



## Chronic and Acute Effects of Smoking on Left and Right Ventricular Relaxation in Young Healthy Smokers\*

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**Background:** Left ventricular (LV) diastolic dysfunction has been observed in cigarette smokers with coronary artery disease. The aim of the study was to assess LV and right ventricular (RV) diastolic function in healthy, young, and slim smokers before and after smoking one cigarette.

**Material and methods:** The participants were 66 healthy volunteers (age < 40 years; body mass index < 25 kg/m<sup>2</sup>): 33 smokers (study group [HS]) and 33 nonsmokers (control group). Echocardiographic examination was done in the HS before smoking one cigarette (HS-1) and after smoking one cigarette (HS-2). To assess diastolic function of LV and RV mitral valve flow (MVF), pulmonary venous flow (PVF) and tricuspid valve flow (TVF) were evaluated.

**Results:** MVF early to late phase ratio (E/A) was significantly lower in HS-1 and HS-2 than in the control group. The PVF systolic to diastolic phase ratio (S/D) was significantly higher in HS-1 and HS-2 than in the control group. These changes suggest LV diastolic function impairment in the HS, but the MVF pattern remained within the normal range. PVF S/D showed systolic dominance (S/D > 1) typical for impaired LV relaxation and abnormal for this age group. TVF E/A was significantly lower in HS-2 than in HS-1 and control subjects and suggests RV diastolic dysfunction.

**Conclusions:** The following conclusion are made: (1) MVF and PVF demonstrate LV relaxation impairment in healthy smokers before and after smoking one cigarette; (2) the assessment of PVF is a good method reflecting LV diastolic function changes, even when MVF remains normal; and (3) TVF shows RV relaxation impairment after smoking one cigarette in healthy smokers.

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**Key words:** cigarette smoking; echocardiography; diastolic function; heart; left ventricle; right ventricle

**Abbreviations:** A = late phase; BMI = body mass index; D = maximal velocity of pulmonary venous flow diastolic phase; DT = deceleration time of early phase of mitral or tricuspid valve flow; E = early phase; E/A = early to late phase ratio; HS = study group; HS-1 = study group before smoking one cigarette; HS-2 = study group after smoking one cigarette; IVRT = isovolumetric relaxation time; LV = left ventricular; MPI = myocardial performance index; MVF = mitral valve flow; PVF = pulmonary venous flow; RV = right ventricular; S = maximal velocity of pulmonary venous flow systolic phase; S/D = systolic to diastolic phase ratio; TVF = tricuspid valve flow; VTI = velocity time integral

Impairment of relaxation, the early phase of ventricular diastole, is the first stage of diastolic dysfunction. Left ventricular (LV) diastolic function

can be determined by Doppler echocardiography-derived mitral valve flow (MVF) velocities.<sup>1–4</sup> The addition of a pulmonary venous flow (PVF) pattern enables more accurate assessment of LV diastolic

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function<sup>1,5,6</sup> The role of the right ventricle in hemodynamic function of the heart is now emphasized. Right ventricular (RV) diastolic function can be assessed by recording the tricuspid valve flow (TVF) pattern, but the studies on this subject are sparse.<sup>7–10</sup> In the last decade, the myocardial performance index (MPI) has been described as a good marker of ventricular global—systolic and diastolic—function.<sup>11,12</sup> Impaired LV diastolic function usually precedes systolic dysfunction<sup>13</sup> and may cause clinical signs of congestive heart failure.<sup>3,14</sup> Cigarette smoking is one of the major risk factors for cardiovascular disease. In smokers with coronary artery disease, abnormalities of LV diastolic function were detected.<sup>15,16</sup> The impairment of LV relaxation observed in healthy smokers was shown in some studies. Most of the researchers<sup>17–19</sup> assessed LV diastolic function by evaluation of MVF. The aim of our study was to examine the LV diastolic function by assessing MVF and PVF, LV MPI, and also diastolic and global RV function in young healthy smokers before and after smoking one cigarette. LV diastolic function may be impaired by obesity,<sup>17</sup> and the Doppler patterns of diastolic filling are strongly dependent on age<sup>20,21</sup>; therefore, the authors conducted the study on young (age  $\leq 40$  years) participants with normal body mass index (BMI). The focus of interest was if smoking impaired the LV and RV function even in healthy, young, and slim persons.

## MATERIALS AND METHODS

### Participants

The inclusion criteria were age  $< 40$  years, BMI  $< 25$  kg/m<sup>2</sup>, normal BP, and normal parameters of echocardiographic examination (wall thickness, left and right chamber size, valvular function, and left and right ventricular systolic function). All the participants were healthy volunteers with normal results of routine physical examination, chest radiography, standard resting ECG, and routine laboratory tests. The inclusion criteria for smokers were additionally smoking  $> 10$  cigarettes per day over the last 5 years. The study group (HS) consisted of 33 healthy smokers (19 women, age 22 to 40 years) who smoked 10 to 25 cigarettes per day for 6 to 20 years. The control group included 33 healthy nonsmokers (16 women, age 20 to 40 years).

### Study Protocol

In all participants, echocardiographic examination in the left lateral position, and heart rate and BP measurements after 10 min of rest were performed. In the HS, the first examination was done after a 2-h nonsmoking period (HS before smoking one cigarette [HS-1]); the second examination was done immediately after smoking one cigarette containing 0.9 mg of nicotine (HS after smoking one cigarette [HS-2]). The duration of the second examination was 9 to 14 min. All participants gave written consent before inclusion in the study. The protocol was approved by the Bioethical Committee of Warsaw Medical University.

### Methods

Echocardiography was performed with a Hewlett-Packard SONOS 2000 (Andover, MA) imaging system. Transducer frequency was 2 MHz. Recording and calculations were performed according to the standards and recommendation of the American Society of Echocardiography.<sup>22</sup>

Echocardiographic studies were recorded on videotape. In LV and RV filling, end-expiratory beats were measured and a mean of three cycles was used for calculations. The analysis of echocardiograms was performed by two independent observers.

### LV Diastolic Function Assessment

From the apical four-chamber view, the transmitral flow at the level of the leaflet tips was obtained and following parameters were defined: the maximal velocity (centimeters per second) of MVF early phase (E) and the maximal velocity of MVF late phase (A), the MVF E/A ratio, and deceleration time (DT; milliseconds) of MVF E. From the apical five-chamber view, the simultaneous recording of the aortic and mitral flows was evaluated and the isovolumetric relaxation time (IVRT; milliseconds) was measured.<sup>1,23</sup> From the apical four-chamber view, PVF was revealed by placing the pulsed-wave Doppler sample volume approximately 1 cm into the right upper pulmonary vein.<sup>1</sup> The following parameters were defined: the maximal velocity of PVF systolic phase (S), the maximal velocity of PVF diastolic phase (D), the PVF S/D ratio, and the maximal velocity of atrial reversal flow.<sup>1,23</sup> Technically sufficient for calculations, Doppler spectrum of atrial reversal flow was detected in 82% of participants. Normal values for persons  $< 40$  years old according to previously reported data<sup>4,6,21,24</sup> were as follows: E/A  $> 1$ , DT  $< 180$  ms, IVRT  $< 75$  ms, S/D  $< 1$ , and atrial reversal flow  $< 0.35$  cm/s as reflecting normal atrial pressure. Impaired relaxation was defined by the diminution of E/A, prolongation of DT and IVRT, and S/D elevation (Fig 1).

### Global LV Function Assessment

LV MPI, defined as the sum of LV isovolumetric contraction and relaxation times (milliseconds) divided by the LV ejection

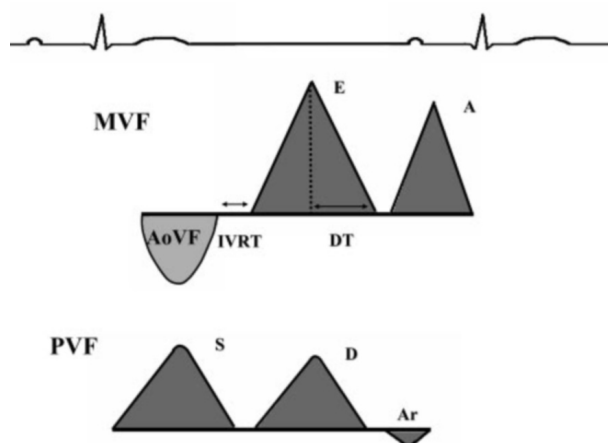


FIGURE 1. The parameters of Doppler MVF and PVF. Impairment of relaxation is reflected in MVF by decreased velocity of E, increased velocity of A, and longer duration of times: IVRT and DT and in PVF by increased velocity of S and decreased velocity of D. Atrial reversal flow (Ar) velocity reflects atrial pressure. AoVF = aortic valve flow.

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