# Effect of shisha vs. cigarette smoking on endothelial function by brachial artery duplex ultrasonography: an observational study

*Brakiyal arter dubleks ultrasonografi ile sigaraya karşılık nargile içmenin endotel fonksiyonuna etkisi üzerine gözlemsel bir çalışma*

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## ABSTRACT

**Objective:** In this study, we sought to investigate the effect of shisha smoking on endothelial function compared to cigarettes, using brachial artery ultrasound (BAUS) imaging in asymptomatic young adults with no other cardiovascular risk factors.

**Methods:** This is an observational case-control study where 30 young shisha smokers, 30 cigarette smokers and 10 healthy, non-smokers, age-matched subjects between 25-35 years old with no cardiovascular risk factors were recruited from all around Egypt. Flow-mediated dilation was assessed using brachial artery duplex ultrasonography.

**Results:** FMD% was significantly impaired among shisha smokers compared to cigarette smokers and non-smokers cigarettes (7.9±3.8% vs. 12±3.4% and 21.5±2.5% respectively p<0.001).

**Conclusion:** Shisha smoking has a more hazardous effect on brachial artery endothelial- dependent flow mediated vasodilation compared to cigarette. *(Anadolu Kardiyol Derg 2013; 13: 759-65)*

**Key words:** Shisha, smoking, waterpipe, cigarettes, duplex ultrasonography, flow-mediated dilation

## ÖZET

**Amaç:** Bu çalışmada başka hiçbir kardiyovasküler risk faktörü belirtisi olmayan genç yetişkinlerde brakiyal arter ultrason (BAUS) görüntüleme kullanarak nargile kullanımının sigaraya karşılık endotel fonksiyonu üzerine etkisini incelemek istedik.

**Yöntemler:** Bu çalışma bir gözlemsel vaka-kontrol çalışması olup; Mısır'ın birçok yerinden alınan 30'u nargile, 30'u sigara içen ve 10'u sağlıklı, içici olmayan, 25-35 yaş arası, yaş olarak eşleştirilmiş, hiçbir kardiyovaskuler risk taşımayan şahıslarla yapılmıştır. Akıma bağımlı dilatasyon brakiyal arter dubleks ultrasonografi ile ölçüldü.

**Bulgular:** %FDM sigara içenlere ve içmeyenlere nazaran nargile içenlerde önemli ölçüde azaltıldı (sırasıyla %12±3,4 ve %21,5±2,5; %7,9±3,8).

**Sonuç:** Nargile kullanımı sigara kullanımına göre brakiyal arter akıma bağımlı dilatasyona daha tehlikeli etkilere sahiptir. *(Anadolu Kardiyol Derg 2013; 13: 759-65)*

**Anahtar kelimeler:** Nargile, sigara içmek, sigara, brakiyal dubleks ultrasonografi, akıma bağlı dilatasyon

## Introduction

Smoking is a major cause of cardiovascular disease mortality (1, 2). Current research, treatment, and policy efforts focus on cigarettes, while many people in developing regions smoke tobacco using waterpipes. The misconception that waterpipe is less harmful than cigarette increases its spread to other segments of society, particularly among young men and women. Waterpipes (also known as gouza, narghile, hubble-bubble, hookah, or shisha) are increasing in popularity, and more must be learned about them so that we can understand their effects on public health, curtail their spread and help their users quit (3).

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Several studies have evaluated the association of waterpipe smoking with respiratory and psychological problems, but to our knowledge, none has studied its effect on endothelium (4, 5).

Waterpipe smoking has become an epidemic throughout the world as it is also spreading rapidly in Europe and the US (3), especially among college and university students (6-9). Approximately 3.3% of the Egyptian population are current shisha smokers (6.2% of men and 0.3% of women) (10).

Waterpipe smoking may affect different systems either directly by contact or the smoke itself (11). Evidence suggests that waterpipe tobacco smoking is associated with a number of deleterious health outcomes including lung cancer, respiratory illness, low birth-weight and periodontal disease (12). It is also associated with markers of atherosclerosis (13), elevation of total plasma lipids (3), a significant elevation of blood pressure and heart rate (14) and deterioration of right ventricular function (15).

Smoking causes endothelial dysfunction through impairment of nitric oxide (NO) production, or increased oxidative stress by a large number of free radicals known to exist in smoke (16). Since endothelial dysfunction is a well-documented early phenomenon in atherosclerosis as it precedes structural changes and clinical manifestations, major research efforts have focused on the detection of endothelial dysfunction in humans (17).

Duplex ultrasound may be used to measure brachial artery reactivity. The vasodilatory response of the brachial artery to increased shear stress is called flow mediated dilation (FMD). Brachial artery flow mediated dilation is a validated, noninvasive physiological measure widely used as a research tool to quantify endothelial function. A diminished FMD response reflects endothelial dysfunction (18, 19).

FMD is diminished in patients with several coronary risk factors, coronary artery disease (20), peripheral arterial disease, stroke, and is an independent predictor of cardiovascular events. FMD represents a useful method for identify asymptomatic atherosclerotic subjects with raised risk of developing atherothrombotic complications and improves with risk-reduction therapy such as antihypertensive or antidiabetic drugs, antiplatelet agents and statins (21).

FMD results are closely correlated with endothelial function in the coronary arteries (22) and showed a 71% sensitivity and an 81% specificity in predicting any coronary artery disease (CAD) (23-25).

Since brachial duplex is a non-invasive easy and available technique, we sought to evaluate endothelial function among waterpipe and cigarette smokers.

## Methods

### Study design

This is an observational case-control study.

### Study population

Subjects were recruited from different public places (e.g. colleges, and universities) in Cairo, and its suburbs in the period from (May to September 2010). Subjects born and permanently living in Cairo as well as subjects born in remote governorates who were temporarily in Cairo for study or work were included.

They were asked to answer a survey about their smoking habits and then were invited to undergo clinical examination and a brachial ultrasound duplex scan to detect brachial artery flow mediated vasodilation (FMD) and assess endothelial function.

Accordingly, smokers were grouped into:

Cigarette smokers-30 cigarette smokers were defined as subjects who were current and regular smokers for more than one year and were not known to have any other cardiovascular risk factor.

Shisha smokers-30 shisha smokers were defined as subjects who were current and regular smokers for more than one year and were not known to have any other cardiovascular risk factor.

Ten non-smokers not known to have any other cardiovascular risk factor were assigned to control group.

The following subjects were excluded; Combined smokers (shisha & cigarettes), patients with established coronary artery disease, patients with any cardiovascular risk factors (eg hypercholesterolemia, hypertension, diabetes, family history of premature atherosclerotic disease, and obese patients), patients with history suggestive of peripheral vascular diseases or those receiving drugs affecting vasomotor function function. All subjects were signed an informed consent.

### Study protocol and study variables

Each individual was subjected to full personal data including age, sex, occupation, residence (urban/rural), level of education & other habits of medical importance (eg alcoholism, tobacco chewing, drug abuse) with special emphasis on the smoking habit, history of coronary artery disease (CAD), peripheral vascular disease, and history of cardiovascular risk factors.

All subjects underwent clinical examination. Blood pressure was measured and systemic arterial hypertension was considered when systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg) (26). Pulse was evaluated in radial, brachial, and dorsalis pedis arteries for rate, rhythm, volume, special character and equality of pulsations. Body mass index (BMI) was calculated as weight in kg/height in meter$^2$ and waist circumference (WC): was measured at a level midway between the lowest rib and the iliac crest. Patients were considered obese if BMI >30 (26) or WC>102 cm for men & WC>88 cm for women (27).

### Smoking

Smoking was defined based on its active presence in the last one year; and a non-smoker was someone who did not smoke in the last 15 years (26).

Outdoor smokers were defined as smokers who reported that most of their smoking time was outdoors or in open spaces.

Indoor smokers were defined as smokers who reported that most of their smoking time was at home, car, restaurants, inside coffees or work places.

Shisha smokers were asked about onset &duration of shisha smoking, number of sessions per day, type of tobacco content (moassel "unflavoured"/fruit flavoured/both), while cigarette smokers were asked about onset and duration of cigarette smoking, number of cigarettes smoked per day. Both were asked about place of smoking (mostly outdoors or indoors, eg home, car, restaurants, inside coffees or work places).

**Brachial ultrasound evaluation of FMD**

Patient preparation: Subjects were instructed not to exercise, not ingest substances that might affect flow-mediated vasodilation (FMD) such as caffeine, high fat foods and vitamin C or use tobacco for at least 4 to 6 h before the study (28).

**Image acquisition:** All subjects were studied in a quiet, temperature-controlled room. They were positioned supine with the arm in a comfortable position. Phillips HD11 ultrasound system machine at the radio-diagnosis department was used. A high frequency (10 MHZ) ultrasound scanning probe was placed at an angle of about 30 degrees to the long axis of the arm in order to insulate the brachial artery (29).

**Table 1. Nicotine concentration (mg/gm) in commercial tobacco used in hubble-bubble smoking purchased from local shops**

| Product name | Nicotine concentration (mg/gm) | Nicotine concentration (mg/Narghileh head) |
|---|---|---|
| Two apple nakhleh | 3.7 | 74 |
| Fakhfackeina apple | 3.15 | 63 |
| Fackfackeina fruit | 3.0 | 60 |
| Fackfackeina strawberry | 3.2 | 64 |
| Zaghlool | 5.75 | 113 |
| Salloom | 6.3 | 126 |
| Alsonboleh | 1.8 | 36 |
| Apple - Egypt | 2.3 | 46 |
| Al-Nakhleh | 2.25 | 45 |
| Apple - Jeddah | 2.6 | 52 |
| Al-Noman | 2.8 | 56 |
| **Flavored** | | |
| Average | 3.35 | 67 |
| Range | (1.8-6.3) | (36-126) |
| Asfahani* | 30 | 600 |
| Ajami* | 41.3 | 826 |
| **Unflavored** | 35.65 | 713 |
| Average | 35.65 | 713 |
| Range | (30-41.3) | (600-826) |
| **Both flavored and unflavored** | | |
| Average | 8.32 | 166.4 |
| Range | (1.8-41.3) | (30-826) |

*Unflavored (plain and dry tobacco)

**Measurements of FMD:** Brachial artery diameter was measured at baseline. Another measurement was obtained 1 minute after induction of reactive hyperemia (by 5-minute inflation of sphygmomanometer cuff on the forearm to a pressure 50 mm Hg above systolic pressure). Flow Mediated Dilation (FMD) was calculated as: FMD (%)=$[(D_2-D_1)\backslash D_1]$ x 100 where $D_2$ is the reactive hyperemia diameter and $D_1$ is the baseline diameter (30).

**Statistical analysis**

The statistical analysis of data done by using SPSS for Windows software version. The following tests were done: t-test for independent samples, ANOVA, and Chi- square test. To test the association between variables correlation co-efficiency test was used. ROC curve was drawn to detect cutoff point with highest sensitivity and specificity. P is significant if < or=0.05 at confidence interval 95%.

## Results

**Baseline clinical characteristics (Table 2)**

This study was conducted on 60 smokers between 25-35 years recruited from different areas in Egypt and 10 volunteers age-matched, non-smokers, as control. Study groups did not differ by age, residence, SBP, DBP, heart rate, BMI and WC (p>0.05).

In this study shisha smokers showed significantly lower educational level (mostly due to low socioeconomic status) as compared to cigarette smokers (p<0.05).

**FMD values (Table 3)**

Shisha smokers showed statistically significant reduced values of FMD% as a parameter of endothelial function when compared to cigarette and control groups (7.9±3.8% vs. 12±3.4% and 21.5±2.5%, respectively p<0.001).

**Effect of duration and severity of smoking on FMD%:** In the present study, there was a significant reduction of FMD% with increased duration of smoking per years (p<0.001) with increased number of sessions per day (p<0.001) and an inverse correlation between FMD and duration of smoking per years(p<0.05) and number of daily cigarette smoked (p<0.01) among cigarette smokers.

**Effect of openness of smoking area on FMD (Fig.1)**

Also indoors shisha smokers showed significant reduction in FMD% values vs. outdoors smokers (6.765±3.405 vs. 11.218±3.301 respectively p<0.005).

**Effect of tobacco type on FMD (Fig. 2.)**

Shisha smokers who smoked both flavored and unflavored tobacco showed the lowest values of FMD % compared to those

**Table 2. Baseline clinical characteristics**

| Variables | Shisha (n=30) | Cigarette (n=30) | Controls (n=10) | F/Chi-square | *p |
|---|---|---|---|---|---|
| Age, years | 28±3 | 29.9±3 | 30±3.6 | 0.9 | >0.05 |
| Gender, n (%) | | | | 6 | <0.05 |
| Male | 25 (83.3) | 30 (100) | 8 (80) | | |
| Female | 5 (16.7) | 0 | 2 (20) | | |
| Education, n (%) | | | | 13 | <0.05 |
| Low | 17 (56.66) | 5 (16.7) | 2 (20) | 7 | |
| Intermediate | 10 (33.3) | 13 (43.3) | 4 (40) | | |
| High | 3 (10) | 12 (40) | 4 (40) | | |
| Residence, n (%) | | | | 0.5 | >0.05 |
| Rural | 6 (20) | 6 (20) | 3 (30) | | |
| Urban | 24 (80) | 24 (80) | 7 (70) | | |
| SBP, mm Hg | 118.8±7 | 120±6 | 116±5 | 2 | >0.05 |
| DBP, mm Hg | 77±5 | 80±4.5 | 77±4.8 | 1.9 | >0.05 |
| Pulse, mm Hg | 76±5.7 | 75.9±5 | 73±5 | 1.1 | >0.05 |
| BMI, kg/m$^2$ | 26.6±8 | 27±1.7 | 26±2.2 | 0.9 | >0.05 |
| WC, cm | 96.7±4 | 98.4±2.2 | 96.6±5.8 | 1.7 | >0.05 |

Data are presented as mean±SD and number (percentage)
*Chi-square test and ANOVA
BMI - body mass index, DBP - diastolic blood pressure, SBP - systolic blood pressure, WC - waist circumference

**Table 3. Flow-mediated vasodilation data**

| Variables | Shisha n=30 | Cigarette n=30 | Control n=10 | F | *p |
|---|---|---|---|---|---|
| $D_1$ | 4.2±0.39 | 4.1±0.45 | 4.3±0.48 | 0.93 | >0.05 |
| $D_2$ | 4.6±0.43 | 4.66±0.48 | 5.2±0.59 | 6.3 | <0.001*** |
| FMD% | 7.9±3.8 | 12±3.4 | 21.5±2.5 | 57.7 | <0.001*** |

Data are presented as mean±SD and number (percentage)
* ANOVA
***Post hoc test (LSD) shows significant difference between Control group vs. Shisha, cigarette
FMD% LSD test shows significant difference between Shisha group vs. Cigarette, control
$D_1$ - baseline diameter of brachial artery, $D_2$ - hyperemia-induced diameter, FMD - flow-mediated vasodilation

who smoked unflavored tobacco only or flavored tobacco only (5.5±3.6 vs. 7.5±3.3 vs. 9.8±3.9 respectively p<0.05).

**The average content of tobacco per shisha serving:** Screening 30 random coffee shops which sell tobacco boxes for shisha serving was done to evaluate the average weight of tobacco used to fill one shisha serving, it was found that an average of (7-12 gr) of tobacco was used. Thus, the nicotine content can therefore be calculated in respect to the commercial type of tobacco used (Table 1).

## Discussion

Brachial artery duplex is a non-invasive, easy, available and relatively cheap method that may be used for evaluation of endothelial function by measuring FMD% among smokers. In this study, shisha smokers showed significantly diminished FMD% and $D_2$ readings compared to cigarette. This may be due to higher tobacco and nicotine content per serving especially among indoors smokers.

This study included 30 asymptomatic shisha smokers, 30 asymptomatic cigarette smokers and 10 non-smokers volunteers. The main age was 28±3.29±3 and 30±3.6 respectively with no significant difference. It was found that 83% of shisha smokers and 100% of cigarette smokers were males. The lack of female smokers may be attributed to the reluctance of females in Egypt to report their smoking habit (31, 32).

Most of shisha smokers in our study (56.6%) received no or little education signifying a low socioeconomic status, while most of cigarette smokers received higher levels of education (43.3%). Our findings about the educational level and residence of smokers may be supported by a survey done by Hassan et al. (33) in 1987 on a much less educated group of 2782 soldiers, from Central

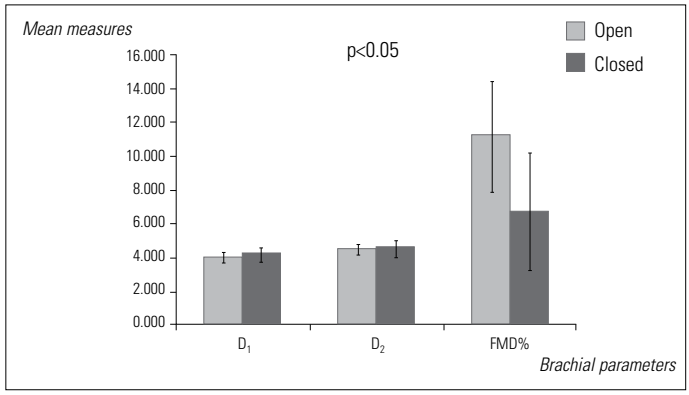


**Figure 1. Brachial artery diameters and FMD in indoor and outdoor smokers**

ANOVA test
d- diameter, FMD - flow-mediated dilatation

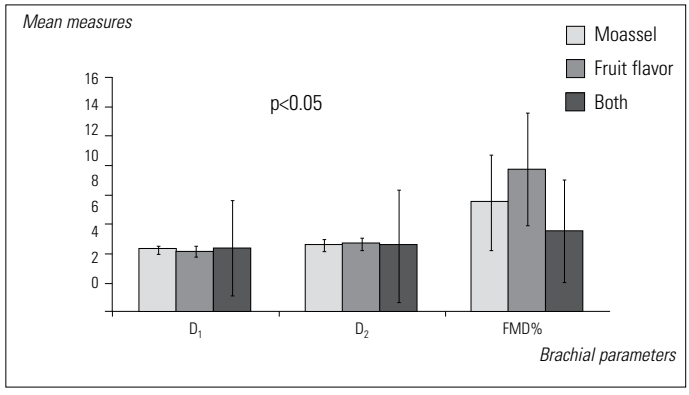


**Figure 2. Brachial artery diameters and FMD in smokers of different types of tobacco**

ANOVA test
d- diameter, FMD - flow-mediated dilatation

Security in Cairo, The survey revealed rates of 27% waterpipe use versus 5% cigarette use. This group reflects the role of education rather than residence as soldiers may be recruited from different parts of Egypt (32).

Most of our shisha smokers (53.3%) tended to smoke 3-5 sessions per day, while most of the cigarette smokers (43.3%) involved in this study smoked 10-20 cigarette per day in average. This would translate into an average 100-200 mg nicotine intake per day if we put in consideration that nicotine present in 20 cigarettes equals 204 mg (34). While an average estimate of nicotine content per serving among shisha smokers can be calculated according to the commercial types as shown in Table (1). If we add this to the fact that the average weight of tobacco per shisha serving is (7-12 gm) as identified from our screened sample of coffee shops, this would point out dramatically how shisha smokers are exposed to higher nicotine content per head (per session) compared to cigarette smokers and in turns expect worse FMD reading which is a parameter of endothelial function. Add to this the number of sessions per day and the duration of smoking per years. In this study, (50%) of shisha smokers and (73.3%) of cigarette smokers smoked for a duration longer than 5 years, so, a reduced FMD of both cohorts would not be surprising.

In the present study, there was a significant reduction of FMD with increased duration of smoking per years ($p<0.001$) and with increased number of sessions per day ($p<0.001$). Therefore, there was a significant inverse correlation between FMD versus smoking duration and number of sessions per day among shisha smokers. This may be explained by a study of Shihadeh et al. (35) in 2006 found that a typical smoking session consists of hundreds of puff cycles executed over a period of approximately an hour with cumulative inhaled volume of the order 100 liters hence, the more frequent number of sessions, the more inhaled shisha tobacco and more exposure to hazards of smoke.

In this study, indoors shisha smokers had a statistically significant lower FMD than outdoors smokers ($p<0.05$). This seems logic as the concentration of environmental tobacco smoke is much higher in closed places, and (compared to cigarette smoking), the number of puffs and volume using shisha are about ten times higher than cigarettes (36, 37).

Our results agree with the study performed by Gül et al. (38) on a total of 61 non-smokers who stayed for 30 minutes in the smoking room, The impairment of endothelial functions has been shown to occur after acute and chronic exposure to passive smoking as assessed by FMD of the brachial artery. Mean FMD was significantly decreased after passive smoking ($p<0.001$).

Interestingly shisha smokers who smoked both types of tobacco (flavored & unflavored) showed the lowest values of FMD%, $p<0.05$. This may be explained by the fact that unflavored tobacco has high nicotine content while flavored tobacco was more often smoked and for longer sessions due to its enjoyable taste produced by the additives, which mask the natural harshness and taste of tobacco smoke, a combination that provided cumulative nicotine exposure, and thus, more prominent endothelial dysfunction.

It is worth noting that all smokers in this study, especially those who showed reduced FMD, were advised to join Smoking Cessation Program present at the Cardiac Rehabilitation Unit in the Cardiology Department, Ain Shams University Hospital, Cairo. However, most of them, especially shisha smokers, showed no intention of stopping smoking despite explaining the relation between endothelial dysfunction and cardiovascular risk. This may be attributed to the dependence effect, lack of awareness, habitual cognitive attitudes associated with smoking.

### Study limitations

Additional studies are needed to evaluate brachial artery duplex ultrasonography as a screening tool for endothelial dysfunction and to quantify its cost -effectiveness among asymptomatic smokers.

## Conclusion

Brachial artery duplex is a non-invasive, easy, available and relatively cheap method that may be used for evaluation of endothelial function by measuring FMD% among smokers. In this study, shisha smokers showed significantly diminished FMD%

and D2 readings compared to cigarette. This may be due to higher tobacco and nicotine content per serving especially among indoors smokers.

Impaired endothelium-dependent dilatation of brachial artery in absence of overt ischemic heart disease can be the earliest sign of coronary artery endothelial dysfunction as smoking disrupts vessel wall morphology long before atherosclerosis is manifest. This calls for more preventive measures as early as school age to promote awareness to smoking hazards specially shisha among those with low educational and socioeconomic status in Egypt.

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**Authorship contributions**

Concept - G.M.S., K.A.E.M., A.S.E.B.; Design - G.M.S., K.A.E.M.; Supervision - G.M.S., K.A.E.M.; Resource - A.S.E.B.; Materials - A.S.E.B.; Data collection&/or Processing - G.M.S., A.S.E.B.; Analysis &/or interpretation - A.S.E.B.; Literature search - G.M.S., K.A.E.M., A.S.E.B.; Writing - G.M.S., K.A.E.M., A.S.E.B.; Critical review - G.M.S., K.A.E.M., A.S.E.B.; Other - G.M.S., K.A.E.M., A.S.E.B.

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