



ORIGINAL ARTICLE

Evaluation of subclinical atherosclerosis in migraine patients by ultrasound radiofrequency data technology: preliminary results

Migren hastalarında ultrason radyofrekans-veri analizi ile subklinik aterosklerozun saptanması, ön sonuçlar

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Summary

Objectives: Migraine is a headache disorder affecting approximately 12% of the population, predominantly female individuals. Migraine has been associated with vascular events such as stroke and cardiovascular disease. The close connection between these vascular disorders and atherosclerosis is well known. Carotid artery intima-media thickness (CAIMT) is a marker for detection of subclinical atherosclerosis. The present study is an analysis of the presence of subclinical atherosclerosis in migraine patients.

Methods: CAIMT was evaluated in 25 female migraine patients and 27 female controls using innovative ultrasound (US) radiofrequency (RF) data technology. Mann–Whitney U test was used to compare measurements in patient and control groups.

Results: There was a statistically significant difference between mean CAIMT of migraine patients and control group ($p < 0.005$): mean CAIMT was $701 \pm 114 \mu\text{m}$ in migraine patients and $400 \pm 64 \mu\text{m}$ in control group.

Conclusion: Migraine patients are more prone to atherosclerosis compared to healthy individuals. CAIMT measurement with sonography can be utilized in follow-up to detect subclinical atherosclerosis.

Keywords: Carotid; intima-media thickness; migraine; ultrasound radiofrequency data technology.

Özet

Amaç: Migren, toplumun yaklaşık %12'sini ve ağırlıklı olarak da kadın bireyleri etkileyen bir baş ağrısı bozukluğudur. Migren, inme ve kalp-damar hastalığı gibi vasküler patolojiler ile ilişkilendirilmiştir. Bu vasküler bozukluklar ile ateroskleroz arasındaki yakın bağlantı iyi bilinmektedir. Karotis arter intima media kalınlığı, subklinik aterosklerozun saptanması için bir göstergedir. Biz bu çalışmada; migren hastalarında subklinik aterosklerozun varlığını incelemeyi amaçladık.

Gereç ve Yöntem: Karotis arter intima media kalınlığı, 25 kadın migren hastasında ve 27 kadın kontrol grubunda yeni bir teknik olan ultrason radyofrekans-veri teknolojisi ile değerlendirildi. Hasta ve kontrol gruplarında fark varlığını analiz etmek için Mann–Whitney U testi kullanıldı.

Bulgular: Migren hastaları ve kontrol grubu arasında ortalama karotis intima media kalınlığı açısından istatistiksel olarak anlamlı fark saptandı ($p < 0.005$). Ortalama karotis intima media kalınlığı migren hastalarında 701 ± 114 mikrometre iken kontrol grubunda 400 ± 64 mikrometre ölçüldü.

Sonuç: Migren hastaları, sağlıklı bireylere oranla ateroskleroza daha yatkındır. Sonografi ile karotis arter intima media kalınlığı ölçümü bu hastalarda subklinik aterosklerozun tanınması amacıyla takiplerde kullanılabilir.

Anahtar sözcükler: Karotis; intima media kalınlık; migren; ultrason radyofrekans-veri analizi.

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Introduction

Migraine is the most common type of headache in young adults, affecting approximately 12% of the population, predominantly female individuals.^[1-3] It is characterized by recurrent attacks of headache accompanied by nausea, vomiting, phonophobia and photophobia.^[4] Though pathological mechanisms involving neuronal inflammation, disorders of neuronal excitability, and pain regulation with trigemino-vascular dysfunction have been proposed, complete pathophysiology is still unclear.^[5]

In the literature, various studies point out the association between migraine and cardiovascular diseases.^[6-10] The close connection between these vascular disorders and atherosclerosis, which is defined as a complex metabolic and inflammatory process related to various comorbid risk factors, is well known. It has been suggested that some of these risk factors, such as hypertension, disturbed lipid profile, insulin resistance, metabolic syndrome, increased body mass index (BMI), and hyperhomocystenemia, may be associated with migraine as well.^[11] Carotid artery intima-media thickness (CAIMT) is a received marker for detection of subclinical atherosclerosis.^[12] The purpose of the present study is to analyze presence of subclinical atherosclerosis in migraine patients.

Material and Methods

After obtaining approval of local ethics committee of our institution, 40 consecutive female migraine patients from neurology outpatient clinic between May 2014 and February 2015 who were under follow-up for migraine for at least 6 months were considered for this study. Exclusion criteria were history of known atherosclerosis, cerebrovascular or cardiovascular disease, arterial hypertension (blood pressure >80/130 mmHg), diabetes mellitus (DM), presence of plaque in CAIMT evaluation, active migraine attack during examination, regular use of medication for chronic condition or contraception, pregnancy or lactation, and refusal to participate in the study. Once exclusion criteria were applied, there were 25 patients who signed informed consent forms and participated in the study. CONSORT diagram of the study is shown in Figure 1. Patients were evaluated for frequency and duration of pain, cigarette smoking, presence of nausea, vomiting, photophobia, phonophobia, eyelid edema, prodromal symptoms,

accompanying neurological findings, lacrimation, nasal congestion, and corneal erythema. Lipid profiles, sedimentation, high-sensitivity C-reactive protein (hs-CRP), and glucose levels were studied in serum.

Control group consisted of 27 female patients from neurology outpatient clinic without any type of headache condition.

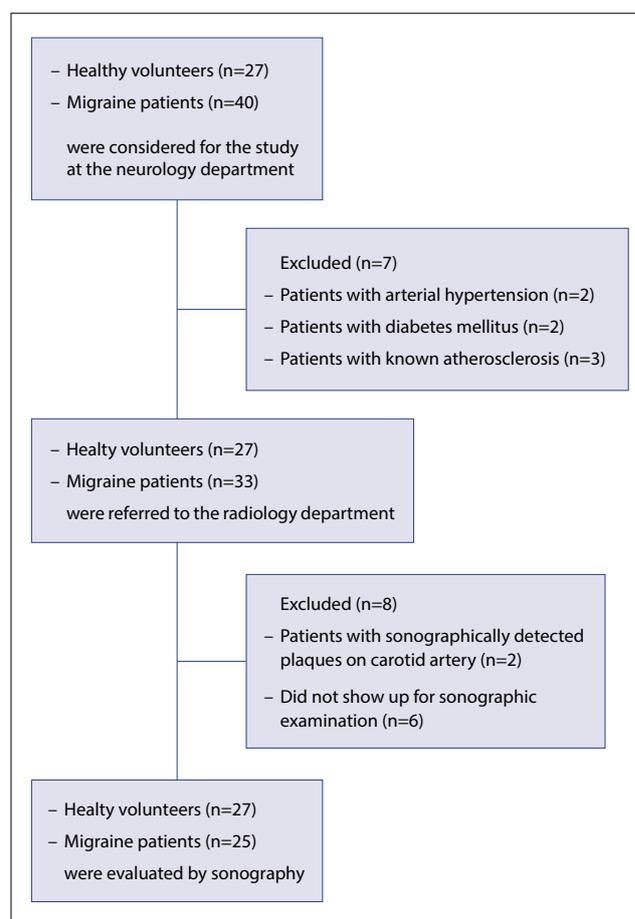


Figure 1. CONSORT diagram of the study.



Figure 2. Carotid artery intima-media thickness (CAIMT) was measured at 567 μm with SD of 23 μm in 23-year-old female migraine patient.

Table 1. Demographic features of the control group and migraine patients

Feature	Control group (n=27)	Migraine patients (n=25)
Age	33±9 years (range: 18–52)	32±9 years (range: 16–51)
Height	165±9 cm (range: 146–178)	164±7 cm (range: 150–175)
Weight	64±12 kg (range: 44–79)	67±14 kg (range: 49–98)
Body mass index	24±4 kg/m ² (range: 15–32)	25±6 kg/m ² (range: 16–39)

Sonographic CAIMT measurements were performed on all participants by radiologist with 16 years of experience in sonography, blinded to clinical information. Patients were asked to lie in supine position and both common carotid arteries (CCA) were evaluated in longitudinal planes with 5–12 MHz linear transducer of Esaote My Lab 90 Platform ultrasound (US) system (Esaote Medical Systems, Rome, Italy) equipped with dedicated software (radiofrequency [RF] data technology, including RF Quality Intima-Media Thickness [RFQIMT]). The software has an algorithm that is able to process data coming from the site as RF signals. US RF data technology allows combination of B-mode imaging with RF data technology for quantitative assessment of properties of arterial walls.^[13] CAIMT was measured in distal CCA, 1 cm proximal to carotid bulb (Figure 2). Average of the 2 measurements was used. Focal protrusions into lumen of at least 100% of surrounding IMT value were considered plaque, and these patients were excluded from the study.^[14]

Statistical analysis was performed using SPSS software (version 16.0; SPSS Inc., Chicago, IL, USA). P values <0.05 were considered statistically significant. Mann–Whitney U test was used to analyze presence of difference in CAIMT in migraine patients and control group. Spearman correlation coefficient analysis was used for analysis of correlation between CAIMT and various features of migraine patients.

Results

Demographic features of study participants are shown in Table 1. Patient and control groups were well-matched for age, BMI, and number of patients. All participants in both patient and control groups were female. Numerical and categorical features of migraine patients are listed in Tables 2 and 3. Statistically significant difference was seen in CAIMT mea-

surements of migraine patients and control group. Mean CAIMT was 701±114 µm (range: 562–905 µm)

Table 2. Numeric features of migraine patients (n=25)

Feature	Mean±SD (range)
Frequency of pain (times/month)	7±7 (1–30)
Duration of pain (hours)	34±26 (2–120)
Cigarettes (package/year)	2±5 (0–20)
Sedimentation	14±5 (5–32)
Hs-CRP	5±6 (0–24)
Glucose (mg/dL)	81±11 (66–110)
Total cholesterol (mg/dL)	158±30 (102–246)
HDL (mg/dL)	52±12 (23–75)
LDL (mg/dL)	92±24 (50–153)
Triglyceride (mg/dL)	97±40 (33–192)

HDL: High-density lipoprotein; hs-CRP: High-sensitivity C-reactive protein; LDL: Low-density lipoprotein; SD: Standard deviation.

Table 3. Categorical features of migraine patients (n=25)

Feature	Frequency
Nausea	25/25 (100%)
Vomiting	8/25 (32%)
Photophobia	21/25 (84%)
Phonophobia	20/25 (80%)
Eyelid edema	15/25 (60%)
Prodromal symptoms	19/25 (76%)
Accompanying neurological findings	2/25 (8%)
Lacrimation	13/25 (52%)
Nasal congestion	3/25 (12%)
Corneal erythema	14/25 (56%)

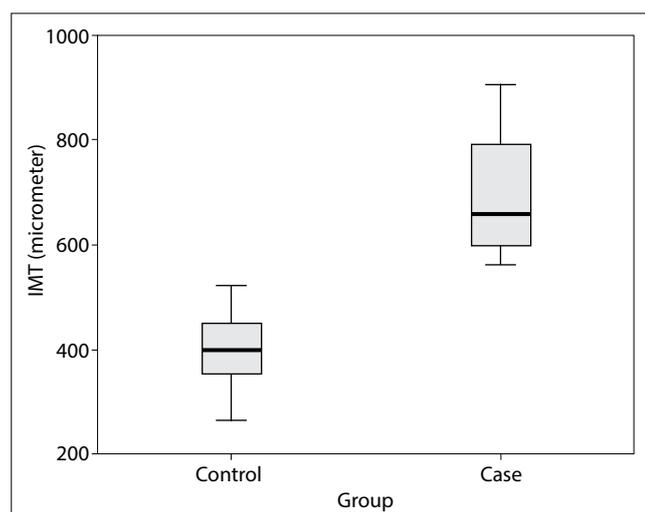


Figure 3. Carotid artery intima-media thickness (CAIMT) values are significantly higher in migraine patients compared to control group ($p < 0.01$).

in migraine patients, whereas it was 400 ± 64 (range: 265–521 μm) in control group ($p = 0.001$) (Figure 3).

When features of migraine patients were analyzed, none demonstrated significant relationship to CAIMT.

Discussion

CAIMT is a safe, cheap, feasible, and accurate method for detecting early changes secondary to atherosclerosis. CAIMT values higher than 0.8 mm are considered anomalous and are reported in our clinic.^[14] It reflects cardiovascular disease risk via rate of increase over time.^[12,15] Demonstrating enhanced subclinical atherosclerosis in migraine patients using CAIMT measurements may provide early modification of traditional risk factors of atherosclerosis, and thus reduce morbidity and mortality rates.

In the present study, CAIMT values of migraine patients were significantly higher when compared to healthy controls. This result demonstrates increased subclinical atherosclerosis in migraine patients.

RFQIMT technique, a novel sonographic method, was utilized. It improves CAIMT measurement quality with contribution of integrated RF data technology, providing real time feedback via quality indicators overlaid on US image of vessel wall by accepting and expressing integral RF signals.^[13] Also, this technique allows for obtaining CAIMT measurements in micrometers. This ensures more precise results

compared to other studies that utilized millimeter as measurement unit.

The association of migraine with atherosclerosis has been examined in the literature. Various studies have reported contradictory results regarding CAIMT values in migraine patients.

There are reports that are consistent with our results. Hamed et al. analyzed the association between migraine, vascular risk profile, endothelial injury, and CAIMT.^[16] In their study, systolic and diastolic blood pressure, serum levels of glucose, insulin, endothelin-1, and CAIMT measurements were higher in migraine patients compared to healthy patients. Thus, they suggested that migraine is associated with specific vascular risk profile, and this strongly suggests that migraine could be a risk factor for atherosclerosis. Besir et al. also reported higher CAIMT values in migraine patients compared to healthy controls.^[11] In addition, there are several published reports suggesting that migraine is a risk factor for stroke.^[7,10,17]

On the other hand, there are studies that did not demonstrate that migraine was a risk factor for cardiovascular events. Liman et al. indicated that there was no significant difference in CAIMT and peripheral arterial tonometry (PAT) ratio in female patients with migraine with aura.^[18] They concluded that in women with migraine with aura, peripheral endothelial function is not disturbed, but they have increased arterial stiffness that may explain increased stroke incidence in this population. Schwaiger et al. investigated both burden of atherosclerosis via carotid and femoral artery IMT measurement, and venous thromboembolism incidence in migraine patients compared to non-migrainous participants.^[19] Results indicated that migraine patients were not predisposed to increased atherosclerosis in carotid and femoral sites but they are at higher risk of venous thromboembolism (VTE). This finding may suggest that increased incidence of VTE is marker of prothrombotic state in migraine patients, which may help enlighten basis for increased stroke rate of migraineurs. Stam et al. suggested migraine patients had no increased risk for atherosclerosis according to their population-based study in which atherosclerosis was quantified by IMT, pulse wave velocity (PWV), and ankle-brachial index (ABI).^[20] Also, in a

study by Tzourio et al., migraine was associated with lower levels of blood pressure and with lower CAIMT values compared to patients without migraine.^[21]

Contrary to reports suggesting that migraine is not associated with atherosclerosis, a significant relationship was demonstrated in the present study. It should be noted that the studies of Schwaiger et al., Stam et al., and Tzourio et al. were all population-based studies with a wide range of age, and some included merely elderly patients. The difference between our results and these studies may be secondary to their relatively elderly subject groups. Subclinical atherosclerosis related to migraine is nearly impossible to detect in such an instance due to various other risk factors of atherosclerosis associated with increased age.

The findings of the present study were consistent with those of Besir et al. and Hamed et al. Their results indicated migraine patients' predisposition to atherosclerosis via well-known risk factors of atherosclerosis and increased values of CAIMT.^[11,16] Both of these studies used similar age profiles to the present study, notably the study by Besir et al., in which young female patients constituted majority of participants.

The results of the present study indicate that in young female migraine patients there is an increased incidence of subclinical atherosclerosis compared to healthy women of similar age group. Underlying mechanism may be secondary to common inflammatory processes of migraine and atherosclerosis, increased arterial stiffness or potential prothrombotic state of the migraine patients.^[22] Early detection or knowledge of this circumstance may help provide for lifestyle changes in young migraine patients, thereby preventing morbidity associated with vascular events.

There were some limitations to the current report. Analysis should be conducted with larger number of patients. Also, results should be validated with follow-up CAIMT measurements of the migraine patients, which is a goal for authors' further study.

In conclusion, migraine patients are more prone to subclinical atherosclerosis compared to healthy in-

dividuals of their age. CAIMT measurement by sonography can be utilized in routine follow-up of migraine patients to detect subclinical atherosclerosis. This may decrease morbidity and mortality rates associated with cardiovascular disease and stroke via early risk factor modifications.

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