

Cardiopulmonary Risk of Waterpipe Smoke: A Meta-Analysis

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Keywords

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Carboxyhemoglobin

ABSTRACT

Purpose: This study aimed to analyze and summarize the effects that waterpipe (WP) smoke has on the cardiopulmonary system through a systematic review and meta-analysis.

Methods: We searched MEDLINE, Embase, Wiley Cochrane Library, Centre for Reviews and Dissemination, CINAHL Plus, and grey literature in March 2017. Our inclusion criteria for the studies were a comparison of WP smokers before and after waterpipe smoking (WPS) or to non-smokers.

Results: Using a random effects meta-analysis, a WPS session was associated with an elevation in systolic blood pressure (SBP) by 6.45 mmHg (95% CI 3.87 to 9.04; $p < 0.0001$), diastolic blood pressure (DBP) by 3.71 mmHg (95% CI 2.34 to 5.08; $p < 0.0001$), mean arterial pressure by 5.54 mmHg (95% CI 3.33 to 7.76; $p < 0.0001$), heart rate by 7.03 bpm (95% CI 4.60 to 9.46; $p < 0.0001$), carboxyl hemoglobin (COHb) by 4.11% (95% CI 3.38 to 4.84; $p < 0.0001$), and expired carbon monoxide (CO) by 22.53 ppm (95% CI 15.99 to 29.08; $p < 0.0001$).

Conclusion: WPS exposure is associated with significant acute increases in cardiopulmonary hemodynamic parameters, along with COHb and expired CO. These findings parallel the acute effects seen with cigarette smoking.

Introduction

According to the 2010 Global Burden of Disease Study, cardiopulmonary diseases are responsible for the top 5 causes of death worldwide¹. Within the United States (U.S.), mortality data from 2015 shows cardiovascular disease (CVD) ranked as the leading cause of death in the U.S.,² with about 80% of CVD being preventable,³ and chronic lower respiratory diseases ranked third². Additionally, within the second leading cause of death in the U.S., cancer, lung and bronchus cancer is the leading cause of mortality in both men and women⁴. One of the greatest risk factors for developing cardiopulmonary disease is cigarette smoking,⁵ but with major public health efforts since 1965, the prevalence of cigarette smoking has been declining⁶.

In contrast to cigarette use, in the last decade, waterpipe (WP) use, commonly referred to as hookah, nargile, shisha, or hubble-bubble, has risen in popularity in Western countries, especially among adolescent populations⁷⁻⁹. In the United States, 8% of adolescents 13 -17 years old and 20% of high-school seniors

reported using a WP, according to the 2011 National Youth Tobacco Survey⁹. The increase in popularity is partially attributable to the misconception that waterpipe smoke (WPS) is less deleterious than cigarette smoke^{8,10}. Nonetheless, similar to cigarettes, an association between WPS and cardiopulmonary disease has been documented¹¹.

Studies have shown that during a typical WPS session, which varies in length from 30 minutes to 90 minutes with the average duration around 45 minutes, there can be acute increases in hemodynamic parameters of cardiopulmonary function such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR), as well as an increase in expired carbon monoxide (CO) and carboxyl hemoglobin (COHb)^{7,12,13}.

Although these common parameters of cardiopulmonary function appear to correlate with WPS in some studies, the short-term and long-term health effects of WPS on the cardiopulmonary system are still not well understood. Thus, this meta-analysis aims to summarize the effects of WPS on several common hemodynamic parameters of cardiopulmonary function and respiratory markers of tobacco exposure.

Methods

A comprehensive literature review was conducted in March 2017 for all relevant publications up to that date in English using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, the Centre for Reviews and Dissemination database Cumulative Index to Nursing & Allied Health Literature (CINAHL Plus), Google Scholar, and the Wiley Cochrane Library. PubMed Reminer was used to help refine the search strategy and ensure all appropriate and relevant terms were included. Medical Subject Heading (MeSH) terms and keywords that were included are detailed in Table 1. A grey literature search was also conducted by hand searching OAIster, Open Grey, Grey Literature Report, and Proceedings of the National Academy of Sciences. All studies comparing the before and after hemodynamic effects of WPS were included, including several that analyzed smokers who used both waterpipes and cigarettes. Studies that did not distinguish between tobacco use or indicate a proper cessation from cigarette smoke were excluded. The references for selected studies were hand searched to identify any additional literature. The process of selecting studies for the final inclusion in this systematic review, as well as the reasons for exclusion, is outlined in Figure 1. Relevant data were extracted on study design and setting, population, the type of WP being used, and outcomes of HR, SBP, DBP, expired CO, and COHb. Two authors independently assessed the relevance and quality of all included studies. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria was used to ensure thorough and transparent evaluation of all included literature¹⁴.

Table 1. MeSH Headings Used to Identify Relevant Studies.

Exposure
1. "Hookah pipe smoking"
2. "Waterpipe smoking"
3. "Water-pipe smoking"
4. "Shisha smoking"
5. "Shisha"
6. "Nargile"
7. "Goza"
8. "Hubble bubble"
9. "1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8"
Outcome
10. "Cardiovascular disease"
11. "Respiratory system"
12. "Blood pressure"
13. "Respiratory"
14. "Baroreflex"
15. "Blood pressure"
16. "Cardiorespiratory"
17. "Cardiopulmonary"
18. "Heart rate"
19. "10 Or 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18"
Combined Terms
20. "9 AND 19"

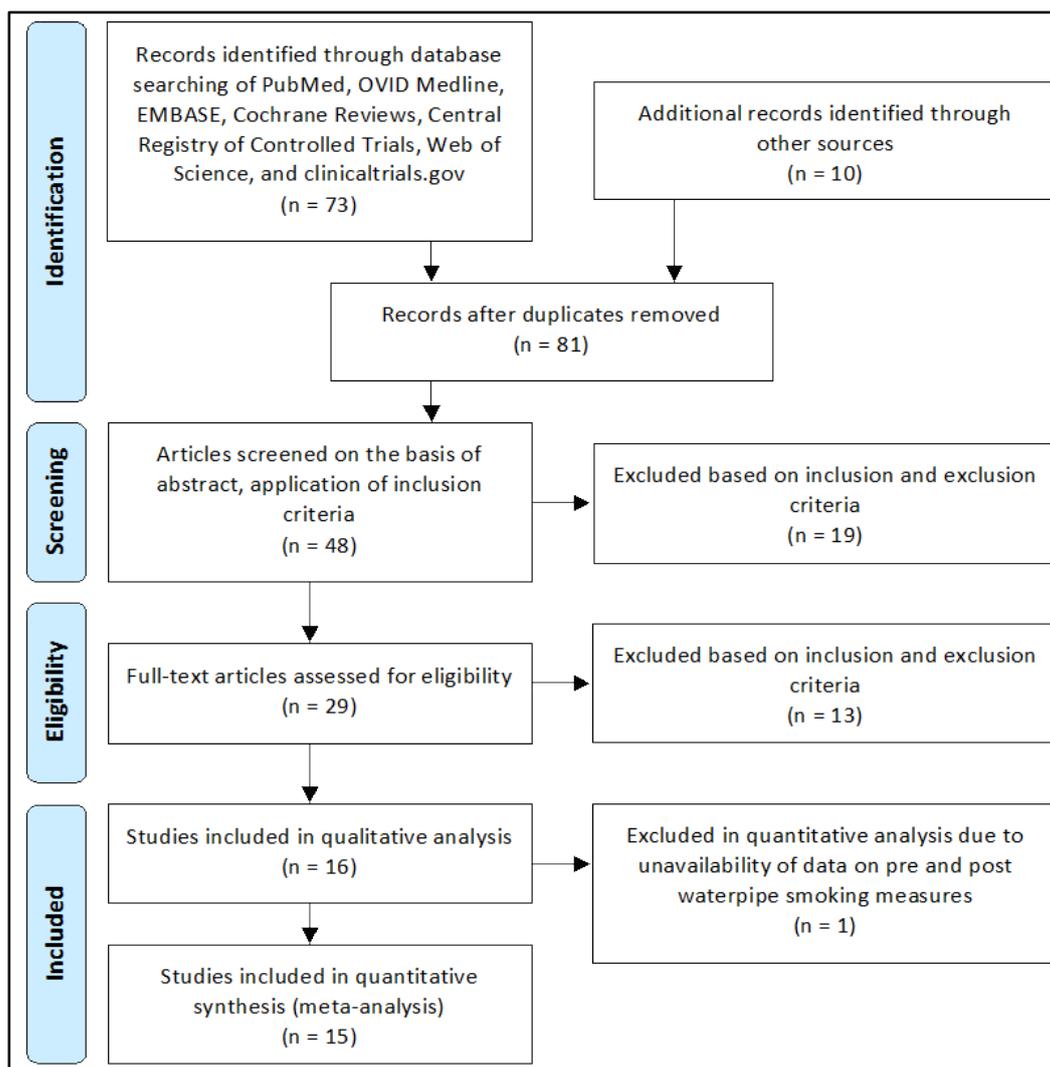
Abbreviations: MeSH, Medical Subject Headings

The quality of the body of evidence for each hemodynamic parameter and respiratory marker of tobacco exposure was assessed in accordance to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group¹⁵. Using this tool, outcomes from each study were graded as high, moderate, low, or very low quality, based on the methodology reported in the individual studies. Risk of bias, inconsistency, indirectness, imprecision, and publication bias were taken into account, and any limitations in these fields resulted in downgrading the quality of evidence.

Using the "meta" and "forestplot" packages in R, meta-analyses were conducted to derive effect estimates of all relevant cardiopulmonary health markers^{16,17}. Mean differences with corresponding 95% confidence intervals were calculated using a random effects model to account for the high heterogeneity (I^2 statistic) and corresponding forest plots were created to graphically depict the results.

Results

As noted in Figure 1, the literature search yielded a total of 73 studies from the databases searched, and another 10 studies were identified through other sources. After the removal of duplicates, 81 studies were screened for titles, and 48 studies remained for abstract screening and application of the inclusion criteria. Of these abstracts, 29 studies were eligible for full-text review, and 15 studies were ultimately included in the meta-analysis altogether. The inter-rater reliability was computed using the Cohen's kappa coefficient and was calculated to be 0.91. The results of the synthesis are summarized in Table 2.



Abbreviations: n, sample size

Figure 1: Process of Inclusion of Studies.

Table 2. Markers of Cardiopulmonary Function in Waterpipe Smoking

Author, Year	Study Design and Location	Sample Size and Characteristics	Waterpipe & Equipment Properties	Comments and Limitations
Shafagoj et al. 2002 ¹²	Cross-sectional design Volunteers smoked for 45-minutes in a well ventilated room Tobacco cessation prior to beginning of study: 84 hours School of Medicine in Amman, Jordan	Age range: 20 – 45 years old Average age in years (Mean ± SD): 27 ± 8 Average WP use in years (Mean ± SD): 3.8 ± 2.3 (smoked at least 3 times per week) n = 18 (100% male) Convenience sampling	WP: Large-size Arghileh 20 grams of HB Mu'asel BP measured by mercury sphygmomanometer CO measured by a trained person using a portable Bedfont EC50-MICRO CO monitor smokerlyser. HR measurement technique not reported	Small sample size Measured maximum CO after first 5 minutes of smoking, which might not be an indicator of smoke inhaled
Al-Kubati et al. 2006 ⁴¹	Cross-sectional design Volunteers smoked for 45-minutes in a laboratory environment Tobacco cessation prior to beginning of study: 12 hours Czech Republic	Age range: 20 – 40 years old Average age in years (Mean ± SD): 27 ± 6 Average WP use in years (Mean ± SD): Not reported n = 20 (100% male) Convenience sampling	WP dimensions NR 5 grams of Maassel shisha SBP, DBP, and HR measured by photo-plethysmographic transducer (Finapres Ohmeda)	Small sample size Only analyzed acute effects

Shaikh et al. 2008 ⁴²	Cross-sectional design Volunteers smoked for 45-min in five different WP cafes Tobacco cessation prior to beginning of experiment: NR Ajman, UAE	Age range: > 17 years old Average age in years (Mean ± SD): NR Average WP use in years (Mean ± SD): Not reported n = 202 (100% male) Convenience sampling	WP dimensions NR Shisha amount or brand NR BP measured by mercury sphygmomanometer HR measured by three fingers on the right wrist over the radial artery	Small sample size Only analyzed acute effects Puff profile not controlled
Al-Safi et al. 2009 ¹³	Randomized cross-sectional Trained pharmacy students interviewed WP users Tobacco cessation prior to beginning of experiment: NR Jordan	Age range: > 17 years old Average age in years for sample (Mean ± SD): 31.4 ± 14.2 Average WP use in years: Not reported n = 14,310 (51.7% male) Random sampling	WP dimensions not specified Shisha amount or brand not specified BP measured by mercury sphygmomanometer MAP and HR were calculated	Self-reported smoking history 78% of sample were students from Jordan
Blank et al. 2011 ⁷	Double-blind design Volunteers smoked for 45-minutes ad lib in a well ventilated laboratory setting Tobacco cessation prior to start of experiment: NR Richmond, VA	Age range: 18 – 50 years old Average age in years (Mean ± SEM): 20.5 ± 2.1 Average WP use every month (Mean ± SEM): 3.8 ± 1.0 Average WP use ≥ 6 months (Mean ± SEM): 20.2 ± 12.9 n = 37 (78% male) Convenience sampling	WP dimensions: Chrome body: 43 cm and acrylic Base ~2.5 mL of the body's conduit submerged by 870 mL water Glazed Ceramic head (7.6 cm) 33 mm quicklight charcoal 10 gram of shisha BP and HR measured by Criticare Systems CO measured by Vitalograph COHb measured by venous blood sampling. NPT7 blood gas analyzer	Participants were casual users Topography data varied from prior studies Experiment conducted in lab setting Smokers smoked alone; not in group setting
Hakim et al. 2011 ¹⁰	Prospective study design Volunteers smoked for 30-min ad lib on an open-air balcony Tobacco cessation prior to start of experiment: at least 6 hours from cigarettes and at least 24 hours from WP smoking Israel	Age range: 18.3 – 65.1 years old Average age in years (Mean ± SD): 32.35 ± 23.36 Average WP use in years: NR n = 45 (66.67% male) Convenience sampling	WP dimensions: 3.5 cm diameter; 1 cm width charcoal disk 10 grams of double-apple flavored shisha from Nakhla BP measured by Omron HEM-712 C BP digital HR measurement technique NR COHb measured by venous blood samples using an Illex cooximeter	Small sample size Focused solely on health individuals Did not analyze aldehydes, PAHs, and nicotine
Cobb et al. 2012 ³⁶	Cross-over study design Volunteers smoked for 45-min with puff topography monitored in a laboratory setting Tobacco cessation prior to start of experiment: 12 hours Richmond, VA	Age range: 18 – 35 years old Average age in years (Mean ± SD): 22.7 ± 4.8 Average WP use in years (Mean ± SD): 2.2 ± 1.6 n = 32 (50% male) Convenience sampling	WP dimensions: Same as Blank et al. 2011 ⁷ 3 mm quicklight charcoal 10 gram of shisha BP and HR measured by Model 507E, Criticare Systems inflatable cuff CO measured by Vitalograph	Description of the demographics of the sample was unclear
Selim et al (a) 2013 ⁴³	Observational case-control study design Tobacco cessation prior to start of experiment: Not reported Cairo, Egypt	Age range: 25 – 35 years old Average age in years of solely WP user (Mean ± SD): 28 ± 3 Average WP use: 50% of WP smokers smoked > 5 years Total n = 70 (90% male) Solely WP smoker n = 30 (83.3% male) Convenience sampling	WP dimensions NR Shisha amount or brand NR BP measurement technique NR	Brachial artery duplex ultrasonography needs to be evaluated as a screening tool for endothelial dysfunction
Selim et al (b) 2013 ⁴⁴	Prospective cohort study design 1 st time coronary angiography patients: May to October 2010 Tobacco cessation prior to start of experiment: NR Cairo, Egypt	Age range: Not specified Average age in years (Mean ± SD): NR Average WP use in years: Not specified Total n = 287 (% male not reported) Solely WP smoker n = 65 (% male NR) Convenience sampling	WP dimensions NR Shisha amount or brand NR BP measurement technique NR	Only one site Self-reported smoking history Most patients were on anti-ischemic treatment

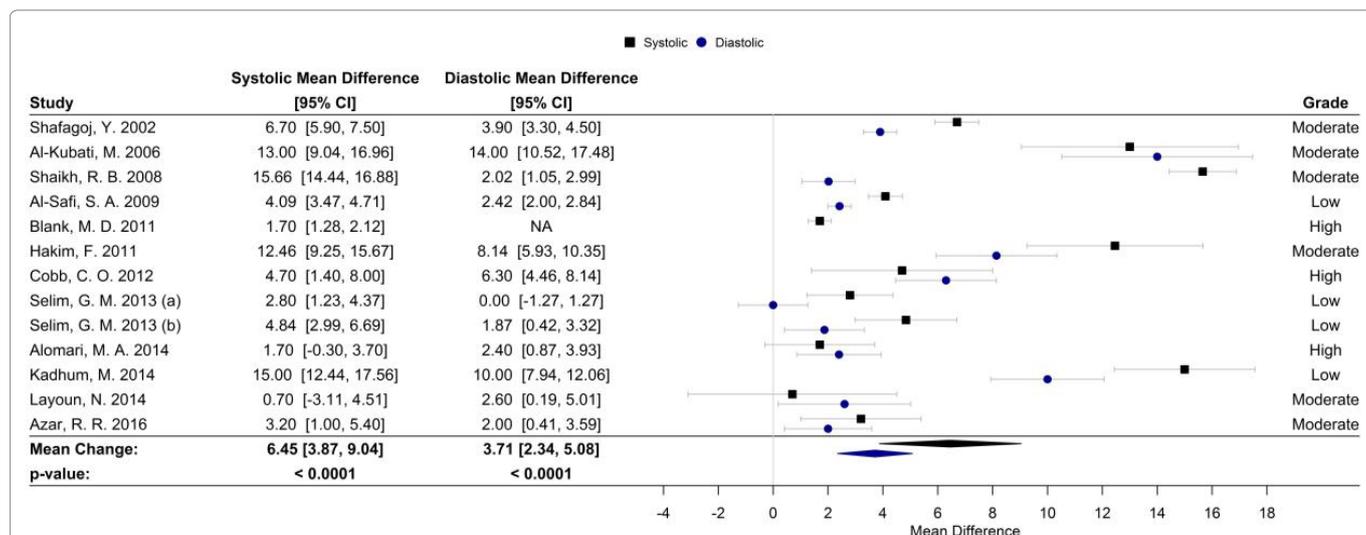
Alomari et al. 2014 ⁴⁵	Time-series design Volunteers smoked ad lib for 30 minutes in a well-vented and air-conditioned room Tobacco cessation prior to start of experiment: NR Jordan	Age range: 18 – 35 years Average age in years (Mean ± SD): 22.7 ± 4.8 Average WP use in years: All participants smoked for >1 year n = 53 (64% male) Convenience sampling	WP dimensions Fast-lit charcoal (Three Kings, Holland) No other WP dimensions provided 10 grams Two Red Apples, Nakhla, Egypt BP measured by Omron HEM-907XL HR measured by Auscultation MAP calculated	Limited information on study demographic
Kadhum et al. 2014 ⁴⁶	Cross-sectional study design Volunteers smoked ad lib for a period between 45 and 90 minutes in WP cafes Tobacco cessation prior to start of experiment: NR London, England	Age range: 18 – 25 years Average age in years (Mean ± SD): NR Average WP use in years: NR n = 61 (80% male) Convenience sampling	WP dimensions: Cafes used the same brand coal No other WP dimensions provided Shisha weight NR BP measured by manual sphygmomanometer HR measured manually by palpation over 30 s MAP measurement technique not reported CO levels measured by portable CO monitor	WPS sessions varied (45 – 90 min) Readings of BP, CO, MAP, and HR not consistent
Layoun et al. 2014 ⁴⁷	Observational non-invasive design Smoked ad lib for a period between 60 and 90 min Tobacco cessation prior to start of experiment: NR Beirut and Mt Lebanon	Age range: NR Average age in years for WP smokers (Mean ± SD): 29.26 ± 9.78 Average WP use per week (Mean ± SD): 11.12 ± 17.27 Total n = 132 (32% WP smokers) Solely WP smokers n = 42 (78.6% male) Convenience sampling	WP dimensions: Commercially available quick-lighting type charcoal No other WP dimensions provided 20 grams of Muassel shisha BP and HR measured by Beurer BM16	Difficulty controlling puff topography and amount inhaled No biomarkers of exposure
Shishani et al. 2014 ⁸	Repeated-measures design Smoked ad lib between 45 and 60 minutes in a fenced outdoor area until a defined target volume was achieved. Tobacco cessation prior to start of experiment: 24 hours Washington, USA	Age range: 18 – 30 years Average age in years for WP smokers (Mean ± SD): 23 ± 3.1 Average WP use: Smoked WP at least 10 times in past year but no more than twice a week in the 3 months before the experiment n = 22 (59% male) Convenience sampling	WP dimensions: 30 mm diameter; 5.6 grams; Golden Coal No other WP dimensions provided 15 grams of Al Fakher shisha BP and HR measured by Welch-Allyn monitor CO measured by Bedford Micro + Smokerlyzer	Small sample size Sessions took place in a laboratory setting
Azar et al. 2016 ⁴⁸	Trial design study Smoked ad lib at 6 different restaurants Tobacco cessation prior to start of experiment: 1 hour for cigarette and 12 hour WP Lebanon	Age range: NR Average age in years for WP smokers (Mean ± SD): 36 ± 13 Average WP use: NR Total n = 194 WPS n = 101 (65% male) Convenience sampling	WP dimensions: NR Amount of shisha NR BP and HR measured by automatic sphygmomanometer	Small number of controls Type and dose of exposure varied for participants
Eissenberg et al. 2009 ²⁸	Two-condition crossover design Volunteers smoked ad lib in a laboratory setting Tobacco cessation prior to beginning of experiment: 12 hours Richmond, VA	Age range: 18 – 50 years Average age in years (Mean ± SD): 21.4 ± 2.3 Average WP use per month (Mean ± SD): 5.2 ± 4.0 WPS n = 31 (67.7% male) Convenience sampling	WP dimensions: Same as Blank et al. 2011 ⁷ Three Kings, Holland brand quicklight charcoal 15 grams of shisha HR measured by Model 506, Criticare Systems, fitted with a reusable finger pulse oximeter sensor CO measured by Vitalograph COHb measured by NPT7 blood gas analyzer	Smoking took place in a laboratory setting WP smokers also smoked cigarettes

Abbreviations: BP, blood pressure; bpm, beats per minute; CO, carbon monoxide; COHb, carboxyl hemoglobin; DBP, diastolic blood pressure; HR, heart rate; MAP, mean arterial pressure; mmHG, millimeter of mercury; n, sample size; NR, not reported; s, seconds; SBP, systolic blood pressure; WP, waterpipe; WPS, waterpipe smoke; PAH, polyaromatic hydrocarbons; UAE, United Arab Emirates

Fifteen studies were used in the meta-analyses to determine the effects of WPS on CVD and respiratory markers of tobacco exposure by assessing changes in intermediate hemodynamic parameters affecting cardiopulmonary function, including MAP, SBP, DBP, and HR, as well as expired CO and COHb concentration to assess WPS exposure¹⁸. A pooled analysis of the results revealed an association between a WPS session and an increase in mean SBP and DBP of 6.45 mmHg (95% CI 3.87 to 9.04; $p < 0.0001$) and 3.71 mmHg (95% CI 2.34 to 5.08; $p < 0.0001$), respectively (Figure 2). Additionally, MAP increased by 5.54

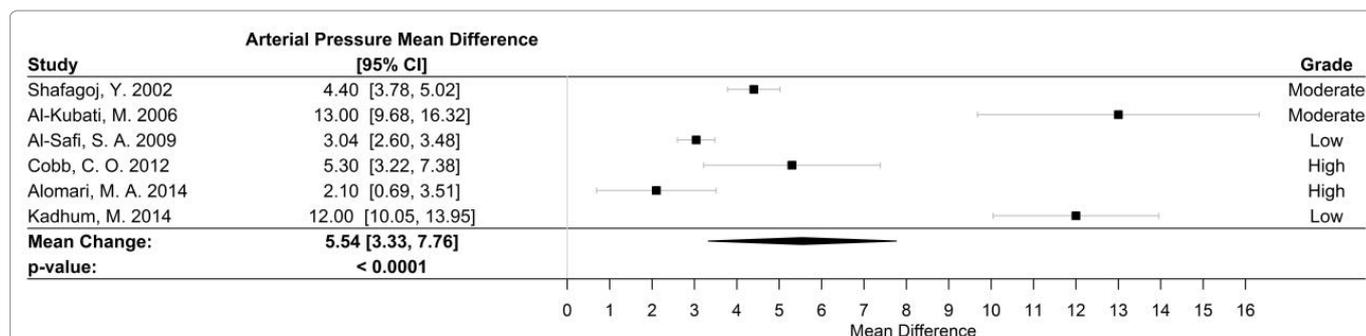
mmHg (95% CI 3.33 to 7.76; $p < 0.0001$), following a WPS session (Figure 3). There was also an increase in COHb levels by 4.11% (95% CI 3.38 to 4.84; $p < 0.0001$) and expired CO by 22.53 ppm (95% CI 15.99 to 29.08; $p < 0.0001$) (Figures 4 and 5, respectively). Figure 6 illustrates that a WPS session is also associated with elevated HR by 7.03 bpm (95% CI 4.60 to 9.46; $p < 0.0001$). All the meta-analyses had substantial heterogeneity (>90%), which we accounted for by pooling the results with a random effects model.

Using GRADE, the quality of evidence for each study was assessed. Three studies received a high GRADE, 8



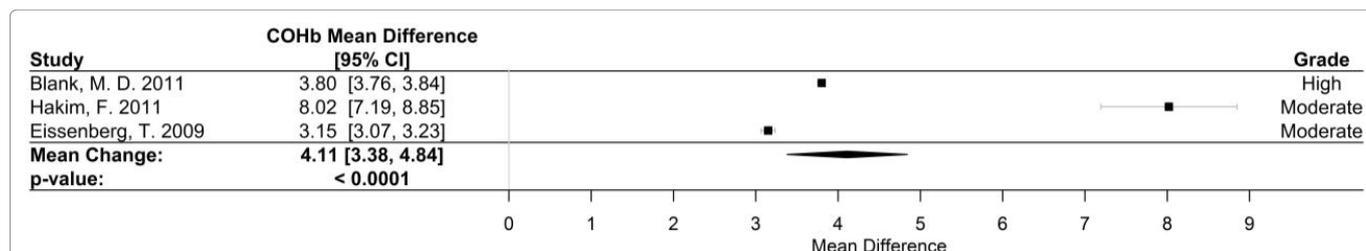
Abbreviations: CI, confidence interval, DBP, diastolic blood pressure, SBP, systolic blood pressure; WPS, waterpipe smoke

Figure 2. Forest plot of the mean difference of a WPS session and an acute elevation in SBP/DBP.



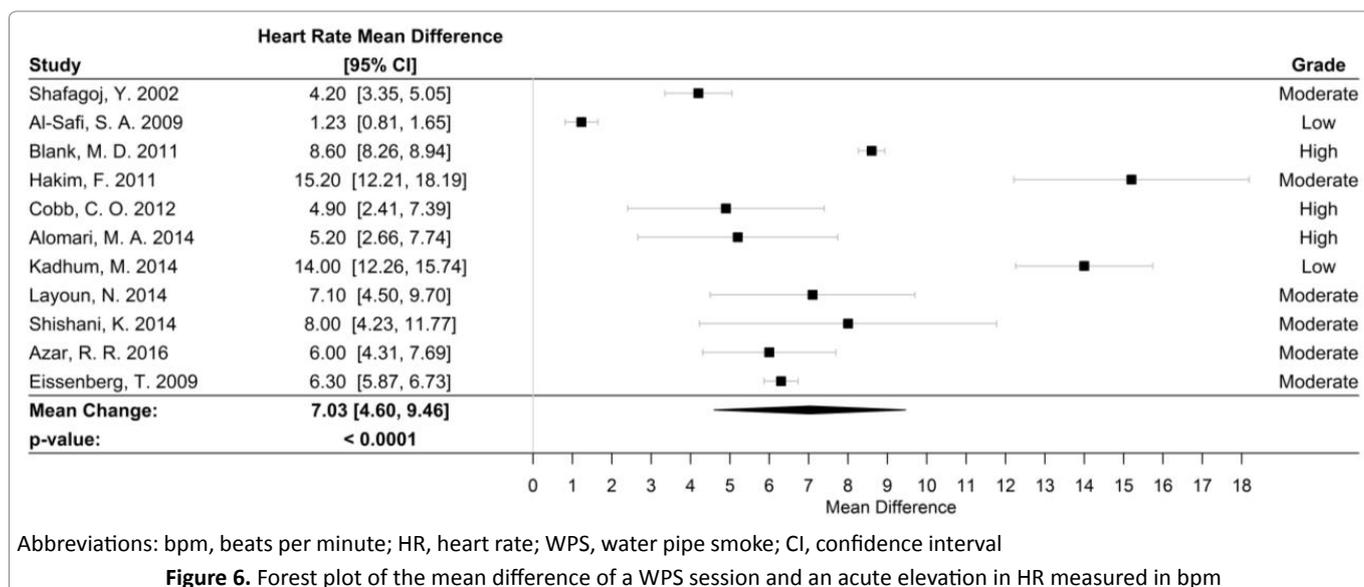
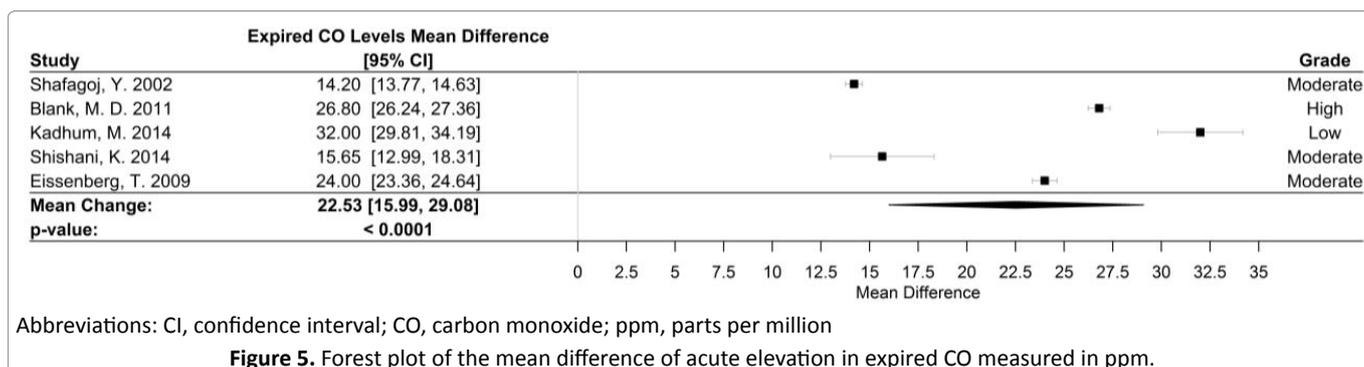
Abbreviations: CI, confidence interval, MAP, mean arterial pressure; mmHg, millimeters of mercury; WPS, waterpipe smoke

Figure 3. Forest plot of the mean difference of a WPS session and an acute elevation in MAP measured in mmHg.



Abbreviations: CI, confidence interval; COHb carboxyhemoglobin; WPS, waterpipe smoke

Figure 4. Forest plot of the mean difference of acute elevation in COHb measured as a percent.



were moderate GRADE, and 4 were low GRADE. To further analyze our data, we conducted a sensitivity analyses by stratifying by the GRADE of the studies and by type of WPS. Upon performing a subgroup analysis of only high/moderate GRADE studies, heterogeneity (I^2 statistic) decreased from >90% to 0.0% in the meta-analysis for the outcome of SBP and 62.3% for DBP. Unfortunately, there was limited overlap in the type and size of the WPS between each study and many studies did not report this level of detail, thereby limiting our ability to conduct sensitivity analyses on these factors.

Discussion

WPS is a common practice with increasing prevalence globally, especially amongst younger generations¹⁹⁻²¹. The perception that WPS carries fewer health risks than cigarette smoking has propelled its growth and contributed to limited regulations,¹⁹⁻²¹ despite the fact that several studies have shown that WPS may have similar health consequences as cigarette smoking²⁰⁻²⁴. The findings from our pooled analyses, showing statistically significant increases in all measured hemodynamic parameters of cardiopulmonary function, parallel the effects seen with smoking cigarettes²⁵.

The nicotine in cigarettes has been found to increase systolic blood pressure 5-10 mmHg and HR by 10-15 bpm;²⁵ similarly, our analysis found an increase in SBP by 6.45 mmHg and HR by 7.03 bpm. More recently, a Mendelian Randomization Meta-Analysis looking at the effect of smoking on blood pressure and resting heart rate measurements revealed that smoking one additional cigarette per day was associated with a 0.08 mmHg increase in SBP, 0.05 mmHg increase in DBP, and 0.21 bpm increase in HR²⁶. Additionally, not only does the literature suggest comparable changes in hemodynamic parameters with acute use of cigarettes or WPS, but also that WPS may actually be associated with higher levels of exposure to some toxicants such as tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons, volatile aldehydes, benzene, nitric oxide, heavy metals, and CO due to the burning of charcoal to heat tobacco- or nontobacco-based shisha in the hookah WP^{20,21,27,28}. In a direct comparison of toxicant exposure between WPS and cigarette smoking, Eissenberg and Shihadeh in 2009 found that WPS was associated with an average increase in expired CO by 23.9 ppm whereas the average expired CO for cigarette smoking was 2.7 ppm²⁸. However, the peak nicotine levels for WPS and tobacco cigarettes were similar in the study,²⁸ which

can explain why WPS has similar effects on hemodynamic parameters as does smoking cigarettes. In fact, the level of nicotine in the blood can increase up to 250% after one session of hookah smoking and remain elevated for 40-45 minutes^{20,21}. Of course, the dose of nicotine and other harmful and potentially harmful constituents varies with the duration and intensity of both hookah and smoking cigarettes.

As with smoking cigarettes, the changes seen in hemodynamic parameters of cardiopulmonary function in this meta-analysis can be attributed to the nicotine and CO exposures obtained with WPS^{20,21,25,30}. Nicotine is an agonist at nicotinic receptors in the brain, at neuromuscular junctions, the adrenal medulla, and autonomic ganglia. It acutely increases norepinephrine and epinephrine release, which in turn increases heart rate, myocardial contractility, and cardiac output^{20,25,30,31}. High levels of CO can lead to decreased oxygen supply to tissues, including myocardial muscles, due to the production of COHb, which prevents the binding and distribution of oxygen to the body^{20,25,32}. Lastly, exposure to additional toxicants in WPS can lead to oxidative stress, which in turn can induce inflammation and endothelial dysfunction^{25,33}. Together, these factors combine to increase myocardial oxygen demand and decrease in oxygen supply, putting strain on the heart, and can also lead to vascular damage^{20,25,30,31}. Although acutely these changes lead to increases in blood pressure and HR, cumulative exposures are beginning to show a trend toward development of cardiopulmonary disease^{20,24}.

This meta-analysis indicates that the acute effect of WPS on the cardiopulmonary system parallels smoking cigarettes and long term studies are also starting to show a trend toward negative health effects³⁴. Similarly, Haddad, et al.²⁹ performed a systematic review and found that WPS may be as harmful as cigarettes in several hemodynamic parameters of cardiopulmonary function, but regulations of WPS remain limited²¹. In the United States, hookah establishments are often exempted from smoke free air laws in several states,²¹ but some hookah establishments must use tobacco-free shisha instead of the traditional tobacco shisha³⁵. Importantly, even tobacco-free shisha can affect hemodynamic parameters. Despite the absence of nicotine, tobacco-free shisha can acutely increase expired CO and COHb levels and has been shown to compromise cardiopulmonary regulation^{7,36}. As the evidence on the negative cardiopulmonary, and overall, health effects of WPS grows, policy changes will be necessary to protect the public³⁷.

In this meta-analysis, we found statistically significant increases in hemodynamic parameters of cardiopulmonary function and expired CO content after WPS exposure, but a limitation was the high heterogeneity of the data. This can be attributed to the geographic diversity of the

studies analyzed, the multiple study protocols, and the various different forms of waterpipes, shisha, and charcoal that exist, as noted by Chaouachi et al³⁸⁻⁴⁰ as a serious limitation of the existing WPS literature. For future studies, standardized approaches to evaluating WPS exposures and outcomes across a varied global population will be necessary to more definitively associate WPS with long term cardiopulmonary disease.

Conclusion

WPS exposure is associated with statistically significant and potentially clinically relevant short term increases in hemodynamic parameters of cardiopulmonary function, including SBP, DBP, MAP, HR, and the amount of expired CO. Importantly, these findings parallel the acute effects seen with smoking cigarettes. Studies looking at the long-term effects of repeated WPS exposures on cardiopulmonary disease are in their infancy, but initial results point towards development of cardiopulmonary disease with cumulative WPS exposure. If the trend toward cardiopulmonary disease persists, health policy changes will need to take place in response to the negative cardiopulmonary health effects of WPS. However, standardized approaches to evaluating WPS exposures and outcomes are necessary for more definitive associations with health outcomes.

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Conflict of Interest

Mr. Matthew Marshall, Ms. Marya Ghazipura, and Drs. Tanzib Hossain, Terry Gordon, and Lung-Chi Chen **have no conflicts of interest to disclose.**

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