Objective measure of smoking status highlights disparities by sex☆

Sherrie Khadanga[a,c,*], **Blair Yant**[b,c], **Patrick D. Savage**[a,c], **Jason Rengo**[a,c], **Diann E. Gaalema**[b,c]

[a]Department of Medicine, Division of Cardiology, University of Vermont, Burlington, VT, United States of America

[b]Departments of Psychiatry and Psychology, University of Vermont, Burlington, VT, United States of America

[c]Vermont Center on Behavior and Health, University of Vermont, Burlington, VT, United States of America

Abstract

Current smoking is the strongest predictor of future morbidity and mortality in those with cardiovascular disease, yet clinically, smoking status is usually ascertained through self-report. We objectively measured smoking status, using exhaled carbon monoxide (CO), for 1122 consecutive patients entering cardiac rehabilitation. Within those with elevated CO levels (4 ppm), females had CO levels almost twice that of males (20.4 vs. 11.6), suggesting higher amounts of smoking.

1. Introduction

Cigarette smoking is the leading cause of preventable death, and the prevalence of smoking is higher among those with cardiovascular disease (CVD) compared to the general population [1–3]. Smoking is a major contributor to the premature development of CVD. Unfortunately, many continue to smoke following a major cardiac event, which is associated with a host of negative health outcomes [2–4]. Despite continued smoking being a powerful predictor of morbidity and mortality, patients are not objectively screened for this risk factor.

*Corresponding author at: University of Vermont Medical Center Cardiac Rehabilitation and Prevention, 62 Tilley Drive, S. Burlington, VT 05403, United States of America. Sherrie.Khadanga@uvmhealth.org (S. Khadanga).
☆The manuscript is not submitted elsewhere, and the content has not been previously published. All authors have read and approved the manuscript and all authors have substantially contributed.

Typically, smoking status in patients with CVD is assessed through self-report. Given the stigma associated with smoking in this population, self-report is not ideal, and it has been estimated that up to 25 % of patients do not accurately report their current status [5]. Objective monitoring would overcome bias in self-reporting. One way to objectively measure recent smoking is through the amount of carbon monoxide (CO) (a gas that is a byproduct of incomplete combustion) in expired breath [6]. CO levels peak immediately after a cigarette is smoked and decrease steadily over time as CO is expelled from the body. The half-life of CO in expired breath is approximately 8 h. Expired CO can be measured quickly and non-invasively, by having the patient exhale into a small, handheld monitor, which reports CO content in parts per million. Different cut-offs representing concerning levels of CO have been proposed, but for a clinical population, sensitive to the effects of CO, a cut-off of 4 ppm of higher has been suggested as requiring further screening as to the source of the CO [7]. CO exposure can also occur from sources other than cigarette smoking and CO, independent of smoking, is harmful to those with CVD [8]. Thus, expired CO monitoring can serve as an objective, non-invasive method to screen for those who are currently smoking [6] as well as identify patients with CO exposure from other sources. The purpose of this study was to assess the prevalence of elevated CO levels in patients attending phase 2 cardiac rehabilitation (CR) and examine patient characteristics based on CO measurements.

2. Methods

Data were prospectively gathered on individuals entering University of Vermont Medical Center CR from 5/2018 to 10/2021. As part of the standard assessment upon CR entry, self-reported smoking status, depression symptom level (Patient Health Questionnaire [PHQ-9]), cardiorespiratory fitness (peak oxygen capacity [VO_{2peak}]), hemoglobin A1c, and CO level (Micro Smokerlyzer, coVita) were obtained. Given that CO is cardiotoxic, patients were told that they were being screened for exposure to a gas that is harmful to the heart and that CO may come from a variety of sources beyond cigarette smoking [7].

Patient characteristics and CR attendance (number of sessions completed) were compared between those with elevated CO (ECO level   4 ppm) vs. low levels of CO exposure (LCO level < 4 ppm). Among those with ECO, sex differences were examined. Statistical methods included non-paired *t*-tests and chi square analysis. Analyses were conducted on de-identified data and, thus, were deemed by the University of Vermont Institutional Review Board as exempt from committee review.

3. Results

The sample consisted of 1122 consecutive patients (29 % female). Exhaled CO values ranged between 0 and 206 ppm. Fifteen percent (*n* = 166) were found to have an elevated CO. Mean CO in the ECO group was 13.9 ± 20.8 ppm despite the fact that only 60 % had self-reported current smoking. When comparing the LCO (*n* = 956) and ECO groups, significant differences were observed. The LCO group compared to ECO group was older (67 ± 11 vs. 63 ± 11, *p* < .01), reported lower depression symptom scores (3.8 ± 4.0 vs. 5.4 ± 4.7, *p* < .001) and had higher educational attainment (14.9 ± 3.0 vs. 13.3 ± 2.8 years, *p*

< .001). Additionally, the LCO group attended more sessions of CR compared to the ECO group (22 sessions vs. 18 sessions, respectively p < .001).

The percentage of patients with ECO did not differ by sex (15 % in both males and females). However, within the ECO group, females had almost twice the CO level of males (20.4 ± 31.1 vs. 11.6 ± 15.1 ppm, respectively $p < .02$ [Fig. 1]). Also, within the ECO group, while the sexes did not differ by age, depressive symptoms, or CR attendance; females in this group did have other indicators of a more at-risk profile including lower fitness (15.5 ± 4.2 vs 20 ± 6.1 mL·kg^{-1}·min^{-1} $p < .002$) and higher hemoglobin A1c (6.6 vs 6.0, $p < .02$) (Table 1).

4. Discussion

Continued smoking in those with CVD is a powerful predictor of future morbidity and mortality [1,2]. Furthermore, CO exposure, independent of smoking, causes angina, fatigue, and reduced exercise capacity and has been associated with the development and progression of CVD [10]. Therefore screening for CO can have benefits in two ways, by identifying additional people needing treatment for cigarette smoking, as well as identifying patients with exposure from non-cigarette sources, such as smoking of other substances, second-hand smoke exposure, or other environmental exposure. Importantly, CO screening also identified additional patients who were smoking who had not been identified through self-report. The high CO levels found in the ECO group would not be consistent with second-hand or environmental exposure. Screening for smoking should therefore not be left to a self-reported measure, as only 60 % of those with elevated CO levels reported current smoking.

Importantly, implementation of CO monitoring in this population also revealed disparities by sex. In the past decade, the smoking rates between males and female have narrowed and there are concerns that eventually current smoking will be more prevalent in females than males. The results from this study suggest we should also be concerned about sex differences in the number of cigarettes smoked as well. Females in this sample had twice the CO levels compared to males; given that expired CO scales with the number of cigarettes smoked [9] it can be assumed females are likely smoking at a higher intensity. This is a surprising result given that at equal level CO exposure, prior studies have found women to have lower CO levels than men due to higher respiratory rates and smaller blood volumes [10].

The current study provides evidence that expired CO monitoring is beneficial for identifying additional patients who are currently smoking as well as those who have environment exposure to CO. While initial cost may be a challenge for implementation, price per measurement is relatively low. A CO monitoring device costs between $500 and $1000. Equipment to calibrate the monitors is about $100/year and the only individual patient supplies needed are the disposable mouth pieces (~$0.20/piece). These costs are far less than other standard medical equipment, such as, for example, a hospital-grade automated blood pressure machine.

The results from this study have several implications for the practical management of CVD patients. CO is cardiotoxic regardless of source, and exposure to it in those with CVD should be minimized [8]. If a patient has an elevated CO they can be asked about potential sources of exposure. Those who report current cigarette smoking can be referred to appropriate treatment. For those not currently smoking, clinicians can query about other sources of exposure (smoking other substances, second-hand smoke exposure, other environmental exposure). The clinician can then counsel the patient on how to reduce their exposure. For example, many patients with CVD do not know the harm associated with second-hand smoke exposure. CO monitoring can also be used repeatedly, over time, to track whether efforts to reduce CO exposure (e. g. smoking cessation) have been successful.

Our finding of the elevated CO levels in females is also of clinical importance. Females with CVD who smoke have disproportionally negative health outcomes from smoking as compared to males [1,2]. For example, females who smoke have higher rates of smoking-related mortality from CVD than males (relative risk 2.86 vs. 2.50 respectively). Given these disparities in health outcomes which would be assumed to be further exacerbated by the differences in CO we observed, extra efforts towards screening and treatment must be directed towards this vulnerable population.

Funding

References

[1]. US Department of Health and Human Services, The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Reports of the Surgeon General, Atlanta, GA, 2014.

[2]. Huxley RR, Woodward M, Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies, Lancet 378 (9799) (2011) 1297–1305, 10.1016/S0140-6736(11)60781-2. [PubMed: 21839503]

[3]. Gaalema DE, Bolívar HA, Khadanga S, Priest JS, Higgins ST, Ades PA, Current smoking as a marker of a high-risk behavioral profile after myocardial infarction, Prev. Med. 140 (2020), 106245, 10.1016/j.ypmed.2020.106245. [PubMed: 32910931]

[4]. Gaalema DE, Pericot-Valverde I, Bunn JY, et al. , Tobacco use in cardiac patients: perceptions, use, and changes after a recent myocardial infarction among US adults in the PATH study (2013–2015), Prev. Med. 117 (2018) 76–82, 10.1016/j.ypmed.2018.05.004. [PubMed: 29746974]

[5]. From Attebring M, Herlitz J, Berndt AK, Karlsson T, Hjalmarson A, Are patients truthful about their smoking habits? A validation of self-report about smoking cessation with biochemical markers of smoking activity amongst patients with ischaemic heart disease, J. Intern. Med. 249 (2) (2001) 145–151, 10.1046/j.1365-2796.2001.00770.x. [PubMed: 11296802]

[6]. Benowitz NL, Bernert JT, Foulds J, et al. , Biochemical verification of tobacco use and abstinence: 2019 update, Nicotine Tob. Res. 22 (7) (2020) 1086–1097, 10.1093/ntr/ntz132. [PubMed: 31570931]

[7]. Gaalema DE, Yant B, Khadanga S, Savage PD, Rengo JL, Ades PA, Carbon monoxide monitoring to objectively measure smoking status in cardiac rehabilitation [published online ahead of print, 2022 apr 7], Health Psychol. (2022), 10.1037/hea0001178.

[8]. Papathanasiou G, Effects of smoking on cardiovascular function: the role of nicotine and carbon monoxide, Health Sci. J. 8 (2) (2014).

[9]. Henningfield JE, Stitzer ML, Griffiths RR, Expired air carbon monoxide accumulation and elimination as a function of number of cigarettes smoked, Addict. Behav. 5 (3) (1980) 265–272, 10.1016/0306-4603(80)90049-0. [PubMed: 7435315]

[10]. Zavorsky GS, Tesler J, Rucker J, Fedorko L, Duffin J, Fisher JA, Rates of carbon monoxide elimination in males and females, Physiol. Rep. 2 (12) (2014), e12237, 10.14814/phy2.12237. Published 2014 Dec 11. [PubMed: 25501428]

P <0.02
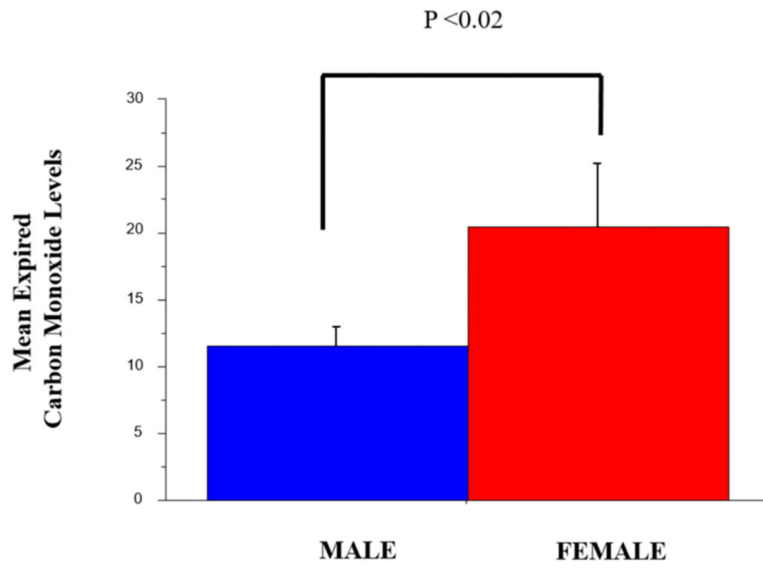
Fig. 1.
Sex differences in CO Measurements among those with elevated CO (4).

Table 1

Patient characteristics overall and by carbon monoxide group.

	All (*n* = 1122)	LCO (<4) (*n* = 956)	ECO (4) (*n* = 166)
Age (years)	67 ± 11	67 ± 11	63 ± 11
Sex, female (%)	322 (28.7)	279 (29.2)	43 (25.9)
Educational attainment (years)	14.6 ± 3.1	14.9 ± 3.0	13.3 ± 2.8
Smoking status (self-report)			
Never smoked	490 (43.7)	465 (48.6)	25 (15.1)
Formerly smoked	533 (47.5)	471 (49.2)	62 (37.3)
Currently smoking	99 (8.8)	20 (2.1)	79 (47.6)
CO (ppm)	3.4 ± 9.1	1.5 ± 0.9	13.9 ± 20.8
HgA1C	6.3 ± 1.2	6.3 ± 1.2	6.2 ± 1.1
VO2peak (mL·kg^{-1}·min^{-1})	19.5 ± 6.4	19.6 ± 6.5	18.7 ± 6.0
BMI	30.0 ± 6.0	30.0 ± 5.9	30.0 ± 6.7
PHQ-9	4.0 ± 4.2	3.8 ± 4.0	5.4 ± 4.7
Sessions of CR completed	22 ± 13	23 ± 13	19 ± 14

Values are presented as either N (%), or as mean ± SD. Abbreviations: LCO: Low Carbon Monoxide; ECO: Elevated Carbon Monoxide; HgA1C: Hemoglobin A1c, CO: Carbon Monoxide; METS: Metabolic Equivalents; VO2: Peak Oxygen Capacity; BMI: Body Mass Index; PHQ-9: Patient Health Questionnaire; CR: Cardiac Rehabilitation.