Dose-Dependent Acute Effects of Passive Smoking on Left Ventricular Cardiac Functions in Healthy Volunteers

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Objective: We have previously shown that acute passive smoking impaired left ventricular diastolic function in healthy volunteers. The aim of this study was to determine whether length of exposure and/or ambient smoke concentration is the key determinant of this outcome.

Methods: We measured blood carboxyhemoglobin (COHb)and lactate level to investigate the acute effects of passive smoking on tissue oxygenation. A total of 90 healthy nonsmoker volunteers were prospectively enrolled into the study. Each of 30 subjects were exposed to carbon monoxide (CO) less than 5.0 ppm smoke in group A for 30 minutes, to CO 5 to 10 ppm smoke in group B for 30 minutes, and to CO less than 5.0 ppm smoke in group C for 60 minutes. Hemodynamic parameters were obtained, blood samples for measuring COHb and lactate levels were taken and echocardiographic examinations were performed at baseline and after exposure to passive smoking.

Results: Mean ± SD CO levels in groups A, B, and C were 4.2 ± 0.5 ppm, 9.2 ± 0.3 ppm, and 4.1 ± 0.8 ppm, respectively. There was no change in left ventricular systolic functions in all groups. Left ventricular diastolic functions were impaired in groups B and C, whereas no change was observed in group A. Carboxyhemoglobin and lactate levels increased after passive smoking in groups B and C. However, group B had significantly higher COHb and lactate levels compared to group C ($P < 0.001$).

Conclusions: Our results suggested that passive smoking at a certain dose in relation with length of exposure and ambient smoke concentration seems to cause relative left ventricular diastolic dysfunction.

Key Words: passive smoking, left ventricular diastolic function, length of exposure, ambient smoke concentration, carboxyhemoglobin levels, lactate levels

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Exposure to passive smoking over a period of time is a form of environmental risk. It is strongly associated with increased cardiovascular morbidity and mortality that has been estimated approximately one third of which is seen in active smokers.[1,2]

Diastolic dysfunction is associated with impaired clinical status and poor prognosis. Even in asymptomatic patients, mild diastolic dysfunction was associated with a 5-fold higher 3- to 5-year mortality in comparison with subjects with normal diastolic functions.[3] We have previously shown that acute exposure to passive smoking impaired left ventricular diastolic functions immediately in healthy volunteers.[4]

Carbon monoxide (CO) is one of the major components of tobacco smoke, which is suspected to play a major role in cigarette smoke–induced cardiovascular diseases. Carboxyhemoglobin (COHb) is a stable complex of CO and hemoglobin that forms in red blood cells when CO is inhaled and hinders delivery of oxygen to the tissues.[5] Lactate accumulation occurs when the supply of oxygen to the tissues is limited; either the muscle cells are working so hard that the supply cannot keep up or the supply itself is not enough for some conditions including ischemia, hypoxia, sepsis, and acute lung injury.[6,7]

In this study, we aimed to evaluate the dose-dependent acute effect of passive smoke exposure on cardiac functions and hemodynamic parameters in healthy volunteers in 3 study groups, which differ from each other according to duration and/or intensity of smoke exposure. We measured blood COHb and lactate level to investigate the acute effects of passive smoking on tissue oxygenation.

MATERIALS AND METHODS

Participants

Ninety healthy nonsmoker volunteers (45 men; mean ± SD age, 25 ± 5 years) were prospectively enrolled into the study. Subjects were excluded from the study if they had a history of hypertension, diabetes mellitus, hyperlipidemia, coronary heart disease, left ventricular hypertrophy, and lung disease. All of the participants had normal blood pressure at the time of the examination. Results of physical examinations, resting electrocardiograms, chest roentgenograms, echocardiographic parameters, and respiratory function tests were all normal. All subjects were in sinus rhythm.

This study complied with the Declaration of Helsinki and was approved by the ethics committee and the institutional review board of Erciyes University Medical School; informed consent was obtained from each patient.

Study Protocol

All subjects were totally free of smoking and alcohol intake and were asked to abstain from caffeine in the preceding 12 hours. They were separated into 3 groups as groups A, B, and C. Each group consisted of 30 volunteers. The subjects rested in a supine position for 10 minutes before baseline measurements. Baseline hemodynamic measurements including systolic and diastolic blood pressures, heart and respiratory rates, and arterial oxygen saturations (obtained by pulse meter) were obtained. Blood samples were taken into a heparinized syringe by venipuncture for COHb and lactate measurements. Baseline echocardiographic examinations were performed in the volunteers. Then, subjects were taken in groups of

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5 in the study room. In group A, the subjects were exposed for 30 minutes in smoking room to tobacco smoke with amount of CO less than 5 ppm. In group B, subjects were exposed for 30 minutes in smoking room to tobacco smoke with the amount of CO approximately 5 to 10 ppm. In group C, the subjects were exposed for 60 minutes in smoking room to tobacco smoke with the amount of CO less than 5 ppm. They stayed on a wheelchair in resting position during exposure and read a magazine or listened to music of their choice, without doing any muscular activity. Immediately after passive smoking, blood samples, hemodynamic measurements, and pulse arterial oxygen saturations were obtained from the subjects. Then the subjects were taken into the next smoke-free room by using a wheelchair, and echocardiographic examinations were performed within 5 minutes. All the subjects were asymptomatic during the study.

Echocardiography

Two-dimensional echocardiography and color tissue Doppler imaging were performed by using a commercially available machine (Vivid 7 GE Medical System, Horten, Norway) with a 3.5-MHz transducer, during at least 3 consecutive cardiac cycles. The recordings were made by an investigator blinded in respect to the patients. All patients were studied in the left lateral recumbent position after a 10-minute resting period for baseline measurements, and second measurements were assessed within 5 minutes after exposure.

Simpson's method in 2-dimensional echocardiographic apical 4-chamber view was used to asses left ventricular volumes and ejection fractions as recommended by American Society of Echocardiography guidelines.[8] Mitral annular systolic myocardial velocities were measured to assess longitudinal systolic functions by using color tissue Doppler imaging (TDI).

Evaluation of diastolic functions was performed by assessing pulsed-wave Doppler of mitral and pulmonary venous inflow and color tissue Doppler of the mitral annulus in each subject. Two-dimensional pulsed-wave Doppler and color TDI data were obtained in apical 4-chamber views during end-expiration. Pulmonary venous inflow velocities were recorded in the apical 4-chamber view by placing the pulsed-wave Doppler sample volume approximately 1 cm into the right upper pulmonary vein. Impaired diastolic functions were defined by the diminution of early diastolic mitral inflow velocity (E)/late diastolic mitral inflow velocity (A) in one of the methods; including pulsed-wave Doppler of mitral inflow or color TDI of mitral annulus and/or prolongation of deceleration time and isovolumic relaxation time, and/or venous systolic velocity/venous diastolic velocity elevation as recommended by the American Society of Echocardiography guidelines.[9]

Biochemical Analysis

Carboxyhemoglobin and lactate levels were measured from heparinized blood samples within 1 minute by using Roche Cobas b121 blood gas analyzer. The expected values for lactate in our laboratory ranged between 0 and 2 mmol/L. High-sensitivity CRP was measured by using BN2 model nephelometer (Dade-Behring).

Smoking Room

Smoking room (2.5 × 6.5 m with a 3-m ceiling) was next to the room where the echocardiographic examinations were performed. We tried to compose a natural environment for passive smoking exposure. There were 5 groups, which consisted of 3 different volunteer smokers. They smoked filtered cigarette respectively in shifts to form study environment. There were always 3 people who were smoking in the smoking room during exposure. Carbon monoxide concentration was measured by using Pulsar single gas detector (Mine Safety Appliances Company, Pittsburg, PA). The detector is equipped with an autocalibration feature, and it was zeroed in on a clean air, and then CO levels in the smoking room were measured

TABLE 1. General Clinical and Laboratory Characteristics of Groups

Variable	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	*P*
Age, yrs	25 ± 4	26 ± 3	25 ± 5	NS
Sex, F/M	15/15	15/15	15/15	NS
Body mass index, kg/m^2	21.2 ± 1.2	20.8 ± 2.5	21.3 ± 1.5	NS
Systolic blood pressure, mm Hg	120 ± 5	121 ± 4	119 ± 7	NS
Diastolic blood pressure, mm Hg	72 ± 4	70 ± 6	71 ± 8	NS
Heart rate, beats per minute	72 ± 6	72 ± 6	70 ± 7	NS
Respiratory rate, breaths per minute	13 ± 1	13 ± 2	12 ± 4	NS
Hemoglobin, g/dL	14.2 ± 1.1	14.8 ± 0.75	14.5 ± 1.5	NS
Hs-CRP, mg/L	1.2 (0.2– 2)	1.0 (0.1–3)	0.8 (0.2–3)	NS
Fasting blood glucose, mg/dL	74 ± 4	72 ± 4	72 ± 5	NS
Total cholesterol, mg/dL	184 ± 31	182 ± 33	192 ± 11	NS
HDL cholesterol, mg/dL	48 ± 13	45 ± 12	48 ± 18	NS
LDL cholesterol, mg/dL	103 ± 16.0	105 ± 22	105 ± 18	NS
Plasma triglyceride, mg/dL	95 (62–115)	98 (73–108)	90 (52–120)	NS
Pulmonary Functions (Spirometry)				
FEV1, mL	3.6 ± 1.7	3.8 ± 1.2	3.5 ± 1.6	NS
FEV1, % predicted	95.0 ± 3.7	95.2 ± 2.0	94.2 ± 8.0	NS
FVC, % predicted	98.0 ± 10	97.3 ± 12	97 ± 15	NS
FEV1/FVC, %	86.3 ± 7.9	85.4 ± 6.8	88.4 ± 5.8	NS

Data are expressed as mean ± SD or median and quartile.

FEV1 indicates forced expiratory volume in first second; FVC, forced vital capacity; HDL, high-density lipoprotein; Hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; NS, not significant.

TABLE 2. Left Ventricular Volumes and Systolic Function Parameters of Groups Before and After Exposure

Variable	Before Exposure	After Exposure	*P*
Group A			
LVSV, mL	84.7 ± 3.0	86.5 ± 2.1	NS
LVDV, mL	30.1 ± 2.6	32 ± 0.8	NS
EF, %	66 ± 2.5	67 ± 0.8	NS
Sm, cm/s	10 ± 1.5	9.8 ± 1.7	NS
Group B			
LVSV, mL	85.4 ± 3.8	86.5 ± 2.1	NS
LVDV, mL	32.1 ± 1.6	34 ± 4.8	NS
EF, %	67 ± 3.6	67 ± 2.8	NS
Sm, cm/s	10 ± 1.1	10.4 ± 2.3	NS
Group C			
LVSV, mL	34.1 ± 9.6	35.2 ± 9.2	NS
LVDV, mL	85.1 ± 6.8	86.4 ± 3.0	NS
EF, %	63 ± 5.0	63 ± 5.0	NS
Sm, cm/s	12 ± 1.8	11.5 ± 1.5	NS

EF indicates ejection fraction; LVSD, left ventricular diastolic volume; LVSV, left ventricular systolic volume; Sm, systolic myocardial velocity.

continuously for all subjects. We have paid attention to keep the amount of CO lower than 5 ppm in group A and C and approximately 5 to 10 ppm in group B by using this detector. Duration of exposure was measured by using a chronometer.

Statistical Analysis

Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. We report continuous data as mean and standard deviation or median and interquartile range. The paired Student *t* test was used for the comparison of parameters before and after passive smoking in all subjects. We compared continuous variables using one-way analysis of variance or the Kruskal-Wallis test among groups. Categorical data were compared with the χ^2 test. Pearson correlation coefficients examined the degree of association between examined variables. $P < 0.05$ was considered significant. All statistical analyses were performed using the SPSS statistical package for Windows version 13 (SPSS, Inc., Chicago, IL).

RESULTS

There was no difference in basal characteristics of the groups as demonstrated in Table 1. Mean ± SD ages in groups A, B, and C were 25 ± 4, 26 ± 3, and 25 ± 5 years, respectively. Mean ± SD CO levels in groups A, B, and C were 4.2 ± 0.5, 9.2 ± 0.3, and 4.1 ± 0.8 ppm, respectively, in the smoking room.

Tables 2, 3, and 4 indicated echocardiographic findings of the groups. Left ventricular systolic function parameters: ejection fraction and mitral annular systolic myocardial velocity did not change after exposure in all groups. As the result of echocardiographic evaluations in group A, no significant changes were observed in conventional and tissue Doppler diastolic parameters. Mitral annular early diastolic myocardial velocity (Em), Em/late diastolic myocardial velocity (Am) decreased, and Am increased in color TDI examination; mitral inflow E and E/A decreased and pulmonary venous diastolic velocity decreased in conventional Doppler examination, which indicated impairment in left ventricular diastolic function in both group B and group C.

Table 5 demonstrated changes in hemodynamic measurement, COHb, and lactate level. Heart and respiratory rate, systolic and diastolic blood pressure, and pulse arterial oxygen saturation changed significantly in groups B and C ($P < 0.05$), whereas no change was obtained in group A. Similarly, mean COHb and lactate levels increased after passive smoking in only groups B and C ($P < 0.001$). However, group B had significantly higher COHb and lactate levels compared to group C (3.63% ± 0.13% vs 1.25% ± 0.07%, 3.80 ± 0.80 vs 2.52 ± 0.40 mmol/L, respectively; $P < 0.001$). In addition, we determined that lactate and COHb level had a remarkable correlation after passive smoking in the whole study population ($r = 0.67$; $P < 0.001$).

DISCUSSION

In this study, we have demonstrated the acute deleterious effect of passive smoking on left ventricular diastolic function, which was related with duration and intensity of smoke exposure in healthy volunteers without structural heart disease. In

TABLE 3. Conventional Doppler Diastolic Parameters of Groups Before and After Exposure

Variable	Before Exposure	After Exposure	*P*
Group A			
E, m/s	0.95 ± 0.08	0.94 ± 0.1	NS
A, m/s	0.62 ± 0.12	0.60 ± 0.26	NS
E/A	1.43 ± 0.13	1.45 ± 0.22	NS
E wave DT, ms	152.0 ± 28	155.8 ± 18.0	NS
IVRT, ms	65.1 ± 8.0	68.1 ± 10.0	NS
Pulmonary S, cm/s	0.60 ± 0.10	0.58 ± 0.12	NS
Pulmonary D, cm/s	0.41 ± 0.16	0.65 ± 0.26	NS
Pulmonary S/D	1.3 ± 0.45	1.2 ± 0.18	NS
Pulmonary Ar, cm/s	0.35 ± 0.08	0.34 ± 0.05	NS
Group B			
E, m/s	0.95 ± 0.1	0.78 ± 0.7	<0.01
A, m/s	0.64 ± 0.12	0.66 ± 0.22	NS
E/A	1.38 ± 0.46	1.35 ± 0.25	<0.01
E wave DT, ms	164.5 ± 34	170 ± 45	NS
IVRT, ms	77.9 ± 13	78 ± 22	NS
Pulmonary S, cm/s	0.49 ± 0.11	0.51 ± 0.42	NS
Pulmonary D, cm/s	0.52 ± 0.13	0.58 ± 0.20	<0.01
Pulmonary S/D	1.30 ± 0.40	1.16 ± 0.68	<0.01
Pulmonary Ar, cm/s	0.25 ± 0.04	0.46 ± 0.10	<0.01
Group C			
E, m/s	0.99 ± 0.12	0.70 ± 0.14	<0.001
A, m/s	0.62 ± 0.14	0.60 ± 0.17	NS
E/A	1.55 ± 0.48	1.43 ± 0.32	<0.001
E wave DT, ms	155 ± 33	158 ± 39	NS
IVRT, ms	85 ± 28	88 ± 34	NS
Pulmonary S, cm/s	0.54 ± 0.13	0.52 ± 0.10	NS
Pulmonary D, cm/s	0.52 ± 0.12	0.59 ± 0.13	<0.01
Pulmonary S/D	1.25 ± 0.34	1.02 ± 0.38	<0.01
Pulmonary Ar, cm/s	0.29 ± 0.07	0.38 ± 0.12	<0.01

Data are expressed as mean ± SD.

A indicates late diastolic mitral inflow velocity; Ar, venous atrial reverse flow velocity; D, venous diastolic velocity; DT, deceleration time; E, early diastolic mitral inflow velocity; IVRT, isovolumic relaxation time; S, venous systolic velocity.

TABLE 4. Color Tissue Doppler Diastolic Parameters of Groups Before and After Exposure

Variable	Before Exposure	After Exposure	*P*
Group A			
Em, cm/s	12.1 ± 2.3	11.8 ± 2.1	NS
Am, cm/s	9 ± 1.0	8.8 ± 1.6	NS
Em/Am	1.40 ± 0.23	1.38 ± 0.26	NS
Group B			
Em, cm/s	13.1 ± 1.8	10.0 ± 1.6	<0.001
Am, cm/s	9.3 ± 0.9	12.2 ± 0.9	<0.001
Em/Am	1.94 ± 0.15	1.75 ± 0.17	<0.001
Group C			
Em, cm/s	14.5 ± 1.1	10.0 ± 1.6	<0.001
Am, cm/s	7.43 ± 2.1	12.2 ± 0.9	<0.001
Em/Am	2.08 ± 0.8	1.75 ± 0.4	<0.001

Data are expressed as mean ± SD.

Em indicates early diastolic myocardial velocity; Am, late diastolic myocardial velocity.

addition, passive smoking caused marked increase in COHb and lactate levels in subjects with impaired diastolic functions.

Several studies have concluded that there is a relationship between coronary heart disease and passive smoking either after acute or chronic exposure.[10–13] Importantly, most of its effects have a rapid onset of action in 30 to 60 minutes as established previously in endothelial function, coronary flow reserve, and arterial blood pressure.[14–19] In this study, we have demonstrated that smoke exposure at a certain level (approximately 9-ppm CO exposure for 30 minutes or approximately 4-ppm CO exposure for 60 minutes in this study) is enough to cause acute impairments in left ventricular diastolic functions. Abnormalities of diastolic filling play an important role in the clinical status and prognosis of patients with most heart diseases. Asymptomatic persons with isolated diastolic dysfunctions carry high risk of heart failure in the future.

Diastolic function is an active energy-consuming process of both relaxation and atrial contraction.[20] So, all cases that lead to energy depletion in myocardium cause diastolic dysfunction. It is found that passive smoking causes an imbalance between myocardial oxygen demand and supply by impairing coronary blood flow and reducing the ability of heart muscle to convert oxygen into the "energy molecule" adenosine triphosphate. In a study in rabbits, activity of the mitochondrial enzyme cytochrome oxidase fell 25% after a single 30-minute exposure to secondhand smoke, and the activity continued to decline with prolonged exposure.[21] After 8 weeks of exposure of 30 minutes per day, its activity was reduced by half. Thus, passive smoking causes impairment in both oxygen purchasing and usage by myocardium and may lead to abnormalities in energy-dependent relaxation of left ventricle, although there is no structural heart disease.

We have determined that passive smoking increased COHb levels according to duration and intensity of exposure. Several studies showed that exposure to tobacco smoke leads to increase in COHb concentrations.[22–24] Hedblad et al.[25] determined that measurement of COHb percent could be a part of the risk assessment in nonsmoking patients considered at risk of cardiac disease. Persons with existing heart disease show increasing electrocardiographic evidence of ischemia and experience more arrhythmias as COHb levels increase, even at low levels.[26–28] The main mechanism of how COHb causes heart disease is production of hypoxia. Increased COHb levels reduce the oxygen-carrying capacity of blood. This effect is more profound in the myocardium than in peripheral tissues because of very high oxygen extraction by the myocardium at rest.[29] Elevated levels of COHb in groups B and C may lead to hypoxia and energy depletion in myocardium so diastolic dysfunction occurred in normal individuals without structural heart disease as in our study population.

In our study, it was also found that passive smoking led to an elevation of lactate level according to duration and intensity of exposure. It was shown that passive smoking significantly increased the amount of lactate in venous blood, which indicated that the heart increasingly relied on anaerobic metabolism during passive smoking.[30] Contrast to aerobic metabolism, energy profit is too low in anaerobic metabolism that contributes to ischemia in tissues. In a previous study, blood lactate concentrations at peak exercise seemed to be a strong independent predictor of ischemia indicating coronary artery disease in men.[31] It was demonstrated that coronary sinus lactate levels greater than 2.85 mmol/L had a sensitivity level of 80.0% and specificity of 72.9% in discrimination between patients with or without acute myocardial infarction. In addition, lactate levels greater than 2.05 mmol/L had sensitivity of 87.5% and specificity 70.7% in discrimination of patients with or without

TABLE 5. Hemodynamic Parameters, SaO2, Lactate and COHb Levels of Groups Before and After Groups

Variable	Before Exposure	After Exposure	*P*
Group A			
SBP, mm Hg	120 ± 5	122 ± 4	NS
DBP, mm Hg	72 ± 4	72 ± 3	NS
HR, beats per minute	72 ± 6	70 ± 4	NS
RR, breaths per minute	13 ± 1	14 ± 1	NS
Lactate, mmol/L	0.38 ± 0.23	0.40 ± 0.40	NS
COHb, %	0.30 ± 0.11	0.32 ± 0.07	NS
SaO_2, %	98 ± 2	96 ± 2	NS
Group B			
SBP, mm Hg	119 ± 7	128 ± 8	<0.05
DBP, mm Hg	71 ± 8	74 ± 7	<0.05
HR, beats per minute	70 ± 7	85 ± 9	<0.001
RR, breaths per minute	12 ± 4	18 ± 3	<0.05
Lactate, mmol/L	0.33 ± 0.17	3.80 ± 0.80	<0.001
COHb, %	0.26 ± 0.08	3.63 ± 0.13	<0.001
SaO_2, %	96 ± 2	86 ± 4	<0.001
Group C			
SBP, mm Hg	121 ± 4	125 ± 10	<0.05
DBP, mm Hg	70 ± 6	73 ± 3	<0.05
HR, beats per minute	72 ± 6	76 ± 4	<0.05
RR, breaths per minute	13 ± 2	16 ± 1	<0.05
Lactate, mmol/L	0.41 ± 0.23	2.52 ± 0.40	<0.001
COHb, %	0.34 ± 0.11	1.25 ± 0.07	<0.001
SaO_2, %	96 ± 3	90 ± 4	<0.001

Data are expressed as mean ± SD.

DBP indicates diastolic blood pressure; HR, heart rate; RR, respiratory rate; SaO_2, pulse arterial oxygen saturation; SBP, systolic blood pressure.

myocardial damage.[32] In our study, we determined that lactate levels in group B and C were 3.80 ± 0.80 and 2.52 ± 0.40 mmol/L in venous blood, respectively.

Previous studies determined the increased blood lactate concentrations in subjects who were immediately or chronically exposed to CO.[33,34] One of our evident findings was a remarkable correlation between lactate and COHb levels after passive smoking. We think that increased COHb levels may be one of the causes of ischemia whereas increase in lactate levels may related to the result of ischemia. It can be said that increment in COHb levels caused insufficient amount of oxygen in blood, which constrained tissues including myocardium, to use anaerobic energy pathways; and this condition may be manifested as increase in lactate levels. Moreover, increased heart and respiratory rates and decreased pulse arterial oxygen saturation may indicate acute developed ischemia.

In addition, when groups B and C were compared with each other according to COHb and lactate level, it was seen that the more intensive exposure led to higher COHb and lactate levels in shorter time compared to less intense but longer exposure. This indicated that more intense smoke exposure is a more important determinant than duration of exposure.

We have demonstrated that systolic and diastolic blood pressures and heart rates increased significantly in subjects with impaired diastolic functions. The important topic is that whether hemodynamic changes affected diastolic parameters over preload alternation. When it is considered that hemodynamic changes occurred in groups B and C, it is possible to say that this effect may be a determining factor. However, we have determined diastolic impairment in each subject of affected subjects by using color TDI of mitral annulus and pulsed wave Doppler of pulmonary venous inflow. Previously, it was reported that Em acted as a preload-independent index of LV relaxation, and preload alternation did not affect Doppler tissue velocities.[35–37] In addition, it was shown that the assessment of pulmonary venous inflow is independent from heart rate.[38] We have previously shown that color TDI demonstrated impaired diastolic function independently from hemodynamic changes, including heart rate and blood pressure.[4]

Limitations

In this study, we did not evaluate echocardiographic measurements again after normalization of COHb and lactate levels in the blood. In addition, we measured lactate levels in systemic venous blood; however, obtaining blood samples from coronary sinus would be a more powerful method to evaluate myocardial oxygenation.

Conclusions

Our results suggested that smoke exposure at a certain dose (approximately 9-ppm CO exposure for 30 minutes or approximately 4-ppm CO exposure for 60 minutes in this study) seems to cause relative diastolic dysfunction. In addition, passive smoking leads to marked increase in COHb and lactate levels. Repetitive and intensified secondhand smoke exposure may lead to serious and permanent left ventricular diastolic dysfunction in normal individuals without structural heart disease.

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