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

Lovro Bojić1, Ratko Ermacora2, Milan Ivanišević1, Davor Galetović1, Zdravko Mandić3, Katia Novak-Lauš3 and Branimir Cerovski4

1 University Department of Ophthalmology, Clinical Hospital Split, Split, Croatia
2 University Department of Internal Medicine, Clinical Hospital Split, Split, Croatia
3 University Department of Ophthalmology, Clinical Hospital «Sisters of Mercy», Zagreb, Croatia
4 University Department of Ophthalmology, Clinical Hospital Center «Rebro», Zagreb, Croatia

ABSTRACT

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), LVEDP and 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 extracocular deposition of abnormal extracellular matrix material and it has been found to be the most common precursor of open-angle glaucoma3. The presence of pseudoexfoliative fibrils has been found in various tissues in the body including the skin, kidney, heart, lungs, gallbladder, blood vessels, optic nerve and cerebral meninges3-4. 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 disease3-7. 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 disease7. However no increase in mortality rates in person with PEX has been shown6. Primary open-angle glaucoma occurs more commonly in eyes with PEX5. Recent evidence indicates that the ocular features of PEX syndrome are in fact only one manifestation of a systemic process2 Cardiovascular abnormalities as well as myocardial ischemia are more often observed in glaucoma patients than in normals10-11. Some of these patients may go through a phase of asymptomatic left ventricular dysfunction, but overt heart failure is not present12,13. 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,
diastolic dysfunction occurs when these process are prolonged, slowed or incomplete. 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 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 filling (E wave, which encompasses 85% of total diastolic filling during diastole), late diastolic filling (A wave, which represents the last of approximately 15% of ventricular filling during diastole), ratio E/A, velocity time integral (VTI) and atrial contribution to the left ventricle filling. From the parasternal short-axis derived M-modes of the left ventricle, the end-diastolic and end-systolic diastolic filling were measured. Left ventricular ejection fraction and fractional shortening were obtained according to the Kessler. Left ventricular diastolic function was evaluated by the pulsed Doppler technique measuring mitral venous flow. The following transmitral Doppler parameters were analysed: E, A, VTI, ratio VTI/E, and ratio VTI/A. LV EDP and PCWP were calculated according to the formula of Stock at al. 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, VTI and VTI/E. Although the significant difference was not found among VTI 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. 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, VTI, PCWP, and LVEDP, a significant difference was found. In healthy 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 VTI and ratio VTI/E/VTI = 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 lead to an impaired relaxation of left ventricle. In the myocardium the presence of PEX materials were closely appro.
REFERENCES


TABLE 1

THE RESULTS OF ECHOCARDIOGRAPHIC AND DOPPLER ECHOCARDIOGRAPHIC EXAMINATIONS

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

EF = ejection fraction; FS = fractional shortening; peak velocity of early mitral flow; A = peak of late mitral flow; VTIE = velocity time integral of the A wave; 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, and these deposits could probably be harmful for myocardial cells causing prolonged relaxation of left ventricle. Some evidence suggests that vascular endothelial function could also contribute to vascular deficit in glaucoma. The increased concentration of endothelin-1 in the plasma of PEX patients was found. 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. 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. Although there was no statisti...
DOPLER EHOKARDIOGRAFSKE KARAKTERISTIKE FUNKCIJE LIJEVOG VENTRIKULA U BOLESNIKA SA PSEUDOEKSFOLIJATIVNIM GLAUKOMOM

SAŽETAK