Mentholated cigarette smoking induced alterations in left and right ventricular functions in chronic smokers

Kronik sigara içenlerde, mentollü sigara içilmesiyle uyarılan sol ve sağ ventrikül işlevlerindeki değişiklikler

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ABSTRACT

Objective: Possible acute effects of smoking mentholated cigarette on left and right ventricular function is not known. The aim of the study was to compare acute effects of normal and mentholated cigarettes smoking on both ventricular diastolic functions in chronic smokers.

Methods: In a single-blinded, cross-over, open label and controlled study acute effect of smoking of the mentholated and the regular cigarettes was evaluated. Eighteen other than healthy regular cigarette smokers and 20 nonsmoker control subjects were included into the study. To compare the acute effects of mentholated and regular cigarette in each subject echocardiographic examination including tissue Doppler imaging (TDI) were performed at baseline, than in the smokers group TDI was measure 20-30 minutes after smoking two either cigarettes.

Results: In response to smoking two cigarettes, mitral E/A values declined from 1.78±0.44 to 1.58±0.41 after the regular cigarette (p=0.0043) and from 1.78±0.44 to 1.53±0.40 after the mentholated cigarette (p=0.0035). Tricuspid E deceleration time values declined from 185.28±20.05 ms to 222.72±26.47 ms after the regular cigarette (p<0.001) and 185.28±20.05 ms to 241.53±47.63 ms after the mentholated cigarette (p<0.001). Smoking of mentholated cigarette, but not regular cigarette smoking, increased tricuspid E deceleration time and right ventricular isovolumic contraction time (p=0.044; p=0.024 respectively) and decreased the right ventricular Em values (p=0.027).

Conclusion: Mentholated and regular cigarette smoking have acute detrimental effects on right and left ventricular systolic and diastolic function. Mentholated cigarettes cause additional unfavorable acute effects on especially right ventricular tissue Doppler velocities, relaxation and contraction indices compared to regular cigarettes. *(Anadolu Kardiyol Derg 2008; 8: 116-22)*

Key words: Menthol smoking, tissue Doppler imaging, myocardial performance index, left ventricular function, right ventricular function

ÖZET

Amaç: Mentollü sigaranın olası akut etkilerinin sağ ve sol ventrikül işlevleri üzerindeki etkisi bilinmemektedir. Mentollü sigara içilmesinin her iki ventrikül işlevlerini regüler sigara içilmesine göre daha fazla bozup bozmadığının araştırılması.

Yöntemler: Tek kör, çapraz, açık uçlu ve kontrollü olarak dizayn edilen çalışmada; 18 sağlıklı regüler sigara içicisi ve 20 sigara kullanmayan sağlıklı gönüllü çalışmaya alındı. Mentollü ve regüler sigaranın akut etkilerini karşılaştırmak için her bir katılımcıya doku Doppler incelemesinin de dahil olduğu ekokardiyografik değerlendirme, başlangıçta ve 2 adet diğer sigara içirildikten 20-30 dakika sonra gerçekleştirildi.

Bulgular: İki sigara içilmesine yanıt olarak, regüler sigaradan sonra mitral E/ A değerleri 1.78±0.44'ten 1.58±0.41'e (p=0.0043) ve mentollü sigara için 1.78±0.44'ten 1.53±0.40'a geriledi (p=0.0035). Triküspit E deselerasyon zamanı değerleri regular sigara için 185.28±20.05'den, 222.72±26.47'e yükselmiştir (p<0.001) ve mentollü sigara için 185.28±20.05'den 241.53±47.63'e yükselmiştir (p<0.001). Mentollü sigara içilmesi triküspit E deselerasyon zamanını, sağ venrikül isovolümik kontraksiyon zamını regüler sigara içilmesine göre daha fazla artırırken (sırasıyla, p<0.044; p=0.024) sağ ventrikül Em değerini daha fazla azaltır (p=0.027).

Sonuç: Mentollü sigara içilmesi, regüler sigara içilmesine göre sol ve sağ ventrikül işlevini daha olumsuz etkilemektedir ama ek olarak mentollü sigara içimi sağ ventrikul relaksasyon ve kontraksiyon fonksiyonlarını normal sigaralara karşın ileri derecede kötü etkilemektedir. *(Anadolu Kardiyol Derg 2008; 8: 116-22)*

Anahtar kelimeler: Mentollü sigara içilmesi, doku Doppler ekokardiyografi, miyokardiyal performans indeksi, sol ventrikül işlevi, sağ ventrikül işlevi

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Introduction

Smoking is the most prevailed and the most preventable risk factor for cardiovascular diseases resulting in two fold increase in coronary artery disease risk (1). Cigarette smoke exerts the most prominent detrimental effects on endothelial system and especially on coronary endothelial system (2-3). Smaller amounts of nicotine than cigarette smoke can cause acute endothelial dysfunction (4). Free radicals contained in the cigarette smoke tar can damage the vascular endothelium (3). Commercially available for recent years, so called mentholated cigarettes are increasingly smoked. Menthol has numerous biological actions. The cooling effect of menthol could result in greater intensity of smoking (deeper inhalation and/ or more prolonged breath holding), resulting in greater exposure to tobacco smoke toxins. The effects of menthol to increase permeability of cell membranes could result in a greater absorption of smoked toxins (5, 6). Some but not all researchers have reported higher carbon monoxide levels after smoking mentholated compared with non-mentholated cigarettes. Ahijevych et al. (7) have also reported higher cotinine levels per cigarette smoked per day in smokers of mentholated compared with nonmentholated cigarettes, suggesting greater nicotine absorption per cigarette. Clark et al. (8) found that mentholated cigarette smoking per se was associated with higher blood cotinine and carbon monoxide levels per cigarette. These reports are consistent with the idea that menthol increases inhalation and/ or absorption of 4000+ tobacco smoke toxins. Also mentholated cigarette smoking did significantly inhibit the metabolism of nicotine (5, 6). However, to date, there is no study comprehensively investigating cardiovascular effects of mentholated cigarettes.

In recent years, conventional echocardiographic Doppler assessment in combination with the newly developed tissue Doppler imaging (TDI) has become a well accepted, practical, and safe noninvasive method for the diagnosis of left and right ventricular systolic and diastolic function in the clinical setting (9, 10). Several previous studies have investigated the acute effect of cigarette smoking on left and right ventricular function (11, 12, 13).

In this study, considering the previous emphasize on the effects of nicotine and tar on cardiovascular system, we have hypothesized that mentholated cigarettes with enhanced systemic exposure to nicotine and other toxic compounds might be more hazardous for left and right ventricular functions than regular cigarettes.

Methods

Study population

For this study, otherwise healthy regular cigarette smokers were consecutively registered from our hospital staff and/or healthy volunteers. Inclusion criteria were smoking steadily regular cigarette from the beginning at least for three years, to be 18-40 years of age, being free of coronary risk factors, and for women to be on regular menstrual cycle. Exclusion criteria were having any disease that could cause left and right ventricular function impairment (e.g. hypertension, diabetes mellitus, and family history for coronary artery disease), drinking alcohol, and obesity (body mass index [BMI] greater than 30 kg/m^2). Subjects using any vasoactive drug and those with electrocardiographic changes implicating coronary heart disease were excluded.

Subjects who fulfilled all inclusion and exclusion criteria, 18 regular cigarette smokers (mean age: 26.11±6.56 years, 6 female) and 20 healthy nonsmoker volunteers (mean age: 27.75±4.51 years, 10 female) were consecutively included in the study.

The study was conducted according to the recommendations set forth by the Declaration of Helsinki on Biomedical Research involving Human Subjects. The institutional ethics committee approved the study protocol. Written informed consent was obtained from each subject.

Study design

In a single-blinded, cross-over, open label and controlled study acute effect of smoking of the mentholated and the regular cigarettes was evaluated. The sample size of the study was calculated with assumption of significance level of 5% and power of the study of 80% based on the results of the previous investigation (11).

Blood glucose, total cholesterol, high-density (HDL) and low-density (LDL) lipoprotein cholesterol levels in at least 12-hour fasting state were determined. Plasma high sensitivity C-reactive protein (hsCRP) levels were measured by a highly sensitive sandwich ELISA technique. Each subject underwent transthoracic echocardiographic examination including TDI measurement.

A complete physical examination was performed. Peripheral arterial pulses and carotid bruits were searched for in particular, and sitting blood pressure was recorded. Each subject was questioned for alcohol consumption, and again for major cardiovascular risk factors.

Study protocol

In the first day of the study, 18 regular cigarette smokers and the 20 control subjects underwent echocardiographic examination after 12 hours fast and cigarette free period to see the baseline measure of left and right ventricular functions. At the second day, each subject from the smokers group smoked two mentholated (0.9 mg nicotine, 11 mg tar, 12 mg carbon monoxide) or regular (0.9 mg nicotine, 12 mg tar, 12 mg carbon monoxide) cigarettes, in a closed room within 15 minutes. Then, within the following 20 to 30 minutes, each subject underwent echocardiographic examination including TDI measurement to see the acute effect of smoked cigarette on left and right ventricular function. Fifteen days later, in the second run of the study, the same procedure was repeated, and each subject from the smokers group smoked two cigarettes from the other kind after 12 hours fast and cigarette free period in a closed room within 15 minutes. Then, within the following 20 to 30 minutes, each subject underwent echocardiographic examination to see the acute effect of the smoked mentholated cigarette.

Echocardiographic examination

Each subject was examined using an Acuson Sequoia C256® Echocardiography System equipped with a 3V2c broadband transducer with second harmonic capability (Acuson, Mountain View, CA, USA). Two-dimensional, M-mode, and subsequent standard and pulsed tissue Doppler echocardiographic examinations were performed in each subject in the lateral decubitus position. The echocardiographic images were recorded on VHS videotapes. Diastolic and systolic interventricular septal (IVS) thickness, posterior wall (PW) thickness, and left

ventricular end-diastolic (LVDD) and left ventricular end-systolic (LVSD) diameters were measured from the parasternal long-axis views. All measurements were performed on M-mode images. The left ventricular mass index (LVMI) and left ventricular ejection fraction (EF) were calculated using conventional formulas.

The pulsed Doppler sample volume was positioned at the mitral and tricuspid leaflet tips. Early diastolic peak flow velocity (E), late diastolic peak flow velocity (A), E/A ratio, and E-wave deceleration time (DT) were measured by Doppler imaging of transmitral and transtricuspid flows.

The TDI program was set to the pulsed-wave Doppler mode. Filters were set to exclude high-frequency signals, and the Nyquist limit was adjusted to a velocity range of -15 to 20 cm/s. Gains were minimized to allow for a clear tissue signal with minimal background noise. All TDI recordings were obtained during normal respiration.

A 5-mm sample volume was placed at the apical four-chamber view on the lateral corner of the mitral annulus (14). The resulting velocities were recorded for 5-10 cardiac cycles at a sweep speed of 100 mm/s, and stored on VHS videotape for later payback and analysis. The following measurements were determined as indexes of regional systolic function: peak velocities (cm/s), time velocity integral of myocardial systolic (Sm) wave. Myocardial early (Em) and atrial (Am) peak velocities (cm/s), Em/Am ratio, and Sm-Em duration (isovolumic relaxation time: IVRTL) were measured, as the time interval occurring between the end of Sm and the onset of Em, were determined as diastolic measurements. Left ventricular ejection time (LVET) was measured from the onset to the end of left ventricular (LV) outflow curve. Right ventricular ejection time (RVET) was measured from the onset to the end of right ventricular (RV) outflow curve. Isovolumetric contraction time of the left ventricle (IVCTL) was the interval from the cessation of mitral inflow to the onset of LV outflow. Also, isovolumetric relaxation time of the right ventricle (IVRTR) was obtained as the time interval from the cessation of RV outflow to the onset of tricuspid valve inflow. Isovolumetric contraction time of the right ventricle (IVCTR) was determined from the cessation of tricuspid inflow to the onset of RV outflow. The myocardial performance index of the right ventricle (MPIR) was calculated by the formula (IVCTR+IVRTR)/RVET. The myocardial performance index of the left ventricule (MPIL) was calculated by the formula (IVCTL+IVRTL)/ LVET (11). All diastolic parameters were measured in three consecutive cardiac cycles and averaged. The same investigator blinded for clinical data performed the echocardiography, and two cardiologists blinded for subjects' data analyzed the echocardiogram recordings.

Statistical analyses

Statistical analyses were performed using SPSS 13.0 (SPSS for Windows 13.0, Chicago, IL, USA). Numeric values are expressed as mean±SD. The baseline values for 2 groups were compared using unpaired Students` t test. The baseline, after mentholated cigarette and regular cigarette measurements were compared using Mann Whitney U Test Bonferroni correction to assess differences among the groups. Changes in the measurements after smoking mentholated cigarette and regular cigarette compared to baseline measurements were tested using Wilcoxon Sign Test. A P value less than 0.05 were considered significant.

Results

The controls and the smokers group were similar regarding age, BMI, blood pressure, heart rate, glucose, cholesterol, and hsCRP values. The IVS thickness, PW thickness, LVDD, LVSD, EF, left atrium diameter and LVMI were similar between the smokers and control groups (Table 1). The analysis revealed that systolic blood pressure, diastolic blood pressure, heart rate, and rate_pressure product (RPP) values were slightly increased by smoking of both types of cigarettes. Mitral E/A ratios were significantly decreased (p=0.043, p=0.035), mitral E wave DT (p=0.016; p=0.028), and MPIL significantly increased by smoking of both types of cigarettes (p=0.018; p=0.016). Lateral E/ A values slightly decreased from baseline for regular and mentholated smoking (p=0.157, p=0.522 respectively). The IVRTL, IVCTL, and LVET values increased for both cigarette types. However only IVRTL for regular cigarette smoking and LVET for mentholated cigarette smoking reached significant levels (p=0.021; p=0.007 respectively). Tricuspid E wave DT significantly increased from baseline for smoking both regular and mentholated cigarettes (p=0.001; p=0.001 respectively). Tricuspid E/A ratios did not reach significance for smoking regular and mentholated cigarettes (p=0.184; p=0.913 respectively). Right ventricular E/ A ratios did not change significantly for regular and mentholated smoking (p=0.372; p=0.267). The IVRTR, IVCTR, MPIR values increased after smoking for both cigarette types. However IVCTR and MPIR values for mentholated smoking reached statistical significance (p=0.008; p=0.043) (Table 2).

In the second run of the study, each smoker smoked two cigarettes from the other kind, and each was evaluated immediately after smoking (within 20-30 minutes following smoking).

Table 1. Demographic, biochemical, and echocardiographic characteristics of the two groups

Variables	Cigarette smokers (n=18)	Controls (n=20)	p
Age, years	26.11±6.56	27.75±4.51	0.371
Male/Female	12/ 6	10/10	0.312
BMI, kg/m^2	23.68±3.40	23.90±3.62	0.845
Baseline SBP, mm Hg	119.44±12.11	114.00±12.73	0.187
Baseline DBP, mm Hg	68.33±9.24	72.00±7.68	0.190
Baseline heart rate, bpm	69.39±7.92	71.85±11.06	0.440
Glucose, mg/dL	87.06±4.70	87.00±4.50	0.970
Total cholesterol, mg/dL	159.00±35.57	160.95±39.13	0.874
Triglyceride, mg/dL	109.39±73.84	111.60±76.95	0.929
HDL chol, mg/dL	42.56±8.23	41.50±7.43	0.680
LDL chol, mg/dL	92.94±21.43	95.00±23.54	0.781
hsCRP, mg/L	1.61±1.26	1.68±1.52	0.877
LVMI, g/m^2	76.22±13.02	76.40±14.66	0.969
Mitral E max, cm/s	86.94±17.92	82.25±10.38	0.607
Mitral A max, cm/s	50.56±9.25	52.60±6.50	0.880
Mitral E/A ratio	1.78±0.44	1.58±0.24	0.636

Data are represented as Mean±SD unpaired Students` t test

BMI - Body mass index, chol- cholesterol, DBP - diastolic blood pressure, HDL - high-density lipoprotein, hsCRP - high sensitivity C-reactive protein, LDL - low-density lipoprotein; LVMI - left ventricular mass index, SBP - systolic blood pressure

Mentholated cigarette smoking increased tricuspid E wave DT, IVCTR and decreased RVEm values more significantly than regular smoking (p=0.044; p=0.024; p=0.027, respectively) (Table 3).

Discussion

The present study revealed that both mentholated cigarette and regular cigarette smoking have acute detrimental effects on left and right ventricular function. Our study is the first to investigate the hazardous effects of smoking mentholated cigarettes on left and right ventricular functions. Our study demonstrated that mentholated cigarette smoking was accompanied by more pronounced impairment of RV relaxation and contraction, as compared with normal cigarette smoking.

Recent data showed that 1/4 of all the cigarette sales in USA are the mentholated cigarettes. "The First Conference on Menthol Cigarettes" (15) emphasized on the prominent increase in mentholated cigarette consuming (15). Concern about mentholation of cigarettes has arisen because of the high rates of lung cancer in African-American smokers, most of whom smoke mentholated cigarettes, compared with whites, who predominantly smoke nonmenthol cigarettes (16, 17). Menthol is known to stimulate cold receptors and to produce a cooling sensation as well as local anesthesia. In animals, menthol inhalation results in longer air retention time in the lungs (5, 18). Furthermore, many African-Americans report the ease of inhalation and ability to inhale more deeply as reasons for smoking mentholated cigarettes (19). Therefore, it is reasonable to suspect that mentholation of tobacco might increase the depth of inhalation and/or the duration of smoke retention in the lungs, resulting in greater carcinogen exposure. Menthol is also known to enhance the dermal absorption of various drugs (20, 21) raised concern that menthol might enhance lung permeability to toxic chemicals in tobacco smoke. Menthol is reported to alter hepatic drug-metabolizing enzyme levels in rats (22). MacDougall et al. (23) have reported that menthol inhibits nicotine metabolism in human microsomes.

Sellers and Tyndale (6) have found that menthol inhibits the metabolism of nicotine and cotinine using human liver microsomes as well as by cDNA expressed CYP2A6. Although cigarette mentholation was not associated with an increased cancer risk in several studies, there are no studies of mentholated cigarettes and risk of cardiovascular disease. The cooler taste of mentholated cigarette might contribute to a false psychological perception of safety compared to non-mentholated cigarettes (15).

We found significant increase in heart rate and therefore rate pressure product caused by mentholated cigarette (Table 3). This could be explained by acute increments of blood nicotine

Table 2. Left ventricular function parameters before and after smoking of the mentholated and regular cigarettes in the smokers group

Variables	Basal	After regular cigarette	After mentholated cigarette	p* Basal vs Regular	p* Basal vs mentholated	p** Mentholated vs Regular
Mitral E max, cm/s	86.94±17.92 (84.50; 51.00-113.009)	90.89±14.30 (89.50; 58.00-118.00)	83.73±9.12 (83.73; 65.00-98.00)	0.150	0.527	0.085
Mitral A max, cm/s	50.56±9.25 (50.50; 30.0-67.00)	60.22±12.49 (57.00; 43.00-80.00)	57.67±13.36 (57.67; 33.00-91.00)	0.017	0.058	0.767
Mitral E deceleration time, ms	177.89±28.99 (170.00; 130.00-228.00)	195.72±23.02 (190.00; 151.00-246.00)	202.80±38.97 (202.80;140.00-303.00)	0.016	0.028	0.481
Mitral E/A ratio	1.78±0.44 (1.82; 0.84-2.64)	1.58±0.41 (1.57; 0.73-2.36)	1.53±0.40 (1.45; 0.86-2.44)	0.043	0.035	0.628
Lateral Sm, cm/s	16.28±3.94 (15.50; 11.00-26.00)	15.61±2.55 (16.00; 9.00-21.00)	15.00±2.35 (15.00; 9.00-20.00)	0.570	0.298	0.305
Lateral Em, cm/s	25.61±3.66 (26.00; 18.00-30.00)	24.89±4.92 (25.00; 15.00-34.00)	23.33±5.19 (23.67; 12.00-35.00)	0.375	0.046	0.355
Lateral Am, cm/s	14.67±3.22 (13.50; 11.00-21.00)	16.44±3.84 (16.00; 8.00-24.00)	14.47±2.95 (14.47; 9.00-22.00)	0.291	0.984	0.219
Lateral E/ A ratio	1.82±0.46 (1.79; 1.16-2.64)	1.59±0.43 (1.49; 0.75-2.38)	1.65±0.44 (1.61; 1.09-3.00)	0.295	0.522	0.910
Lateral IVRT, ms	83.17±13.10 (80; 67.00-107.00)	96.22±17.22 (87.00; 67.00-127.00)	107.53±55.41 (93.00; 60.00-260.00)	0.021	0.239	0.767
Lateral IVCT, ms	80.28±16.51 (80.00; 53.00-113.00)	81.06±15.64 (80.00; 53.00-113.00)	81.47±18.01 (80.73; 53.00-127.009)	1.000	0.491	1.000
Lateral ET, ms	275.94±19.83 (276.50; 243.00-313.00)	265.61±14.82 (263.50; 233.00-300.009)	252.60±28.87 (252.80; 153.00-293.00)	0.124	0.007	0.059
Lateral MPI	0.60±0.09 (0.57; 0.49-0.85)	0.67±0.11 (0.68; 0.46-0.87)	0.79±0.41 (0.69; 0.46-2.27)	0.018	0.016	0.767

Data are represented as Mean± SD and Median, Minimum- Maximum values
* - Wilcoxon sign test,
** - Mann Whitney U test
Am - atrial peak velocity, Em - early peak velocity, ET - ejection time, IVCT - isovolumic contraction time, IVRT - isovolumic relaxation time, MPI - myocardial performance index, Sm - systolic peak velocity

levels due to the fact that mentholated cigarettes might activate sympathetic nervous system, so systolic blood pressure, heart rate and RPP increments were greater than the smoking regular cigarettes. Benowitz et al. (6) observed, blood nicotine levels were slightly higher while smoking mentholated cigarettes, but they may not have had the statistical power to observe a significant effect (6).

In the current study, we found a decrease in the ratio between early and late velocity after smoking regular or mentholated cigarette. Assessment of LV function by TDI has been suggested to be more sensitive than conventional Doppler methods, because it is independent of filling pressure (24, 25). Therefore, we combined the 2 techniques and observed that the early systolic velocity and E/A velocity measured at the lateral sides of the mitral annulus by TDI decreased after smoking both regular and mentholated cigarettes, while late diastolic velocities increased more significantly for mentholated than for regular cigarettes. Stork et al. (12) studied the effect of cigarette smoking on left ventricular diastolic function in 22 smokers who had no evidence of organic heart disease by echocardiography and observed that acute cigarette smoking significantly impaired the energy-conserving process of early diastolic relaxation, independent of its role as a risk factor for atherosclerosis. Later, Stork's group (26) also investigated, by means of echocardiography, in patients with coronary heart disease, LV relaxation and filling before and after inhalation of a cigarette. The authors observed that acute cigarette smoking caused a shift of mitral blood flow from early to late diastole and a prolongation of isovolumetric relaxation; they thereby concluded that cigarette smoking, by affecting LV filling and isovolumetric relaxation, significantly impaired LV diastolic function independently of its role as a risk factor for coronary atherosclerosis. Similarly, Kyriakides and associates (13) studied the effect of acute smoking on LV function in patients with coronary artery disease. The authors

Table 3. Right ventricular function parameters before and after smoking of the mentholated and regular cigarettes in the smokers group

Variables	Basal	After regular	After mentholated	p* Basal vs Regular	p* Basal vs mentholated	p** Mentholated vs Regular
SBP, mmHg	117.50±16.20 (112.50;90.00-145.00)	120.00±17.15 (120.00;95.00- 160.00)	130.67±22.02 (130.33;95.00-180.00)	0.922	0.116	0.238
DBP, mmHg	70.83±9.28 (70.00;60.00-85.00)	71.11±11.32 (70.00;60.00-95.00)	73.47±9.25 (73.47;60.00-92.00)	0.997	0.733	0.780
Heart rate, beats/min	90.83±9.63 (91.00;68.00-110.00)	99.39±10.45 (95.00;85.00-115.00)	101.20±11.54 (103.10;72.00-115.00)	0.061	0.018	0.780
Rate&pressure product	10693.33±1943.82 (10540.00; 6800.00-13860.00)	11995.00±2514.62 (11810.00; 8075.00-17600.00)	13280.58±3002.32 (13223.00; 8550.00-19800.00)	0.311	0.013	0.319
Tricuspid E max, cm/s	62.67±10.68 (63.50;46.00-85.00)	61.94±12.78 (63.00;39.00-86.00)	66.87±7.32 (67.00;50.00-79.00)	0.983	0.038	0.214
Tricuspid A max, cm/s	40.78±11.67 (37.00;26.00-74.00)	44.44±9.41 (41.00; 35.00-74.00)	66.87±7.32 (43.01;28.00-65.00)	0.020	0.222	0.963
Tricuspid E deceleration time, ms	185.28±20.05 (186.00;150.00-219.00)	222.72±26.47 (224.5;167.00-278.00)	241.53±47.63 (241.53;138.00-349.00)	0.001	0.001	0.044
Tricuspid E/A ratio	1.60±0.32 (1.61;1.15-2.34)	1.43±0.35 (1.33; 0.67-2.00)	1.61±0.36 (155;1.03-2.19)	0.184	0.913	0.181
RV Sm, cm/s	16.61±3.90 (16.00;10.00-25.00)	18.28±2.93 (18.00;12.00-26.00)	16.87±3.36 (16.87;10.00-25.00)	0.112	0.831	0.072
RV Em, cm/s	21.56±4.94 (21.50; 12.00-32.00)	22.67±4.69 (22.00;12.00-33.00)	20.27±4.07 (20.13;12.00-30.00)	0.254	0.406	0.027
RV Am, cm/s	16.72±3.38 (17.50;12.00-23.00)	18.89±4.78 (19.00;8.00-29.00)	17.00±4.34 (17.00; 8.00-25.00)	0.118	0.836	0.192
RV E/ A ratio	1.31±0.30 (1.28;0.67-2.00)	1.31±0.59 (1.13;0.70-3.13)	1.24±0.30 (1.19;0.79-2.00)	0.372	0.267	0.719
RV IVRT, ms	83.72±19.09 (80.00;60.00-127.00)	93.28±20.32 (87.00;60.00- 133.00)	97.39±19.71 (97.3;60.00-133.00)	0.190	0.144	0.443
RV IVCT, ms	75.44±17.48 (73.00;40.00 -107.00)	79.11±16.19 (80.00;53.00-120.00)	88.33±15.38 (88.33;53.00-120.00)	0.367	0.008	0.024
RV ET, ms	250.72±30.32 (253.00; 160.00-293.00)	255.00±24.30 (253.00;227.00-300.00)	250.50±30.52 (247.00;209.00-320.00)	0.906	0.965	0.443
RV MPI	0.65±0.14 (0.61; 0.39-0.92)	0.68±0.15 (0.65;0.45-1.03)	0.76±0.16 (0.78; 0.38-1.03)	0.381	0.043	0.097

Data are represented as Mean± SD and Median, Minimum- Maximum values
* - Wilcoxon sign test,
** - Mann Whitney U test
Am- atrial peak velocity, DBP- diastolic blood pressure, Em- early peak velocity, ET- ejection time, IVCT- isovolumic contraction time, IVRT- isovolumic relaxation time, MPI- myocardial performance index, RPP- rate pressure product, RV - right ventricle, SBP- systolic blood pressure, Sm- systolic peak velocity

observed a decrease in peak E velocity and peak E/A ratio and concluded that each cigarette provokes disturbances in LV diastolic function.

Using pulsed-wave TDI, we recorded the systolic mitral annular velocity, which reflects LV function. Recently, Alam et al. (27) used conventional and TDI techniques to study the acute effects of smoking on left ventricular function in 36 healthy subjects. Those authors did not find any smoking-related, acute change in LV systolic function after participants smoked cigarettes but did observe a significant change in transmitral flow measurements and concluded that cigarette smoking significantly changed diastolic function. Karakaya et al. (11) show that acute cigarette smoking impaired left ventricular diastolic function in smokers as evaluated by conventional Doppler and TDI techniques. We found similar results to aforementioned studies confirming the smoking induced diastolic dysfunction as decreased mitral E/A ratios and increased mitral E deceleration time. We could not find any difference between the mentholated and regular cigarette smoking for mitral inflow parameters. Like other studies, we found that lateral Sm and lateral Em and lateral E/A ratios values decreased and lateral Am and lateral IVRT increased. Lateral IVRT values for regular cigarette smoking reached statistical significance however lateral E/A ratios for mentholated smoking did not (p=0.021 and p=0239, respectively). Both of the cigarette types increased left ventricular MPI and there was not significant difference between them.

The echocardiographic evaluation of right ventricular function is difficult because of the geometry of the ventricle and its position beneath the sternum (28). In the current study, RV systolic function was found to be unchanged after smoking a cigarette. However, using conventional Doppler we noted that tricuspid valve inflow measurements were significantly altered except tricuspid E wave deceleration time. Mentholated cigarette smoking impaired tricuspid E wave DT more than regular smoking (p= 0.044). The velocity measured at the lateral sides of the tricuspid annulus by TDI was significantly altered after the smoking a cigarette. Myocardial performance index is a Doppler-derived nongeometric measure of ventricular function. It has been reported that MPI is a useful index for the evaluation of RV function and appears to be relatively independent of changes in preload or afterload in a clinical setting (28, 29). It has also been reported that the index is not significantly affected by heart rate, tricuspid regurgitation, RV pressure, or RV dilatation (28). Karakaya et al. (11) showed that acute cigarette smoking impaired right ventricular diastolic function in smokers as evaluated by conventional Doppler and TDI techniques. They found that MPIR increased after regular cigarette smoking significantly (11). Our results were definitely in accordance with the aforementioned studies. In the present study, RV systolic function did not change, RV E/ A ratios slightly decreased, IVRTR, IVCTR, right ventricular ET, MPIR increased after both regular and mentholated cigarette smoking, however IVCTR and MPIR increase, reached statistical significance after only smoking of mentholated cigarette (p=0.008, p=0.043). Mentholated smoking impaired IVCT more than regular cigarette smoking (p=0.024). There were no differences in increase in MPIR after smoking of mentholated and regular cigarettes (p=0.094).

Menthol could affect human nicotine metabolism and, therefore, could affect the metabolic activation or detoxification of tobacco related toxic compounds. According to our findings; mentholated cigarettes cause additional unfavorable acute effects on left and right ventricular diastolic function compared to regular cigarettes.

Study limitations

Limited sample size and the lack of measurements of biomarkers such as cotinine and carbon monoxide levels might affect the accuracy of our results. In this study, smoking conditions was not identical to the real smoking habit and nobody always smoke in a closed room. Therefore, the results could not exactly be applicable to the real world. However, considering the fact that this is a study with a small sample size it was not possible to mimic real smoking habits.

Conclusion

The present study revealed that both mentholated cigarette and regular cigarette smoking have acute detrimental effects on right and left ventricular systolic and diastolic function. The present study revealed that both mentholated cigarette and regular cigarette smoking have acute detrimental effects on right and left ventricular systolic and diastolic function. Additional implication of our study is that mentholated cigarettes cause additional unfavorable acute effects on especially right ventricular tissue Doppler velocities, relaxation and contraction indices compared to regular cigarettes. Further studies are needed, investigating possible chronic effects of mentholated cigarettes on left and right ventricular function.

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