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Is Expired Air Carbon Monoxide Testing Effective for Screening of Cigarette Use in Orthopaedic Patients?

Sean Sterrenberg[1], David Gallacher[1], Melissa Schmidt[2], Rebecca Rugel[2], Summer Gerke[2], Kenneth Gundle[1], Ryan Wallenberg[2]

[1]Oregon Health Sciences University, [2]Portland Veterans Affairs Medical Center

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Smokerlyzer Study, PVAMC
Tech. support phone: **+14062125430** email: **sterrenb@ohsu.edu**

ABSTRACT

Background: Tobacco use is associated with increased post-operative complications and is often underreported by patients. Traditional biochemical testing methods, including serum and urine cotinine assays, do not differentiate active smoking from nicotine replacement therapy (NRT). This study intends to evaluate the effectiveness of a novel point-of-care carbon monoxide (CO) breath test to verify smoking status and differentiate active smoking from NRT pre-operatively in a cohort of veteran orthopaedic patients.

Methods: This is a single-institution, prospective cohort study of adult orthopaedic patients at the Portland VA Medical Center to implement and evaluate a point-of-care CO breath test, the Smokerlyzer® Micro EC50, for pre-operative smoking status verification. Patients who are indicated for orthopaedic surgery in the pre-operative clinic will be offered inclusion. Self-reported smoking status will be obtained pre-operatively to categorize patients as non-smoker, quitters, or active smokers. Exhaled CO and serum cotinine levels will be obtained at the initial clinic visit, pre-operative visit, and day of surgery. Primary endpoints are concordance between self-reported smoking status and CO levels, and concordance between exhaled CO and serum cotinine levels.

Discussion: Pre-operative smoking cessation interventions have been shown to decrease smoking rates on the day of surgery and promote abstinence 30 days post-operatively. NRTs are commonly used to promote smoking cessation, however their effect on surgical outcomes are not known. This study aims to validate the use of point-of-care testing that differentiates active smoking from NRT, and identify patients at risk for smoking status misclassification. Results would provide preliminary data to directly test NRT use, separate from tobacco use, and surgical outcomes.

Specific Aims:

1. To determine if expired air CO levels can be used to identify patients that are at risk of smoking status misclassification pre-operatively, including patients that are on nicotine replacement therapy.
2. To evaluate the concordance between self-reported smoking and expired air CO levels in the veteran orthopedic population.
3. To evaluate the concordance between pre-operative expired air CO and typical serum levels in the orthopedic population.

Hypotheses:

1. Expired air CO testing will allow for differentiation between active smokers and those on nicotine replacement therapy compared to serum cotinine testing.
2. Self-reported “quitters” will have lower agreement between self-reported smoking status and biological testing compared to self-reported “non-smokers” and “active smokers.”
3. Compared to serum cotinine testing, expired air CO testing will allow for non-inferior accuracy in verifying smoking status.

EXTERNAL LINK

https://www.bedfont.com/shop/smokerlyzer/micro

GUIDELINES

Guidance on Conducting the Study

All patients being indicated for elective orthopaedic surgery will be included in this study. All related tests should be obtained when the patient is originally indicated for surgery (at the initial visit) and again at least within 4 weeks of a planned elective surgery (at the pre-operative visit), and finally on the day of surgery.

Study Population

All adult veteran patients who are seen in pre-operative joints clinic and fracture clinic at Portland Veteran Affairs Medical Center who are indicated for a planned orthopaedic surgical procedure will be offered inclusion in this study. Patients who are indicated for a planned orthopaedic procedure and are interested in participating in the study will be referred to an approved study team member for inclusion. Patient demographics will include adult patients, age 18 or older, of any ethnic background or health status who are indicated for a planned orthopaedic surgical procedure in the above clinics.

An a priori power calculation was performed using sample-size calculations for Cohen's Kappa Test. According to a recent study published by the CDC, smoking prevalence in the VA population is approximately 27%. Based on the assumption there is approximately a 27% prevalence of smoking in the general VA population, and assuming a power of 0.8 and an alpha of 0.5, we performed a simulation for a desirable Cohen's Kappa coefficient between 0.6 and 0.7 to 0.99, with a predicted sample size (n) between 77 and 247 patients, respectively. Based on current clinical practice at the Portland VAMC, we anticipate less than 10% of patients will be removed from the study due to screening failures, receiving care outside the VA or declining surgery, death prior to indicated surgery, or being lost to follow up. The study should continue until 250 participants who were able to complete all three breath tests have been enrolled. At that time, recruitment will stop and data will be analyzed by study team members.

Inclusion Criteria

a) The patient will be an in-patient or outpatient at the Portland VAMC and under the care of the Orthopaedic Surgery Department.
b) Any adult patient that is seen in joints or fracture clinic that is indicated for a surgical orthopaedic procedure.

Exclusion Criteria

a) Patients who are unable to provide informed consent, for example those who are intubated/sedated
b) Patients who are involved in a concurrent trial that includes interventions on smoking
c) Patients who are treated non-operatively
d) Prisoners
e) Patients who are under the age of 18
f) Patients who are pregnant

Research Design and Methods

This will be a single-institution, prospective, non-randomized cohort study of orthopaedic patients at the Portland Veterans Affairs Medical Center (VAMC) to implement and evaluate the use of expired air carbon monoxide (CO) testing as a point-of-care screening tool for pre-operative smoking status in orthopaedic patients. Orthopaedic patients who are indicated for surgery in the orthopaedic joints and fracture clinic will be offered inclusion, with an anticipated enrollment of 250 patients, and a recruitment duration of 12-18 months based on current surgical volume. Self-reported smoking status will be obtained pre-operatively to categorize patients as non-smoker, quitters, or active smokers. Additionally, expired CO levels ~~levels~~will be obtained from all recruited patients at three time points: 1. Initial clinic visit (time patient is indicated for surgery); 2. Routine p~~P~~re-operative visit (within 4 weeks of day of surgery); 3. Day of surgery. The current standard of care is to obtain pre-operative serum cotinine blood assays at time of surgical indication and within 4 weeks prior to surgery to validate smoking status, which will not be changed during this study. The experimental portion of this study will be to additionally collect exhaled CO levels at these two routinepre-operative visits as well as on the day of surgery. Day of surgery expired CO results will be blinded to the surgeon until after surgery. Results will be followed post-operatively at clinic follow up. Primary endpoints will be concordance between self-reported smoking status and CO testing, and concordance between CO and serum cotinine test concordance in patients stratified by their self-reported smoking status (i.e. non-smoker, quitter, and active smoker).

All patients indicated for orthopaedic surgery in the joints and fracture clinic will be invited to participate in this study. Once a patient has been indicated for surgery by an attending physician and the patient agrees to participate in the study, an approved study member will obtain informed consent for inclusion into the study. Initially, patients will be evaluated with a standardized self-reported smoking questionnaire, serum cotinine blood test (unchanged from current standard of care), and carbon monoxide breath test, at this first clinic visit which will be deemed the "Indications clinic visit," as this is the time patients have been indicated for surgery. Patients will be classified as a Non-Smoker, Quitter, or Active Smoker based on the self-reported smoking status questionnaire.

Results from the smoking questionnaire, initial and subsequent carbon monoxide test results will be documented on hard copy and stored in a locked cabinet owned by the PI and located in the VA orthopaedic clinic on the 8thfloor. All research data, including the smoking questionnaire as well as the results from the Smokerlyzer, will be on hard copy and will accessible to the study team outside of CPRS. No research data will be entered into CPRS for the purpose of this research study. Smokerlyzer results may be entered into CPRS for clinical care, as is standard of practice, however, this data will not be used for research purposes. Any Smokerlyzer or Smoking

questionnaire data used for research analysis will be derived from hard copies outside of CPRS. Serum cotinine results will automatically populate within CPRS when results have been ascertained by the laboratory.

Patients will be seen again in clinic at a routine “Pre-operative visit,” which will occur within 4 weeks of surgery, where they will then undergo repeat serum cotinine and exhaled CO testing. Both the “indications” and “pre-operative” visits will be considered routine visits for clinical care, and no visit will be made solely for the purpose of research. Day of surgery exhaled CO testing will be performed by a pre-designated approved study team member in the pre-operative area prior to surgery and results will be blinded to the patient and surgeon until after the surgery.

Serum cotinine level of >15 ug/L will be considered positive for recent nicotine use. Exhaled Carbon Monoxide levels >6ppm will be considered positive for active smoking, and <6ppm will be considered negative for active smoking.

All recruited patients will complete a standardized self-reported smoking questionnaire. The hard copy of t~~T~~his data will be filed with their record in a locked cabinet owned by the PI and located in the VA orthopaedic clinic on the 8thfloor. Carbon Monoxide testing will be obtained using a Smokerlyzer® Micro EC50 device (Bedfont Scientific Ltd, Kent, U.K.) according the manufacturer's recommendations. Results will be recorded on a hard copy which will be kept and secured with the smoking questionnaire. Serum cotinine samples will be ordered through CPRS, collected by nurses who obtain regular pre-operative screening labs which is standard of care, and results will be reported within CPRS in the normal fashion.

Data will be analyzed by study team members at the Portland VAMC. Statistical analysis will be performed using the R language environment. Means will be compared using independent samples t-tests; a one-way analysis of variance (ANOVA) will be performed to analyze differences in serum cotinine levels and expired air carbon monoxide levels between the three subgroups of patients (smokers, non-smokers and ex-smokers). Independent categorical data will be analyzed using chi-squared tests. Intraclass correlation coefficient will evaluate repeated measures using linear regression. The Kappa coefficient will calculate agreement between the results of the serum cotinine levels and expired air carbon monoxide levels. A two-tailed p-value of < 0.05 will be considered statistically significant.

Limitations of the study include the inherent limitations with the use of the Smokerlyzer Mrico EC50 device, which has reported false positive readings in patients with COPD, OSA, and other upper respiratory conditions, as well as false negatives for patients with intermittent smoking activity.

MATERIALS TEXT

Equipment: Smokerlyzer® Micro EC50 device, D-piece

Supplies: SteriBreath^{TM}mouthpiece

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GENERAL OUTLINE

Study participant recruitment takes place in the orthopaedic clinic and a patient is offered enrollment into the study once the surgeon has indicated them for an orthopaedic surgical procedure. Upon enrollment, the patient agrees to the following tests on three separate occasions:

1. Visit 1 (The day surgery is decided): The patient will fill out the Tobacco Use Quesionnaire, undergo a blood draw for serum cotinine and serum nicotine assays, and perfrom the exhaled carbon monoxide breath test.

2. Visit 2 (Pre-operative visit within 4 weeks of surgery): The patient will again undergo a blood draw for serum cotinine and serum nicotine assays, and perfrom the exhaled carbon monoxide breath test.

3. Visit 3 (Day of surgery): The patient will perfrom the exhaled carbon monoxide breath test prior to their surgery. These results will be blinded to the surgeon until after the surgery.

	Visit 1 (The day surgery is decided)	**Visit 2** (Pre-operative visit, within 4 weeks of surgery)	**Visit 3** (Day of Surgery)
Tobacco Use Questionnaire	**X**		
Serum Cotinine/Nicotine Assay	**X**	**X**	
Exhaled CO Breath Test	**X**	**X**	**X** *blinded to surgeon

2 **VISIT 1 (the day surgery is decided)**

Consent is obtained by a study team member, and the patient is enrolled into the study.

3 **VISIT 1 (the day surgery is decided)**

The patients fill out a “Tobacco Use Questionnaire.”

Tobacco Use Questionnaire

1. Have you smoked cigarettes in the past 3 months? Yes No
(If you answered yes, complete the questions below, if you answered no, skip to question #2)

a. How frequently do you smoke?
   i. Daily
   ii. Weekly (intermittently)
   iii. Monthly (intermittently)
   iv. Yearly (rarely)

b. When was your last cigarette?
   i. Today
   ii. In the last 1-2 days
   iii. In the past week
   iv. In the past month

c. How many cigarettes do you smoke per day?
   i. 1-4 per day
   ii. <10 per day
   iii. Between ½ pack to 1 pack per day
   iv. More than 1 pack

d. How many years have you smoked daily?
   i. < 1 year
   ii. 2-5 years
   iii. 5-10 years
   iv. >10 years

2. How long ago did you quit smoking?
   i. I've never smoked
   ii. <1 year
   iii. 2-5 years
   iv. >5 years

3. Do you live or work in an environment where you are exposed to second hand smoke?
   i. Yes
   ii. No

4. Do you use other forms of nicotine?
   i. Nicotine replacement therapy (gum, patches)
   ii. Cigars (if used greater than weekly)
   iii. Other tobacco products (chewing tobacco)
   iv. None

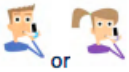
5. Do you smoke other products that are not cigarettes?
   i. Marijuana
   ii. Cigars
   iii. E-cigarettes
   iv. None

6. Have you ever been diagnosed with a lung or breathing disease?
   i. COPD
   ii. Asthma
   iii. Obstructive sleep apnea
   iv. Other _____
   v. None

4 **VISIT 1 (the day surgery is decided)**
Nursing staff performs venupuncture, and a blood sample is obtained. Serum Nicotine and Serum Cotinine assays are ordered and the sample is sent to the lab. Results automatically are recorded within the electronic medical record system.

5 **VISIT 1 (the day surgery is decided)**
Patient is instructed to perform a breath test using the Smokerlyzer® Micro EC50 device as described per the manufacturer, with the exception that the breath hold is pre-set to only 6 seconds. Results are recorded.

Taking a breath test

1. Attach a breath sampling D-piece™ and new SteriBreath™ mouthpiece
2. Turn on the monitor by pressing the power button once
3. Press 'breath test' symbol on screen,  or
4. To cancel the breath test, press 
5. Inhale and hold breath for the pre-set 15 second countdown
6. A beep will sound during the last three seconds of the countdown.
7. Blow slowly into mouthpiece, aiming to empty lungs completely
8. The ppm and equivalent %COHb and/or %FCOHb levels will rise and hold onscreen.
9. On the piCO™ and piCO^{baby}™, when the test is finished  will appear at the bottom of the screen
10. On the Micro^{+}™, when the test is finished  will appear at the bottom of the screen
11. If a high reading has been recorded, you can mute the sound by pressing 
12. To repeat breath test, press  once to return to the home screen and repeat steps 3-8
13. To save the reading (Micro^{+}™ only) press  and select the relevant patient profile
14. Remove the D-piece™ between tests to purge sensor with fresh air
15. To switch off, press and hold the power button for 3 seconds, unit will also power off after 2 minutes of inactivity to save power.

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6 **VISIT 2 (Pre-operative visit within 4 weeks of surgery)**
Nursing staff performs venupuncture, and a blood sample is obtained. Serum Nicotine and Serum Cotinine assays are ordered and the sample is sent to the lab. Results automatically are recorded within the electronic medical record system.

7 **VISIT 2 (Pre-operative visit within 4 weeks of surgery)**
Patient is instructed to perform a breath test using the Smokerlyzer® Micro EC50 device as described per the manufacturer, with the exception that the breath hold is pre-set to only 6 seconds. Results are recorded.

8 **Visit 3 (Day of surgery)**

On the day of surgery the patient will undergo a third round of carbon monoxide testing with the Smokerlyzer® Micro EC50 device repeating manufacturer instruction steps 1-15, with the exception that the breath hold is pre-set to only 6 seconds. This testing occurs in the pre-op holding area and is performed by perioperative nursing staff. Results are recorded but are blinded to the surgeon until after the surgery.