Postero-anteriorchest X-ray

Figure 1B. Foot-anklegraphy

cardiovascular morbidity and mortality in hemodialysis patients (Chen and Moe, 2012). VC is not simply calcification of vessel wall and is an active process, which shows inflammatory features such as atherosclerosis (Hruska et al.,2009). Basically VC is resulted from the impairment of the balance between the inhibitors and activators of calcification (Ketteler and Biggar, 2009). The known risk factors for VC include an advanced age, duration of dialysis, vitamin D therapy, hyperpara-thyroidism and multiplication of increased calcium x phosphorus product. VC is often seen in the coronary arteries thoracic and abdominal aorta, common carotid arteries and lower extremities. Cardiac computed tomography is the major method for identification of the calcification of aorta and cardiac valves, but it has challenging aspects because it is difficult to access it and due to the need for equipment. Various non-invasive radiological methods (postero-anterior chest X-ray (Figure 1A), foot-ankle graphy (Figure 1B), hand-wrist graphy, upper extremity long bone graphies (Figure 1C), femur (Figure 1D), pelvic graphies (Figure 1E) and knee graphy (Figure 1F), as well as lateral lumbar vertebral graphy etc.) can show VC and guide the clinicians for further investigations (Karohl et al., 2009).

Carotid artery calcification (CAC) may be an indicator of coronary artery calcification and CAC monitored on the panoramic radiograph is a strong marker of cardiovascular and cerebro vascular events in the future (Ralph et al., 2011 ; Alves et al., 2014). In Turkey, about 37.000 deaths in 2014 year are reported to be caused by cerebrovascular events (Turkish Statistical Institute). CAC is commonly seen in the carotid bifurcation region and is the main cause of stroke. CAC is monitored as an irregular, circular and heterogeneous nodular opacity within the soft tissue in the paravertebral area between the cervical 3 (C3) and cervical 4 (C4) vertebrae (Alves

Figure 1C. Hand-wristgraphy

Figure 1D. Femurgraphy

Figure 1E. Pelvicradiography

Figure 1F. Kneegraphy

Figure 1. Radiographs and vascularcalcification of hemodialysis patient

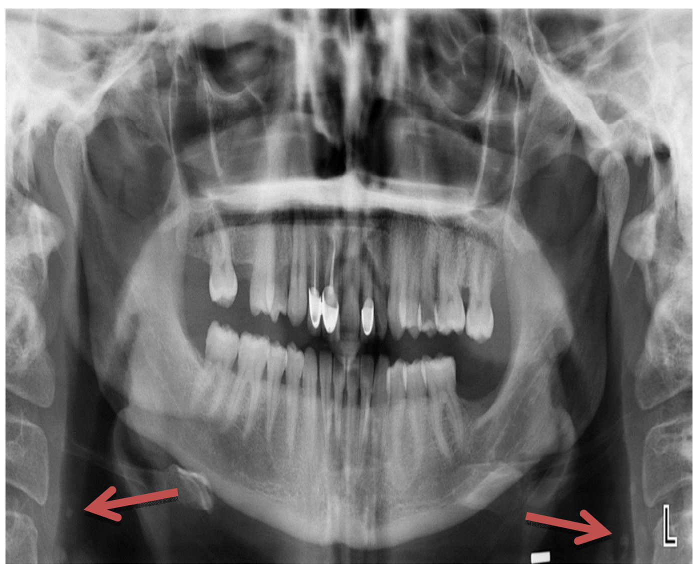

Figure 2. Panoramicradiographyshowingcarotidarterycalcification

et al., 2014). CAC may be observed as unilateral or bilateral (Figure 2).

Panoramic radiographs (PRs), which is the main imaging modality in dental examination can give information about the dental and paradental tissues as well as about the pathologies of bones, vessels and soft tissues that are involved in the visualization area. Although the primary goal of PRs is not to show CAC, in recent years many studies have shown CAC on PRs in general population (Pornprasertsuk-Damrongsri and Thanakun, 2006) and patients with type 2 diabetes (Friedlander et al., 2002), hemodialysis and kidney transplantation (Kansu et al., 2005), obstructive sleep apnea syndrome (Friedlander et al., 1999), and metabolic syndrome (Pornprasertsuk Damrongsri et al., 2009). The objective of this study was to determine the incidence of CAC on PRs in Turkish hemodialysis patients and evaluate the association of CAC with duration of hemodialysis and traditional risk factors.

MATERIAL AND METHODS

This study was designed as a retrospective, single center study evaluating hemodialysis patients who presented to Akdeniz University, Faculty of Dentistry, the Department of Oral and Maxillofacial Radiology for routine examination between January 2013 and March 2016. A total of 143 patients (70 male, 73 female, 49% - 51%) with 92 being hemodialysis (HD) patients receiving hemodialysis therapy of four hours for three times a week in different hemodialysis centers (40 male, 52 female, 43.5% - 56.5%) and 51 control subjects who presented for routine dental examination (21 female, 30 male, 41.2% - 58.8%) were included in the study. The mean duration of dialysis was 66.2 ± 24.3 months (minimum 4, maximum 148) in HD patients.

Demographic data were obtained through the patient files. The body mass index (BMI) was calculated as weight/height^2 (kg/m^2). All patients medical records were reviewed for traditional atherogenic risk factors: hypertension, diabetes, hyperlipidemia, BMI, smoking and history of family cardiovascular disease. The control group consists of subjects free of systemic disease and chronic kidney disease. Patients with a PRs of poor quality for evaluation and whom C3 and C4 vertebrae were not included in the visualization area were excluded from the study. In addition, patients with previous maxillofacial and neck surgery, stenting and carotid artery endarterectomy and those with a history of cerebrovascular disease were also excluded.

All PRs were taken with PLANMECA, OY 00880 *(Helsinki, Finland)* device. PRs were taken by giving an appropriate dose of radiation in the patients standing with the cervical vertebrae in the vertical position as much as possible. Depending on the subject's jaw size the unit's operation ranged between 8-10 mA and 65-80 kVp. Kodak T-Mat G panoramic film with Kodak Lanex Medium intensifying screen *(Eastman Kodak Co.,NY)* was used and were processed accordng to the manufacturer's recommendations using an automatic processor *(Velopex Extra-X; Medivance Instruments Limited, United Kingdom).* All PRs were analysed in subdued ambient dimlight using transmitted light from a standard view box.

CAC was evaluated on PRs as monitoring of the heterogeneous radiopaque opacity so as to evaluate both CAC within the soft tissue in C3 and C4 inter vertebral space (Figures 2). The PRs were evaluated for the presence (unilateral/bilateral) or absence of CAC. To determine the presence and location of calcification, patients with all CACs were also reevaluated by colour doppler ultrasonography.

All PRs were evaluated by two oral and maxillofacial radiology specialists who were not aware of the patients receiving hemodialysis with 2-week intervals for the presence of CAC. If the two expert agreed, a positive carotid artey calcifications was accepted. The study was approved by the local ethics committee. The study was performed in accordance with the Helsinki Declaration ethical principles.

Laboratory analyses

Venous blood samples for biochemical analyzes were taken 12 hours after fasting and before mid-week hemodialysis session. Measurements of height (m), weight (kg) and blood pressure of all patients were achieved. The BMI was calculated as weight/ height^2 (kg/m^2). To determine the adequacy of the hemodialysis Kt/V (Daugirdas formula SPKt/V = -Ln (R-0.008×t) + (4+3.5R) UF) and urea reduction ratio (URR) = (urea pre-dialysis - urea post-dialysis)/ urea pre-dialysis x100) was used. In laboratory analyzes, fasting blood glucose (FBG), blood urea nitrogen, creatinine, albumin, calcium, phosphorus (PO4), intact parathyroid hormone (PTH), ferritin, alkaline phosphatase, triglyceride, total cholesterol (LDL-C), high density cholesterol (HDL-C), C-reactive protein (CRP) and uric acid levels were measured. The low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald method (LDL = TChol-HDL-TG / 5.0 [mg / dL]).

Patients with a BMI of 25-29.9 were considered over weight, those with a BMI of >30 were considered as obese and >35 morbidly obese. Diabetes mellitus was defined as a patient who takes oral antidiabetics and/or insülin or a patient with glucose higher 126 mg/dL. Hypertension was defined as a patient who takes antihypertensive drug or a patient with a predialysis stage systolic blood pressure higher than 140 mmHg and/or a diastolic blood pressure higher than 90 mmHg. Hyperlipidemia was defined as a patient who takes antihyperlipidemic drug or a patient with total cholesterol higher 200 mg/dL and/or LDL- cholesterol>130 mg/dL and/or triglyceride>150 mg/dL.

Statistical method

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences; 21.0, SPSS Company, Illinois, USA) for Windows (21.0, SPSS Company, Illinois, USA) software. Data are presented as mean ± standard deviation (SD) or as a percentage for categorical variables. Comparison of the incidence of CAC between the groups and sexes was made using Chi-square test. Multivariate logistic regression models were used to assess the association of hemodialysis patient and its traditional risk factors with CAC, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). To assess intra- and inter-examiner reliabilities, the intra-class correlation coefficient (ICC) was used. The ICC value for the intra- and inter-reliability was as high as 0.96 (P< 0.001) and 0.93 (P< 0.001), respectively, indicating excellent reliability. A P value of <0.05 was considered statistically significant.

Table 1. Comparison of traditional atherogenic risk factors of hemodialysis patients and controls

Parameter	Hemodialysis group	Control group	All patient	P^+
Patient, [n]	92	51	143	0.07
Gender, [F/M]	52/40	21/30	73/70	0.20
Age, [Years]	51.2 ±18.9	49.5±13.4	50.5 ± 15.3	0.13
Female	50.8 ±17.7	48.9±10.3	49.3 ± 13.5	0.17
Male	52.6 ±18.5	51.8 ±14.6	52.3 ± 17.3	0.15
DM [n,%]	26, 28.2	7, 13.7	33, 23.1	**0.02**
Hypertension [n,%]	38, 41.3	6, 11.7	44, 30.7	**0.01**
Hyperlipidemia[n,%]	24, 26.1	7, 13.7	31, 21.6	**0.04**
Smoking [n,%]	33, 35.8	18, 35.2	51, 35.6	0.23
BMI, [kg/m^2]	28.9 ± 4.1	29.8 ± 4.7	29.3 ± 4.4	0.16
History of family CVD [n,%]	23, 25.2	9, 17.6	32, 22.3	0.08

$^{+:}$PearsonChi-squared tests, Data are given as mean, standart deviation (SD)**, CAC**= Carotid artery calcification, **F**=Female, **M**=Male, **BMI=**Body mass index, **DM=** Diabetes Mellitus, **CVD=**Cardiovascular disease

Table 2. Distribution of hemodialysis patients and controls with or without carotis artery calcification

	Hemodialysis group			Control group			All group			P^+ value
	M	F	Total	M	F	Total	M	F	Total	
Unilateral(n) (within %)	6 50%	5 31%	11 39%	0 0%	1 20%	1 16%	6 46%	6 28%	12 35%	0.03
Bilateral(n) (within %)	6 50%	11 69%	17 61%	1 100%	4 80%	5 84%	7 54%	15 72%	22 65%	0.16
Total (n) (within %)	12 100%	16 100%	28 100%	1 100%	5 100%	6 100%	13 100%	21 100%	34 100%	0.012
CAC positive (n,%)	28, 30.4			6, 11.8			34, 23.7			0.01

+: Chi-square test, M=Male, **F=**Female

RESULTS

The mean age was 51.2 ± 18.9 years (minimum 15, maximum 80) in HD group, 49.5 ± 13.4 (minimum 23, maximum 74) in the control group (P = 0.12) and 50.5 ± 15.3 years (minimum 15, maximum 80) all group. There was no significant difference in the age, gender and BMI between the two groups (P value respectively; 0.13, 0.20, 0.16). Among other traditional risk factors, diabetes, hypertension and hyperlipidemia were more significantly observed in the hemodialysis group (P<0.05) (Table 1). Demographics data and traditional atherogenic risk factor incidence and percentage of CAC are shown in Table 1.

A total of 28 (30.4%) patients with hemodialysis and 6 (11.8%) patients from the control group had CAC (P = 0.012). The mean ages of the CAC (+) patients in the hemodialysis patients and control group were 55.4 ± 13.4 years and 52.1 ± 12.5 years; respectively (P = 0.08). Among 28 HD patients with calcification, 11 had unilateral CAC (39%) and 17 had bilateral CAC (61%), while among the patients in the control group, one had unilateral CAC (16%) and five had bilateral CAC (84%) (Table 2).

There was no significant difference in gender between the HD and the control group in terms of bilateral CAC frequency (P value 0.23, 0.06, respectively). Similarly, there was no significant difference between genders in terms of unilateral CAC frequency in the HD and control group. Among the HD patients with unilateral CAC, right CAC was observed in seven and left CAC in four patients. Whereas one patient in the control group had right CAC. The prevalence of unilateral CAC was higher in HD group. There was no significant difference between the groups in terms of prevalence of bilateral CAC (Table 2). The prevalence of the right CAC was higher than the left CAC in HD patients with unilateral CAC, but there was no significant difference between the durations of dialysis (P = 0.34).

Bilateral CAC was more common in female patients among the HD patients. The left CAC was more commonly observed in male patients (three males and one female). No significant difference was found between the sexes in both HD patients and the control group in terms of the prevalence of CAC in patients aged 40 years and over, and the prevalences of left CAC, right CAC, and bilateral CAC (P>0.05).

Mean age and mean durations of hemodialysis were significantly higher (P = 0.04, P = 0.03, respectively) in patients with CAC (+) compared to CAC(-) HD patients (Table 3). The mean durations of dialysis were respectively 80.0 ± 27.9 and 96.2 ± 31.2 months in unilateral and bilateral CAC (+) HD patients and no

Table 3. Demographic, clinical and laboratory measurements of the hemodialysis patient

Parameters	CAC positive (*n* = 28)	CAC negative (*n* = 64)	*P*value+
Gender, [Female/Male]	16/12	36/28	
Age, [years]	55.4 ± 13.4	44.9 ± 11.1	**0.04**
Female	56.1 ± 14.6	46.3 ± 14.2	**0.02**
Male	54.9 ± 14.8	43.9 ± 20.0	**0.01**
Duration of hemodialysis, [months]	87.8 ± 24.5	45.1 ± 15.6	**0.03**
Weight, [kg]	77.8 ± 15.9	73.1 ± 18.2	0.24
BMI, [kg/m^2]	29.3 ± 5.3	28.5 ± 4.4	0.67
SBP, [mm Hg]	147.4 ± 25.4	139.2 ± 21.5	**0.04**
DBP, [mm Hg]	91.3 ± 18.2	83.7 ± 19.4	**0.03**
Smoking (n,%)	11, 39.2	22, 34.3	0.09
DM	13, 46.4	13, 20.3	**0.02**
HT	15, 53.5	23, 35.9	**0.03**
FBG, [mg/dL]	154.4 ± 18.5	94.2 ± 8.9	**0.02**
BUN, [mg/dL]	96.2 ± 19.9	92.6 ± 18.1	0.13
Urea reduction ratio	71.6 ± 11.3	69.8 ± 10.3	0.18
Kt/V	1.8 ± 0.5	1.7 ± 0.6	0.41
Albumin, [g/dL]	3.8 ± 1.2	4.0 ± 1.6	0.34
Hemoglobin, [g/dL]	11.2 ± 2.3	11.4 ± 2.6	0.40
Ferritin, [ng/mL]	698.2 ± 159.4	728.2 ± 127.0	0.38
Calcium, [mg/dL]	9.4 ± 2.2	8.3 ± 1.9	**0.04**
Phosphorus, [mg/dL]	5.2 ± 1.5	4.1 ± 1.2	**0.03**
CaxP product	48.8 ± 6.4	34.4 ± 7.1	**0.04**
PTH, [pg/mL]	537.7 ± 128.1	361.2 ± 189.3	**0.02**
ALP (IU/L)	252.5 ± 42.0	133.9 ± 28.2	**0.02**
CRP, [mg/dL]	4.8 ± 1.1	2.1 ± 0.9	**0.01**
Uric acid, [mg/dL]	6.8 ± 1.9	7.1 ± 2.3	0.30
Total cholesterol, [mg/dL]	219.5 ± 21.2	175.3 ± 33.2	**0.03**
HDL-C, [mg/dL]	38.3 ± 6.6	47.2 ± 11.8	**0.04**
LDL-C, [mg/dL]	105.1 ± 25.9	71.1 ± 31.2	**0.02**
Triglyceride, [mg/dL]	336.9 ± 94.8	209.3 ± 98.3	**0.01**

[+:]Chi-squared tests, $P< 0.05$: statistically significant difference, Data are given as mean, standart deviation (SD), **BMI=**Body mass index,**DM=**Diabetes Mellitus, **HT=**Hypertension,**CKD=**Chronic kidney disease, **SBP=**Systolic blood pressure, **DBP=**Diastolic blood pressure, **CRP=**C-reactive protein, **FBG=**Fasting blood glucose,**LDL=**Low-density lipoprotein, **HDL=** High-density lipoprotein, **PTH=**Parathyroid hormone

significant difference was observed between them (P= 0.18). The mean durations of dialysis were respectively 88.5 ± 19.4 and 83.4 ± 16.7 months in the male and female HD patients among the CAC (+) HD patients (P = 0.08). No statistically significant difference was observed between age (P = 0.22) and durations of dialysis (P = 0.15) between male and female HD patients.

When the correlation of CAC with age was evaluated; 75% of CAC (+) patients in HD patients aged over 40 years and 53% aged over 50 years. CAC (+) was found in 21 of 41 patients who aged over 40 years (51.2%), 14 of 28 patients who aged over 50 years (50%) and 66% of nine patients who aged over 65 in HD group. CAC (+) was observed in 7 of 51 patients who aged under 40 years (13.7%). The prevalence of CAC (+) was significantly higher in the patients who aged over 40 years than in those aged under 40 years (P<0.000). Whereas, four of six patients with CAC (+) observed in the control group aged over 40 years (66.6%). The durations of HD were respectively 75.4 ± 12.6 months and 56.5 ± 10.7 months in patients who aged before and after 40 year old (P<0.005). Of the CAC (+) HD patients, eight were males (38%) and 13 females (62%). The prevalence of CAC was higher in female HD patients who aged over 40 years. Of the 17 patients with bilateral CAC (+), two (11.7%) aged under 40 years and 15 (88.3%) aged over 40 years, while six (54.5%) of 11 patients with unilateral CAC (+) aged over 40 years and five (44.5%) aged under 40 years. Bilateral CAC was observed in 15 (71.4%) of 21 CAC (+) HD patients. Bilateral CAC was more common in patients who aged over 40 years, while unilateral CAC was more common in patients who aged under 40 years.

Data of CAC (+) and CAC (-) HD patients are presented in Table 3. There were no significant differences in the URR, Kt/V, hemoglobin, albumin, ferritin, uric acid values between the CAC (+) and CAC(-) HD patients (P>0.05). But PTH, C-reactive protein, alkaline phosphatase, calcium, phosphorus, and Ca-P product were significantly higher (P = 0.02, P = 0.02, P =

Table 4. Multivariate logistic regression analysis for the CAC by traditional and non traditional risk factors.

Variable	OR (95% CI)	P-value
Age (>40 year)	1.34 (1.04-2.23)	0.002*
Gender (Male)	0.98 (0.88-1.03)	0.23
Diabetes mellitus	1.45 (1.27-3.22)	0.004*
Hyperlipidemia	1.38 (1.29-1.83)	0.001*
Current smoking	1.04 (0.93-1.11)	0.14
Hypertension	1.47 (1.40-2.19)	0.003*
History of Family CVD	1.01 (0.91-1.04)	0.11
Obesity [BMI>30kg/m^2]	1.22 (1.16-1.74)	0.03*
Surgical parathyroidectomy	1.19 (1.11-1.39)	0.04*
Calcium-based phosphorus binders	1.08 (1.02-1.17)	0.09
Vitamin D analog(paricalcitol)	1.24 (1.15-1.95)	0.04*

OR=Odds ratio, **CI=**Confidence interval, **CAC=**Carotid artery calcification, **CVD=**Cardiovascular disease, **BMI=**Body mass index.

0.02, *P* = 0.04, *P* = 0.03 and *P* = 0.04, respectively) in CAC(+) patients compared to CAC(-) patients (Table 3). There were no significant differences between CAC(+) and CAC(-) groups in calcimimetics (cinacalset) and non-calcium based phosphorus binders (sevelamer) used (*P*>0.05).The surgical parathyroidectomy, vitamin D analog (paricalcitol), and calcium-based phosphorus binders were statistically higher in the CAC(+) group than the CAC(-) group (*P*<0.05).

HD patients with CAC positive were older, had longer duration of hemodialysis and of traditional risk factors (diabetes, hypertension, hyperlipidemia and obesity) as compared to patients CAC negative. History of family CVD, smoking and male gender showed no association with carotid artery calcification (Table 4). Multi variate logistic regression analysis is shown in Table 4.

DISCUSSION

Atherosclerosis is a process characterized by the development of atheroma plaques that cause prominent thickening and stiffening of the vessel walls, with plaque content consisting of lipids, inflammatory cells and cytokines (Uslu et al., 2016). Especially coronary artery disease and cerebrovascular disease related to atherosclerosis are important causes of morbidity and mortality in ESRD (Lee et al., 2017). Atherosclerosis is mostly localized in the branching and bifurcation regions of the large arteries or veins. Arterial calcification is observed in the intima and medial layers of the vein.

Intimal and medial calcifications (Mönckeberg sclerosis) are often associated in CKD. While intimal calcification frequently shows an irregular and sporadic localization, medial calcification is observed as smooth and peripheral in the arterial walls. The presence of arterial medial calcification is recognized as an important prognostic indicator of mortality from all causes and cardio vascular causes in HD patients, independently from the traditional atherogenic risk factors (London et al., 2003). VC in CKD has drawn attention in 1976 for the first time and it was observed in 79% of dialysis patients and 44% in CKD before dialysis (Kuzela et al., 1977). Carotid artery calcifications are closely related to cerebrovascular events and showed that the detectection of CAC on PRs may help prevent stroke (Tamura et al., 2005, Soares et al., 2015).

PRs is a frequently used imaging method in the dental practice, providing information about the oral and fascial structures as well as the pathologies of bones, soft tissues and cartilage. When evaluating CAC, (stylohyoid process and stilomandibular ligament, hyoid bone, epiglottisis, superior horn of the thyroidcartilage and triticeal cartilage) and pathological radiopacities (calcified lymph node, phlebolith, salivary gland stones, tonsillolithiasis) should be carefully assessed (Alves et al., 2014). Consequently, dentists play an important role in an diagnosis of CAC. The suspected lesions for CAC were not included in our study and all radioopacities were guided ultrasonographic reevaluated. CAC was described on PRs for the first time for Friedlander and Lande and it was reported that CAC may indicate the risk for stroke in asymptomatic patients who aged over 50 years (Friedlander and Lande, 1981; Friedlander and Baker, 1994). CAC is often observed on PRs as a heterogeneous radiopacity within soft tissue in 1.5-2.5 cm inferoposterior to the mandibular angle close to hyoid bone near C3-C4 vertebrae (Kansu et al., 2005).

The prevalence of CAC has been reported as 0.43%-9.9%in general population studies (Hubar 1999; Johansson et al., 2011), 37% in patients who had experienced stroke (Friedlander et al.,1994), 22.4% in patients with metabolic syndrome (Pornprasertsuk-Damrongsri et al., 2009), 36% in type 2 diabetic patients using insulin, 24% in type 2 diabetics who do not receive insulin therapy (Friedlander et al., 2002), 22% in patients with obstructive sleep apnea (Friedlander et al., 1999), 31% in postmenopausal women (Friedlander and Altman, 2001), 17.6% in hemodialysis patients and 15.7% in patients with kidney transplantation (Kansu et al., 2005). All these study have shown higher prevalence of CAC in comparison with normal healty population. The different appearance of CAC frequency in the general population may be due to dissimilar ethnicity, age group, nutritional status, number of patients and frequency of atherosclerotic risk factors. The prevalence of CAC have been reported to be higher among healthy postmenopausal women compared with normal healthy population. In the present study, the prevalence of CAC was 30.4% in hemodialysis group and 11.4 in the control group. The higher prevalence of CAC in healthy population might be related to sedanter lifestyle. As expected, in this study the prevalence of CAC in HD group was high, consistently with the literature. According to the studies investigated prevalence of CAC in systemic diseases, the incidence of CAC was higher in HD patients. This may be related to type 2 diabetes mellitus and hypertension that are the most common causes of ESRD as well as to the incidence and severity of additional atherosclerotic risk factors existing in CKD. In our study, the prevalence of CAC was higher in the control group compared to the other study on different societies. It should be kept in mind, however, that the atheromal plaques in the carotid arteries are not calcified and that all calcified atheromatous plaques may not be visible in the PRs.

The fact that the prevalence of CAC, stroke and cardio vascular events increase with age is well-know (Ralph et al., 2011; Kumagai et al., 2007; Madden et al., 2007). In this study, the prevalence of CAC was significantly higher in patients who aged over 40 years than those aged under 40 years. In addition, bilateral CAC was more commonly observed in patients who aged over 40 years, this indicate the importance of advanced age together with the duration of hemodialysis as an atherosclerotic risk factor.

Among general population studies evaluating the prevalence of CAC with the persons who aged over 40 years; the prevalence of CAC was reported as 5.03% by Şişman et al. (Şişman et al., 2007), 2.1% by Bayram et al. (Bayram et al., 2006), 1.97% by Immanimoghaddam et al (Immanimoghaddam et al., 2012). In this study, the prevalence of CAC was 10-20 times higher in hemodialysis patients compared to general population. This is consistent with the fact that the risk of death from cardiovascular diseases is 10-30 times higher in hemodialysis patients compared with general population (Kansu et al., 2005).

CAC is reported to be commonly seen in women (Hubar 1999; Bayram et al., 2006) as unilateral (Pornprasertsuk-Damrongsri and Thanakun 2006; Şişman et al., 2007). In this study, CAC was more common in women, but bilateral CAC (+) positivity was higher both in HD and the control group.

The correlation of diabetes mellitus with the presence of CAC was statistically significant ($P<0.05$). The overall relative risk of stroke and recurrent stroke were reported to be greater in patients with DM (Hankey et al., 1998). Uthman et al.'s studies have shown increased CAC prevalence in diabetic and hyperlipidemic patients (Uthman and Al-Saffar, 2008). Similarly, Friedlander et al. CAC frequency was found to be increased in diabetic patients and there was no difference between patients who did not use insulin and those who did not use it (Friedlander et al., 2002).

Traditional risk factors can be classified as unmodifiable (such as age, gender) and modifiable (smoking, hypertension, hyperlipidemia, diabetes). In this study, CAC was identified as a risk factor for age, diabetes, hypertension and hyperlipidemia according to the multivariate logistic regression analysis conducted to evaluate the association of athero sclerotic risk factors with CAC. There was no significant relationship between gender, smoking, history of family cardiovascular disease, and CAC. In many studies, the association between diabetes (Friedlander et al., 2002; Pornprasertsuk-Damrongsri et al., 2009; Johansson et al., 2011; Uthman and Al-Saffar, 2008), hyperlipidemia (Alves et al., 2014; Pornprasertsuk-Damrongsri and Thanakun, 2006; Kumagai et al., 2007), hypertension (Alves et al., 2014; Pornprasertsuk-Damrongsri and Thanakun, 2006; Johanssonet al., 2011) and increased CAC frequency has been demonstrated. In this study, Kumagai et al. (Kumagai et al., 2007), Tamura et al. (Tamura et al., 2005) did not assess risk as a risk factor for smoking, in addition to the lack of a significant association between smoking and CAC frequency, similar to the Imanimoghaddam et al (Imanimoghaddam et al., 2012). These results may depend on such factors as the design of the studies, age of the patients participating in the study, and their characteristics.

As limitations of this study, the first CAC could not be evaluated with invasive imaging methods. The latter were not included in patients with a relatively small number of patients who were unable to identify PRs and who had atheroma plaque. Confirmation of CAC will invasive more detailed information.

CONCLUSION

The prevalence of CAC is higher in hemodialysis patients compared to general population.The increased age, type 2 diabetes, hypertension, hyperlipidemia, and parathyroi dectomy are associated with a high CAC prevalence.

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Conflicting Interest

No conflict of interest was declared by the authors.

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