Journal of Cardiology 63 (2014) 223–229

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Aortic stiffness is increased in patients with premature coronary artery disease: A tissue Doppler imaging study

Barış Güngör (MD), Hale Yılmaz (MD), Ahmet Ekmekçi (MD), Kazım Serhan Özcan (MD)*, Mohamedou Tijani (MD), Damirbek Osmonov (MD), Baran Karataş (MD), Ahmet Taha Alper (MD), Ferit Onur Mutluer (MD), Ufuk Gürkan (MD), Osman Bolca (MD)

Department of Cardiology, Siyami Ersek Cardiovascular and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 18 June 2013
Received in revised form 1 August 2013
Accepted 14 August 2013
Available online 21 September 2013

Keywords:
Aortic stiffness
Premature coronary artery disease
Tissue Doppler imaging

ABSTRACT

Background: Atherosclerosis and arterial stiffening may coexist and the correlation of these parameters in patients with premature coronary artery disease (CAD) has not been well elucidated. Tissue Doppler imaging of the ascending aorta may be used in the assessment of elastic properties of the great arteries.
Objective: To investigate the correlation between aortic stiffness and premature CAD using parameters derived from two-dimensional and tissue Doppler imaging (TDI) echocardiography of the ascending aorta.
Methods: Fifty consecutive subjects younger than 40 years old who were hospitalized with diagnosis of acute coronary syndrome and had undergone coronary angiography were recruited. The control group included 70 age–sex matched individuals without a diagnosis of CAD. Aortic stiffness index (SI), aortic distensibility (D), and pressure-strain elastic modulus (E_p) were calculated from the aortic diameters measured by two-dimensional M-mode echocardiography and blood pressure obtained by sphygmomanometry. Aortic systolic velocity (S_{Ao}), and early (E_{Ao}) and late (A_{Ao}) diastolic velocities were determined by pulse-wave TDI from the anterior wall of ascending aorta 3 cm above the aortic cusps in parasternal long-axis view.
Results: Stiffness index was higher [median 5.40, interquartile range (IQR) 5.98 vs. median 4.14 IQR 2.43; $p = 0.03$] and distensibility was lower (median 2.86×10^{-6} cm^2/dyn, IQR 2.51×10^{-6} cm^2/dyn vs. median 3.46×10^{-6} cm^2/dyn, IQR 2.38×10^{-6} cm^2/dyn; $p = 0.04$) in patients with CAD compared to the control group. E_{Ao} was significantly lower in the CAD group (7.2 ± 1.8 cm/s vs. 9.2 ± 2.4 cm/s, $p < 0.01$). The difference in E_{Ao} remained significant when CAD patients with a left ventricular ejection fraction >55% was compared to the control group. S_{Ao} and A_{Ao} velocities of ascending aorta were similar in control and CAD groups. There was a significant correlation between E_{Ao} velocity and aortic stiffness index ($r = -0.28$, $p = 0.01$), distensibility ($r = 0.19$, $p = 0.04$) and elastic modulus ($r = -0.24$, $p = 0.01$). In multivariate regression analysis, decreased levels of high-density lipoprotein cholesterol [odds ratio (OR): 1.12 95% CI 1.06–1.19; $p = 0.01$] and E_{Ao} (OR: 1.41 95% CI 1.12–1.79; $p = 0.01$) measurements remained as the variables independently correlated with premature CAD in the study group.
Conclusion: Arterial stiffness is increased in patients with premature CAD. E_{Ao} of the anterior wall of ascending aorta measured with pulse-wave TDI echocardiography is correlated with arterial stiffening and is decreased in patients with premature CAD.

Introduction

The normal aging process is associated with an increase in vascular stiffness which is accelerated by atherosclerosis, hypertension, and diabetes mellitus [1–4]. Several studies have revealed that increased aortic stiffness (AS) is a risk factor for cardiovascular (CV) diseases and also is a predictor of CV morbidity and mortality [5–9]. In addition, arterial stiffening is increased in individuals with a family history of premature coronary artery disease (CAD) which may indicate a genetic predisposition to CAD [10].

Two-dimensional and tissue Doppler imaging (TDI)-derived parameters of ascending aorta have been found to be abnormal, indicating increased AS in subjects with CAD, hypertension, and diabetes mellitus [11,12]. However, the direct correlation of AS with CAD is hard to examine as most of these patients are old and have comorbidities such as hypertension and diabetes mellitus.

* Corresponding author at: Acıbadem Mah, Tekin Sokak, Erdem Sitesi, E Blok, Daire: 16, Kadikoy, Istanbul 34087, Turkey. Tel.: +90 532 674 24 29/216 545 47 36; fax: +90 216 337 97 19.
E-mail addresses: serhandr@gmail.com, serhan_oz@yahoo.com (K.S. Özcan).

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http://dx.doi.org/10.1016/j.jjcc.2013.08.008

Investigation of these parameters in patients with premature CAD may yield valuable information as most of these patients do not have confounding factors that increase AS.

Thus, the aim of this study was to investigate the correlation of the aortic wall velocities assessed by TDI echocardiography with CAD in subjects younger than 40 years of age.

Methods

The study population consisted of 50 patients (male 41, female 9) who were younger than 40 years of age and were hospitalized with the diagnosis of acute coronary syndrome in Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, Istanbul between January 2010 and June 2012. Clinical data including past medical history, smoking status, family history, and medications were obtained from patient interview and chart review. Fasting blood samples were collected on the first day of hospitalization.

Hypercholesterolemia, hypertension, and diabetes mellitus were defined either as self reported, documented diagnosis obtained from chart review, or current treatment with medication. Hypertension was defined as a systolic pressure > 140 mmHg and/or a diastolic pressure > 90 mmHg or if the individual was taking antihypertensive medications. Diabetes mellitus was defined as a fasting glucose level >126 mg/dl and/or if the patient was taking anti-diabetic medication. Hypercholesterolemia was defined as total cholesterol of at least 200 mg/dl or use of cholesterol-lowering agents. Positive family history for CAD was defined as documented evidence of CAD in a first-degree relative before 60 years of age. Individuals who reported smoking of at least one cigarette per day during the year before examination were classified as smokers. Cardiac medications taken at study entry were recorded. The weight and stature were measured and body mass index (BMI) values were calculated as weight (kg)/height (m^2).

All of the subjects underwent diagnostic coronary angiography during index hospitalization. CAD was diagnosed as the presence of a lumen diameter reduction >50% in ≥1 major coronary artery. Percutaneous coronary intervention was performed as indicated.

Exclusion criteria were: age >40 years; left ventricular ejection fraction (LVEF) <50%; severe valvular disease; history of coronary artery bypass grafting operation; heart rhythm other than sinus.

The control group was composed of 70 (58 male, 12 female) subjects who were admitted to the outpatient clinic. All of the control subjects had normal findings in the physical examination, 12-lead electrocardiography, and transthoracic echocardiography. The echocardiographic examination was performed after 6 hours of abstinence from smoking. All patients gave informed consent to participate in the study and the local ethical committee approved the study.

Echocardiography

All patients underwent echocardiography in the left lateral decubitus position on the day of discharge. Studies were performed using a commercially available system (VIVID 7; General Electric Vingmed Ultrasound, Milwaukee, WI, USA). Images were obtained using a 3.5-MHz transducer, at a depth of 16 cm in the parasternal (long- and short-axis) and apical (2- and 4-chamber) views. Standard 2-D and color Doppler data, triggered to the QRS complex, were saved in cineloop format. A minimum of 3 consecutive beats were recorded from each view, and the images were digitally stored for offline analysis. All of the images were obtained at end-expiration as recommended. All echocardiographic findings were analyzed by one of the authors, who were blinded to the subjects' past histories.

Aortic diameters were measured at a level 3 cm above the aortic cusps in long axis from the parasternal view (Fig. 1). M-mode diameter measurements were made in systole (point of maximal anterior motion of aorta) and at end-diastole (q wave on electrocardiogram). The means of five diameter measurements in sequential cardiac cycles were used for data analysis. Systemic arterial blood pressure (BP) was measured at the right brachial artery by manual sphygmomanometer with the patient supine using an adequately sized cuff. BP was measured three times on each occasion at 2 min intervals and averaged. Pulse pressure (PP) was obtained by subtracting the diastolic BP from the systolic BP. Antihypertensive drugs were not discontinued on the day of the examination. Control subjects refrained from smoking for at least 12 h before the echocardiographic examination. Patients with CAD had not smoked during the hospitalization period which accounts for 3–4 days before the examination.

The elastic properties of the aorta were indexed by calculation of aortic distensibility (D), stiffness index (SI) and pressure strain elastic modulus (E_p) and were as follows: $D = 2\,(A_s - A_d)/[A_d\,(P_s - P_d)]$, $SI = \ln(P_s/P_d)/[(A_s - A_d)/A_d]$ and $E_p = (P_s - P_d)/[(A_s - A_d)/A_d]$, respectively, where A_s is the aortic diameter at end-systole, A_d is the aortic diameter at end-diastole, P_s is the systolic BP, P_d is the diastolic BP, and ln is the natural logarithm [13–15].

Measurements of cardiac chambers were made by transthoracic echocardiography according to established criteria [16–18]. Peak early (E) and late (A) diastolic velocities, deceleration time, left ventricular (LV) isovolumic relaxation time (IRT) were obtained from apical four-chamber view using standard Doppler practices [19–21].

Tissue Doppler imaging

Aortic upper-wall velocities were measured by TDI at the same point as in the M-mode measurements (Fig. 1). Gain and filter settings were adjusted to optimize the image. High temporal resolution (>100 frames/s) and a sweep speed set to 100 mm/s were used. The TDI of expansion peak velocity during systole (S_{Ao}) and early (E_{Ao}) and late (A_{Ao}) contraction peak velocities during diastole were obtained with a 1-mm sample volume size. The resulting velocities were recorded for 5–10 cardiac cycles and stored for later playback and analysis. The averages of velocities measured from the septal and lateral mitral annulus on the transthoracic four-chamber views were reported as S_a, E_a, A_a [22,23].

Statistics

The data were analyzed using SPSS version 13.0 software (SPSS, Chicago, IL, USA). All of the data are expressed as arithmetic mean ± SD or median (interquartile range; IQR) for skewed variables. The differences between the groups were explored using the Student's *t*-test and the Mann–Whitney *U*-test. Differences in proportions between groups were assessed for statistical significance using the chi-square test. As the LVEF was significantly different between the two groups, we also performed an ANCOVA analysis, putting the aortic stiffness parameters as the dependent variables, patient group as the fixed factor and LVEF, E_a, and smoking status as the covariate. The relationships between parameters were evaluated by Spearman's rank correlation analysis or linear regression analysis. Multiple stepwise logistic regression analysis was performed to examine the correlates of CAD. Differences were considered statistically significant when the p-value was <0.05.

Reproducibility for the measurements of the aortic velocities by TDI method was examined in 25 randomly selected cases. Intra-observer and inter-observer variability were estimated by measuring the Lin's concordance correlation coefficient. Concordance correlation coefficients were 0.92 (95% CI 0.843–0.966) for S_{Ao},