Original Article / Özgün Araştırma

Assessment of Arterial Stiffness in Hemodialysis Patients, Using Speckle Tracking Carotid Strain Ultrasonography

Benek İzleme Karotis Gerilme Ultrasonografisini Kullanarak Arteriyel Sertliğin Hemodializ Hastalarında Değerlendirilmesi

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Abstract

Objective: The newly introduced ultrasonographic based speckle tracking carotid strain (STCS) imaging method is a promising technique that enables cardiovascular risk assessment by measuring arterial stiffness and strain parameters in carotid arteries. The present study evaluates the application of this technique in an end-stage renal disease (ESRD) patient group.

Materials and Methods: In total, 100 patients (50 ESRD, 50 controls) were included in this study. Arterial stiffness and strain parameters were measured in the longitudinal and axial planes from both carotid arteries with the STCS technique. The measurements were analyzed between the groups and a multiple regression model was implemented to identify independent predictors of carotid stiffness and strain parameters.

Results: The study found a significant difference between ESRD and the control group in β-stiffness index, arterial distensibility (AD), elastic modulus and pulse wave velocity both in longitudinal and axial plane for stiffness parameters. Strain parameters for radial and circumferential strain parameters for both planes were significantly different between the two groups. In the multivariate linear regression analyse, estimated glomerular filtration rate was positively and independently associated with both axial and longitudinal AD and arterial compliance (all $p<0.05$).

Conclusion: The study demonstrated the feasibility and clinical value of the STCS method in the assessment of vascular stiffness, and its potential use as a tool in cardiovascular risk assessment in an ESRD patient group.

Öz

Amaç: Ultrasonografi zemininde geliştirilen yeni bir teknik olan benek izleme karotis gerilme (BİKG) görüntüleme yöntemi, karotis arterlerdeki arter sertliği ve gerilme parametrelerini ölçerek kardiyovasküler risk değerlendirmesini sağlayan umut verici bir tekniktir. Bu çalışma, bu tekniğin son dönem böbrek yetmezliği (SDBY) hasta grubunda uygulanabilirliğini değerlendirmektedir.

Gereç ve Yöntemler: Bu çalışmaya toplam 100 olgu (50 SDBY, 50 kontrol) dahil edildi. Arter sertliği ve gerinim parametreleri, BİKG tekniği ile her iki karotis arterden uzun aks ve aksiyal planda ölçüldü. Bu ölçümler gruplar arasında analiz edildi ve ayrıca karotis sertliği ve gerinim parametrelerinin bağımsız öngörücülerini belirlemek için çoklu regresyon modeli uygulandı.

Bulgular: Sertlik parametreleri için hem uzun aksta hem de aksiyal düzlemde β-sertlik indeksi, arteriyel esneyebilirlik, elastik modül ve nabız dalga hızında SDBY

Keywords
Atherosclerosis, cardiovascular disease, carotid artery, end-stage renal disease, speckle tracking carotid strain, ultrasonography

Anahtar Kelimeler
Ateroskleroz, kardiovasküler hastalık, karotis arter, son dönem böbrek yetmezliği, benek izleme karotis gerilme, ultrasonografi

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ve kontrol grubu arasında anlamlı fark vardı. Her iki düzlem için radyal ve çevresel gerinim parametreleri iki grup arasında önemli ölçüde farklıydı. Çok değişkenli lineer regresyon analizinde, tahmini glomerüler filtrasyon hızı, hem aksiyal hem de uzun aksta arteriyel genişleyebilirlik ve arteriyel uyum ile pozitif ve bağımsız olarak ilişkiliydi (tümü p<0,05).

Sonuç: Çalışma, SDBY'li hastalarda vasküler sertliğin değerlendirilmesinde BİKG yönteminin uygulanabilirliğini ve klinik değerini göstermiştir ve bu teknik bu hasta grubunda kardiyovasküler risk değerlendirmesinde kullanılabilecek potansiyele sahip bir yöntemdir.

Introduction

End-stage renal disease (ESRD) is a serious public health issue that causes premature deaths. Half of the deaths in ESRD patients are caused by cardiovascular diseases, at a rate 20 times higher than the normal population (1).

Carotid artery system is an important indicator of the atherosclerotic status of the whole body (2). Standard carotid ultrasonograpy (USG) is an imaging modality that allows us to evaluate morphological changes in atherosclerosis such as carotid intima-media thickness (CIMT) and carotid plaque. Whereas speckle tracking carotid strain (STCS) USG is a newly introduced USG tecnique that allows us to measure not only morphological information but also functional information about the carotid system by measuring stiffness and strain parameters (3,4). These functional changes occur before the morphological changes (5). These changes, allowing for earlier detection of cardiovascular disease, especially for patients at risk (6,7).

Arterial analysis software using the STCS method measures differences in arterial diameter generated by each heartbeat. With the diameter and pressure measurements, variables related to arterial stiffness such as arterial compliance (AC), arterial distensibility (AD), β-stiffness index (β-SI), elastic modulus (EM), and pulse wave velocity (PWV) and variables related to arterial strain such as displacement, strain and strain rate can be calculated. The literature indicates that the STCS method can identify the changes in arterial stiffness parameters due to increased cardiovascular risk at a subclinical level in different patient groups (5,6,8-12).

Measurement of arterial stiffness and strain parameters with the STCS technique helps in the early detection of potential cardiovascular incidents. The present study evaluates the application of this technique in an ESRD patient group.

Materials and Methods

Study Population

A total of 100 subjects (50 ESRD who received hemodialysis and 50 controls) who underwent a carotid USG examination between 1 April 2021 to 31 May 2022 were included in the study. Both groups were paired according to age, gender and body mass index (BMI) (Table 1). Patients with severe common carotid artery (CCA) stenosis (>70%), a history of intervention to the CCA or to the neck region were excluded from the study. Approval from the Institutional Ethics Committee of Aydın Adnan Menderes University was provided (protocol no: 2022/78, date: 28.04.2022) with informed consent obtained from those included in the study.

Calculation of Stiffness and Strain Parameters

Carotid USG was performed with a Samsung RS80 USG device using a L3-12A (Samsung Medison Co., Ltd. Seoul, Korea) linear array transducer. The arterial analysis software programme (Samsung Medison Co., Ltd., Seoul, Korea) was applied to measure strain and stiffness parameters (Figure 1). CCA displacement was automatically calculated to evaluate the functional capabilities. The segment 5-10 mm beneath the carotid bulb was analyzed. Control points on the CCA were determined by the user. The frame created by the control points was set to automatically follow the optical flow algorithm.

Before the USG examination, subjects were rested in the supine position, in dim lighting and at ideal room temperature for a minimum of 10 minutes. Then the systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured with pulse wave analysis of the brachial artery using a Reister sphygmomanometer (Reister 1312 minimus II, Rudolf Riester GmbH, Jungingen Germany). The SBP and DBP were entered into the software. Two different planes (longitudinal and axial) used for each CCA were performed. The mean value of each plane measurements were noted for right and left CCA. In each plane, all stiffness parameters and radial strain parameters were measured by the software. The circumferential strain parameters for the axial plane were also calculated (Figure 1a, b).

The mean value of the CIMT was calculated with the same software for each CCA in the longitudinal plane. Both the anterior and posterior wall interfaces that define the blood-intima boundaries in the carotid artery (minimum 5 spots in all) were selected on a still image, then the movement of the points were automatically monitored by the software (Figure 1c, d).

Statistical Analysis

The Statistical Package for Social Science version 21.0 was applied for the statistical processing of the data (International Business Machine Corporation, Armonk, NY, USA). Descriptive statistics were presented as numbers, percentages, and mean ± standard deviation values. The conformity of continuous variables to normal distribution was evaluated with descriptive statistics, kurtosis and skewness coefficients, histogram, and Shapiro-Wilk test. For categorical data a chi-square test was used. Where data had normal distribution a t-test was used, but otherwise the Mann-Whitney U test was used for comparing two independent groups. To identify the independent predictors of CCA stiffness and strain parameters, a multiple regression model was implemented. After adjusting for BMI, presence of diabetes mellitus (DM) and presence of hypertension (HT), the impact of estimated glomerular filtration rate (eGFR) on stiffness and strain parameters was given. The model fit was evaluated using proper residual and goodness-of-fit statistics. The type 1 error level was determined as 0.05.

Results

Baseline Characteristics

A total of 50 control subjects (56.8±15.5 years, 60% male, 40% female) and 50 ESRD (57.2 years ±15.9, 60% male, 40% female) were included in the study (Table 1). Both groups were matched in terms of gender and age. In terms of the biochemical data in blood, eGFR, total cholesterol and low-density lipoprotein in the ESRD group was lower, while creatinine, blood urea nitrogen and triglyceride levels were higher than the normal group (Table 1).

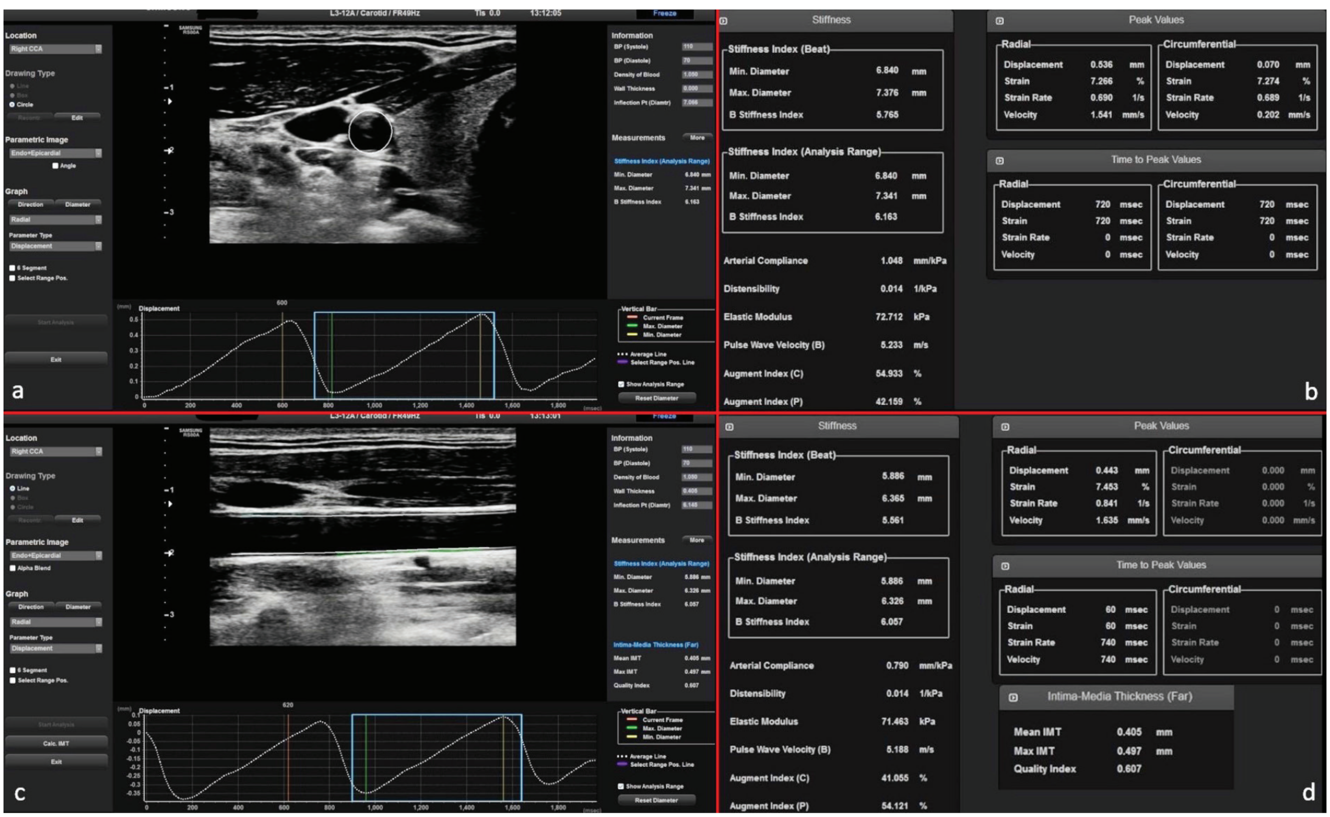

Figure 1. Evaluation of the right CCA in normal patient in (a) axial plane with related (b) stiffness and strain parameters report page, in (c) longitudinal plane with related (d) CIMT, stiffness and strain parameters report page
CCA: Common carotid artery, CIMT: Carotis media thickness

Carotid Stiffness and Strain Findings

Strain examination was successfully performed on all participants. In the evaluation of the stiffness parameters in the longitudinal plane (Table 2); while there was a significant increase in β-SI, EM, PWV parameters, in AD parameter there was a significant decrease in the ESRD group compared to the control group (all $p<0.05$). With only the AC stiffness parameter, no significant difference was observed between the groups. In the radial strain parameters in the longitudinal plane, only with the strain parameter there was a significant decrease in the ESRD group ($p=0.014$), while there was no difference between the two groups with other strain parameters (Table 2).

The results in the axial plane are consistent with the results in the longitudinal plane (Table 3). A statistical difference was observed between the ESRD and control group in all of the stiffness parameters in the axial plane. A significant increase was observed in β-SI, EM and PWV stiffness parameters, on the other hand there was a significant decrease in AC and AD stiffness parameters in ESRD group (all $p<0.001$). In the radial strain parameters in the axial plane, as in the longitudinal plane, there was a significant decrease in ESRD group in the strain parameter ($p=0.001$), while there was no difference with displacement and strain rate parameters. In the axial circumferential strain parameters, there was a significant decrease in displacement and strain parameters in ESRD group (all $p<0.05$) and no difference was observed for the strain rate parameter (Table 3).

In the multivariate linear regression analysis adjusted for BMI, the presence of DM, HT, and eGFR

Table 2. Comparison of the parameters in the longitudinal plane between the groups

	Control (n=50)	ESRD patients (n=50)	p-value
Right Mean CIMT* (mm)	0.67±0.2	0.75±0.26	0.095
Left Mean CIMT* (mm)	0.68±0.21	0.82±0.29	0.013
β-SI*	6.67±1.96	9.44±4.46	0.001
AC* (mm/kPa)	0.79±0.35	0.67±0.31	0.071
AD* (/kPa)	0.0135±0.0053	0.0097±0.0053	<0.001
EM* (kPa)	85.58±29.35	131.51±62.12	<0.001
PWV* (m/s)	5.58±0.93	6.72±1.51	<0.001
Strain parameters (radial)			
D** (mm)	0.46±0.13	0.45±0.18	0.459
S** (%)	7.35±1.92	6.66±3.01	0.014
SR** (1/s)	0.75±0.22	0.94±0.69	0.158

ESRD: End stage renal disease, *CIMT: Carotis media thickness, β-SI: β-stiffness index, AC: Arterial compliance, AD: Arterial distensibility, PWV: Pulse wave velocity, EM: Elastic modulus, **D: Displacement, S: Strain, SR: Strain rate

Table 1. Baseline characteristics and laboratory works of both groups

	Control (n=50)	ESRD (n=50)	p-value
Age (years)	56.8±15.5	57.2±15.9	0.904
Sex (male)	30 (60%)	30 (60%)	1
Sex (female)	20 (40%)	20 (40%)	1
Central systolic blood pressure (mmHg)	118.9±16.5	134.5±23	<0.001
Central diastolic blood pressure (mmHg)	75.4±11.1	81±16.8	0.064
Body mass index (kg/m^2)	26±4.3	25.1±5.4	0.186
Hypertension	15 (30%)	26 (52%)	0.025
Diabetes mellitus	8 (16%)	22 (44%)	0.002
eGFR (mL/min/1.73 m^2)	94.1±13.2	6.7±1.9	<0.001
Creatinine (mg/dL)	0.8±0.1	7.8±2.1	<0.001
Blood urea nitrogen (mg/dL)	15.3±11	51.5±15.6	<0.001
Total cholesterol (mg/dL)	203.8±42.1	167.9±47.6	<0.001
High-density lipoprotein (mg/dL)	54.4±15.9	49.5±16.3	0.076
Low-density lipoprotein (mg/dL)	124.8±36.4	87.4±37.5	<0.001
Triglyceride (mg/dL)	124.1±58.9	155.3±84.5	0.019

eGFR: Estimated glomerular filtration rate, ESRD: End stage renal disease was negatively and independently associated with both axial and longitudinal β-SI, EM and PWV. In the multivariate linear regression analysis adjusted for BMI, the presence of DM, HT, and eGFR was positively and independently associated with both axial and longitudinal AD and axial AC (all $p<0.05$). From the strain parameters perspective, eGFR was positively and independently associated with axial radial displacement, axial radial strain and axial circumferential strain, and also was only negatively and independently associated with longitudinal radial strain rate (all $p<0.05$). On the other hand, eGFR had no impact on one stiffness parameter (longitudinal AC) and on most of the strain parameters (all $p>0.05$) (Table 4).

Discussion

The STCS technique was successfully performed on all participants of the present study. Both groups were compared by evaluating the stiffness and strain parameters of CCAs. A significant difference was observed between the groups in all stiffness parameters in both the longitudinal and axial planes except AC in the longitudinal plane. A significant difference was also observed in terms of the strain parameter in the longitudinal plane, displacement and strain parameters in the axial plane.

Vascular remodeling characterized by increased vascular stiffness was observed in patients with ESRD. This remodeling process also affects the elastic properties of the vascular structure (13,14). Increase in fibroelastic intimal thickness, calcification in vascular walls, inflammation and increased collagen cause changes in intrinsic elastic properties in vascular walls and this causes an increase in stiffness in the CCA of ESRD patients (15,16).

To the author's knowledge, there is only one study in the literature by Lee et al. (13) in which arterial stiffness of the CCA was evaluated using the STCS method in patients with ESRD. With respect to stiffness parameters, Lee et al. (13) observed statistically significant differences in AD, EM and PWV parameters (all $p<0.005$). In terms of strain parameters, Lee et al. (13) observed that there was a significant decrease in the strain ratio in both the longitudinal and axial planes in the ESRD group. As a result, it has been determined that the STCS method is much more valuable than the conventional aortic stiffness indices in cardiovascular risk classification in the ESRD patient group (13). The present study returned similar results to Lee et al. (13). These results show that many stiffness parameters (especially AD, EM and PWV) and some strain parameters (strain and strain ratio) are significantly different between the two groups and provide valuable information in cardiovascular risk classification of ESRD patients.

In order to support and reinforce this result, we performed a multivariate analysis evaluation.

Table 3. Comparison of the parameters in the axial plane between the groups

	Control (n=50)	ESRD patients (n=50)	p-value
β-SI*	6.97±1.82	11.03±5.64	<0.001
AC* (mm/kPa)	0.94±0.37	0.67±0.29	<0.001
AD* (/kPa)	0.0126±0.0047	0.0088±0.0049	<0.001
EM* (kPa)	89.44±27.02	150.18±74.08	<0.001
PWV* (m/s)	5.71±0.86	7.15±1.69	<0.001
Strain parameters (radial)			
D** (mm)	0.48±0.12	0.41±0.17	0.006
S** (%)	6.93±1.68	5.80±2.66	0.001
SR** (1/s)	0.76±0.24	0.77±0.51	0.145
Strain parameters (circumferential)			
D** (mm)	0.063±0.016	0.058±0.035	0.018
S** (%)	6.91±1.67	5.76±2.62	0.001
SR** (1/s)	0.75±0.24	0.77±0.51	0.135

ESRD: End stage renal disease, *β-SI: β-stiffness index, AC: Arterial compliance, AD: Arterial distensibility, PWV: Pulse wave velocity, EM: Elastic modulus, **D: Displacement, S: Strain, SR: Strain rate

Table 4. Multivariate linear regression analysis*				
Parameters	β	95% CI	SE	p
Axial β-SI**	-0.316	-0.164 to -0.043	0.031	0.001
Axial AC**	0.359	0.053 to 0.175	0.031	<0.001
Axial AD**	0.30	0.056 to 0.176	0.030	<0.001
Axial EM**	-0.349	-0.182 to 0.063	0.030	<0.001
Axial PWV**	-0.330	-0.084 to 0.027	0.014	<0.001
Longitudinal β-SI**	-0.260	-0.142 to -0.020	0.031	0.009
Longitudinal AC**	0.153	-0.017 to 0.114	0.033	0.147
Longitudinal AD**	0.316	0.046 to 0.170	0.031	0.001
Longitudinal EM**	-0.312	-0.167 to -0.045	0.031	0.001
Longitudinal PWV**	-0.297	-0.077 to -0.019	0.015	0.002
Axial Radial D**	0.211	0.002 to 0.108	0.027	0.044
Axial Radial S**	0.205	0.003 to 0.108	0.026	0.039
Axial Radial SR**	0.002	-0.063 to 0.064	0.032	0.984
Axial Circumferential D**	0.183	-0.008 to 0.111	0.030	0.088
Axial Circumferential S**	0.209	0.004 to 0.108	0.026	0.036
Axial Circumferential SR**	-0.002	-0.064 to 0.062	0.032	0.985
Longitudinal Radial D**	-0.004	-0.052 to 0.051	0.026	0.974
Longitudinal Radial S**	-0.124	-0.020 to 0.081	0.025	0.235
Longitudinal Radial SR**	-0.222	-0.128 to -0.004	0.031	0.036

*Adjusted for body mass index, presence of diabetes mellitus, presence of hypertension, CI: Confidence interval, ESRD: End stage renal disease, SE: Standart error, **β-SI: Stiffness index, AC: Arterial compliance, AD: Arterial distensibility, PWV: Pulse wave velocity, D: Displacement, S: Strain, SR: Strain rate

In the analysis performed after correction of BMI, presence of DM and presence of HT, especially since the two groups were not homogeneous, all stiffness parameters except for longitudinal AC, were negatively or positively correlated with eGFR independently. Only axial radial displacement, axial radial strain, axial circumferential strain, and longitudinal radial strain rate parameters were found to be negatively or positively correlated with eGFR from a strain parameters perspective. Multivariate analysis showed that even after correcting for the secondary differences of the groups, the relationship between the depth of the ESRD and especially the stiffness parameters showed continuity.

The limitations of the study include the inability to evaluate the prognostic value of CCA strain parameters on clinical outcomes due to the cross-sectional nature of the study. Since measurements were made only once by a single radiologist, no intra- and inter-observer variability evaluation could be made. Further limitations of the study include the fact that STCS values are affected by smoking, age, hyperlipidemia, DM and other metabolic diseases, and the lack of clinical homogeneity between the groups in this respect.

Conclusion

The study demonstrated the feasibility and clinical value of the STCS method in the assessment of vascular stiffness in patients with ESRD. STCS is a method that has the potential to offer benefits in cardiovascular risk assessment and even in cardiovascular risk control in an ESRD patient group. Further multicenter randomized studies with a higher number of patients in this patient group will make significant contributions to the literature in this area.

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Ethics

Ethics Committee Approval: Institutional Ethics Committee of Aydın Adnan Menderes University was provided (protocol no: 2022/78, date: 28.04.2022).

Informed Consent: Informed consent was obtained from those included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.G., H.A., Concept: M.G., Z.G.A., Y.Y., Design: M.G., H.A., Y.Y., Data Collection or Processing: M.G., Z.G.A., Analysis or Interpretation: M.G., G.T., Y.Y., Literature Search: M.G., Y.Y., Writing: M.G., Y.Y.

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