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Prevalence of Carotid Artery Calcification in Hemodialysis Patients: A Case–Control Study

Hemodiyaliz Hastalarında Karotis Arter Kalsifikasyonunun Prevalansı: Bir Vaka Kontrol Çalışması

Ayşe Hanne SARI[1], Güldane MAĞAT[2]

[1]*Erzurum Ağız ve Diş Sağlığı Merkezi, Türkiye*
[2]*Necmettin Erbakan Üniversitesi, Diş Hekimliği Fakültesi, Klinik Bilimler Bölümü, Ağiz, Diş ve Çene Radyolojisi AD, Türkiye*

ABSTRACT: The aim of this study is to determine the prevalence of carotid artery calcification (CAC) in panoramic dental radiographs of chronic hemodialysis patients and to compare the values obtained with the healthy group. Panoramic radiographs of 76 patients (38 with hemodialysis and 38 with control) (age range 15–79 years; mean age 52.89 years) were examined. CAC was defined as the presence of heterogeneous nodular opacities in the soft tissue in C3–C4 intervertebral area on panoramic radiographs. Using Chi-squared tests, calcification prevalence rates were statistically compared. The Statistical Package for the Social Sciences (version 20.0; SPSS, Inc., an IBM Company, Chicago, IL, USA) was used. A probability p <0.05 was considered statistically significant. The prevalence of CAC on the right and left sides was 23.7% (18 patients) and 17.1% (13 patients) for all groups in this study, respectively. The prevalence of right and left CAC in the case group was 34.2% and 26.3%, respectively, while these values were 13.2% and 7.9%, respectively, in the control group. These differences between the case-control groups were statistically significant (p<0.05). While the rate of CAC increased with age (p<0.05), gender was not an effective factor on CAC (p>0.05). Age rather than disease was more effective on CAC according to the regression analysis. CAC was higher in hemodialysis patients than control groups. However, it should be considered that the age has a greater effect on CAC. These patients with such calcifications should be referred for further evaluation and treatment of carotid arteries, coronary arteries and vascular risk factors.

Keywords: Carotid artery calcification, chronic hemodialysis, panoramic radiography, risk factors, vascular calcification

ÖZET: Bu çalışmanın amacı kronik hemodiyaliz hastalarının panoramik diş radyografilerinde karotis arter kalsifikasyonu (KAK) sıklığını belirlemek ve elde edilen değerleri sağlıklı grupla karşılaştırmaktır. 100 hastanın (50'si hemodiyaliz hastası, 50'si kontrol hastası) (yaş aralığı 15-79; ortalama yaş 52,89 yıl) panoramik radyografileri incelendi. KAK, panoramik radyografilerde C3-C4 intervertebral alanda yumuşak dokuda heterojen nodüler opasitelerin varlığı olarak tanımlandı. Ki-kare testleri kullanılarak kalsifikasyon görülme oranları istatistiksel olarak karşılaştırıldı. Sosyal Bilimler için İstatistik Paketi (versiyon 20.0; SPSS, Inc., bir IBM Şirketi, Chicago, IL, ABD) kullanıldı. p<0.05 olasılığı istatistiksel olarak anlamlı kabul edildi. Bu çalışmadaki tüm gruplarda sağ ve sol tarafta KAK prevalansı sırasıyla %24 (24 hasta) ve %18 (18 hasta) idi. Olgu grubunda sağ ve sol KAK prevalansı sırasıyla %36 ve %28 iken kontrol grubunda bu değerler sırasıyla %12 ve %8 idi. Vaka-kontrol grupları arasındaki bu farklar istatistiksel olarak anlamlıydı (p<0,05). KAK oranı yaşla birlikte artarken (p<0,05), cinsiyet KAK üzerinde etkili bir faktör değildi (p>0,05). Regresyon analizinde KAK üzerinde hastalıktan ziyade yaş daha etkiliydi. Karotis arter kalsifikasyonu hemodiyaliz hastalarında kontrol gruplarına göre daha yüksekti. Ancak yaşın KAK üzerinde etkisinin daha büyük olduğu göz önünde bulundurulmalıdır. Bu tür kalsifikasyonları olan hastaların karotid arterler, koroner arterler ve vasküler risk faktörleri açısından ileri değerlendirme ve tedavi için yönlendirilmesi gerekmektedir.

Anahtar Kelimeler: Karotis arter kalsifikasyonu, kronik hemodiyaliz, panoramik radyografi, risk faktörleri, vasküler kalsifikasyon

Sorumlu Yazar: Prof. Dr. Güldane Mağat, e mail: gul_dent@hotmail.com

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INTRODUCTION

Dialysis is a type of renal replacement therapy that uses artificial equipment to supplement the kidneys' filtration function, removing excess water, solutes, and toxins from the blood. It helps maintain homeostasis in individuals with acute kidney injury, characterized by a rapid loss of kidney function, or chronic kidney disease, marked by a prolonged and gradual decline in renal function. There are mainly three types of dialysis: hemodialysis, hemofiltration and peritoneal dialysis (1).

Hemodialysis is the most commonly used treatment for patients whose kidneys have significantly reduced functionality. It is known to enhance survival in those with end-stage renal failure. This therapeutic procedure employs extracorporeal circulation of the patient's blood to address the azotemia, fluid, electrolyte, and acid-base imbalances characteristic of uremic syndrome (2). It is known that people who undergo hemodialysis due to chronic renal failure have a high risk of developing atherosclerotic complications (3). Vascular calcifications may occur in adult patients receiving long-term hemodialysis treatment, with increased stiffness of the carotid artery and aorta. These calcifications in the carotid artery are observed on panoramic films as unilateral or bilateral radiopaque vertical linear nodules in the soft tissues of the neck at the level of the intervertebral space between C3 and C4 (4). These calcified nodules may lead to increased cardiovascular morbidity and mortality in hemodialysis patients (5). Since atherosclerosis is an important risk factor for cardiovascular diseases in these patients, early detection of calcifications can be lifesaving (6). Atherosclerotic changes resulting from thickening of the carotid artery intima and media layers are associated with the presence of both cardiovascular disease and stroke.

The carotid artery calcification (CAC) is an important factor that increases the risk of cardiovascular morbidity and mortality in hemodialysis patients. Therefore, regular evaluation of hemodialysis patients for CAC and implementation of appropriate treatment strategies may help reduce cardiovascular risk. Panoramic radiographs, which are routinely used in dental practice, can also be used as a noninvasive, inexpensive and easily reproducible method for the detection of CAC (6, 7). This study aimed to detect the presence of CAC on dental panoramic radiographs of chronic renal failure patients undergoing hemodialysis.

MATERIAL AND METHOD

This study was conducted in accordance with ethical standards and guidelines to ensure the protection of patient rights and privacy. Prior to the inclusion of panoramic radiographs in the research, informed consent was obtained from all participants, allowing for the use of their medical images for academic purposes. All patient data were anonymized to maintain confidentiality, and the study was approved by the relevant ethics committee at Necmettin Erbakan University Faculty of Dentistry (approved number 2024/472). The ethical considerations adhered to the principles outlined in the Declaration of Helsinki, ensuring that the rights and welfare of the participants were prioritized throughout the study.

Sorumlu Yazar: Prof. Dr. Güldane Mağat, e mail: gul_dent@hotmail.com

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In this study, the sample size for the case and control groups was determined based on power analysis using G*Power software. The calculations were conducted for Fisher's exact test, considering a significance level of 5% ($\alpha = 0.05$) and a statistical power of 95% ($1-\beta = 0.95$). The analysis indicated that a minimum of 25 participants per group was required (8). However, to enhance statistical power and minimize variability, the total sample size was determined as 100 participants (50 cases, 50 controls).

The study included panoramic radiographs of patients undergoing hemodialysis treatment who presented to the Necmettin Erbakan University Faculty of Dentistry, Department of Oral and Maxillofacial Radiology, between 2014 and 2024. The inclusion criteria specified that participants must have had panoramic radiographs clearly displaying the C3 and C4 vertebral regions, taken using the Morita Veraviewepocs 2D panoramic unit, with settings of 60-70 kVp, 5-7 mA, and an exposure time of 6-8 seconds. Additionally, patients were required to provide informed consent for the use of their radiographic images in the research and must be aged 15 years or older. Conversely, the exclusion criteria eliminated patients with unclear panoramic radiographs due to movement or artifacts, those with a history of orthodontic treatment or permanent tooth extraction, individuals with facial trauma or systemic diseases affecting dental and bone development, and patients whose radiographs did not include the C3 and C4 regions.

Panoramic radiographs were taken with a Morita Veraviewepocs 2D panoramic unit (J Morita MFG Corp., Kyoto, Japan) at 60-70 kVp, 5-7 mA and 6-8 s exposure time in accordance with the manufacturer's recommendations. Suspicious findings of carotid artery calcification (CAC) were characterized by the presence of one or more unilateral or bilateral radiopaque masses located in the intervertebral space between the C3 and C4 vertebrae on panoramic radiographs (Figure 1). The presence or absence of CAC was assessed by two dentomaxillofacial radiologists, one with over 10 years of clinical experience and the other with 4 years of experience. Panoramic radiographs that were unclear due to patient movement during imaging, contained artifacts, or failed to include the C3 and C4 vertebral regions were excluded from the analysis

Out of the 98 panoramic radiographs obtained, 50 met the inclusion criteria and were selected for the study. Additionally, a control group consisting of 50 healthy panoramic radiographs, matched by age and gender to the case group, was established.

To ensure the reliability of CAC assessments, interobserver and intraobserver agreement were calculated. Two independent radiologists evaluated all panoramic radiographs, and a subset of cases was reassessed after a two-week interval to determine intraobserver agreement. Cohen's kappa and intraclass correlation coefficient (ICC) were used to quantify agreement, with values ranging from 0.88 to 0.96, indicating excellent reproducibility of CAC detection.

The calcification occurrence rates were statistically compared using Chi-square tests. Data analysis was performed using the Statistical Package for the Social Sciences

Sorumlu Yazar: Prof. Dr. Güldane Mağat, e mail: gul_dent@hotmail.com

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(SPSS, version 20.0; IBM Corp., Chicago, IL, USA). A p-value of less than 0.05 was considered statistically significant

RESULTS

The distribution of all evaluated panoramic images according to age groups and gender is shown in Table 1. A total of 100 panoramic images (50 cases-50 controls) were evaluated. The mean age of the participants was 53.42 ± 14.74 years. The predominant age group among the participants was 57-79 years (n=52), while the lowest participations were from the 15-35 age group (n=12) (Table 1). There was no statistically significant difference in the gender distribution among the age groups (p=0.187).

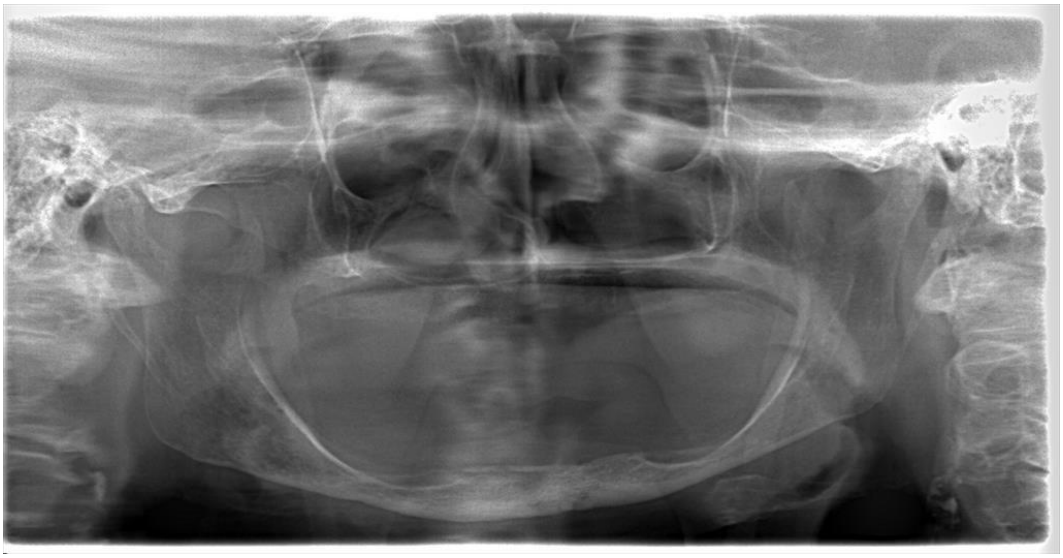

Figure 1. Bilateral, irregularly shaped calcified atherosclerotic plaques

Table 1. The distribution of carotid artery calcification status according to the gender, age, and case-control groups

Parameters	n	%	Carotid Artery Calcification					
			Right		p value	Left		p value
			Yes	No		Yes	No	
Gender								
Female	63	63.0	18 (72.0%)	45 (60.0%)	0.344	11 (57.9%)	52 (64.2%)	0.792
Male	37	37.0	7 (28.0%)	30 (40.0%)		8 (42.1%)	29 (35.8%)	
Age Groups								
15-35 years	12	12.0	0 (0.0%)[a]	12 (100.0%)[a]		0 (0.0%)	12 (100.0%)	
36-56 years	36	36.0	5 (13.9%)[a]	31 (86.1%)[a]	0.002*	6 (16.7%)	30 (83.3%)	0.147
57-79 years	52	52.0	20 (38.5%)[b]	32 (61.5%)[b]		13 (25.0%)	39 (75.0%)	
Case-Control Group								
Case	50	50.0	19 (76.0%)[a]	31 (41.3%)[a]	0.005*	15 (78.9%)[a]	35 (43.2)[a]	0.009*
Control	50	50.0	6 (24.0%)[b]	44 (58.7%)[b]		4 (21.1%)[b]	46 (56.8%)[b]	

* p<0.01 Each same superscript letter indicates a subset of right carotid artery calcification categories whose column ratios are not significantly different from each other at the .05 level.

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Table 1 shows the distribution of the carotid artery calcification status according to age and gender. Gender was not an effective factor on artery calcification, whereas age was effective on right artery calcification (p<0.01) (Table 1). The incidence of CAC increased statistically significantly with age.

When evaluated in terms of case-control group, the rate of CAC was statistically higher in the case group than in the control group (p<0.01) (Table 1).

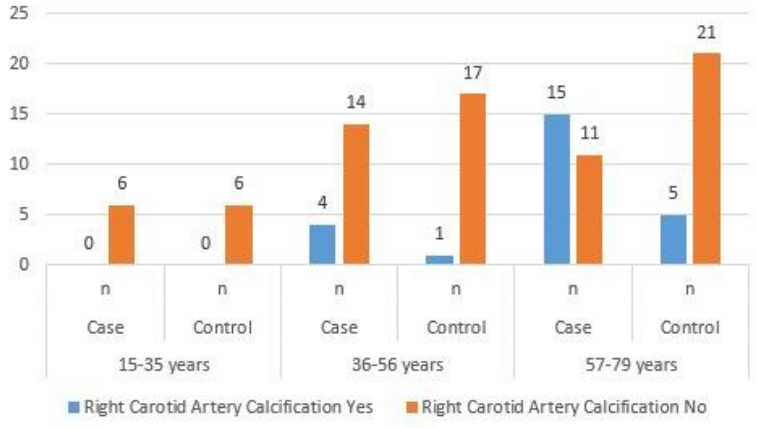

Figure 2. Distribution of the incidence of carotid artery calcification according to age groups and case-control groups

Table 2 Presentation of Hierarchical Binomial Logistic Regression Analysis (Right Side Carotid Arter Calcification

Predictor	Estimate	SE	Z	p-value	Odds Ratio	Lower (95% CI)	Upper (95% CI)	Deviance	AIC	R^2_{MCF}
Intercept [a]	-19.8459991	18004.177	-0.0011023	0.99912	2.4043E-09	0	inf	112.46703	114.46703	0.00000000
Model 1								98.304735	104.30473	0.12592395
Age Groups (Ref. 15-35 years)										
36-56 years & 15-35 years	0.070694529	0.02357651	3.00E+00	0.002713	1.07325333	1.024786782	1.124012063			
57-79 years & 15-35 years	0.079142361	0.0256075	3.09E+00	0.001998	1.0823584	1.029374835	1.138069107			
Model 2								87.691039	95.691039	0.220295584
Case-Control Groups (Ref. Case)	-1.70889586	0.56174701	-3.04210942	0.002349	0.1810656	0.060209809	0.544508499			

[a] Ref: Represents reference level, R^2_{MCF}: McFadden's R^2

When the difference between the case-control groups was evaluated with age held constant, the incidence of calcification was statistically higher in hemodialysis patients aged 56-79 years (case-75.0%; control-25.0%) (p=0.009) (Figure 2).

The results of the hierarchical binomial logistic regression analysis for the right-side CAC indicate that age and case-control group status are significant predictors of the outcome variable. The intercept was estimated at -19.85 (p = 0.9991). In Model

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1, age groups were compared using 15-35 years as the reference category. The 36-56 years group had an odds ratio (OR) of 1.07 (95% CI: 1.02-1.12, p = 0.0027), while the 57-79 years group had a higher OR of 1.08 (95% CI: 1.03-1.14, p = 0.0020), suggesting an increasing likelihood of right-side CAC with age. Model 2 examined the effect of case-control group status, showing that the control group had a significantly lower likelihood of right-side CAC compared to the case group (OR = 0.18, 95% CI: 0.06-0.54, p = 0.0023). Model 1 had an AIC of 104.30 and McFadden's R^2 of 0.1259, whereas Model 2 demonstrated a better fit with an AIC of 95.69 and McFadden's R^2 of 0.2203, indicating an improved explanatory power when incorporating case-control status (Table 2).

Table 3 Presentation of Hierarchical Binomial Logistic Regression Analysis (Left Side Carotid Arter Calcification)

Predictor	Estimate	SE	Z	p-value	Odds Ratio	Lower (95% Cl)	Upper (95% Cl)	Deviance	AIC	R^2_{MCF}
Intercept [a]	-20.28724673	21836.09759	-0.00092907	0.99925871	1.54654E-09	0	inf	97.244592 93	99.244592 93	0.000000000
Model 1								90.923262 07	96.923262 07	0.065004445
Age Groups (Ref. 15-35 years)										
36-56 years & 15-35 years	20.94473075	21836.09759	9.59E-04	0.99923 4686	124790 3465	0	inf			
57-79 years & 15-35 years	21.50610776	21836.09759	9.85E-04	0.99921 4173	218768 0654	0	inf			
Model 2								82.290311 67	90.290311 67	0.15378008
Case-Control Groups (Ref. Case)	-1.661054 43	0.616908	-2.692548 04	0.00709 0832	0.18993 8597	0.056687922	0.636408422			

[a] Ref: Represents reference level, R^2_{MCF}: McFadden's R^2

The results of the hierarchical binomial logistic regression analysis for the left-side CAC indicate that age and case-control group status are significant predictors of the outcome variable. The intercept was estimated at -20.29 (p = 0.9993). In Model 1, age groups were compared using 15-35 years as the reference category. The 36-56 years group had an odds ratio (OR) of 1.24 × 10^7 (95% CI: 0 - Inf, p = 0.9992), while the 57-79 years group had an even larger OR of 2.18 × 10^9 (95% CI: 0 - Inf, p = 0.9992), suggesting an extreme model estimation issue. Model 2 examined the effect of case-control group status, showing that the control group had a significantly lower likelihood of left-side CAC compared to the case group (OR = 0.19, 95% CI: 0.06-0.64, p = 0.0071). Model 1 had an AIC of 96.92 and McFadden's R^2 of 0.0650, whereas Model 2 demonstrated a better fit with an AIC of 90.29 and McFadden's R^2 of 0.1538, indicating an improved explanatory power when incorporating case-control status (Table 3).

DISCUSSION

This research was undertaken to investigate the prevalence of carotid artery calcification (CAC) among patients undergoing hemodialysis, a population known to experience elevated

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cardiovascular risks. Existing literature has established a strong correlation between chronic kidney disease, prolonged hemodialysis, and the development of vascular calcifications, which significantly contribute to morbidity and mortality rates in these individuals (9, 10). Utilizing panoramic radiographs as a non-invasive and readily available imaging modality, this study aimed to assess the occurrence of CAC in chronic hemodialysis patients and to juxtapose these findings with those from a healthy control group. Early identification of CAC through this method could facilitate prompt clinical interventions, ultimately aiming to mitigate cardiovascular complications in this at-risk population (11).

Panoramic radiograph is a reliable, reproducible and non-invasive method for detecting and monitoring asymptomatic atherosclerosis (12-14). While panoramic radiography is a non-invasive, widely accessible, and cost-effective imaging method, it has limitations in detecting CAC compared to ultrasound or CT angiography, which offer higher sensitivity and specificity. Given that panoramic radiography is primarily used for dental assessments, its ability to visualize vascular calcifications may be influenced by image resolution, anatomical superimpositions, and the experience of the interpreting radiologist (8). Future studies should discuss the sensitivity and specificity of panoramic radiography for CAC detection in greater depth, particularly in comparison with gold-standard imaging techniques such as Doppler ultrasound and CT angiography.

Atherosclerosis is a leading cause of heart attacks and strokes worldwide, resulting in the deaths of thousands. The disease has a complex etiopathogenesis, involving a series of biological mechanisms influenced by various factors (15, 16). Traditional risk factors include diabetes mellitus, obesity, high blood pressure, and poor diet and eating habits. Recent research suggests additional contributing factors such as chronic kidney disease, menopause, head and neck radiotherapy, and obstructive sleep apnea syndrome (17, 18).

When the general population and end-stage renal disease patients were compared, a significant increase in intima-media thickness and plaque formation in the carotid artery was observed in hemodialysis patients compared to the age- and gender-matched healthy control group (19-22). Consistent with these data, in our study, the incidence of CAC in panoramic radiographs was 48% in hemodialysis patients (16% bilaterally and 32% unilaterally) and 16% (4% bilaterally and 12% unilaterally) in the control group, and it was observed at a statistically higher rate in the case group than in the control group. Previous similar studies reported that the CAC percentages detected on digital panoramic radiographs in hemodialysis patients ranged from 15.9% to 22.5% (23-25), while the CAC rates in the general population ranged from 0.43% to 9.9% (26).

The effect of hemodialysis on the formation of calcified atheroma plaques has not been fully clarified, but it is thought that hemodialysis-related factors such as catheter use and chronic inflammation due to high serum urea levels may contribute to the formation of calcified atheroma plaques (27, 28). In hemodialysis patients with end-stage renal disease, these vascular

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calcifications are associated with increased stiffness of large and elastic arteries such as the aorta and carotid (23).

The findings of this study highlight the significant relationship between age and CAC as observed in panoramic images. The mean age of participants was 53.42 years, with the predominant age group being 57-79 years, which aligns with existing literature indicating an increased prevalence of CAC with advancing age (29-31). The statistically significant increase in CAC incidence among older adults underscores the importance of age as a risk factor for cardiovascular diseases, particularly in populations undergoing hemodialysis, where the incidence of CAC was notably higher (75.0% in cases versus 25.0% in controls for the 56-79 age group) (31, 32). This finding is consistent with previous studies that have documented a correlation between age and the prevalence of CAC, suggesting that older individuals are at a higher risk for atherosclerotic changes in the carotid arteries (33, 34).

Moreover, the study found no statistically significant difference in gender distribution among the age groups ($p=0.187$), indicating that while age is a critical factor in the development of CAC, gender may not play a significant role in this context (35, 36). This is further supported by research suggesting the prevalence of CAC is similar across genders, although some studies have reported variations in specific populations (37). The lack of gender influence on CAC prevalence in this study aligns with findings from other studies that have also noted no significant gender differences in CAC incidence (38, 39).

The comparison between case and control groups revealed a statistically significant higher rate of CAC in the case group, emphasizing the potential of panoramic radiography as a screening tool for identifying individuals at risk for cardiovascular events (40, 41). This is particularly relevant for hemodialysis patients, who are known to have a higher prevalence of cardiovascular complications due to factors such as malnutrition and oxidative stress, which can exacerbate arterial calcification (31, 32). The results suggest that routine evaluation of panoramic images could serve as an effective method for early detection of CAC, potentially leading to timely interventions that could mitigate the risk of serious cardiovascular events such as stroke or myocardial infarction (42, 43).

The findings indicate that age is a significant predictor of right-side CAC, with the odds of calcification increasing in older age groups. This aligns with previous studies suggesting that vascular aging, chronic inflammation, and metabolic disturbances contribute to the progressive calcification of arterial walls. However, for left-side CAC, the extremely large odds ratios ($OR = 1.24 \times 10^7$ and $OR = 2.18 \times 10^9$) suggest a model estimation issue, possibly due to small sample size or data separation problems. These findings should be interpreted with caution, and future studies may benefit from larger datasets or alternative statistical approaches such as penalized regression or Firth logistic regression to improve model stability.

The study also found that case-control group status was a significant predictor of CAC in both right and left carotid arteries.

Sorumlu Yazar: Prof. Dr. Güldane Mağat, e mail: gul_dent@hotmail.com

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The control group had significantly lower odds of calcification than the case group, reinforcing the role of systemic disease (e.g., chronic kidney disease, diabetes, cardiovascular disease) in CAC progression. This supports the importance of early screening and preventive measures in high-risk patients to mitigate the development of carotid artery calcification and its associated complications.

In both right-side and left-side CAC models, the inclusion of case-control status improved model performance, as indicated by higher McFadden's R^2 values in Model 2. However, the AIC values remained relatively high, suggesting that additional factors influencing CAC were not captured in the current model. Future studies should consider incorporating hypertension, dyslipidemia, inflammatory markers, and lifestyle factors such as smoking to enhance model performance and better understand CAC pathogenesis.

The study has several limitations that should be considered when interpreting the results. Firstly, the reliance on panoramic radiography as the sole imaging modality for detecting CAC may limit the diagnostic accuracy, as this method is generally less sensitive than advanced imaging techniques such as cone-beam computed tomography or ultrasonography. Secondly, while the sample size of 100 panoramic images is notable, it may not be sufficiently large to draw definitive conclusions about the general population, and a larger sample size would enhance the statistical power of the findings and allow for more robust subgroup analyses. Additionally, the retrospective design of the study may introduce selection biases, potentially affecting the representativeness of the case and control groups. The absence of longitudinal data restricts the ability to establish causal relationships between age, gender, and the development of CAC, as the study only provides a snapshot of participants' health status at a single point in time. Lastly, the study did not account for potential confounding factors such as lifestyle choices, comorbidities, and medication use, which are known to significantly impact cardiovascular health and could skew the results if not adequately controlled for in the analysis. These limitations highlight the need for caution in interpreting the findings and suggest that further research is warranted to address these issues.

CONCLUSION

This study highlights the significant association between CAC and age in hemodialysis patients, emphasizing the potential of panoramic radiography as a non-invasive screening tool. Early detection of CAC could facilitate timely referrals and preventive interventions. Future research should investigate systemic risk factors, compare panoramic radiography with advanced imaging methods, and conduct longitudinal studies to assess CAC progression and cardiovascular outcomes. Expanding sample sizes and including diverse populations will further improve the clinical applicability of findings.

Sorumlu Yazar: Prof. Dr. Güldane Mağat, e mail: gul_dent@hotmail.com

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Author Contributions: Design: AHS, GM, Data collection or data entry: AHS, GM Analysis and interpretation: GM Literature review: GM, AHS Writing: GM, AHS

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