Assessment of Carbon Monoxide in Exhaled Breath using the Smokerlyzer Handheld Machine: A Cross-Sectional Study

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ABSTRACT

INTRODUCTION: Nicotine dependence is known to be a chronic remitting and relapsing addictive disorder. Among cancer patients who smoke, nicotine addiction has been found to be more when compared with smoking healthy individuals. Smokerlyzer machine can be used to test smoking substance use and de-addiction services can be provided at Preventive Oncology units. The objectives of the study include: (i) To assess eCO using a Smokerlyzer hand-held machine and correlate it with the smoking status, (ii) To assess the cut-off value for smoking use, and discusses the benefits of this method.

METHODS: In this cross-sectional study, healthy individuals at the workplace were tested for exhaled CO (eCO), which is used as a biological marker for monitoring the tobacco smoking. We discuss the feasibility of testing and its implications for cancer patients. The Bedfont EC50 Smokerlyzer machine was used to measure the concentration of CO in the end-tidal expired air.

RESULTS: Among 643 study subjects, we found a statistically significant difference ($P < .001$) of median (IQR) eCO (measured in ppm) among smokers and non-smokers 2(1,5) vs 1(1,2). A significant and moderate positive correlation (Spearman rank correlation coefficient: .463) was observed between eCO and subjects who used cigarettes (measured in pack years). The ROC curve shows a cut off value for eCO as 2.5 with sensitivity 43.6% and 1 – specificity 2.76% (Specificity: 97.24%), which was rounded to 3. The area under the curve is 74.9%, which indicates a moderate discrimination performance of the test. The diagnostic accuracy of the test is 82.89%, which shows the proportion of correct test results.

CONCLUSION: Estimating eCO in health care settings will enable monitoring the smoking substance use which has important impact on clinical outcomes. In cancer hospitals, when the goal is complete abstinence a stringent CO cutoff in the range of 3-4 ppm should be used.

KEYWORDS: Breath tests, smoking, carbon monoxide, smoking cessation, neoplasm, carboxyhaemoglobin

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Introduction

The WHO statistics 2021 reports that the age-standardized tobacco use prevalence among adults (≥18 years) in India is 27.0%.[1] As per the 2016-17 Global Adult Tobacco Survey2 India, ~29% of all adults (≥15 years) were reported to use tobacco.[2] In the State of Karnataka, 8.8% of all adults (16.8% of men, .7% of women) currently smoke tobacco[2] Cancer patients tend to have antecedent addiction to tobacco consumption (eg: smoking).[3] Nicotine dependence is known to be a chronic remitting and relapsing addictive disorder.[3] Among individuals using smoke forms of tobacco, nicotine addiction has been found to be more among cancer patients than among those without cancer.[4] In India, one in four cancer patients continue to smoke.[5] Following the cancer diagnosis, continued substance use (eg: smoking) can result in reduced tolerance to treatment, failure of therapy, worse surgical outcomes, poor quality of life, tumor progression, poor survival outcomes and recurrence/other primary tumors and secondary cancers.[4] It results in poor response to radiation therapy and more radiation-related side effects, when compared with patients who have quit the substance use. It also exacerbates other chronic illness such as coronary/peripheral artery disease, chronic obstructive pulmonary disease and stroke.[4]

Carbon monoxide (CO) is a highly poisonous gas that is produced in car exhaust fumes, faulty gas boilers, poorly ventilated fossil/wood fuelled heating apparatus and in tobacco smoke.[6] Combustion of tobacco releases nicotine together with a multitude of harmful chemical constituents, including CO.

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However, non-combustible nicotine sources (nicotine replacement therapy: NRT, smokeless tobacco, electronic cigarettes) are less likely to release any chemical constituents including CO.[7] Sustained exposure to these chemical constituents over time is known to be carcinogenic.[4] Smoking cessation initiatives can reduce the risk of developing tobacco related malignancies. Even healthy individuals who intend to quit the substance use, can be tested using the Smokerlyzer machine and treated with 'tobacco cessation initiatives' at Preventive Oncology units in Cancer hospitals. The benefits of abstinence from smoking include improved psychological well-being and self-esteem, general mental health and cognitive functioning.[8]

It is imperative to confirm abstinence from smoking in cancer settings beyond self-reporting, as its continued use determines the effectiveness of cancer treatment. Some biological methods used for verifying abstinence include measuring exhaled CO (eCO) as well as concentration of nicotine/cotinine in plasma, saliva and urine. Cotinine can be detected for several days after exposure, as its half-life is 10 to 30 hours.[9] However, patients on nicotine replacement therapy (NRT) show a higher level of cotinine as it is a metabolite of nicotine. eCO provides a good estimate of smoking substance use and is not affected by NRT. It can only be detected upto 24 hours after exposure, as it has a short half-life (2 to 3 hours).[9] A cut-off point of 8-10 parts per million (ppm) is commonly cited as indicative of recent smoking.[9]

CO binds with haemoglobin in the red blood cells to form carboxy haemoglobin (COHb), preventing these cells from carrying oxygen and thus impairing its delivery at the tissue level. The binding capacity of CO with haemoglobin is 200 times more readily than that of oxygen. An individual who smokes one pack of cigarettes/day can have 3% to 6% COHb level in the blood, with two packs/day the level could be 6% to 10% and as much as 20% with three packs/day.[6] CO also binds to myoglobin and cytochrome oxidase, and its binding with the latter causes the release of mitochondrial free radicals, which attract the leukocytes. This results in damage to the endothelial cells, as well as the vasculature of the brain and lipid peroxidation of the membranes of the brain.[10] As CO is primarily eliminated by respiration, there exists a strong correlation between breath CO and COHb.[11] The clinical arena uses a COHb concentration ≥2% for distinguishing smokers from non-smokers.[12]

CO has adverse impact on the functioning of heart, blood circulation, breathing capacity and outcome of pregnancy.[13] Testing for CO in the breath of an individual is a quick, non-invasive and cost-effective means of validating his/her smoking status. A higher reading on assessment indicates a higher dependence on nicotine. However, the levels of smoking are also influenced by psychosocial, behavioral and biological factors.[14] CO monitor is an independent clinical tool which provides evidence for assessing and treating patients with smoke-forms of tobacco dependence.[6] After holding the breath, the amount of CO in expired alveolar air is well correlated with COHb.[13] Biomarkers such as thiocyanate (SCN), cotinine, nicotine and COHb have been used to estimate the byproducts of inhaled cigarette smoke in serum, saliva or urine.[15] However, these methods are tedious, expensive and do not provide immediate assessment.

The study setting includes outreach screening activities coordinated from the Preventive Oncology Unit of a Cancer hospital, and the rationale is to assess the feasibility of testing for eCO and correlating it with the smoking status of healthy subjects. The objectives of the study include: (i) To assess eCO using a Smokerlyzer hand-held machine and correlate it with the smoking status, (ii) To assess the cut-off value for smoking use, and discusses the benefits of this method.

This concept will have pragmatic implications when applied for screening smoking abstinence among cancer patients. With evidence derived from healthy subjects, the scaling out[16] of this intervention among cancer patients will borrow strength from our study. A peak expiratory flow rate (PEFR) measurement using the peak flow meter was done among subjects with history of asthma and/or with a yellow/red zone reading on the Smokerlyzer machine. The progressive decline in lung function over time among chronic obstructive pulmonary disease (COPD) patients is exacerbated by smoking substance use.[17] Given the young age group of our study subjects (<40 years), only asthmatic bronchitis component of COPD was assessed in our study.

Methods

Study Design and Setting

This cross-sectional study was done as a screening test for the employees (non-cancerous) at multiple workplaces (Information technology companies, Traffic police management cell, Corporate marketing office etc), which reduced the possibility of bias. Also, a simple random sampling method was used to select the subjects. The assessment of subjects was performed in accordance with the relevant guidelines and regulations, and written informed consent was obtained. The Institutional Ethics Committee has approved the study.

Participants and Sample Size

The study was conducted during the period March to April 2021, and the sample size was 643 individuals. We chose the confidence level (α = 95%), margin of error (e = 2.2%), population proportion (P = 8.88%),[2] and derived the precise sample size of 643. All the subjects were adults aged >18 years and our study does not include minors. History of smoking substance use includes current everyday and occasional smokers who have smoked during the previous one year,[18] and consumed a cumulative of >100 cigarettes in their lifetime.[19] Those who had never smoked or had not smoked in the previous 5 years including those who had consumed fewer than 100 cigarettes in

their lifetime were considered non-smokers.[20] Individuals with a history of myocardial infarction within the previous 4 weeks and diagnosis of alcohol dependence in the previous six months were excluded from the study. Given the high prevalence of smoking among individuals with psychiatric disorders than in the general population,[20] they were also excluded from the study.

Data Collection

History of smoking substance use was assessed by self-reporting, as the subjects were interviewed using a questionnaire. Since e-cigarettes/vaping/heated tobacco products have been banned in India since December 2019, we did not account them for assessing exposure to tobacco/nicotine.

Jarvis protocol[21] was used to measure CO in the expired air (eCO), where-in subjects were asked to slowly exhale preceded by deep inhalation. After 20 seconds of breath holding (to avoid ambient CO affecting exhaled air CO), the Bedfont EC50 machine (Smokerlyzer machine of choice) was used to measure the concentration of CO in the end-tidal expired air. This was used as a biological marker for monitoring tobacco smoking. Another device which has been used for similar purpose includes the photo acoustic spectrometer Bruel & Kjaer 1312. Others include laser spectrophotometer and near-infrared analyzer.[21]

As depicted in Figure 1, the Bedfont EC50 'Smokerlyzer' is a breath CO monitor which provides the reading in 'ppm' (number of CO molecules in a million parts of air). It also provides COHb% which is the percentage of red blood cells carrying CO instead of oxygen. The quality of air could influence the amount of eCO in breath, however there is lack of evidence regarding its affect (as well as partner's smoking habit) on routine CO screening.[22]

The detection principle includes an electrochemical sensor, which assess CO in the initial part of expiration. The subject exhales through a disposable pipe which fits to the machine through a one-way valve and the sample is captured by diffusion. The standard values provided by 'Bedfont'[6] includes: eCO levels of <6 ppm which corresponds with COHb% concentration of <1.59% which indicates the normal level (Green zone). The range of eCO between 7 to 10 ppm or COHb% between 1.75% to 2.23% indicates a light smoker or a passive smoker or a smoker breathing in poor air quality (Yellow zone). The range of eCO between 11 to 30 ppm or COHb% between 2.39% to 5.43% indicates a regular smoker (Red zone).

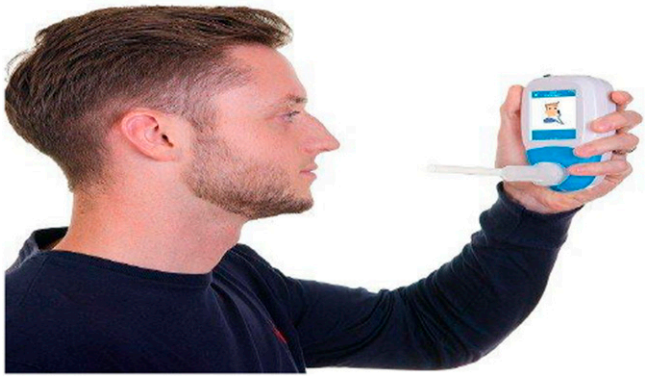

Figure 1. Bedfont EC50 smokerlyzer handheld machine.

Individuals in yellow or red zone were subjected to the standard peak flow meter test. It measures an individual's ability to push air out of his/her lungs. This could be used as a screening tool for Asthma and chronic obstructive pulmonary disease (COPD) before a diagnostic assessment with Spirometry.[13] The peak expiratory flow rate (PEFR) is usually used to assess the narrowing of airways before an attack of asthma. COPD is attributed to smoking tobacco, where-in the number of pack-years consumed and the duration of smoking influences the severity of the disease including progressive loss of lung function due to alveolar damage.[23] Our study subjects in yellow and red zones were presumed to consume the substance for a long duration, and hence an assessment of their lung function was done simultaneously.

Statistical Analysis:

Statistical analyses were performed using R version 4.2.1 software. Categorical data were expressed as numbers and percentages. Shapiro-wilk test of normality for eCO (measured in ppm) and COHb% were significant ($P < .05$). Given the non-normality of data, correlation was analyzed by Spearman rank correlation coefficient test. A *P*-value <.05 was considered statistically significant.

Results

A total of 643 individuals were assessed in the study. Among them, 132 (20.5%) were female and 511 (79.5%) were male. The mean age of the study subjects was 35.7 yrs. 73.3% of study subjects were non-smokers (n = 471) and 26.7% were smokers (n = 172).

Table 1 compares the difference in median values (in ppm) of eCO levels among the study subjects, who were stratified based on the smoking substance use. Mann Whitney U test shows a statistically significant difference ($P < .001$) of median eCO among smokers and non-smokers (2 vs 1).

Pack-year was calculated using the formula: (no. of cigarettes smoked/day)*(no. of years smoked)/10 (Denominator is '10' given that each pack of cigarette contains 10 units).

Figure 2 depicts the dose response relationship graph with smoking pack years on the x-axis and eCO in ppm on the y-axis. Using Spearman rank correlation, a moderate positive correlation was observed between patients who used cigarettes (measured in pack years) and eCO (ppm). The strength of association observed is .463, which was statistically significant ($P < .001$). The direction of correlation is positive, and the plotted data points are scattered and in an upward direction, which indicates a moderately positive correlation.

Table 1. Comparison of eCO (ppm) with history of smoking.

STUDY SUBJECTS	MEDIAN ECO (IN PPM)	IQR (Q1, Q3)	*P* VALUE
Smokers	2	(1,5)	<.001
Non-smokers	1	(1,2)	

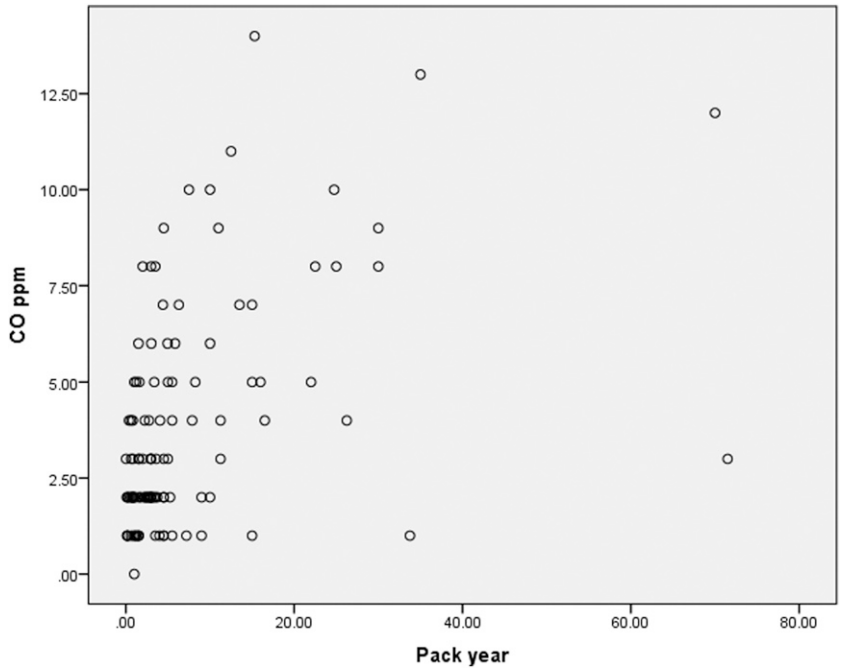

Figure 2. Dose response relationship between smoking (pack years) and eCO.

Table 2. PEFR analysis among males and females.

SEX	PEFR* IN LTS/MT**	FREQUENCY	PERCENTAGE
Female	>300	2	1.52
	≤ 300	13	9.85
Male	>425	19	3.72
	≤ 425	37	7.24

*Difference in PEFR strata for each sex is as per the average lung function given their mean height & weight.
**lts/mt: litres/minute.

Among study subjects either falling in the yellow/red zone of Smokerlyzer machine or with history of bronchial asthma, a peak flow meter was used to measure the PEFR. Table 2 depicts the minimum cut-off levels for adequate PEFR: males is 425 and females is 300 lts/mt. Our study results reveal that among subjects with history of bronchial asthma and/or eCO falling in the yellow/red zone of the Smokerlyzer, a low PEFR was found among 7.24% males and 9.85% females.

Figure 3 depicts the ROC curve plot using the variables eCO and history of smoking (dichotomized as yes/no, and considered

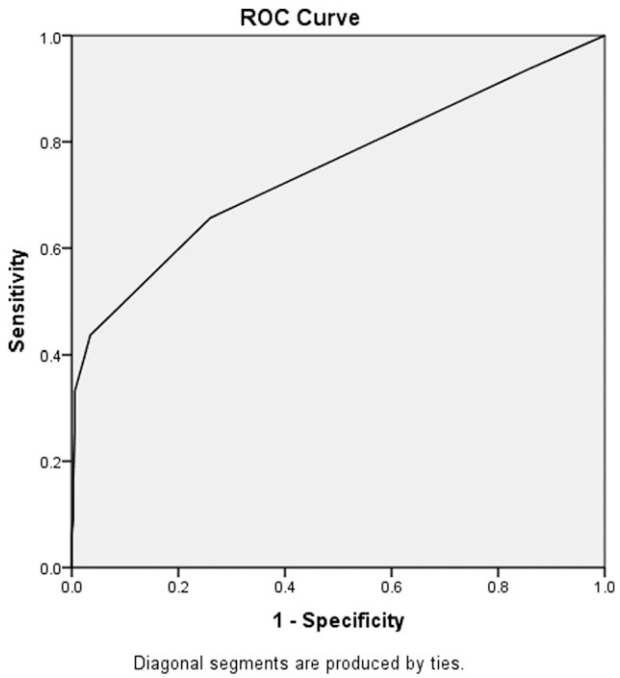

Figure 3. Receiver Operating Characteristic (ROC) curve.

Table 3. Range of cut-off values with the respective sensitivity and specificity.

SL. NO.	SENSITIVITY	SPECIFICITY	CUT-OFF	PPV	NPV	DIAGNOSTIC ACCURACY
1	65.70%	69.00%	1.5	43.63%	84.64%	68.12%
2	43.60%	97.24%	2.5	85.23%	82.52%	82.89%
3	33.14%	99.58%	3.5	96.61%	80.31%	81.80%
4	25.58%	99.58%	4.5	95.65%	78.56%	79.78%
5	16.28%	99.79%	5.5	96.55%	76.55%	77.45%

gold standard). Youden index provides the cut off value for eCO as 2.5 with sensitivity 43.6% and 1 – specificity 2.76% (Specificity: 97.24%). This cut-off value is rounded-off to 3, as the Smokerlyzer machine does not provide decimal values. Also, there is no change in sensitivity and specificity, as there are no data values between 2.5 to 3 in our data set. The area under the curve (AUC) is 74.9% (ie .749), which falls in the range of .7 to .9[9]. Hence, the discrimination performance of the test (Smokerlyzer machine in measuring eCO) is moderate (qualitative measure).

The range of cut-off (threshold) values depicted in Table 3, are determined based on the exposure assessment and the desired balance between true positive rate (TPR) and false positive rate (FPR). Researchers can wisely choose the relevant cut-off, based on whether the machine is being used for screening or diagnostic purpose, and the clinical context. The diagnostic accuracy was quantified as 82.89%, which indicates a moderate accuracy of testing for eCO using the Smokerlyzer machine, for both smokers and non-smokers.

Discussion

The estimation of eCO in health care settings, primarily in cancer hospitals will enable monitoring the smoking substance use, which in-turn has an important impact on clinical outcomes. As self-reporting of smoking may not be reliable, an unbiased indicator such as eCO will enable assessing its use among patients. The Smokerlyzer hand-held machine measures breath CO which is a quantitative guide for smoking, and unlike the biomarker cotinine it is not affected by the use of nicotine replacement therapy (NRT). The challenge of testing eCO is the half-life of CO (~4 ½ hours).[20] CO exposure during the previous 3 to 5 hours can be detected by this test, and it cannot detect tobacco exposure beyond the previous day.[21]

In our study, 26.7% of the study subjects used the substance (n = 172). We found a significant difference (P < .001) for the median eCO level for smokers: 2 ppm (IQR:1,5) and non-smokers: 1 ppm (IQR:1,2). Deveci S.E[11] et al report the mean eCO level as 17.13 ± 8.5 ppm for healthy smokers, 3.61 ± 2.15 ppm for healthy non-smokers and 5.2 ± 3.38 ppm for passive smokers. The authors[11] report a cutoff of 6.5 ppm when smokers and non-smokers were assessed together, with a sensitivity of 90% and specificity of 83%. Given the high prevalence of continued smoking substance use among cancer patients (~25%), a stringent eCO cutoff in the range of 3-4 ppm should be used for cancer patients when the goal is complete abstinence.[4] As per Nilsen's schema,[24] this implementation theoretical approach of translating research into practice is categorized as 'Process model', and the framework for adapting the evidence from healthy subjects to cancer patients includes 'Dynamic Adaptation'.

Self-assessment of smoking status may cause under-reporting, which has the potential to bias risk estimates. Evidence indicates that smoking use is inaccurately reported due to social stigma and the quitting expectancies of the health-care team. Non-differential misclassification is possible during self-reporting (interview method) of smoking use. Recall bias is common among all exposed subjects with high levels of eCO, as they tend to differentially recall smoking use to a greater extent when compared with individuals in the green zone of eCO measurement. A structured questionnaire could have increased the accuracy of self-reporting the smoking use. Lack of validation standards for assessment of smoking, is another concern. However, the alternative method of exposure assessment includes measuring cotinine (nicotine biomarker) levels in the biospecimen (urine) for distinguishing smokers from non-smokers. This involves expenditure for collection and analysis, and hence we relied on self-reports of exposure to tobacco smoke.

Irving J.M et al[15] report a clear dose-response relationship between eCO level and cigarette consumption, with high correlation and good level of agreement when measured by both EC50 and Ecolyzer machines. Reynolds C.M.E[22] et al used a cut-off point of ≥3 ppm to identify ongoing smokers. In this study,[22] 39.6% (25/63) of maternal smokers did not report their smoking status to the midwives when scheduling their first antenatal visit. During the encounter with midwives, only 15% of women reported their current smoking status. The rate increased to 25% when eCO test was combined with self-reporting of smoking. Non-disclosure of smoking by patients results in missed opportunities for providing assistance to quit the substance use. For determining abstinence from smoking among cancer patients, assessment of eCO should be a necessary construct of screening tests.

The Smokerlyzer monitor also provides an accurate guide of COHb concentration among both smokers and non-smokers.[12]

The half-life of COHb is 5 to 6 hours[10] and a concentration of ≥2% is generally used clinically for distinguishing smokers from non-smokers.[12] In our study, a strong and significant correlation was observed between eCO and COHb% (Spearman rank correlation coefficient: .882). In the Bedfont EC50 machine, the COHb% levels are a result of an algorithm based calculation depending on the eCO levels rather than the actual COHb% measurement. This explains the high correlation in our study. As an approximate guide, the COHb% can be estimated by dividing the eCO concentration in the expired air by the value'6'.[12] Herath P et al[20] report the dynamic equilibrium of eCO with CoHb%. Given the close relationship between eCO levels and COHb%, our study suggests the advantage of replacing the invasive analysis of blood sample with the non-invasive method of assessing the expired air. This correlation should be further assessed by comparing the results with the standard Ecolyzer machine.

Jarvis M.J et al's[13] study compares the results from two instruments which estimate eCO in expired air (Bedfont EC50 vs National Coal Board's COTracer). These measures were in-turn compared with the results from the standard expired air eCO monitor (Ecolyzer 2000) and with blood COHb% concentration. The eCO levels measured by EC50 and COTracer machines closely correlated with COHb% (r = .95 and .98, n = 75) as well as with the values from Ecolyzer (r = .98, n = 75). In our study, since sensitivity (43.63%) is low and specificity (97.24%) is high we can infer that the chosen cut-off point is stringent. Although these 2 measures have been used in the ROC curve for calculating the eCO cut-off point, they may not be useful for making a decision on a positive Eco testing among individuals with history of smoking. In this context, PPV (84.64%) and NPV (82.52%) have been retained as the metrics of choice which in-turn focus on the practical usefulness of the test in clinical practice.

In our study, we used a composite indicator to assess the cumulative exposure to smoking. The pack-years thus computed include the number of packs of cigarettes smoked per day (10 units/pack in the Indian context). This indicator was an improvisation of the 'Brinkman index' used in Herath P's[20] study. We found a moderate positive correlation among subjects who used cigarettes (measured in pack years) and eCO (ppm) levels. The strength of association was .463 (Spearman rank correlation), which was significant. Although this indicates that eCO assessment is an objective measurement of the cumulative smoking status, evidence[25] shows that eCO levels correlate with the number of cigarettes smoked during the past 24 hours. Deveci S.E[11] et al report a significant positive correlation between eCO levels and daily cigarette consumption as well as the duration of smoking among healthy smokers (r = +.55, P < .001, and r = +.265, P < .01 respectively). Our approach enables assessing the recent smoking status (measure of abstinence) among individuals with smoking substance use.

The dose-time effect of smoking (exposure) on eCO levels (outcome) has been assessed by computing the cumulative dose (smoking pack-years) over the time period of adult age (18 yrs of age to present). Our premise was that the recalled history of lifetime consumption is a better measure of true exposure (smoking use) than is the current activity. However, the exposure measurement error in our study includes both the systematic bias and validity co-efficient. The first error is due to measuring smoking in-terms of pack years rather than intensity over the previous 24 to 48 hours. The second error is due to the self-reporting of smoking use, where-in we should have ideally assessed exposure by analyzing the cotinine levels in the biospecimen (urine). Its half-life is 17 hours, which makes it suitable to distinguish smokers and non-smokers.

The ROC curve in our study has determined the optimal cut-off point for eCO as 2.5 ppm (round-off to 3). Any value above this ceiling will identify the smoking status, and this value is impacted by the dose (intensity, frequency and time period of exposure) of smoking among the study subjects. Among cancer patients, the eCO cut-off point could be much higher given the inherent high dose of smoking use when compared with the general population. In our study, the discrimination performance of the Smokerlyzer machine in measuring eCO was found to be moderate (qualitative assessment by considering AUC measure '0.749'), and the diagnostic accuracy was quantified as 82.89%. This indicates the proportion of correct test results (true positives and true negatives) among all the test results.

In our study, since sensitivity is low and specificity is high we can infer that the chosen cut-off point is stringent. Although these 2 measures have been used in the ROC curve for calculating the eCO cut-off point, they are not helpful for making a decision about smoking individuals testing positive with a positive (>3 ppm) eCO testing. PPV (84.64%) and NPV (82.52%) have been retained in Table 3 as the metrics of choice, which in-turn focus on the practical usefulness of the test in clinical practice. Our study results should enable using eCO levels as a tool to discriminate short term abstinence (for atleast 24 hours) from continued smoking.

Evidence shows that eCO measurement is a valuable guide even among emphysema patients.[12] In our study, among subjects with history of bronchial asthma and/or eCO falling in the yellow/red zone of Smokerlyzer machine, a low PEFR was found among 7.24% males and 9.85% females. Jarvis M.J et al[13] report the impaired diffusion of CO from blood to the alveoli among emphysema patients, where-in for a given concentration of eCO in expired air an association was found with high levels of COHb% in the blood of emplysema patients (correlation between eCO and COHb%: .98 for normal smokers and .92 for emphysema patients). Biologically, eCO tends to exist in a dynamic equilibrium with COHb%. Pezzuto A et al's[17] study assessed the benefit of smoking cessation and triple inhaler therapy in combustible cigarette smokers with severe COPD. This study[17] used an eCO cut-off measure of <7 ppm, with those who quit smoking reporting an improvement in lung function. The results show a significant increase in FEV1 and

walking test with a decrease in eCO by 15 ppm, when compared with the sustainers (reduced cigarette consumption without quitting). These results substantiate the pivotal role of smoking cessation in improving the clinical function of the respiratory system.

This proof-of-concept study establishes the feasibility and rationale for the utility of smokerlyzer machine in assessing the smoking substance use among healthy subjects. Our results affirm the benefits of such assessment, and advance the potential of such intervention among cancer patients. Further research including clinical trials should be specifically designed for validation among cancer patients.

Limitations

(1) Our study design was cross-sectional in nature. Ideally, we need to design a prospective cohort study among occupational groups, with sample size calculated based on the rate of outcome and not on the prevalence of exposure,

(2) Most of our study subjects were <40 yrs of age and were males working in the Information technology sector or traffic police services. In our study, ideally, we need to compute the smoking prevalence of subjects >40 yrs of age and among an equal proportion of males and females from various occupational groups. However, there is lack of evidence regarding the effect of occupational exposure on routine eCO screening,[15]

(3) In our study, one exhaled breath was used to capture the sample. The process of diffusion may not capture the asymptotic reading after a single exhalation (carryover effect from the previous subject reading). Jarvis M.J et al[13] report a higher second reading on the EC50 machine when compared to the first (mean values 17.3 and 15.7 ppm: $p < .001$). Ideally, we should have taken two successive readings,

(4) Other constituents of exhaled breath (eg: hydrogen) might interfere with the measurement of breath eCO, when an electrochemical sensor (such as in EC50) is used for the analysis. However, Bedfont EC50[6] reports a hydrogen cross interference of ≤6%. Methods with high specificity and sensitivity such as laser-based absorption spectroscopy techniques[7] should be used to detect breath eCO,

(5) In our study, we did not consider the association of breath CO levels due to systemic or respiratory inflammation, and other factors such as diet and exercise, beyond the exposure due to smoking substance use. Also, the exposure assessment in our study dld not include the biomarker cotinine in urine,

(6) We did not derive eCO cutoff for lighter (<10 cigarettes/day) and heavier smokers separately.

Conclusion

Cancer patients who continue to smoke have misconceptions that a moderate amount (half pack of cigarettes/day) might not be harmful.[23] The Smokerlyzer machine enables assessing the eCO level, which is a measure of continued smoking. As a component of the smoking cessation intervention, the risk should be communicated to the patients. Healthcare professionals need to seize the valuable opportunity during patient interactions, for testing and counseling them on quitting the substance use. This analogy is applicable to healthy individuals as well, who intend to quit the substance use. The Smokerlyzer method is one of the least expensive and non-invasive methods of verifying abstinence from smoking. It could be ideally used in 'stop smoking services', and further research will resolve its use for monitoring the outdoor exposure.

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Author contributions

VR conducted the literature review and drafted the manuscript, MM performed the statistical analysis, RN conceived the design of the work, provided inputs regarding the biological associations, revised the draft and provided final approval.

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