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Short Report

Doppler-Echocardiographic Characteristics of Left Ventricular Function in Patients with Pseudoexfoliation Glaucoma: A Preliminary Report

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A B S T R A C T

Glaucoma is associated with an increased incidence of cardiovascular disease and risk factors. The aim of the study was to assess the left ventricular (LV) function in patients with pseudoexfoliation (PEX) glaucoma using doppler-echocardiographic examinations. Two-dimensional and pulsed Doppler echocardiography of transmitral flow was performed in 21 patients with (PEX) glaucoma and 24 controls. LV systolic contraction and ejection were assessed using the LV ejection fraction (EF) and fractional shortening (FS). LV diastolic filling assessed parameters were: early, fast diastolic filling (E wave), late diastolic filling (A wave), ratio E/A, velocity time integral E wave (VTIE) and A wave (VTIA), their ratio (VTIE/VTIA), pressure at the end of filling (LVEDP) and a pulmonary capillary wedge pressure (PCWP). A significant difference was found concerning LV filling flow parameters in E, E/A, VTIA and ratio VTIA/VTIE. No significant difference was found in EF, FS, A, VTIE, LVEDP and PCWP tested parameters.Our study indicates the possibility of slightly impaired diastolic function of LV in patients with PEX glaucoma assessed by Doppler-echocardiographic examinations.

Key words: *Doppler-echocardiography, pseudoexfoliation, glaucoma, left ventricle*

Introduction

Pseudoexfoliation (PEX) syndrome is characterized by the intra-and extraocular deposition of abnormal extra cellular matrix material and it has been found to be the most common precursor of open-angle glaucoma[1]. The presence of pseudoexfoliative fibrils has been found in various tissues in the body including the eyes, skin, kidney, heart, lungs, gallbladder, blood vessels, optic nerve and cerebral meninges[1–4]. Although the clinical consequences of this systemic involvement are not fully clear, the increasing evidence suggest for an association of PEX and cardiovascular and cerebrovascular disease[5–7]. In the Blue Mountains Eye Study (Australia) PEX syndrome was found to correlate positively with a history of myocardial infarction suggesting a vascular systemic effects of this disease[7]. However no increase in mortality rates in person with PEX has been shown[8]. Primary open-angle glaucoma occurs more commonly in eyes with PEX[9]. Recent evidence indicates that the ocular features of PEX syndrome are in fact only one manifestation of a systemic process[2.] Cardiovascular abnormalities as well as myocardial ischemia are more often observed in glaucoma patients than in normals[10–13]. Some of these patients may go through a phase of asymptomatic left ventricular dysfunction, but overt heart failure is not present[14,15]. Conceptually diastole encompasses the time period during which the myocardium loses its ability to generate force and shorten and returns to an unstressed length a force. By extension,

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diastolic dysfunction occurs when these process are prolonged, slowed or incomplete[16].

The aim of this study was to assess the LV myocardial function in patients with PEX glaucoma by using two-dimensional echocardiography as well as pulsed Doppler echocardiography.

Patients and Methods

The study enrolled 21 patients with PEX glaucoma (9 males and 12 females, median age 69 years, range 51–78 years), and 24 healthy volunteers (11 males and 13 females, median age 65 years, range 50–74 years). The criteria used for inclusion in the study were as follows: patients were defined as suffering from PEX glaucoma, based on having controlled IOP on current local therapy (IOP <21 mmHg), open angle on gonioscopy with dandruff like flakes of PEX material, PEX material on the pupillary margin and on the anterior lens surface. No evidence of underlying ocular or systemic cause of high IOP, glaucomatous visual field defect and papillary excavation (C/D vertical >0.3). A 15-day-washout period from previous beta-blocker therapy was enforced to minimize a systemic side effect of the topically applied beta-blocker. Healthy volunteers on no medication without significant past ocular history matched with the PEX glaucoma group for age and sex were recruited as a control group. The criteria for exclusion were: patients with valvular and pericardial heart disease, left ventricular hypertrophy, diabetes mellitus and systemic hypertension. Latent coronary artery disease was excluded after normal upright exercise testing.

All patients were examined using two-dimensional echocardiography studies and pulsed Doppler echocardiography with a 3.5 MHz transducer (Diasonics DRF 4000, USA). Myocardial function was expressed in terms of left ventricular developed pressure and ejection fraction. The cardiac cycle consisted of the contraction and ejection phase of systole and the relaxation and filling phase of diastole. Left ventricular (LV) systolic contraction and ejection were evaluated using the LV ejection fraction (EF) and fractional shortening (FS). LV diastolic filling parameters tested were early fast diastolic inflow (E wave, which encompasses 85% of total diastolic filling) and late diastolic inflow (A wave, which represents the last of approximately 15% of ventricular filling during diastole), ratio E/A, velocity time integral E wave (VTIE) and A wave (VTIA) and their ratio VTIE/VTIA, pressure at the end of left-ventricular filling (LVEDP) and pulmonary capillary wedge pressure (PCWP).The ratio of the atrial velocity time integral represents the atrial contribution to the left ventricular filling.

From the parasternal short-axis derived M-modes of the left ventricle, the end-diastolic and end-systolic dimensions were measured. Left ventricular ejection fraction and fractional shortening were obtained according to the Kessler[17]. Left ventricular diastolic function was evaluated by the pulsed Doppler technique measuring mitral venous flow[17,18]. The following transmitral Doppler parameters were analysed: E, A,VTIE,VTIA ratio VTIE/VTIA[18–20]. LVEDP and PCWP were calculated according to the formulas of Stork at al.[20] Oral consent was obtained for each participant in the study after the nature of the procedure was fully explained.

Statistical analysis was performed using Statistica for Windows (Stat Soft Inc, USA, Version 6.0). All data were analyzed by a descriptive analysis. Comparisons between the two groups were made using the non-parametric Mann-Whitney U test. The Chi-square test and Student′s t-test were used to compare patient's data such as sex and age. Findings with an error probability value of <0.05 were considered to be statistically significant.

Results

The results of echographic and Doppler examinations are presented in Table 1. Using the Student's t-test and chi-square test for independence, we did not find a significant difference between the two groups in age ($t=-1.8$; $p=0.07$) and sex (chi-square=0.04; $p=0.8$). Systolic function assessed by EF and FS was not significantly different between patients with PEX glaucoma and controls. Among diastolic filling parameters a significantly different was found in E, E/A, VTIA and VTIA/VTIE. Although the significant difference was not found among VTIE and A parameters, it is obviously that this difference exists.

Discussion

The higher prevalence of cardiovascular disease particularly of an ischemic nature in elderly glaucoma patients was suggestive of a generalized vascular abnormality[21–23]. Diastolic function of the left ventricle plays a major role in producing the signs and symptoms of heart failure in disease of the myocardium. Among all mitral flow parameters used to evaluate left ventricular diastolic filling, except A, VTIE, PCWP and LVEDP, a significant difference was found. In healthy young persons LV relaxation is fast and most of ventricular filling occurs in early diastole. A decreased E-wave velocity, E/A ratio less than 1.0, prolonged VTIA and ratio VTIA/VTIE = 1.0 found in patients with PEX glaucoma probably could suggest of the early stage of asymptomatic myocardial dysfunction as a consequence of slightly impaired myocardial relaxation. At the time of Doppler echographic examination, the glaucoma patients were without treatment with beta-blockers topically which probably could have an influence on the parameters tested. It is quite possible that these differences in the Doppler waveforms indicate the asymptomatic dysfunction of myocardial relaxation in patients with PEX glaucoma, however with advancing age left ventricular relaxation progressively slows and this can leads to a impaired relaxation of left ventricle[24]. In the myocardium the presence of PEX materials were closely appo-

TABLE 1
THE RESULTS OF ECHOCARDIOGRAPHIC AND DOPPLER ECHOGRAPHIC EXAMINATIONS

	Subjects with PEX glaucoma (n=21)	Control subjects (n=24)	p-value (Mann-Whitney U-test)
EF (%)	59.8 ± 7.9	62.3 ± 4.9	0.2
FS (%)	30.2 ± 6.2	32.9 ± 3.2	0.15
E (cm/s)	63.0 ± 15.2	82.9 ± 22.1	0.003
A (cm/s)	76.6 ±19.1	72.4 ± 15.0	0.56
E/A	0.8 ± 0.1	1.1 ± 0.2	0.00008
VTIE (cm)	8.9 ± 2.2	9.8 ± 1.8	0.18
VTIA (cm)	9.3 ± 2.8	7.6 ± 1.6	0.03
VTIA/VTIE	1.0 ± 0.3	0.8 ± 0.1	0.02
LVEDP (mmHg)	13.1 ± 3.5	13.3 ± 2.3	0.57
PCWP (mmHg)	13.9 ± 3.6	13.8 ± 2.8	0.81

EF=ejection fraction; FS = fractional shortening; peak velocity of early mitral flow; A = peak of late mitral flow; VTIE = velocity time integral of the E wave; VTIA = velocity time integral of the A wawe; LVEDP = left ventricular end-diastolic pressure; PCWP = pulmonary capillary wedge pressure. Values are given as mean ±SD

sed to the myocardial cells and their basement membranes[1,2,4] and these deposits could probably be harmfully for myocardial cells causing prolonged relaxation of left ventricle. Some evidence suggests that vascular endothelial function could also contribute to vascular deficit in glaucoma[25,26]. The increased concentration of endothelin-1 in the plasma of PEX patients was found[27]. An abnormal vascular endothelial function has been shown to occur in heart failure and consequently our findings theoretically could be explained as a part of systemic vascular dysregulation[28]. This is in accordance with findings of Waldmann et al. which indicates that the major cause of the silent myocardial ischemia in glaucoma is not solely explainable by arteriosclerosis changes of coronary arteries but rather by functional vascular dysregulation[9]. Although there was no statistical difference in A and VTIE tested diastolic parameters, the A and VTIE value was higher in patients with PEX glaucoma. Further controlled studies may be required to clarify this. In conclusion, our study indicates the possibility of slightly impaired diastolic function of LV in patients with PEX glaucoma assessed by Doppler-echocardiographic examinations.

As for the limitations, this study was performed using relatively a small number of patients and assessing the presence of abnormalities of diastolic filling in patients with normal left ventricle ejection fraction is difficult to interpret as well. Doppler criteria for diagnosis myocardial diastolic dysfunction in persons over 50 years should include also assessing of the isovolumic relaxation time and E-wave deceleration time[24]. Our results should be confirmed by larger studies.

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DOPLER EHOKARDIOGRAFSKE KARAKTERISTIKE FUNKCIJE LIJEVOG VENTRIKULA U BOLESNIKA SA PSEUDOEKSFOLIJATIVNIM GLAUKOMOM

S A Ž E T A K

Glaukom je povezan sa kardiovskularnim bolestima. Cilj studije je procjena funkcije lijevog ventrikula (LV) kod bolesnika sa pseudoeksfolijativnim (PEX) glaukomom koristeći se dopler ehokardiografskim ispitivanjima. Dvodimenzionalna i pulsna dopler ehokardiografija transmitralnog utoka krvi u srce urađena je kod 21-og bolesnika sa PEX glaukomom i 24 zdrava ispitanika. Kontrakcija i ejekcija lijevog ventrikula je procijenjena pomoću ejekcijske frakcije lijevog ventrikula (EF) i frakcionalnog skraćivanja (FS). Diastolički parametri punjenja LV bili su: rano, brzo dijastoličko punjenje (E-val), kasno dijastoličko punjenje (A-val), omjer E/A, integral brzine kretanja u odnosu na vrijeme E-vala (VTIE) i A vala (VTIA), njihov međusobni omjer (VTIE/VTIA), tlak na kraju punjenja lijevog ventrikula (LVEDP) i tlak u plućnim kapilarama (PCWP). Značajne razlike između promatranih parametara punjenja LV nađene su kod E, E/A, VTIA i VTIE/VTIA. Nisu nađene značajnije razlike u EF, FS, A, VTIE, LVDP i PCWP. Na osnovu dopler ehokardiografskih ispitivanja naša studija ukazuje na mogućnost blagog oštećenja dijastoličke funkcije lijevog ventrikula kod bolesnika sa PEX glaukomom.