Association between coronary artery disease and responsiveness of aortic stiffness and pulsatile diameter change to nitroglycerin

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Abstract

Aim: This study aimed to evaluate the difference between the effect of nitroglycerin on the aortic stiffness measured by transthoracic M-mode ultrasonography in patients with and without coronary artery disease (CAD).

Material and Methods: This study was conducted on one hundred patients with a presume diagnosis of CAD. The patients who had a SYNTAX score (SS) ≥1 according to the results of coronary angiography constituted the CAD group (n:60), while patients who had a SS=0 constituted the control group (n:40). The stiffness of the ascending aorta and arterial blood pressure were measured before and 10 minutes after the sublingual administration of 800 mcg nitroglycerin. A comparison of each parameter before and after nitroglycerin was evaluated for statistical significance using paired sample t-test.

Results: In the control group, after nitroglycerin administration, there was a statistically significant reduction in the pulsatile diameter change (from 2.30±0.79 to 1.74±0.91) and significant increase in stiffness index (from 6.24±2.41 to 9.07±5.88). In the CAD group, after nitroglycerin administration, there was no statistically significant difference in terms of pulsatile diameter change (from 1.42±0.88 to 1.28±0.68) and stiffness index (from 13.52±7.64 to 13.10±7.85).

Conclusion: The effect of nitroglycerin on the aortic stiffness measured by transthoracic M-mode ultrasonography differs in the CAD and control groups. Our findings warrant further studies with a larger population to describe the practicability of this method for the CAD diagnosis.

Keywords: Aorta; Coronary Artery Disease; Stiffness; Nitroglycerin.

INTRODUCTION

The stiffness of the aorta may cause an abnormal pressure pattern that increases the afterload of the left ventricle. In that way, it may induce a left ventricular hypertrophy, left ventricular diastolic and systolic dysfunction as well as coronary ischemia. It is a well-known that atherosclerotic stiffness is an independent predictor of all cause-mortality in different groups of patients (1).

Several previous studies demonstrated that the elasticity of the ascending aorta decreases in the presence of coronary artery disease (CAD) (2,3). For example, the blood flow to the vasa-vasorum of the ascending aorta decreases in patients with CAD because the blood vessels that supply the vaso-vasorum of the ascending aorta originate from the coronary arteries (4). Moreover, similar grades of atherosclerosis, which was found in an autopsy analysis of patients, develop on the distribution of coronary and aortic atherosclerosis. Consequently, atherosclerosis may affect the aortic elasticity (5,6). The decreased aortic elasticity causes an increase of the central pulsatile pressure, thereby results in an increased vessel wall tension. The increased vessel wall tension eventually leads to atherosclerosis by causing endothelial dysfunction (7).

Nitroglycerin may increase distensibility of peripheral muscular arteries (8). However, the effect of nitroglycerin
on the stiffness of aorta, as an elastic artery, has not been precisely clarified. There is also conflicting data about the impact of nitroglycerin on aortic stiffness in the presence of CAD. Shimizu et al. reported a reduction in the arterial stiffness, measured by cardio-ankle vascular index, in healthy subjects and patients with CAD after nitroglycerin administration (9). On the other hand, Yamamoto et al. demonstrated that after nitroglycerin administration, there was only a decreased aortic stiffness in healthy subjects in contrast to CAD patients (10).

The aim of the study was to evaluate the difference between effects of nitroglycerin on the aortic stiffness measured by transthoracic M-mode ultrasonography in patients with and without CAD.

MATERIAL and METHODS

Patient selection and study protocol

This study was conducted on the patients admitted for elective coronary angiography with a presumed diagnosis of CAD. In the present study, all patients underwent a coronary angiography. The patients who had SYNTAX score (SS) ≥ 1 according to the results of coronary angiography constituted the CAD group, while the patients who had a SS=0 constituted the control group. The stiffness of the ascending aorta and arterial blood pressure were measured before and 10 min after the sublingual administration of 800 mcg nitroglycerin. A detailed clinical history, including cardiovascular risk factors and all medication was obtained from all participants. In the study, all patients continued to their medications.

The patients who had at least one of the following factors were excluded from the study. These were: hemodynamic instability, cerebrovascular incident, severe valvular heart disease, heart failure (ejection fraction (EF) of <45%), chronic renal failure, atrial fibrillation, any aortic vessel disease such as aortic aneurysm, Marfan syndrome, aortic coarctation, and a previous aortic valve surgery, a prior revascularization such as percutaneous coronary angioplasty or coronary aortic by-pass surgery, a previous history of myocardial infarction. In addition, the patients whose echocardiographic image quality was insufficient were excluded from the study.

The patients’ baseline demographic characteristics and all medications including age, gender, height, weight, hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking, angiotensin converting enzyme inhibitor, angiotensin receptor blocker, beta blocker, calcium channel blocker, and nitrate use were recorded. The body mass index (BMI) was calculated for each patient using a following equation; weight divided by height squared (kg/m²). The patients were considered to have diabetes mellitus if their fasting blood sugar levels ≥ 126 mg/dL or used oral hypoglycemic agents, insulin sensitizers, or insulin. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or self-reported use of antihypertensive medication. The criterion for hyperlipidemia was total cholesterol level ≥ 220 mg/dL or receiving a lipid-lowering therapy.

Each subject provided an informed written consent prior to participate in the study. The study was approved by our university Ethics review board, and it was conducted in accordance with the principles of the Declaration of Helsinki.

Blood pressure measurement

Blood pressure was measured using sphygmomanometer with a standard cuff from the right arm. The echocardiographic examination was simultaneously performed during the blood pressure monitoring. The first and fifth Korotkoff sounds were accepted as systolic and diastolic blood pressure values, respectively. The pulse pressure (PP) and the mean blood pressure (MBP) were calculated using the following formulas:

\[
PP = SBP - DBP
\]

\[
MBP = (2 x DBP + SBP) / 3
\]

Echocardiographic examination

Transesophageal echocardiography was performed using 3.5 MHz phased probe with a Philips HD11 XE device at the lateral decubitus position. A continuous electrocardiography (ECG) monitoring was performed during the procedure. M-mode and 2D measurements were performed on the parasternal long axis view in accordance with guidelines of American Society of Echocardiography. The left ventricle EF was calculated with using the Teichholz method (11,12). After an observing the ascending aorta on the parasternal long-axis, M-mode transducer was placed passing through the ascending aorta region at 3 cm distal to the aortic valve in order to obtain the trace for calculation of systolic and diastolic diameters of the ascending aorta (Figure 1) (13,14). A systolic diameter was measured from the maximum point of forward motion in the aortic trace, while a diastolic diameter was measured from the location according to the R wave peak on the ECG. The mean systolic and diastolic measurements were calculated from a three consecutive measurements. The aortic elasticity parameters such as stiffness index (SI) and aortic dispensability (AD) were calculated using the following formulas (13,14):

\[
SI = \ln \left(\frac{SBP}{DBP}\right) / \text{pulsatile diameter change}
\]

\[
AD = \left(\text{cm}^2 \cdot \text{dyn}^{-1} \cdot 10^{-6}\right) = 2x \left(\text{pulsatile diameter change}\right) / PP \times \text{diastolic diameter}
\]

All echocardiography were performed and analyzed by one cardiologist who was blinded to clinical data of the patient. Intra-observer variability was calculated as the difference in two measurements of the same patient by one observer divided by the mean value. Intra-observer variability's were less than 5% for aortic elasticity measurements.
Systolic and diastolic diameter measurements of the ascending aorta with M-mode echocardiography. Before (1A) and after (1B) sublingual administration of nitroglycerin, there was no change in pulsatile diameter change in a CAD patient. Before (1C) and after (1D) sublingual administration of nitroglycerin, there was a prominent decrease in pulsatile diameter change in a non-CAD patient after nitroglycerin. AoS: Aortic systolic diameter, AoD: Aortic diastolic diameter

Angiographic evaluation
All patients underwent a selective coronary angiography using the Judkins percutaneous trans-femoral technique. Coronary angiograms were recorded in digital media for quantitative analysis (Dicom-viewer; MedCom GmbH, Darmstadt, Germany). Coronary angiograms were analyzed by two independent interventional cardiologists, who were blinded to patients’ data. The CAD was classified according to SYNTAX scoring. Each lesion ≥1.5 mm in diameter and with ≥50% stenosis was scored and the total score of each patient was calculated using the online SYNTAX score Calculator, version 2.1 (www.syntaxscore.com). Patients with SS ≥1 were considered to have CAD, while those with SS=0 were considered as control group.

Statistical analysis
The definitive statistics was separately performed for the samples in the CAD and control groups for the presentation of the demographic characteristics of the study group. The mean value ± standard deviation was used for continuous variables. The frequencies and percentages (%) were used for a categorical data. The Chi-square test was used to determine whether there was a difference between the groups with respect to the variables such as gender, hypertension, diabetes mellitus, cigarette smoking, hyperlipidemia, angiotensin receptor blocker, beta blocker, calcium channel blocker, and nitrate. Independent sample t-test was used to determine whether there was a difference between the groups with respect to the variables such as weight, height, BMI, EF, age, aortic elasticity parameters, blood pressure and heart rate. Paired sample t-test was used for a comparison between the results obtained before and after nitroglycerin administration. The correlation of the Δ stiffness index and the Δ pulsatile diameter change with SS was assessed using Pearson correlation analyses. The Δ stiffness index and the Δ pulsatile diameter change with the best specificity and sensitivity for predicting presence of CAD was calculated using receiver-operating characteristic (ROC) curve analysis. Statistical analyses were performed using SPSS v.11.5 and Med Calc v11.0 package software. A statistical significance level was accepted as p<0.05.

The effect size (Cohen’s d) and power value (1-β) of the stiffness index and the pulsatile diameter change comparison between patients with and without CAD were calculated using G*Power software (version 3.1.9.2). The alpha level used for this analysis was < 0.05. The effect size and power value of the stiffness index comparison were 1.28 and 0.95, respectively, and the effect size and power value of the pulsatile diameter change comparison were 1.05 and 0.95, respectively. The mean stiffness index of patients with and without CAD was 13.5 ± 7.6 and 6.2 ± 2.4, respectively. The minimum number of patients to be enrolled in this study was calculated, and it was found to be 13 for those with CAD and 13 for those without CAD. The mean pulsatile diameter change average of patients with and without CAD was 1.4 ± 0.9 and 2.3 ± 0.8, respectively. The minimum number of patients to be enrolled in this study was calculated, and it was found to be 21 for those with CAD and 21 for those without CAD.

RESULTS
According to the results of coronary angiography, 60 subjects who had a SS≥1 constituted the CAD group, while 40 subjects who had a SS=0 constituted the control group. The groups were similar in terms of baseline demographic characteristics excluding age, gender, aortic distensibility, pulsatile diameter change and stiffness index (p<0.05, for all) (Table 1).

In the CAD group, a comparison between the hemodynamic and aortic characteristics before and after administration of nitroglycerin demonstrated a statistically significant reduction in the systolic blood pressure, the mean blood pressure, and the pulse pressure (p<0.05, for all). A reduction in the diastolic blood pressure was also statistically significant between both groups (p=0.045). In addition, the increase of heart rate was statistically significant between both groups (p<0.001) (Table 2). There was no statistically significant difference in terms of aortic pulsatile diameter change, aortic distensibility, and stiffness index (Table 2).

In the control group, a comparison between the hemodynamic and aortic characteristics before and after administration of nitroglycerin showed a statistically significant reduction in systolic blood pressure, mean blood pressure and pulse pressure (p<0.05, for all). A reduction in diastolic blood pressure was also statistically significant between both groups (p=0.047). The increase of heart rate was statistically significant between both groups (p=0.001) (Table 2). There was a statistically significant reduction in pulsatile diameter change and a significant increase in the stiffness index (p<0.001 and p<0.001, respectively). There was no statistically significant difference in terms of aortic distensibility between both groups (Table 2).
Both groups were similar with respect to the pressure and heart rate changes after nitroglycerin administration (p > 0.05 for all). In terms of the aortic elasticity parameters, the stiffness index was found to be a statistically significant (p = 0.024), while the aortic distensibility was statistically insignificant after nitroglycerin administration (Table 2). There was also a statistically significant difference in terms of pulsatile diameter change after nitroglycerin administration between the groups (p = 0.014) (Table 2).

In the receiver operating characteristic (ROC) curve analysis, the area under curve (AUC) of the ∆ stiffness index was 0.690 (95% CI: 0.590–0.779, p < 0.001). The optimal cut-off value for the ∆ stiffness index that indicated a CAD was ≤ -0.667 with 55% sensitivity and 82.5% specificity (Figure 2).

Similarly, the AUC of the ∆ pulsatile diameter change was 0.666 (95% CI: 0.564–0.757, p = 0.007). The optimal cut-off value for the ∆ pulsatile diameter change that indicated a CAD was > -0.03 with 70% sensitivity and 70% specificity (Figure 3).

In correlation analyses, there was a moderate inverse correlation between the ∆ stiffness index and the SS (r = -0.475, p < 0.001), and a weak-moderate correlation between the ∆ pulsatile diameter change and the SS (r = 0.327, p = 0.011) (Table 3).

### Table 1. Demographic and definitive characteristics of the groups

<table>
<thead>
<tr>
<th></th>
<th>Total cohort (n=100)</th>
<th>Control group (n=40)</th>
<th>CAD group (n=60)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male n (%)</td>
<td>55 (55.0%)</td>
<td>15 (37.5%)</td>
<td>40 (66.7%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.71±3.83</td>
<td>27.92±4.22</td>
<td>27.58±3.57</td>
<td>0.668</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>60.38±9.96</td>
<td>61.23±8.38</td>
<td>59.82±10.91</td>
<td>0.491</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.51±10.57</td>
<td>53.78±10.00</td>
<td>60.00±10.28</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypertension n (%)</td>
<td>51 (51.0%)</td>
<td>19 (47.5%)</td>
<td>32 (53.3%)</td>
<td>0.568</td>
</tr>
<tr>
<td>Diabetes mellitus n (%)</td>
<td>24 (24.0%)</td>
<td>9 (22.5%)</td>
<td>15 (25%)</td>
<td>0.281</td>
</tr>
<tr>
<td>Cigarette smoking n (%)</td>
<td>30 (30.0%)</td>
<td>9 (22.5%)</td>
<td>21 (35%)</td>
<td>0.181</td>
</tr>
<tr>
<td>ARB use n (%)</td>
<td>13 (13.0%)</td>
<td>6 (15%)</td>
<td>7 (11.7%)</td>
<td>0.627</td>
</tr>
<tr>
<td>ACEI use n (%)</td>
<td>21 (21.0%)</td>
<td>8 (20%)</td>
<td>13 (21.7%)</td>
<td>0.84</td>
</tr>
<tr>
<td>Beta blocker use n (%)</td>
<td>24 (24.0%)</td>
<td>8 (20%)</td>
<td>16 (26.7%)</td>
<td>0.444</td>
</tr>
<tr>
<td>CCB use n (%)</td>
<td>10 (10.0%)</td>
<td>2 (5%)</td>
<td>8 (13.3%)</td>
<td>0.156</td>
</tr>
<tr>
<td>Nitrate use n (%)</td>
<td>10 (10.0%)</td>
<td>4 (10%)</td>
<td>6 (10%)</td>
<td>1.000</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>124.40±16.94</td>
<td>123.75±18.04</td>
<td>124.88±16.31</td>
<td>0.756</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>77.15±11.22</td>
<td>78.50±11.99</td>
<td>76.25±10.68</td>
<td>0.328</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>47.25±10.62</td>
<td>45.25±10.74</td>
<td>48.58±10.42</td>
<td>0.125</td>
</tr>
<tr>
<td>Pulsatile diameter change (mm)</td>
<td>1.77±0.95</td>
<td>2.30±0.79</td>
<td>1.42±0.88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic distensibility (cm².dyn⁻¹.10⁻⁶)</td>
<td>2.10±1.37</td>
<td>2.86±1.28</td>
<td>1.59±1.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stiffness index</td>
<td>10.61±7.06</td>
<td>6.24±2.41</td>
<td>13.52±7.64</td>
<td>0.183</td>
</tr>
<tr>
<td>Heart Rate (beats/min)</td>
<td>67.09±11.23</td>
<td>65.82±11.22</td>
<td>67.93±11.25</td>
<td>0.360</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>92.90±12.43</td>
<td>93.58±13.37</td>
<td>92.44±11.86</td>
<td>0.656</td>
</tr>
<tr>
<td>SYNTAX Score</td>
<td>-</td>
<td>-</td>
<td>18.8±8.6</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ACEI- angiotensin converting enzyme inhibitor; ARB- angiotensin receptor blocker; CCB- calcium channel blocker; CAD- coronary artery disease; DBP- diastolic blood pressure; LVEF- left ventricular ejection fraction; MBP- mean blood pressure; SBP- systolic blood pressure

### Table 2. Hemodynamic and aortic characteristics of the groups before and after nitroglycerin administration

<table>
<thead>
<tr>
<th></th>
<th>CAD group (n=60) after NTG</th>
<th>CAD group (n=60)</th>
<th>p-value for CAD group before and after NTG</th>
<th>Control group (n=40) after NTG</th>
<th>Control group (n=40)</th>
<th>p-value for Control group before and after NTG</th>
<th>p-value for Δ changes of variables between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>124.83±16.31</td>
<td>114.08±0.35</td>
<td>&lt;0.001</td>
<td>123.75±18.04</td>
<td>113.00±12.70</td>
<td>&lt;0.001</td>
<td>1</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>76.25±10.68</td>
<td>74.08±10.68</td>
<td>0.045</td>
<td>78.50±11.99</td>
<td>75.88±9.05</td>
<td>0.047</td>
<td>0.784</td>
</tr>
<tr>
<td>Pulsatile diameter change (mm)</td>
<td>1.42±0.88</td>
<td>1.28±0.68</td>
<td>0.134</td>
<td>2.30±0.79</td>
<td>1.74±0.91</td>
<td>&lt;0.001</td>
<td>0.014</td>
</tr>
<tr>
<td>Aortic distensibility (cm².dyn⁻¹.10⁻⁶)</td>
<td>1.59±1.20</td>
<td>1.73±1.07</td>
<td>0.328</td>
<td>2.86±1.28</td>
<td>2.53±1.45</td>
<td>0.183</td>
<td>0.154</td>
</tr>
<tr>
<td>Stiffness index</td>
<td>13.52±7.64</td>
<td>13.10±7.85</td>
<td>0.700</td>
<td>6.24±2.41</td>
<td>9.07±5.88</td>
<td>&lt;0.001</td>
<td>0.024</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>92.44±11.86</td>
<td>93.58±13.37</td>
<td>0.007</td>
<td>88.25±9.60</td>
<td>88.25±9.60</td>
<td>0.001</td>
<td>0.882</td>
</tr>
<tr>
<td>Heart Rate (beats/min)</td>
<td>67.93±11.25</td>
<td>72.05±11.61</td>
<td>&lt;0.001</td>
<td>65.82±11.22</td>
<td>70.25±11.28</td>
<td>0.001</td>
<td>0.822</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>48.58±10.42</td>
<td>40.00±8.34</td>
<td>&lt;0.001</td>
<td>45.25±10.74</td>
<td>37.12±8.54</td>
<td>&lt;0.001</td>
<td>0.817</td>
</tr>
</tbody>
</table>

Abbreviations: DBP- diastolic blood pressure; MBP- mean blood pressure; NTG- nitroglycerin; SBP- systolic blood pressure. Δ changes: subtraction of before nitroglycerin administration levels from after nitroglycerin administration levels
DISCUSSION

In our study, the presence of CAD was found to be associated with aortic elasticity parameters such as aortic distensibility and stiffness index. The result of our study is found to be a parallel with a current literature (14-17).

An analysis of the aortic elasticity involves the aorta and its main branches with distinguished characteristics from the smaller and more muscular peripheral arteries such as radial and brachial arteries. The stiffness index and aortic distensibility, which show mechanical features of the aortic wall, are known as aortic elasticity parameters. The aortic elasticity is calculated from a relationship between blood pressure and aortic diameter that is based on an establishment of an association with the aortic diameter change against the pressure of tensile strength (13).

In our study, after nitroglycerin administration, a significant increase was found in stiffness index in the control group, whereas no difference was found in the CAD group. There was no statistically significant difference with respect to pulsatile diameter change in CAD group. However, a significant reduction was found in pulsatile diameter change in the control group. The significant increase in stiffness index may be due to the significant reduction in pulsatile diameter change in the control group because the control group showed a similar baseline blood pressure level and a similar level of change after nitroglycerin administration. The different effects of pulsatile diameter change on the aortic distensibility and stiffness index result from their different dependence to blood pressure when a calculation was performed (18). The pulsatile diameter change is affected by pulse pressure, the mean arterial pressure, and absolute aortic elasticity. Because the mean arterial pressure is almost same in the central and peripheral arteries, a reduction in this parameter showed a similar increasing effect on pulsatile diameter change in both groups. The only explanation for the significant difference in terms of pulsatile diameter change between the groups may be a different level of reduction in the central pulse pressure, which could not be perceived in the peripheral pulse because we were only able to measure the blood pressure from the arm. Our study indirectly indicates that nitroglycerin administration leads to a higher reduction in the central pulse pressure in the control group when compared to the CAD group. This issue should be elucidated by further studies with an aim in direct measuring of the aortic root blood pressure after nitroglycerin administration in those groups.

Nitroglycerin provides a reduction in wave reflection which causes a late systolic pressure peak in the aorta (19). Nitroglycerin has a strong effect on the peripheral muscular arteries with a reduction in wave reflection. Thus, it causes a reduction in the late systolic pressure peak, central systolic blood pressure, and central pulse pressure (19,20). It has been reported that nitroglycerin administration provides a more remarkable reduction in the systolic blood pressure and pulse pressure in the aorta.
when compared to the brachial artery (21,22). It has been also demonstrated that vasodilator response of the smooth muscles in the vessel wall to nitroglycerin is impaired in atherosclerosis (23-25). Nitroglycerin may have shown a different grade of effect on the wave reflection in the CAD and control groups because the peripheral muscular arterial dilatation provided by nitroglycerin administration could not be remarkable in the CAD group when compared with the patients in the control group. Even though the results of our study indirectly support the conclusion that nitroglycerin may show different grades of impact on the wave reflection in CAD and control groups, further studies are needed to clarify this issue.

Several limitations of this study should be considered. First, the sample size was small; hence it may affect the statistical power of the study. Second, our findings may only be pivotal for the detection of CAD with a small sample size, that's why definitive conclusions should not be drawn. Third, as the half of the study patients had hypertension, the effect of medications on the aortic elasticity parameters cannot be excluded. Finally, in our study, the blood pressure was measured using sphygmomanometer as same in a daily life practice because the blood pressure measurement in the ascending aorta usually requires an invasive intervention.

CONCLUSION

Our findings showed that the pulsatile diameter significantly decreased, while the aortic stiffness index significantly increased after nitroglycerin administration in the control group. However, these changes were not encountered in the CAD group. The aortic stiffness measured by transthoracic M-mode ultrasonography response to nitroglycerin differently in the CAD and control groups. Our findings warrant further studies with a larger population to describe the practicability of this method for the CAD diagnosis.

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REFERENCES

11. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440-63.
22. Kelly RP, Gibbs HH, O'Rourke MF, et al. Nitroglycerin has
more favourable effects on left ventricular afterload than apparent from measurement of pressure in a peripheral artery. Eur Heart J 1990;11:138-44.

