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Comparison of IQOS (heated tobacco) and cigarette smoking on cardiac functions by two-dimensional speckle tracking echocardiography

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ABSTRACT

Aims: IQOS is a novel tobacco product claimed to be safer than conventional cigarette smoking due to the heat-not-burn system. This study aimed to evaluate the acute effects of IQOS smoking on myocardial systolic and diastolic functions and also compare the acute impacts of IQOS with cigarette smoking.

Methods: In this prospective study, twenty-seven healthy participants who were using IQOS were included. Transthoracic echocardiography was performed three times for each participant; before smoking any tobacco product (group1), after IQOS smoking (group 2), after cigarette smoking (group3). In addition to conventional echocardiographic measurements, left ventricle (LV) and right ventricle (RV) strain analyses were performed by speckle tracking echocardiography.

Results: In comparison with non-smoking status, LV global longitudinal strain (GLS) decreased after IQOS and cigarette smoking ($-18.9 \pm 2.4\%$ in baseline vs. $-17.9 \pm 2.4\%$ in IQOS vs. $-17.9 \pm 2.8\%$ in cigarette smoking; $p = 0.003$, $p = 0.001$; respectively). LV global circumferential strain (GCS) reduced after IQOS and cigarette smoking ($-19.8 \pm 4.4\%$ in baseline vs. $-18.3 \pm 3.9\%$ in IQOS vs. $-17.5 \pm 3.9\%$ in cigarette smoking; $p = 0.005$, $p < 0.001$; respectively). RV GLS was significantly lower in groups smoking IQOS and cigarette ($-23.2 \pm 4.6\%$ in baseline vs. $-21.4 \pm 4.1\%$ in IQOS vs. $-19.4 \pm 4.1\%$ in cigarette smoking; $p < 0.001$, $p = 0.001$; respectively).

Conclusion: IQOS (heat-not-burn) tobacco smoking impairs myocardial systolic and diastolic functions in the acute phase like conventional cigarette smoking. The use of IQOS is rising among young adults in recent years, so further studies should be designed to evaluate the chronic effects of IQOS on myocardial function.

1. Introduction

For many years the adverse effects of cigarette smoking on the cardiovascular system are well known. Smoking increases coronary artery disease risk by inducing endothelial dysfunction, thrombosis, and inflammation in the long term (US Department of Health and Human Services, 2004; Benowitz et al., 2002). Cigarette smoking has several acute adverse effects on the cardiovascular system, such as increased blood pressure, heart rate, and vasoconstriction due to sympathetic nervous system activation (Winniford et al., 1986). Cigarette smoking causes diastolic dysfunction and coronary vasospasm within 30 min after smoking (Farsalinos et al., 2013; Alshehri et al., 2013; Sugiishi and Takatsu, 1993). In recent years, novel tobacco devices, including electronic cigarettes (e-cigarettes) and heat-not-burn systems are popular as an alternative to cigarette smoking. The main harmful effects of tobacco products are known to be due to combusted tobacco exposure. Novel devices have aimed to decrease combusted tobacco consumption and be safer than cigarette smoking (O'Connor et al., 2005). Electronic cigarettes were introduced into the platform as help for cigarette smokers to quit smoking (Benowitz and Fraiman, 2017). IQOS (abbrev. I Quit Ordinary Smoking) is the brand name of a novel heated tobacco product produced by Philip Morris International over the past few years (Philip Morris International, 2019). IQOS, in other words, the heat-not-burn system releases nicotine without fire or smoke, contrary to conventional cigarette smoking. IQOS gets this property by heating tobacco to 350 degrees, while conventional cigarettes are heating tobacco to 600–900 degrees. IQOS is composed of a rechargeable head and tobacco unit, which includes compressed tobacco leaves inserted into the head of the device. The heater of the device includes silver, gold, and ceramic coating to create aerosolization from tobacco leaves without

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combustion. Although the manufacturers of IQOS have declared to have fewer toxic effects as a result of low exposure to toxic chemicals due to the lower temperatures than conventional cigarettes, the FDA's Tobacco Products Scientific Advisory Committee established that Philip Morris International failed to prove that IQOS reduces the risks of tobacco-related diseases (U.S. FDA, 2018). There is limited data in the literature about the cardiac effects of IQOS and, several studies claiming lower adverse effects with IQOS are ongoing (Fried and Gardner, 2020).

Echocardiography is a well-established diagnostic tool for the assessment of systolic and diastolic functions of the myocardium. Speckle-tracking echocardiography (STE) has gained importance to determine early systolic and diastolic dysfunctions of the left and right ventricle by strain and strain rate imaging. Strain and strain rate imaging, also known as myocardial deformation, are superior to conventional echocardiography to quantify regional myocardial functions. Right ventricle (RV) assessment is insufficient with conventional echocardiographic methods because of the complex anatomy, anterior retrosternal position, and poor endocardial border. STE's advantages are being independent of volume overload, angle-independent, and showing RV myocardial functions without ejection fraction (EF) (Vitarelli and Terzano, 2009).

Previous studies have shown that chronic cigarette smoking has harmful effects on myocardial deformation parameters that were the early indicator of systolic and diastolic functions (Eroglu et al., 2009; Yaman et al., 2019). In light of these findings, we aimed to evaluate the acute effects of IQOS smoking on myocardial systolic and diastolic functions by STE comparison with conventional cigarette smoking.

2. Methods

Thirty-eight volunteer IQOS users were recruited for the study prospectively. Participants with a history of chronic cardiac diseases, hypertension, diabetes mellitus, kidney failure, or poor image quality were excluded from the study. Four participants who refused or could not complete the study protocol were excluded. Participants who had a high body-mass index (BMI) (>30 kg/m^2), moderate-severe heart valve disease, systolic dysfunction or diastolic dysfunction, high levels of systolic blood pressure (SBP) (≥140 mmHg), or diastolic blood pressure (DBP) (≥90 mmHg) or history of chronic medical treatment were excluded from the study. Twenty-seven participants were included in our study after exclusions. A flow chart figure of the study population is shown in Fig. 1.

All participants were selected from current smokers. IQOS users who have never smoked any tobacco product before were omitted. The patients' height and fasting weight were measured; body surface area (BSA) (m^2) was calculated. For each participant, 12-lead electrocardiography (ECG) was recorded.

2.1. IQOS and conventional smoking protocol

All participants had their own IQOS (Philip Morris Products S.A, Switzerland) equipment, including a power bank, battery, and tobacco sticks. Device versions used in our study were IQOS 2.4 plus and IQOS 3 duo. The difference between these IQOS versions is that IQOS 3 duo permits two consecutive stick uses without charging. Participants were asked to charge their device and smoke only one IQOS stick before the echocardiographic evaluation session. The devices' setting was checked as follows; to be the same for all devices and allow heating tobacco sticks for 6 min to provide 12–14 puff with two-second puff duration. The tobacco sticks used in our study population were regular and turquoise (smooth menthol blend) which were manufactured by Philip Morris Products S.A containing the same amount of tar (>0.0005) and nicotine (0.5 mg). Participants were questioned about the duration and amount (pack/year) of IQOS smoking. For the cigarette smoking protocol, all smokers were asked to use one brand of tobacco cigarette (Marlboro gold light manufactured by Philip Morris Products S.A) of the same

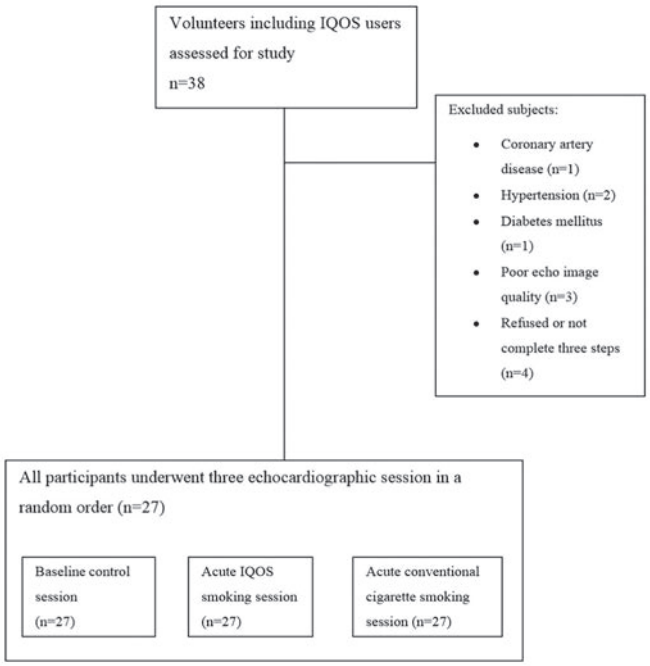

Fig. 1. The flow chart of the study population is shown.

nicotine (0.8 mg) and tar (9 mg) yields. Two-dimensional (2D) transthoracic echocardiography (TTE) was repeated three times for each participant. Each echocardiographic examination was performed with at least 8 h of fasting and without caffeine intake. Baseline echocardiographic measurements were taken without smoking any tobacco product for at least 8 h fasting (group 1). Echocardiography was performed 10 min after IQOS smoking (group 2) and cigarette smoking (group 3) on separate days with random order by a minimum 24 h wash-out period. In this way, each participant had an echocardiographic examination three times on different days. Ten puff of IQOS or cigarette smoking for 5 min was asked to the participants. SBP and DBP were measured manually at baseline, after IQOS and cigarette smoking immediately before echocardiographic evaluation. Heart rate (HR) was recorded during echocardiography for each session.

The local Ethical Committee approved the study, and all patients provided written informed consent.

2.2. Conventional echocardiographic evaluation

Echocardiographic evaluation was performed with the available system (Vivid E9 system; General Electric Healthcare, Milwaukee, Wisconsin) according to the guidelines of the American Society of Echocardiography and European Association of Echocardiography (Lang et al., 2015). All echocardiographic evaluations were performed in the left lateral decubitus position after at least 10 h of fasting, without alcohol or caffeine intake, and after at least 10 min of rest.

Conventional echocardiographic images were recorded from the parasternal long-axis (PSLAX), parasternal short axis (PSAX), apical 4-chamber (A4C), apical 2-chamber (A2C), and apical long-axis (APLAX) views from each participant. Left ventricular (LV) end-diastolic diameter, end-systolic diameter, interventricular septum, and posterior wall thickness were measured in PSLAX, EF was calculated by biplane Modified-Simpson method.

Pulsed Doppler recordings of the mitral valve inflow were performed at diastole. Early peak diastolic velocity (E), late diastolic velocity (a), E/a ratio were measured. Pulsed-wave tissue Doppler imaging (TDI) velocities were measured from the A4C plane. In the A4C view, the cursor was placed at the septal and lateral side of the mitral annulus; also,

lateral side of the tricuspid annulus, peak systolic velocity (Sm), early diastolic velocity (Em), late diastolic velocity (Am) were estimated. The tricuspid annular systolic excursion (TAPSE) was measured by M-mode in the RV-focused A4C view.

2.3. 2D speckle tracking evaluation

2D STE images were recorded during end-expiration with a frame rate of 60–100 frames/s. At least three consecutive beats were stored. The images were analyzed offline using a customized software package (Echo Pac for PC, GE Vingmed). End-systole (aortic valve closure) was defined from pulse wave velocity of the LV outflow tract; end-diastole was defined as the peak R wave on ECG. Region of interest (ROI) was pointed manually, and speckle patterns of the six segments of the LV myocardium were tracked manually for optimization; if necessary, adjustments were done. The bull's eye plot was derived from global longitudinal strain (GLS) of APLAX, A4C and A2C views to assay mean LV GLS. Global circumferential strain (GCS) was obtained at the papillary muscle level at PSAX. ROI was pointed, and speckles were tracked manually in a circular pattern. The software calculated the GCS of the LV myocardium from six segments.

RV GLS and RV free wall strain (FWS) were measured manually in RV-focused apical 4C view. ROI was pointed manually, and RV endocardium was identified from the lateral annulus to the septal annulus of the tricuspid valve. ROI width was adjusted manually if necessary. RV GLS was measured from 6 segments of RV, and RV FWS was measured from 3 segments of the RV lateral wall.

2.4. Statistical analysis

Statistical analysis was performed using the SPSS (version 20.0, SPSS Inc., Chicago, Illinois) software package. Continuous variables were expressed as the mean ± standard deviation (mean ± SD), and categorical variables were expressed as percentages (%). The Kolmogorov-Smirnov test was used to evaluate the distribution of variables. Comparisons of continuous variables between baseline, IQOS, and cigarette smoking groups were made using paired-samples Student's *t*-test. For categorical variables, the chi-square test was used. A p-value<0.05 was considered statistically significant.

3. Results

A total of twenty-seven healthy participants with chronic IQOS smoking history (mean age 39.2 ± 9.3 years) were included in our study; 61.5% of them were male. The mean amount of IQOS smoking was 1.3 ± 1.1 pack-years. 42.3% of the participants were using turquoise (menthol) tobacco sticks (Table 1). As compared HR, SBP, DBP and, echocardiographic parameters between regular stick users and turquoise (menthol) stick users, there were no significant differences (82.8 ± 10.4 bpm vs. 80.4 ± 6.2 bpm, $p = 0.467$; 112.2 ± 20.3 mmHg vs. 117.5 ± 11.1 mmHg, $p = 0.411$; 71.4 ± 11.9 mmHg vs. 69.9 ± 12.3 mmHg, $p = 0.751$). The data is not shown, including the comparison of echocardiographic parameters between IQOS sticks.

Table 1
Demographical characteristics.

Clinical parameters	Mean ± Std. Deviation
Age (years)	39.2 ± 9.3
Male n (%)	16 (61.5)
Height (cm)	171.4 ± 8.3
Weight (kg)	76.7 ± 13.5
IQOS duration (year)	1.3 ± 1.1
IQOS amount (pack/year)	1.3 ± 1.1
IQOS menthol sticks (%)	11 (42.3)
BMI (kg/m^2)	26.2 ± 5.1

BMI, body mass index.

HR significantly increased after IQOS smoking in comparison to non-smoking status (74.4 ± 9.4 bpm vs. 81.8 ± 8.7 bpm, $p < 0.01$) however, SBP and DBP were not changed (111.3 ± 13.5 mmHg vs. 114.1 ± 16.8 mmHg, $p = 0.229$; 71 ± 10 mmHg vs.71.9 ± 10.1 mmHg; $p = 0.515$; respectively). As compared with non-smoking condition, HR, SBP and DBP increased after cigarette smoking (74.4 ± 9.4 mmHg vs. 82.6 ± 8.8 mmHg, $p < 001$; 111.3 ± 13.5 mmHg vs. 120.5 ± 12.7 mmHg, $p < 0.001$; 71 ± 10 mmHg vs. 75.5 ± 10 mmHg, $p = 0.006$; respectively). When comparing IQOS and cigarette smoking, the rise in HR was similar between the two groups; however, there was a more noticeable increase in SBP and DBP after cigarette smoking than IQOS smoking ($p = 0.376$, $p = 0.007$, $p = 0.02$). Comparisons of HR, SBP, and DBP between groups are shown in Table 2.

3.1. Echocardiographic parameters

There is no significant difference between groups regarding LV, LA, RV, RA diameters. There is no impact on LV EF with IQOS and cigarette smoking. There is a reduction in TAPSE after IQOS and cigarette smoking (Table 2). As shown in Table 3, E velocity decreased after IQOS smoking and cigarette smoking (72.6 ± 14.6 cm/s vs. 66.8 ± 12 cm/s vs. 67.3 ± 14.1 cm/s; $p = 0.002$, $p = 0.053$). A velocity increased significantly after cigarette and IQOS smoking compared to baseline ($p = 0.02$, $p = 0.009$). E/A ratio significantly decreased after IQOS and cigarette smoking as compared to non-smoking condition (1.5 ± 0.3 vs. 1.2 ± 0.3 vs. 1.2 ± 0.4; $p < 0.001$, $p = 0.001$; respectively). When comparing IQOS and cigarette smoking, there was no statistically significant difference regarding E velocity, A velocity, and E/A ratio.

Em velocity of mitral valve lateral annulus reduced after IQOS and cigarette smoking in comparison to non-smoking status (12.5 ± 4.3 cm/s vs. 11.6 ± 3.6 cm/s vs. 10.7 ± 3.8 cm/s; $p = 0.02$, $p = 0.004$; respectively). Am was similar between the three groups. Sm of mitral valve lateral annulus decreased after IQOS and cigarette smoking (10.1 ± 2.2 cm/s vs. 9.8 ± 2.4 cm/s vs. 9.1 ± 2.3 cm/s; $p = 0.021$, $p = 0.001$; respectively). Also, when compared IQOS with cigarette smoking, the reduction of Sm was significant in the cigarette smoking group ($p = 0.007$). Em/Am ratio was lower in IQOS and cigarette-smoking than baseline measurements (1.4 ± 0.6 vs. 1.2 ± 0.5 vs. 1.3 ± 1.0; $p = 0.043$, $p = 0.006$), there was no significant difference between IQOS and cigarette smoking ($p = 0.085$).

The evaluation of RV TDI showed that Em of tricuspid valve lateral annulus decreased after IQOS and cigarette smoking in comparison to non-smoking condition (11.8 ± 2.7 cm/s vs. 10.7 ± 2.4 cm/s vs. 10.5 ± 2.4 cm/s; $p = 0.03$, $p = 0.001$; respectively). Am of tricuspid valve lateral annulus increased after IQOS and cigarette smoking ($p = 0.003$, $p = 0.025$; respectively). There was no significant difference between IQOS and cigarette smoking regarding Em and Am of RV lateral annulus ($p = 0.377$, $p = 0.414$; respectively). Sm of RV lateral annulus was similar between the three groups. Em/Ea ratio of tricuspid valve lateral annulus decreased after IQOS and cigarette smoking as compared to baseline (0.9 ± 0.3 cm/s vs. 0.7 ± 0.2 cm/s vs. 0.7 ± 0.2; $p < 0.001$, $p < 0.001$; respectively) however, there was no significant difference between IQOS and cigarette smoking conditions ($p = 0.877$).

3.2. Myocardial deformation parameters

LV GLS decreased significantly after IQOS and cigarette smoking as compared to non-smoking status (−18.9 ± 2.4% in baseline vs. −17.9 ± 2.4% in IQOS vs. −17.9 ± 2.8% in cigarette smoking; $p = 0.003$, $p = 0.001$; respectively) (Table 4). There was no statistically significant difference for LV GLS between IQOS and cigarette smoking groups ($p = 0.395$). LV GCS was lower in IQOS and cigarette smoking groups than non-smoking status (−19.8 ± 4.4% in baseline vs. −18.3 ± 3.9% in IQOS vs.17.5 ± 3.9% in cigarette smoking; $p = 0.005$, $p < 0.001$; respectively). When comparing IQOS with cigarette smoking, the reduction of GCS was much more in cigarette smoking ($p = 0.007$). RV GLS was significantly

Table 2
Comparison of blood pressure, heart rate, and conventional echocardiographic parameters between groups.

	Baseline (Group 1)	IQOS (Group 2)	Smoking (Group 3)	p-Value Group 1–2	p-Value Group 1–3	p-Value Group 2–3
HR (beat/min)	74.4 ± 9.4	81.8 ± 8.7	82.6 ± 8.8	**<0.001**	**<0.001**	0.376
SBP (mmHg)	111.3 ± 13.5	114.1 ± 16.8	120.5 ± 12.7	0.229	**<0.001**	**0.007**
DBP (mmHg)	71 ± 10	71.9 ± 10.1	75.5 ± 10	0.515	**0.006**	**0.024**
LVEDD (mm)	46.4 ± 4.3	46.1 ± 4.1	46.3 ± 4.5	0.258	0.164	1.0
LA diameter (mm)	38.7 ± 5.4	38.8 ± 4.8	38.3 ± 5.2	0.774	0.131	0.156
LV EF(%)	64.0 ± 4.5	64.5 ± 3.8	64.4 ± 3.9	0.237	0.371	0.929
RA diameter (mm)	38.4 ± 3.9	38.2 ± 4.0	38.3 ± 3.9	0.556	0.678	0.814
RV diameter (mm)	33.8 ± 3.8	34.2 ± 3.2	34.2 ± 3.3	0.61	0.126	1.0
TAPSE (mm)	21.6 ± 2.3	20.9 ± 2.5	20.2 ± 2.9	**0.033**	**0.025**	0.155

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEDD, left ventricular end-diastolic diameter; LA, left atrium; LV EF, left ventricle ejection fraction; RA, right atrium; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion. Bold value indicates the significance of $p < 0.05$.

Table 3
Comparison of myocardial diastolic function parameters between groups.

	Baseline (Group 1)	IQOS (Group 2)	Smoking (Group 3)	*p*-Value Group 1–2	*p*-Value Group 1–3	*p*-Value Group 2–3
E wave velocity (cm/s)	72.6 ± 14.6	66.8 ± 12	67.3 ± 14.1	**0.002**	0.053	0.916
A wave velocity (cm/s)	50.8 ± 14.3	55.8 ± 14.2	57.9 ± 16.5	**0.021**	**0.009**	0.357
E/A ratio	1.5 ± 0.3	1.2 ± 0.3	1.2 ± 0.4	**<0.001**	**0.001**	0.634
Em (cm/s)	12.5 ± 4.3	11.6 ± 3.6	10.7 ± 3.8	**0.022**	**0.004**	0.100
Am (cm/s)	9.5 ± 2.2	9.5 ± 2.2	10 ± 2.9	1.000	0.460	0.270
Sm (cm/s)	10.1 ± 2.2	9.8 ± 2.4	9.1 ± 2.3	**0.021**	**0.001**	**0.007**
Em/Am ratio	1.4 ± 0.6	1.2 ± 0.5	1.3 ± 1.0	**0.043**	**0.006**	0.085
RV Em (cm/s)	11.8 ± 2.7	10.7 ± 2.4	10.5 ± 2.4	**0.030**	**0.001**	0.377
RV Am (cm/s)	13 ± 3.1	15 ± 4.5	14.5 ± 3.4	**0.003**	**0.025**	0.414
RV Sm (cm/s)	13.5 ± 2.2	13.1 ± 2.1	12.8 ± 2.5	0.432	0.141	0.247
RV Em/Am ratio	0.9 ± 0.3	0.7 ± 0.2	0.7 ± 0.2	**<0.001**	**0.001**	0.877

Em, peak early diastolic velocity of the left ventricle; Am, peak late diastolic velocity of the left ventricle; Sm, the systolic myocardial velocity of the left ventricle; RV Sm, right ventricle systolic myocardial velocity; RV Em, right ventricle peak early diastolic velocity; RV Am, right ventricle peak late diastolic velocity; RV Sm, right ventricle systolic myocardial velocity. Bold value indicates the significance of $p < 0.05$.

Table 4
Comparison of myocardial deformation parameters between groups.

	Baseline (Group 1)	IQOS (Group 2)	Smoking (Group 3)	*p*-Value Group 1–2	*p*-Value Group 1–3	*p*-Value Group 2–3
LV GLS (%)	18.9 ± 2.4	17.9 ± 2.4	17.9 ± 2.8	**0.003**	**0.001**	0.395
LV GCS (%)	19.8 ± 4.4	18.3 ± 3.9	17.5 ± 3.9	**0.005**	**<0.001**	**0.007**
RV GLS (%)	23.2 ± 4.6	21.4 ± 4.1	19.4 ± 4.1	**<0.001**	**0.001**	0.125
RV FWS (%)	25.3 ± 6.1	23.9 ± 6.2	21.2 ± 5.6	0.139	0.08	**0.03**

LV GLS, left ventricle global longitudinal strain; LV GCS, left ventricle global circumferential strain; RV GLS, right ventricle global longitudinal strain; RV FWS, right ventricle free wall strain. Bold value indicates the significance of $p < 0.05$.

lower in IQOS and cigarette smoking group in comparison to non-smoking status (−23.2 ± 4.6% vs. −21.4 ± 4.1% vs. −19.4 ± 4.1%; $p < 0.001$, $p = 0.001$; respectively). There was no statistically significant difference between IQOS and cigarette smoking ($p = 0.125$). RV FWS was lower in cigarette smoking than non-smoking and IQOS smoking conditions (−25.3 ± 6.1% vs. −23.9 ± 6.2% vs. −21.2 ± 5.6%; $p = 0.08$, $p = 0.03$; respectively). Fig. 2 illustrated the comparison of LV GLS, LV GCS, RV GLS, and RV FWS between baseline, IQOS, and cigarette smoking status.

4. Discussion

To the best of our knowledge, this is the first study to evaluate the acute effects of IQOS smoking on cardiovascular health compared to cigarette smoking. The main findings of our study were; 1) HR increased after IQOS and cigarette smoking. Although SBP and DBP increased after cigarette smoking, IQOS had no acute adverse effect on blood pressures, 2) Diastolic function parameters impaired after IQOS and cigarette smoking, 3) LV global longitudinal and circumferential strain reduced after IQOS and cigarette smoking. LV GCS decreased much more after cigarette smoking than IQOS smoking. Also, TAPSE and RV GLS were reduced after IQOS and cigarette smoking.

The concern remains, including the safety and usage of electronic devices and the heat-not-burn system as a smoking cessation method. FDA stated the lack of data about the safety of e-cigarettes in 2015 and recommended avoiding e-cigarettes due to increased exposure to nicotine which is the primary toxic chemical and cause of premature death among the young population (Crowley and Health Public Policy Committee of the American College of Physicians, 2015; Mirbolouk et al., 2018). However, in recent years, switching from cigarette smoking to electronic cigarettes (e-cigarettes) and the heat-not-burn system has increased, especially among the young population. The use of e-cigarettes and the heat-not-burn system by the young population who have never smoked is rising day by day. The cardiovascular effects of novel tobacco products remain unclear. *E*-cigarettes are claimed to be safer than conventional cigarette smoking and suggested for quitting smoking by some trials (Hajek et al., 2019). E-cigarettes do not include tobacco but have some chemicals in liquid form. The main components of these chemicals are propylene glycol, glycerine, and nicotine, which are also components of tobacco products. In comparison, e-cigarettes have lower

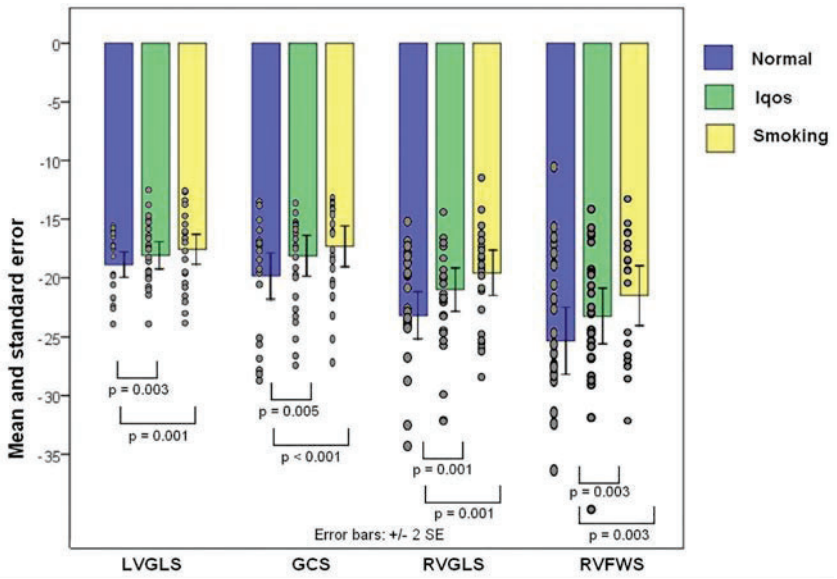

Fig. 2. Bar graph with individual data points comparing the myocardial deformation parameters regarding left ventricular global longitudinal strain (LVGLS), left ventricular circumferential strain (GCS), right ventricular global longitudinal strain (RVGLS), right ventricular free wall strain (RVFWS) between baseline (n = 27), after IQOS smoking (n = 27), and cigarette smoking (n = 27) status. Paired-samples Student's *t*-test was performed. Error bars represent the standard error of the myocardial deformation parameters.

nitrosamine levels than tobacco (Farsalinos and Polosa, 2014). E-cigarettes include some chemicals different from tobacco smoking, which induce oxidative stress and cardiotoxicity. Although the absolute values were very low, the metallic compound of the e-cigarettes may contain these chemicals such as; nickel, tin, silver, cadmium, and lead, which can contact the liquid component of e-cigarettes (Luo et al., 2007). Most e-cigarettes have a variety of flavors such as menthol, coffee, tobacco, or fruit-based that might contain alcohol, diacetyl, and aldehydes, known as toxic chemicals (Barrington-Trimis et al., 2014). Farsalinos et al. (2014) evaluated the acute effects of e-cigarettes on diastolic dysfunction and found no detrimental effect on myocardial relaxation, unlike cigarette smoking.

IQOS (Philip Morris International, Neuchâtel, Switzerland) is a newer heated tobacco product widely used in recent years, also available in Europe and about 30 countries. Several arguments are supporting heat-not-burn system safety. Heated tobacco products perform by heating tobacco to 350 °C temperature; they are not combusting like cigarettes in 900 °C temperatures. IQOS is claimed to be less detrimental than conventional cigarette smoking by force of the heat-not-burn mechanism. The chemicals included by the heat-not-burn system are tobacco-specific nitrosamines, benzene, acrolein, and particulate matter. Chemical toxicants and nicotine compounds are different between electronic cigarettes, IQOS, and other tobacco products (Cheng, 2014; Farsalinos and Polosa, 2014). A previous study showed that, although the nicotine concentration of IQOS is similar to conventional cigarettes, tobacco-specific nitrosamines of IQOS is one-fifth, carbon monoxide of IQOS is one-hundredth of conventional cigarettes (Bekki et al., 2017). Also, when the particulate matter is compared, submicronic particle matter is lower in IQOS than conventional cigarettes (one-quarter of conventional cigarettes) (Protano et al., 2016). Effects of particulate matter on the cardiovascular system are increased blood pressure, ventricular arrhythmia, and left ventricular remodeling (Brooks et al., 2010; Prabhakaran et al., 2020). Especially submicronic particulate is responsible for lung and heart damage via entering systemic circulation easily. The heat-not-burn system is claimed to have lower side effects due to including lower amounts of submicronic particulates (Protano et al., 2016); in furtherance, we showed no adverse effect on blood pressure by IQOS. A previous study observed the chemical content of different IQOS sticks. Glycerol released by IQOS has no toxic effects; however, it can be highly carcinogenic when converted to acrolein. This highly carcinogenic component was discovered in Amber, Blue, Bronze, Sienna, and Yellow IQOS sticks except menthol. A 3-methyl furan is a highly toxic compound and is found in all flavors (Ilies et al., 2020). In our study population, participants had their IQOS sticks, including regular and menthol, so we failed to compare other flavors' effects. As we compared regular and menthol sticks, there was no significant difference, including blood pressures, HR, and systolic-diastolic functions. It is assumed that regular sticks are most similar to the new brand Amber sticks. Peruzzi et al. (Peruzzi et al., 2020) speculated that Bronze sticks have more minor pollutions effects than the other; the particulate matter was similar between Amber and menthol sticks.

Acute exposure to cigarette smoking increases heart rate and blood pressure by inducing the sympathetic nerve system (Narkiewicz et al., 1998). As we focused on pathogenesis, it is well known that acute exposure to smoking is associated with oxidative stress that significantly induces atherogenesis and endothelial dysfunction (Loffredo et al., 2011). Smoking impairs the anti-oxidant mechanism by increasing the production of reactive oxygen radical toxicity (Biondi-Zoccai et al., 2019). Also, acute smoking causes coronary spasm due to endothelial dysfunction and catecholamine rise in patients with coronary artery disease (Winniford et al., 1986). However, there is limited data about the impact of IQOS and e-cigarettes on cardiovascular health; a SURVAPES randomized trial was designed to compare the acute effects of e-cigarettes, IQOS, and traditional cigarettes on atherosclerosis (Biondi-Zoccai et al., 2019). They found that e-cigarettes and the heat-not-burn system are less harmful to oxidative stress, platelet aggregation, and blood pressure than traditional cigarettes. Heat-not-burn products are less impactful than e-cigarettes on nitric-oxide-derived peptides associated with platelet activation, thrombosis, and cardiovascular risk (Biondi-Zoccai et al., 2019). In the present study, HR had increased after IQOS and conventional cigarette exposure, while there was no statistically significant difference between the two smoking regimes. Both SBP and DBP are higher in the cigarette smoking group than the non-smoking condition and IQOS smoking. Acute exposure to IQOS smoking resulted in lower blood pressure levels than cigarette smoking. Although there is no doubt about the detrimental effects of conventional cigarettes on the cardiovascular system, there is limited data about the contents of IQOS and its impact on public health. In the present study, many effects of IQOS on myocardial functions were similar to conventional cigarettes. We compared IQOS with traditional cigarettes. It would be beneficial to make a head-to-head comparison of the effects of traditional cigarettes, e-cigarettes, and IQOS smoking on myocardial functions.

Echocardiography is the main diagnostic tool for the detection of

myocardial systolic and diastolic dysfunctions. Main echocardiographic parameters including LV, LA diameters, and LV EF are similar between IQOS, cigarette smoking, and non-smoking status. It is well known that normal ranges of left and right heart chambers are higher in males than females (*Eur. Heart J. Cardiovasc. Imaging*, 2016). Most of our study population were male, which might affect the LV and RV chamber sizes. We attributed these findings to a small study sample. Although there was no statistically significant difference between sex regarding echocardiographic measurements, it would be beneficial to include sex commensurate in future studies. Cigarette smoking causes mitochondrial damage at the cellular level due to oxidative stress and inflammation by free radicals (Ambrose and Barua, 2004; Gvozdjáková et al., 1984). Myocardial cellular damage progresses to delaying myocardial relaxation. Mitral valve inflow velocities such as E velocity, A velocity, and E/A ratio, TDI parameters of mitral and tricuspid valve annulus are used to assess diastolic function. Previous studies have shown that acute exposure to cigarette smoking causes diastolic dysfunction in healthy smokers (Farsalinos et al., 2013; Lichodziejewska et al., 2007). Farsalinos et al. (2013) demonstrated that acute exposure to cigarette smoking causes impaired diastolic function evaluated by TDI parameters and speckle tracking echocardiography. In our study, we compared the effects of IQOS and cigarette smoking on myocardial systolic and diastolic dysfunctions. E velocity and E/A ratio decreased after IQOS and cigarette smoking similarly; A velocity increased after IQOS and cigarette smoking. The Em/Am ratio of LV and RV lateral annulus were lower in IQOS and cigarette smoking groups. In light of these findings, IQOS is not safer than conventional cigarette smoking on myocardial relaxation in the acute phase.

Myocardial deformation parameters regarding strain and strain rate are the early indicators of systolic myocardial dysfunction. LV strain has three components: longitudinal, circumferential, and radial fibers, assessed by speckle tracking echocardiography. Although radial and circumferential strain can be found normal in the early stages of the diseases, the longitudinal strain begins to deteriorate at very early stages (Lancellotti and Cameli, 2017). A previous study found that LV GLS and RV GLS evaluated by TDI were lower in chronic smokers (Vitarelli and Terzano, 2009). In the present study, LV GLS and LV GCS were reduced after acute IQOS and cigarette smoking. When comparing LV GLS between IQOS and conventional cigarette smoking, there was no statistically significant difference. However, IQOS is less detrimental than cigarette smoking on LV GCS. Sm of mitral valve lateral annulus reduced after IQOS and cigarette smoking. The reduction of Sm was much more prominent in the cigarette smoking group than in the IQOS group. TAPSE is helpful for the assessment of RV global systolic function and a good predictor of cardiovascular outcomes. TAPSE has several limitations, such as; load-dependent, so it may not reflect the actual global RV systolic function and indicate the basal RV wall displacement while RV has three-dimensional anatomical complexity (Rusedski et al., 2010). RV strain is a valuable marker to evaluate RV systolic function; it is independent of volume overload and anatomical complexity (Vitarelli and Terzano, 2009). TAPSE and RV GLS decreased after IQOS and cigarette smoking in the present study compared to non-smoking conditions. When comparing IQOS to cigarette smoking, there was no difference in RV functions between the two groups. Although RV FWS was lower in IQOS and cigarette smoking, there was no statistically significant difference compared to baseline measurements, though the results demonstrated that cigarette smoking reduces RV FWS more than IQOS smoking. We attribute these findings to the involvement of septum in RV GLS. RV FWS is a better indicator of RV systolic function than RV GLS because LV GLS might affect RV GLS via septum. Cigarette smoking had harmful effects on RV systolic functions; however, the effects of IQOS on RV functions are unclear in our study. Although Sm of RV lateral wall was lower in IQOS and cigarette smoking groups than baseline measurements, there was no statistically significant difference.

5. In conclusion

IQOS (heated tobacco) impairs myocardial systolic and diastolic functions in the acute phase like conventional cigarette smoking; however, IQOS had no immediate adverse effect on blood pressure. The use of IQOS is rising among young adults in recent years, so further studies should be designed to evaluate the chronic effects on myocardial functions.

5.1. Limitations

IQOS use is limited in our country; for this reason, small numbers of participants were included. Echocardiographic examination was performed for each same 27 participants at three times. Adding a control group who never smoke would make our study more robust. Also, randomizing the participants to the IQOS, cigarette smoking, smokers with non-smoking status, or control groups who never smoke would be more advantageous. All of the study population was ex-smokers which might affect baseline systolic and diastolic functions of the myocardium. Most of the study population were male gender. Although there is no statistically significant difference regarding echocardiographic parameters according to sex, it may be a limitation of our study. We asked participants to admit with fasting situation to echocardiographic examinations. This is not indicative of everyday life data. As is known, fasting induces parasympathetic activity, decreases heart rate, and may impact echocardiographic parameters (Mattson et al., 2017). In our study, we compared IQOS with traditional cigarettes. It would be beneficial to compare the effects of traditional cigarettes, e-cigarettes, and IQOS smoking on myocardial functions.

Author contributions

Dr. Yaman had access to the data and takes responsibility for the integrity and accuracy of the data and analysis.

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CRediT authorship contribution statement

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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