



# Effect of Chronic Khat Chewing on Intima-Media Thickness of Common Carotid Arteries in Yemeni volunteers

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## ABSTRACT

**Objective:** To assess the changes occurring in both common carotid arteries (CCAs) intima-media thickness (IMT) in Yemeni chronic khat chewers using B-mode ultrasonography.

**Methods:** This cross-sectional study was conducted among 195 participants (103 regular khat chewers and 92 non-khat chewers) conveniently selected at the Radiology Department of the University of Science and Technology Hospital (USTH) in Sana'a from August 2017 to August 2018. Data about gender, age, BMI, chewing khat and the period of chewing were collected from participants using a structured questionnaire. B-mode ultrasonography of bilateral CCAs was then performed to measure the IMT. Data were analyzed using suitable statistical tests, and P-values <0.05 were considered statistically significant.

**Results:** The majority of participants with CCA-IMT were males (91.8%) and aged 27 years or younger (59.0%), with a mean age of  $27.9 \pm 6.8$  years. Khat chewers constituted more than half of patients with CCA-IMT. There was no statistically significant difference in the mean values of RT CCA-IMT and LT CCA-IMT between khat chewers and non-khat chewers. The CCA-IMT was significantly higher among male khat chewers compared to male non-chewers ( $P = 0.004$ ). However, there was no statistically significant difference between khat chewers and non-chewers with respect to the age of 20 years or older ( $P = 0.301$ ) and BMI of  $18.5 \text{ kg/m}^2$  or higher ( $P = 0.888$ ). Age showed a significant positive correlation with RT CCA-IMT ( $r = 0.380$ ;  $P < 0.001$ ) and LT CCA-IMT ( $r = 0.458$ ;  $P < 0.001$ ) in Khat chewers. In contrast, age showed a significant positive correlation with LT CCA-IMT only in non-khat chewers ( $r = 0.236$ ;  $P = 0.024$ ). On the other hand, BMI showed a significant positive correlation with LT CCA-IMT ( $r = 0.254$ ;  $P = 0.010$ ) among khat chewers, but no significant correlation was found in CCA-IMT of both sides among non-khat chewers. Among khat chewers, there was a significant positive correlation with RT CCA-IMT ( $r = 0.273$ ;  $P = 0.005$ ) and LT CCA-IMT ( $r = 0.194$ ;  $P = 0.049$ ).

**Conclusion:** Khat chewing does not lead to a significant difference in CCA-IMT among Yemeni chewers compared to non-chewers. However, the period of chewing may slightly affect the CCA-IMT among khat chewers. Age has a significant positive correlation with CCA-IMT in khat chewers and LT CCA-IMT in non-khat chewers, which could help to determine the contribution of different predisposing factors to atherosclerosis. A significant positive correlation can be found between BMI and LT CCA-IMT among khat chewers.

**Keywords:** Khat Chewing, Intima media thickness, Carotid, Yemen

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## 1. Introduction

Khat (qat, or kat) is an evergreen shrub that belongs to the family Celastraceae, and its chewing is a deep-rooted sociocultural custom in Yemen.<sup>(1)</sup> It has amphetamine-like properties as clinically observed.<sup>(2)</sup> Chewing khat, together with cigarette smoking, is a risk factor for cardiovascular diseases (CVDs),<sup>(3)</sup> and this can be attributed to the abnormal increase in pulse rate and arterial blood pressure (PB) in systolic and diastolic phases.<sup>(2, 4, 5)</sup>

Chronic Khat chewing can be associated with diastolic hypertension (HTN), leading to a sustained effect on the cardiovascular system and HTN at the population level.<sup>(3, 6, 7)</sup> In addition, regular khat chewing can increase the risk of acute myocardial infarction and stroke as a cerebrovascular complication.<sup>(8-10)</sup> The association between khat chewing and stroke has been suggested.<sup>(9-11)</sup>

Although the correlation between atherosclerosis and stroke has been discussed,<sup>(12-14)</sup> the correlation between chronic khat chewing and atherosclerosis has not been established. However, atherosclerosis may characterize the suggested causal link between khat chewing and stroke. The ultrasound investigation of common carotid arteries (CCAs) is crucial in the assessment of subclinical atherosclerosis, which improves cardiovascular risk prediction and chronic Khat chewing effects on the cerebrovascular systems.<sup>(9, 15)</sup> Moreover, the intima-media thickness (IMT) of CCAs is a useful parameter to detect the early development of atherosclerosis,<sup>(16-17)</sup> and it became an important predictor of morbidity and mortality of cardiovascular diseases.<sup>(15, 18)</sup>

High-resolution B-mode ultrasonography is the most useful non-invasive modality to measure CCA-IMT with reliability to detect subclinical atherosclerosis.<sup>(15, 18, 19)</sup> It is commonly used to measure normative CCA-IMT and to study different factors affecting it such as body mass index (BMI), HTN, diabetes mellitus (DM) and age.<sup>(16)</sup>

A recently published study revealed a significant increase in the carotid IMT in Somali regular khat chewers compared to controls using B-mode ultrasonography, being higher among khat chewers who were smokers compared to non-smokers.<sup>(20)</sup> Moreover, significant correlations were found between the duration of chewing and age with the presence of the plaques.<sup>(20)</sup>

To the best of our knowledge, there were no published studies about the effects of chronic khat chewing on CCA-IMT independently of confounding factors like smoking. Therefore, the present study aimed to determine such effects on carotid atherosclerosis.

## Methods

### 2.1. Study design, setting and population

This was a cross-sectional study conducted at the Radiology Department of the University of Science and Technology Hospital (USTH) in Sana'a from August 2017 to August 2018. This one-year study recruited 195 participants (103 regular khat chewers and 92 non-khat chewers) conveniently selected during the study period.

### 2.2. Data collection and IMT measurement

Data about gender, age, BMI, chewing khat and period of khat chewing in years were collected from participants using a structured questionnaire.

Volunteers were included if they were Yemeni adults (khat and non-khat chewers) of any gender provided that they were non-smokers, non-hypertensive, non-diabetic, and without cardiopulmonary disorders, history of severe dyslipidemia or known kidney diseases to avoid the confounding effects of such conditions.

B-mode ultrasonography of bilateral CCAs was performed to measure the IMT using a high-resolution ultrasound system (model: TUS-Aplio 400/Toshiba-MEC-US) equipped with a linear high-frequency probe. Two radiologists approved the



procedures for this prospective study, and a qualified sonographer performed the measurements.

CCAs were scanned to assess IMT in the supine position with supported knees. The operator seated on the right of the patient, and neck scanning was enhanced by tilting and rotating the head away from the side being examined, with possible appropriate adjustment for the head and neck position. Several approaches of ultrasound probe were used to investigate the CCAs in the longitudinal views obtained from different anterior and lateral or posterolateral approaches for getting the best view of vessels. Then, the values of IMT were determined manually (Figure 1).



**Figure 1.** B-mode ultrasound measurement of RT CCA- IMT in a khat chewer

### 2.3. Data analysis

Data were analyzed using IBM SPSS Statistics, version 21.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as mean  $\pm$  standard deviation (SD), where the normality of data distribution was tested using the Kolmogorov-Smirnov test. Qualitative data were expressed as frequencies and proportions. The independent sample t-test was used to compare the means of variables between khat chewers and non-khat chewers. Pearson's correlation was also used to analyze the correlations between continuous variables. *P*-values  $<0.05$  were considered statistically significant.

## 3. Results

### 3.1. Characteristics of study participants

Of 195 participants, the majority were males (91.8%) and aged 27 years or younger (59.0%), with a mean age of  $27.9 \pm 6.8$  years. More than half of the participants were khat chewers (Table 1).

**Table 1.** Characteristics of the study participants subjected to B-mode ultrasonography at the Radiology Department of USTH, Sana'a, Yemen (August 2017-August 2018)\*

Characteristics	n (%)
<b>Gender</b>	
Male	179 (91.8)
Female	16 (8.2)
<b>Age (years)</b>	
$\leq 27$	115 (59.0)
$>27$	80 (41.0)
Range	16-45
Mean male age $\pm$ SD	$27.9 \pm 6.8$
Mean female age $\pm$ SD	$26.2 \pm 6.6$
<b>Khat chewing</b>	
Yes	103 (52.8)
No	92 (47.2)

\*The total number of participants included in the study was 195; SD, standard deviation.

### 3.2. Comparison of CCA-IMT between khat chewers and non-khat chewers

Table (2) shows that there was no statistically significant difference in the mean values of RT CCA-IMT between khat chewers and non-khat chewers ( $0.70 \pm 0.12$  vs.  $0.70 \pm 0.09$ , respectively;  $P=0.693$ ). In addition, no statistically significant difference was found in the mean values of LT CCA-IMT between khat chewers and non-khat chewers ( $0.71 \pm 0.14$  vs.  $0.70 \pm 0.88$ , respectively;  $P=0.496$ ).

**Table 2.** Comparison between the mean values of CCA-IMT in khat chewers and non-khat chewers in Sana'a city, Yemen (August 2017-August 2018)

Side of CCA-IMT	Khat chewers (n=103)	Non-khat chewers (n=92)	P-value
	Mean (mm) SD		
RT CCA-IMT	$0.70 \pm 0.12$	$0.70 \pm 0.09$	0.693
LT CCA-IMT	$0.71 \pm 0.14$	$0.70 \pm 0.88$	0.496

CCA-IMT, common carotid artery intima-media thickness; n, number with CCA-IMT; SD, standard deviation; RT, right; LT, left.



### 3.3. Comparison of CCA-IMT between khat chewers and non-khat chewers

Table (3) shows that CCA-IMT was significantly higher among male khat chewers compared to male non-chewers ( $P = 0.004$ ). However, there was no statistically significant difference between khat chewers and non-chewers for the age of 20 years or older ( $P = 0.301$ ) and BMI of 18.5 kg/m<sup>2</sup> or higher ( $P = 0.888$ ).

**Table 3.** Comparison of CCA-IMT between khat chewers and non-khat chewers in Sana'a city, Yemen (August 2017-August 2018)

Characteristics	Khat chewers (N= 103)	Non-khat chewers (N= 92)	P-value
	n (%)	1 (%)	
Gender male	100 (97.1)	79 (86.0)	0.004
Age ≥20 years	97 (94.2)	83 (90.2)	0.301
BMI ≥18.5 kg/m <sup>2</sup>	90 (52.6)	81 (47.4)	0.888

CCA-IMT, common carotid artery intima-media thickness; n, number with CCA-IMT.

**Table 4.** Correlation of age, BMI and period of khat chewing with CCA-IMT among khat chewers and non-khat chewers in Sana'a city, Yemen (August 2017-August 2018)

Variables	Khat chewers				Non-khat chewers			
	RT CCA-IMT		LT CCA-IMT		RT CCA-IMT		LT CCA-IMT	
	r	P-value	r	P-value	r	P-value	r	P-value
Age (years)	0.380	<0.001	0.458	<0.001	0.084	0.427	0.236	0.024
BMI (kg/m <sup>2</sup> )	0.037	0.710	0.254	0.010	-0.02	0.846	0.122	0.247
Period of khat chewing (years)	0.273	0.005	0.194	0.049	-	-	-	-

CCA-IMT, common carotid artery intima-media thickness; RT, right; LT, left; r, correlation coefficient; BMI, body mass index.

## 4. Discussion

Previous studies have not assessed the effects of chronic khat chewing on CCA-IMT as an independent risk factor. In this context, a single study was performed among Somali khat chewers, but they were also smokers.<sup>(21)</sup> Therefore, the present study was conducted among Yemeni khat chewers compared to non-khat chewers after exclusion of volunteers who were smokers, hypertensive, obese, or had a history of cardio-cerebrovascular diseases.

The diagnostic B-mode ultrasound of CCAs is a valuable modality in assessing IMT, which reveals a good correlation with age and atherosclerosis degree and is considered as a morbidity and mortality predictor for CVDs.<sup>(18)</sup> This study revealed that a slight alteration of CCA-IMT among Yemeni

### 3.4. Correlation of age, BMI and period of khat chewing with CCA-IMT

Table (4) shows that age had a significant positive correlation with RT CCA-IMT ( $r = 0.380$ ;  $P < 0.001$ ) and LT CCA-IMT ( $r = 0.458$ ;  $P < 0.001$ ) in Khat chewers. In contrast, age showed a significant positive correlation with LT CCA-IMT only in non-khat chewers ( $r = 0.236$ ;  $P = 0.024$ ). On the other hand, BMI showed a significant positive correlation with LT CCA-IMT ( $r = 0.254$ ;  $P = 0.010$ ) among khat chewers, but no significant correlation was found in CCA-IMT of both sides among non-khat chewers. Among khat chewers, there was a significant positive correlation with RT CCA-IMT ( $r = 0.273$ ;  $P = 0.005$ ) and LT CCA-IMT ( $r = 0.194$ ;  $P = 0.049$ ).

khat chewers and non-khat chewers in Sana'a city, with no statistically significant difference between the two groups. In disagreement with this finding, a cohort study concluded that CCA-IMT before khat chewing is significantly altered after the chewing process.<sup>(22)</sup>

In the present study, CCA-IMT showed a significant positive correlation with age in khat chewers for both sides and only the LT one in non-khat chewers. This finding is consistent with those reported elsewhere.<sup>(12-14, 20-25)</sup> It is noteworthy that no statistically significant difference was found in CCA-IMT between Yemeni khat chewers and non-chewers among participants aged 20 years or older.

The present study also revealed that IMT was different according to the age of non-khat chewers, with a positive correlation that reflects a decade increments of 0.4 and 0.167 for RT and LT, respec-



tively. This value is higher than that reported among Koreans with metabolic syndrome.<sup>(26)</sup> However, it is consistent with the values reported among different populations elsewhere.<sup>(18, 27, 28)</sup> In addition to age, other risk factors have been reported to be associated with CCA-IMT, including smoking, BP, obesity, diabetes, alcohol consumption and lifestyle habits.<sup>(29, 30)</sup>

The non-significant difference between LT CCA-IMT and RT CCA-IMT among the study participants in the present study disagrees with that reported from Rome, Italy.<sup>(31)</sup> On the other hand, the significant difference in CCA-IMT by gender in the present study is in line with that found among Sudanese people.<sup>(18, 27)</sup>

The non-significant positive correlation of BMI with CCA-IMT among non-khat chewers in the present is in contrast to the findings of previous studies elsewhere.<sup>(18, 32-34)</sup> Among khat chewers, the period of khat chewing showed a significant positive correlation with both RT and LT CCA-IMT. This finding is in agreement with the fact that khat chewing can be a predisposing factor to atherosclerosis and plaque formation.<sup>(20, 35)</sup> However, the effect of chronic khat chewing on CCA-IMT was markedly less compared to that of age, which was the only significant predictor of CCA-IMT. The lower effect of chronic khat chewing on CCA-IMT compared to other factors, such as age and cigarette smoking, has been documented.<sup>(20, 36, 37)</sup>

This study is limited by the fact that the study sample was not randomly selected. However, it provides information on the effect of chronic khat chewing on CCA-IMT among Yemenis, independently of smoking.

## 5. Conclusions

Khat chewing does not lead to a significant difference in CCA-IMT among Yemeni chewers compared to non-chewers. However, the period of chewing may slightly affect the CCA-IMT among khat chewers. Age has a significant positive correlation with CCA-IMT in khat chewers and LT CCA-

MIT in non-khat chewers, which could help to determine the contribution of different predisposing factors to atherosclerosis. A significant positive correlation can be found between BMI and LT CCA-MIT among khat chewers.

## Ethical considerations

Ethical approval of this study was obtained from the Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Science and Technology, Sana'a, Yemen. In addition, a written agreement was received from the Radiology Department of the USTH, and written informed consent was obtained from the participants after explaining the objective of the study and scanning procedures to them.

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## Authors' contributions

AMA conceived the study idea, performed the investigations, analyzed data and drafted the manuscript. EAA developed the theoretical part, supervised the implementation of the study and contributed to manuscript drafting and revision. AAMM verified data analysis and contributed to manuscript drafting and revision. All authors read and approved the final draft of the manuscript.

## Competing interests

The authors declare that they have no competing interests associated with this article.

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