Brief report

Optimal Carbon Monoxide Criteria to Confirm Smoking Status Among Postpartum Women

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Abstract

Introduction: Although expired-air carbon monoxide (CO) is a well characterized biomarker of cigarette smoking, limited research has assessed whether the standard clinical CO cutoffs need to be altered for postpartum women and whether these cutoffs remain constant across the postpartum year. Accordingly, the present study evaluated the effectiveness of using CO as a method to confirm smoking status relative to salivary cotinine among postpartum women and assessed optimal CO criteria to confirm smoking status across the postpartum year. Differences in optimal CO criteria to confirm smoking status also were examined between black and white postpartum women.

Methods: Women ($N = 208$) for the present study had quit smoking for their current pregnancy and were enrolled in a larger postpartum relapse prevention intervention. Smoking status was assessed at 12, 24, and 52 weeks postpartum using both expired-air CO and salivary cotinine.

Results: Receiver-operating characteristic analyses indicated that CO provided moderately high diagnostic accuracy to distinguish between women who were and were not smoking when using salivary cotinine as the reference criterion to confirm smoking status. CO cutoffs of 2 and 3 parts per million (ppm) had the highest overall efficiency and combined sensitivity and specificity across the postpartum year. Results were consistent for black and white women.

Conclusions: These findings indicate that optimal CO criteria to confirm smoking status remains stable throughout the postpartum year and support a need to utilize CO cutoffs much lower than the standard clinical CO criterion of 8 ppm to confirm abstinence among postpartum women.

Implications: Findings from the present study confirm the value of CO as a biomarker of smoking status among postpartum women. Results indicate that CO cutoffs of 2 and 3 ppm were optimal for confirming smoking status across the entire postpartum year in both black and white women. These findings offer a replication and extension of previous work and indicate that optimal CO criteria to confirm smoking status remain stable throughout the postpartum period and further support a need to utilize CO cutoffs much lower than the standard clinical criterion of 8 ppm to confirm smoking status among postpartum women.

Introduction

Maternal smoking during the postpartum period increases health risks for both mothers^{1–5} and their infants,^{6–10} and many women who quit smoking during pregnancy relapse during the first year postpartum.^{11–13} Identifying women at risk for postpartum smoking relapse

has implications for prevention and treatment efforts. However, there is little consensus regarding appropriate tests and optimal cutoffs to confirm smoking status across the postpartum period.¹⁴ Given that demand characteristics are particularly likely to influence the accuracy of self-reported smoking status among new mothers,^{14–16}

objective verification of smoking status is particularly important among postpartum women.

Cotinine, a metabolite of nicotine, is considered the best biomarker for verifying smoking status.^{17–19} Although pregnancy-related changes in the rates of nicotine and cotinine metabolism require that the guidelines for confirming smoking status be amended during pregnancy,^{14,20} these metabolic effects do not persist postpartum.^{14,20} However, the practical use of cotinine to confirm smoking status among postpartum women is limited by the costly and timely procedures required to collect and assay biological samples. Expired-air carbon monoxide (CO) offers a more rapid, lower cost, and less invasive method for confirming smoking status.²¹ Despite the widespread acceptance of CO as an acceptable biomarker of smoking,¹⁴ limited research has assessed whether the standard clinical CO cutoffs need to be altered for postpartum women and whether these cutoffs remain constant across the entire postpartum year.

A report by Higgins and colleagues¹⁶ provided an initial step in investigating the use of different biomarkers and associated cutoffs to confirm smoking status among pregnant and recently postpartum women. The authors found that a CO cutoff half that of the standard clinical cutoff¹⁴ was optimal for confirming smoking status among women during pregnancy and up to 6 months postpartum. However, we are aware of no additional work that has sought to replicate or extend these previous findings. Accordingly, the present study aimed to further evaluate the effectiveness of using CO as a method to confirm smoking status relative to salivary cotinine among postpartum women and assessed optimal CO criteria to confirm smoking status across the entire postpartum year. Given racial differences in smoking habits^{22,23} and nicotine and cotinine metabolism,^{24,25} the present study also sought to verify whether optimal CO criteria to confirm smoking status are consistent between black and white postpartum women.

Methods

Participants and Procedures

Participants were enrolled in a randomized controlled trial investigating the efficacy of a postpartum relapse prevention intervention that included a specialized focus on women's postpartum concerns about mood and weight.²⁶ Women were required to have smoked daily for at least 1 month during the 3 months prior to their current pregnancy, smoked at least five cigarettes per day before quitting, not smoked during the past 2 weeks, and been motivated to remain abstinent postpartum. At study enrollment, smoking cessation was confirmed using the timeline follow-back methodology²⁷ and a CO level less than or equal to 8 parts per million (ppm).¹⁴

Women reported demographic information during their third trimester of pregnancy between 34 and 38 weeks gestation. Smoking status was assessed at 12, 24, and 52 weeks postpartum using expired-air CO and salivary cotinine. CO was gathered using the Vitalograph BreathCO monitor (Vitalograph Inc, Lenexa, KS). Saliva samples were procured using a cotton Salivette swab (Salimetrics LLC, State College, PA), which each participant held in her mouth for approximately 2 minutes or until the swab was saturated with saliva. Saliva samples were stored at -80°C and analyzed using enzyme immunoassay. Abstinence was defined as a salivary cotinine level of 15 $\mu\text{g/L}$ or less.^{28,29}

Statistical Analysis

For each assessment, sensitivity, specificity, predictive values, and efficiency were computed for CO cutoffs ranging from 1 to 15.

Sensitivity was determined for each CO cutoff as the proportion of women whose CO values indicated smoking out of all women who were verified as smoking by salivary cotinine. Specificity was determined for each CO cutoff as the proportion of women whose CO values indicated abstinence out of all women who were verified as being abstinent by salivary cotinine. The positive predictive value was determined as the proportion of women who were verified as smoking by cotinine out of all women whose CO values indicated smoking. The negative predictive value was determined as the proportion of women who were verified as being abstinent by salivary cotinine out of all women whose CO values indicated abstinence. Efficiency was determined as the proportion of times each CO cutoff correctly classified women as being abstinent or smoking.

The area under the receiver-operating characteristic curve was estimated using the nonparametric method to determine the diagnostic accuracy of CO in discriminating between smoking status using salivary cotinine as the reference criterion at each assessment.^{30,31} Sensitivity was plotted against the inverse of specificity for all CO cutoffs, with an area under the curve of 1.0 indicating perfect identification of smoking status and an area under the curve of 0.5 indicating no discrimination between smoking status. Separate analyses were run for black and white women to assess agreement in results between racial categories.

Results

A total of 208 women with complete CO and salivary cotinine data across all assessments were included in the current study. On average, women were 25.12 ($SD = 5.78$) years of age and 52% were black. Salivary cotinine results indicated that 43% ($n = 90$), 39% ($n = 81$), and 36% ($n = 74$) of women were abstinent at the 12, 24, and 52 week assessments, respectively. Because results were found to be consistent between black and white women, only findings from the overall sample are reported.

When CO was used to discriminate between smoking status, the area under the curve was 0.85 (95% CI = 0.80, 0.90), 0.89 (95% CI = 0.85, 0.93), and 0.88 (95% CI = 0.84, 0.93) at the 12, 24, and 52 week assessments, respectively (Figure 1). These data indicate that CO has a moderately strong ability to accurately discriminate

Figure 1. Receiver-operating characteristic curves for varied expired-air carbon monoxide cutoffs in discriminating between smoking status using salivary cotinine as the reference criterion across the postpartum year.

between women whose salivary cotinine levels confirmed them as having abstained from or resumed smoking. Across all assessments, CO cutoffs of 2 and 3 ppm had the highest combined sensitivity and specificity (Table 1). However, a CO cutoff of 2 ppm consistently produced higher sensitivity whereas a CO cutoff of 3 ppm consistently produced higher specificity. For example, at 12 weeks postpartum, a CO cutoff of 2 and 3 ppm respectively identified 77% and 59% of women who were verified as smoking by salivary cotinine and 81% and 92% of women who were verified as abstinent by salivary cotinine.

CO cutoffs of 2 and 3 ppm also had the highest values of efficiency in confirming smoking status although a CO cutoff of 2 ppm consistently had greater efficiency than did a CO a cutoff of 3 ppm. A CO cutoff of 2 ppm also consistently had a higher negative predictive value whereas a CO cutoff of 3 ppm consistently had a higher positive predictive value. For example, at 12 weeks postpartum, women with a negative CO reading had a 73% chance of being verified as abstinent by salivary cotinine when a CO cutoff of 2 ppm was used but only had a 63% chance of being verified as abstinent by salivary cotinine when a CO cutoff of 3 ppm was used. Conversely,

Table 1. Sensitivity, Specificity, and Predictive Values for Each Expired-Air Carbon Monoxide (CO) Cutoff in Confirming Smoking Status Using Salivary Cotinine as the Reference Criterion

CO	Sensitivity	Specificity	Sensitivity + Specificity	PPV	NPV	Efficiency
12-week assessment						
1	0.94	0.39	1.33	0.67	0.83	0.70
2	0.77	0.81	1.58	0.84	0.73	0.79
3	0.59	0.92	1.52	0.91	0.63	0.74
4	0.43	0.98	1.41	0.96	0.57	0.67
5	0.36	0.99	1.35	0.98	0.54	0.63
6	0.32	0.99	1.31	0.97	0.53	0.61
7	0.28	0.99	1.27	0.97	0.51	0.59
8	0.19	1.00	1.19	1.00	0.48	0.54
9	0.18	1.00	1.18	1.00	0.48	0.53
10	0.13	1.00	1.13	1.00	0.47	0.50
11	0.07	1.00	1.07	1.00	0.45	0.47
12	0.04	1.00	1.04	1.00	0.44	0.46
13	0.03	1.00	1.03	1.00	0.44	0.45
14	0.00	1.00	1.00	1.00	0.43	0.43
15	0.00	1.00	1.00	1.00	0.43	0.43
24-week assessment						
1	0.97	0.43	1.40	0.73	0.90	0.76
2	0.79	0.86	1.65	0.90	0.72	0.82
3	0.70	0.93	1.63	0.94	0.66	0.79
4	0.60	0.95	1.55	0.95	0.60	0.74
5	0.47	0.98	1.44	0.97	0.54	0.66
6	0.35	1.00	1.35	1.00	0.49	0.60
7	0.31	1.00	1.31	1.00	0.48	0.58
8	0.23	1.00	1.23	1.00	0.45	0.53
9	0.17	1.00	1.17	1.00	0.44	0.50
10	0.10	1.00	1.10	1.00	0.42	0.45
11	0.07	1.00	1.07	1.00	0.41	0.43
12	0.06	1.00	1.06	1.00	0.40	0.42
13	0.02	1.00	1.02	1.00	0.40	0.40
14	0.01	1.00	1.01	1.00	0.39	0.39
15	0.00	1.00	1.00	1.00	0.39	0.39
52-week assessment						
1	0.93	0.50	1.43	0.77	0.79	0.77
2	0.79	0.82	1.62	0.89	0.69	0.80
3	0.69	0.93	1.63	0.95	0.63	0.78
4	0.63	0.97	1.60	0.98	0.59	0.75
5	0.55	0.99	1.54	0.99	0.55	0.71
6	0.47	1.00	1.47	1.00	0.51	0.66
7	0.37	1.00	1.37	1.00	0.47	0.60
8	0.26	1.00	1.26	1.00	0.43	0.52
9	0.18	1.00	1.18	1.00	0.40	0.47
10	0.17	1.00	1.17	1.00	0.40	0.47
11	0.13	1.00	1.13	1.00	0.39	0.44
12	0.08	1.00	1.08	1.00	0.37	0.40
13	0.04	1.00	1.04	1.00	0.36	0.38
14	0.02	1.00	1.02	1.00	0.36	0.37
15	0.00	1.00	1.00	1.00	0.36	0.36

PPV = positive predictive value; NPV = negative predictive value. Bolded values indicate optimal CO cutoffs.

women with a positive CO reading had an 84% chance of being verified as smoking by salivary cotinine when a CO cutoff of 2 ppm was used compared to a 91% chance of being verified as smoking by salivary cotinine when a CO cutoff of 3 ppm was used.

Discussion

The present study aimed to identify optimal CO criteria to confirm smoking status across the entire postpartum year among both black and white postpartum women using salivary cotinine as the reference criterion. Similar to previous findings among pregnant and postpartum women^{16,32} and the general population,^{31,33,34} our findings support a need to adopt lower CO cutoffs than what are typically reported to document smoking status. Unlike the previous study by Higgins and colleagues,¹⁶ which documented a CO cutoff of 4 ppm to be optimal to confirm smoking status during the first 6 months postpartum, we found that slightly lower CO cutoffs of 2 and 3 ppm consistently provided the highest accuracy to detect smoking and verify abstinence across the entire postpartum year. Our findings also were the first to demonstrate that these lower CO cutoffs are appropriate for use in both black and white postpartum women. Compared to the standard clinical CO cutoff of 8 ppm,¹⁴ these lower CO cutoffs improved accuracy in verifying abstinence by nearly 30%. Thus, previous reports using higher CO cutoffs among postpartum women may have underestimated the number of women smoking in postpartum populations.

Although CO cutoffs of 2 and 3 ppm were comparable in their combined sensitivity and specificity, a CO cutoff of 2 ppm consistently had higher sensitivity to detect smoking whereas a CO cutoff of 3 ppm consistently had higher specificity to verify abstinence. However, because sensitivity and specificity only provide information on the ability of a test to identify individuals with or without the condition, they provide no indication of the diagnostic accuracy of a test and thus have limited clinical utility. Accordingly, predictive values, which estimate the likelihood that a test result will be a true positive or a true negative, are more informative. In the present study, a CO cutoff of 2 ppm was more accurate in classifying women as being abstinent but had a greater tendency to misclassify women who were smoking compared to a CO cutoff of 3 ppm. As such, the choice to use one cutoff over the other would depend on the purpose of assessing smoking status. For example, it may be preferred to use a lower CO cutoff of 2 ppm when determining eligibility of postpartum women to participate in a research study in which smoking is an important exclusion criteria. Alternatively, studies aimed at developing smoking cessation interventions for postpartum women may prefer to use a higher CO cutoff of 3 ppm to avoid incorrectly rejecting successful approaches.

There are several limitations to this study worth noting. First, optimal cutoffs determined through receiver-operating characteristic analysis are dependent upon the prevalence of the condition within the analytic sample.³⁵ Thus, optimal CO cutoffs to confirm smoking status may differ in populations where the rates of smoking are much higher or lower than are those in the present sample. Second, CO readings can be influenced by environmental factors, such as air pollution or secondhand smoke. Accordingly, these findings may differ in varied environmental settings although likely not dramatically.³⁶ Finally, smoking status was confirmed using the recommended cutoff for salivary cotinine concentration.¹⁴ Although cotinine concentrations are similar when assessed through saliva, urine, or plasma samples,^{17,37} optimal CO cutoffs to confirm smoking status may

differ according to which biological sample cotinine is assayed from and what cotinine cutoff is chosen to confirm smoking status.

Despite these limitations, having effective and lower cost methods for determining smoking status is essential to the success of research and clinical interventions directed toward identifying and reducing smoking among postpartum women. Our findings confirm the value of CO as a biomarker of smoking status within this population. We found that CO cutoffs of 2 and 3 ppm were optimal for confirming smoking status across the entire postpartum year in both black and white women. These findings both replicate and extend previous work¹⁶ and indicate that optimal CO criteria to confirm smoking status remain stable throughout the postpartum period and further support a need to utilize CO cutoffs much lower than the standard clinical criterion of 8 ppm to confirm smoking status among postpartum women.

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Declaration of Interests

None declared.

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