Original investigation

A Comparison of the Fagerström Test for Cigarette Dependence and Cigarette Dependence Scale in a Treatment-Seeking Sample of Pregnant Smokers

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Abstract

Introduction: Valid and reliable brief measures of cigarette dependence are essential for research purposes and effective clinical care. Two widely-used brief measures of cigarette dependence are the six-item Fagerström Test for Cigarette Dependence (FTCD) and five-item Cigarette Dependence Scale (CDS-5). Their respective metric characteristics among pregnant smokers have not yet been studied.

Methods: This was a secondary analysis of data of pregnant smokers ($N = 476$) enrolled in a smoking cessation study. We assessed internal consistency, reliability, and examined correlations between the instruments and smoking-related behaviors for construct validity. We evaluated predictive validity by testing how well the measures predict abstinence 2 weeks after quit date.

Results: Cronbach's alpha coefficient for the CDS-5 was 0.62 and for the FTCD 0.55. Measures were strongly correlated with each other, although FTCD, but not CDS-5, was associated with saliva cotinine concentration. The FTCD, CDS-5, craving to smoke, and withdrawal symptoms failed to predict smoking status 2 weeks following the quit date.

Conclusions: Suboptimal reliability estimates and failure to predict short-term smoking call into question the value of including either of the brief measures in studies that aim to explain the obstacles to smoking cessation during pregnancy.

Introduction

Valid and reliable brief measures of cigarette dependence are essential for research purposes and effective clinical care. One such instrument is the Fagerström Test for Cigarette Dependence (FTCD).¹ Known previously as the Fagerström Tolerance Questionnaire² and Fagerström Test for Nicotine Dependence^{3,4} the six-item FTCD is the most widely-used, brief measure of cigarette dependence.⁵ The five-item Cigarette Dependence Scale (CDS-5)⁶ is also a brief and valid measure of cigarette dependence. The CDS-5 has psychometric

properties similar to its parent measure, the CDS-12, but with less comprehensive content in terms of tapping compulsion, withdrawal symptoms, loss of control, time allocation, neglect of other activities, and persistence in smoking despite harm.

Results of direct comparisons between the FTCD and the CDS have been mixed, with the vast majority of studies involving contrasts between the FTCD and CDS-12. In general, the FTCD and CDS-12 are moderately associated with each other and both are correlated positively with cigarettes per day and age at first daily smoking,^{6–8} yet neither measure is associated significantly with the

number of past quit attempts.⁸ CDS-12 has greater internal consistency and test-retest reliability and measures changes in dependence over time better than the FTCD.^{6,8} Previous studies have shown that both are associated with saliva (or blood) cotinine levels. In black light smokers,⁹ CDS-12 showed a stronger association with serum cotinine than FTCD; however, an internet study with a sample of French language smokers⁶ demonstrated that the FTCD was more strongly associated with saliva cotinine compared to the CDS-12. Regarding the prediction of abstinence, CDS-12 was a better predictor of abstinence at the 8-day follow-up than FTCD, although only the FTCD was a significant predictor of smoking status at the 31-day follow-up.¹⁰

Comparisons between the FTCD and CDS-5 are rare. In the French longitudinal survey used to develop the CDS instruments,⁶ CDS-5 had higher test-retest and internal consistency reliability than FTCD. Both scales were associated with saliva cotinine concentration to the same degree ($r = 0.46$); however, CDS-5 exhibited a stronger relationship with craving compared to FTCD. CDS-5 scores also decreased among daily smokers who switched to occasional smoking by the 18-day follow-up assessment, although neither instrument predicted smoking abstinence at follow-up.

We know of only one investigation comparing the reliability and validity of the FTCD and CDS-5 in a treatment population. In that study of smokers with substance use disorders receiving smoking cessation treatment, Rohsenow et al.⁷ concluded that the FTCD and CDS-5 were equivalent measures of tobacco dependence, but the CDS-5 was less reliable. The FTCD was highly correlated with CDS-5, indicating overlap but substantial unique variance. The FTCD and CDS-5 correlated positively with cigarettes per day and age of first daily smoking. The CDS-5, but not the FTCD, correlated significantly with the number of quit attempts. Neither CDS-5 nor FTCD predicted abstinence within 7, 14, or 30 days following initiation of treatment.

One of the most important subpopulations of smokers is pregnant smokers. Smoking during pregnancy is not only harmful for the mother but also for the fetus; it is strongly associated with low birth weight, premature delivery, and several medical and psychiatric disorders in the offspring not only in childhood but also later in life.^{11–20} Although pregnant smokers are aware of the harmful effect of smoking,^{21,22} those who do not quit are probably those who are the most dependent on cigarettes. Therefore, assessment of cigarette dependence among pregnant smokers is a major issue and instruments assessing it should be extensively studied to learn which one is the best measure of cigarette dependence and the best predictor of postquit abstinence.

Whether the FTCD or CDS-5 is a better measure of cigarette dependence in pregnant smokers is an important question. A significant amount of shared variance in the two measures is the number of cigarettes per day.⁷ Pregnant smokers smoke less and have accelerated nicotine metabolism²³ introducing measurement bias in such research. Cotinine concentration has been suggested as a proxy for cigarette dependence²⁴; however, no threshold of urinary/saliva/blood cotinine exists to identify dependent pregnant smokers. To our knowledge, only one previous report assessed the predictive value of serum cotinine level in predicting abstinence among pregnant smokers and found that higher cotinine level predicted lower likelihood of abstinence at 1 month and at delivery.²⁵

With these aims in mind, we analyzed data from a sample of pregnant smokers enrolled in a smoking cessation trial to: (1) determine the psychometric properties of both instruments by examining

internal consistency, reliability, and correlations between the instruments; (2) evaluate construct validity by comparing the FTCD and the CDS-5 using proxies of cigarette dependence including saliva cotinine, cigarettes per day, age initiated regular smoking, previous quit attempts, craving, and withdrawal symptoms; and (3) assess predictive validity by testing how well the measures predict abstinence.

Methods

Participants

The Study of Nicotine Patch in Pregnancy trial²⁶ (Identifier: <http://ClinicalTrials.gov> NCT00507975) was a randomized, double-blind, placebo-controlled, parallel-group, multicenter study designed to assess the efficacy of 16-hour nicotine patches whose dose was individually adjusted according to saliva cotinine and could range from 10 to 30 mg/d. Pregnant smokers older than 18 years, between 12 to 20 weeks of gestation who smoked at least 5 cigarettes per day and had a score at least 5 on a scale of motivation to quit (range 0–10) were enrolled. Potential participants attended the inclusion visit for detailed information about the study, counseling for smoking cessation, and data collection. The next visit was scheduled following a grace period of at least 2 weeks allowing participants to quit smoking, in line with marketing authorization of nicotine replacement therapy in pregnant smokers in France. Participants who failed were randomly assigned to nicotine or placebo patch, and set a quit date. Treatment started on the quit date. A total of 476 pregnant smokers were included in the Study of Nicotine Patch in Pregnancy study, and 403 were randomized to receive nicotine or placebo patch. Among the 476 pregnant smokers included, a total of 73 participants were not randomized: 53 withdrew consent, 15 reduced cigarette consumption below five cigarettes per day, three had serious obstetrical disorders precluding randomization, one did not show up, and one took an antidepressant (which was one of the exclusion criteria).

Data of the included pregnant smokers were analyzed for psychometric properties and construct validity. A total of 306 pregnant women's data were available 2 weeks after quit date and were included in the analysis of the predictive validity of CDS-5 and FTCD. Full details of the Study of Nicotine Patch in Pregnancy study have been published.²⁶ All participants, including potential subjects, signed written consent forms. The study was approved by the Ethics Committee of the Pitié-Salpêtrière Hospital, Paris, France.

Measures

We administered French versions of the FTCD and CDS-5. The FTCD and CDS-5 have established construct validity in French populations, with Cronbach's alpha coefficients of 0.66 and 0.84, respectively.⁶ Also included were smoking-related characteristics indicative of dependence including single-item measures: salivary cotinine concentration, current number of cigarettes smoked per day (CPD), number of previous quit attempts, and age of regular smoking initiation. We assessed simultaneously French versions of the Tobacco Craving Questionnaire (FTCQ-12)²⁷ to assess craving and the Minnesota Nicotine Withdrawal Scale (MNWS)²⁸ to evaluate withdrawal. The 12 items on the FTCQ-12 and the eight items on the MNWS were each summed to yield a general craving score and a total withdrawal score, respectively. The FTCQ-12 and MNWS have established construct validity in French smokers.^{27,29} In the current investigation, Cronbach's alpha for the general craving score and total withdrawal score was respectively, 0.74 and 0.77. Craving and

withdrawal are ordinarily most prominent during the first 2 weeks of quitting³⁰; thus, we evaluated the incidence of smoking 2 weeks after the quit date (abstinent = 0, smoking = 1), which was verified by breath carbon monoxide (≤ 8 parts per million; Smokealyzer, Bedfont Scientific Ltd, Rochester, Kent, United Kingdom). The saliva cotinine sample was collected between 11:00 and 20:00 hours 2–3 weeks before randomization simultaneously with recording of CDS-5, FTCD, demographic and smoking characteristics, and when the pregnant women smoked *ad libitum*. A cotton roll was placed in the gingival cleft for 1 minute and placed immediately into the Salivette tube (Sarstedt, Nümbrecht, Germany), kept at 4°C and sent in less than 24 hours to the central biochemistry laboratory (Hôpital Pitié-Salpêtrière, Laboratoire de Biochimie) for determination. The quantification limit for cotinine was 7.5 µg/mL and the between-run coefficient of variation 5%–8%.³¹

Data Analyses

Cronbach's alpha for the FTCD and CDS-5 were calculated to confirm internal consistency reliability. Correlations (Pearson's r) between the FTCD and CDS-5 were examined to determine the amount of shared variance. To assess construct validity, we compared Pearson's r of both measures with all smoking-related characteristics. Variables were checked for normality and corrected for skewness if necessary. We also conducted standard multiple regression analyses with both CDS-5 and FTCD to determine which instrument was the best predictor of saliva cotinine (raw concentration and log-transformed) including the control term: partners' smoking. To assess whether measures of dependence predicted smoking cessation, we estimated separate logistic regression models to determine the association between all variables of interest with smoking status 2 weeks after the quit date. Consistent with Rohsenow et al.⁷ treatment group was included in the analyses as a control term. We also conducted receiver operating characteristic analyses to compare the performance of FTCD and CDS-5 in classifying smokers and abstainers. Descriptive statistics, reliability analyses, correlations, and logistic regressions were analyzed using STATISTICA (StatSoft, Inc, Tulsa, OK). All statistical tests were two-tailed. Results were considered significant at $P \leq .05$. Receiver operating characteristic analyses were performed using Web-based Calculator for receiver operating characteristic curves.³²

Results

Participant Characteristics

Table 1 presents the sociodemographic and smoking-related characteristics of the included pregnant smokers. Compared to randomized pregnant smokers, those who were included, but not randomized and thus did not receive the study medications ($n = 73$), were on average younger (28.0 vs. 29.5, $P < .02$), started regular smoking at an earlier age (15.9 vs. 16.5, $P < .03$), and were experiencing significantly greater withdrawal symptoms at enrollment (MNWS withdrawal = 8.4 vs. 7.0, $P < .03$).

Psychometric Properties and Construct Validity

Cronbach's alpha for CDS-5 was 0.62 and for the six-item FTCD was 0.55. The CDS-5 and FTCD correlated positively with each other ($r = 0.76$, $P < .001$). Table 2 presents the correlations between other indicators of dependence and the FTCD and CDS-5. Both were significantly correlated with CPD, FTCQ-12 general craving and

Table 1. Characteristics of the 476 Study Participants

	Mean (SD) or N (%)
Sociodemographic characteristics	
Age (years)	29.0 (5.8)
Employed	259 (54%)
Housewife	108 (23%)
Other	109 (23%)
Married or living with partner	402 (85%)
Income/yr	
<€12 000	161 (34%)
€12 000 to €30 000	240 (51%)
>€30 000	75 (15%)
Spouse smokes	353 (74%)
Smoking-related characteristics	
Saliva cotinine (µg/mL)	145.1 (78.7)
Cigarettes smoked per day (CPD)	12.1 (6.0)
Expired air carbon monoxide (CO) (parts per million)	11.6 (6.9)
Age initiated regular smoking (years)	16.3 (2.6)
Previous quit attempts	1.4 (1.6)
French Tobacco Craving Questionnaire (FTCQ-12) score (12–78)	43.4 (11.7)
Minnesota Nicotine Withdrawal Scale (MNWS) score (0–24)	7.5 (4.9)
Five-item Cigarette Dependence Scale (CDS-5) score (1–25)	17.7 (3.0)
Fagerström Test for Cigarette Dependence (FTCD) score (0–10)	4.5 (2.1)
Percent cigarette dependent (FTCD = 6 or greater)	152 (32%)
Incidence of smoking 2 weeks after quit date ($n = 306$)	271 (88.5%)

Table 2. Correlation Coefficients (Pearson's r) for Other Indicators of Dependence With the Fagerström Test for Cigarette Dependence (FTCD) and Five-Item Cigarette Dependence Scale (CDS-5)

	FTCD	CDS-5
Cigarettes smoked per day ^a (CPD)	0.63	0.60
Age initiated regular smoking ^a	–0.15	–0.14
Previous quit attempts ^b	–0.05	–0.02
FTCQ-12 general craving score	0.38	0.43
MNWS total withdrawal score ^a	0.19	0.27

FTCQ-12 = French Tobacco Craving Questionnaire; MNWS = Minnesota Nicotine Withdrawal Scale. Values in bold are significant at $P < .003$.

^aSquare root-transformed to correct skewness.

^bLog-transformed to correct skewness.

MNWS general withdrawal scores, but neither questionnaire was significantly associated with previous quit attempts (both $P > .23$). FTCD was somewhat more strongly associated with CPD and age of first daily smoking compared to the CDS-5. CDS-5 was somewhat more strongly associated with FTCQ-12 general craving score and MNWS general withdrawal score than FTCD.

Table 3 summarizes the results of the standard multiple regression analyses of FTCD and CDS-5 with saliva cotinine concentration as the dependent variable. FTCD was significantly correlated with raw cotinine and log¹⁰ cotinine ($r = 0.351$ and 0.341 , both $r^2 = 0.12$, $P < .01$). CDS-5 was also significantly correlated with raw cotinine and log¹⁰ cotinine, but the association was weaker ($r = 0.286$ and 0.290 ; both $r^2 = 0.08$, $P < .01$). However, in the multiple regression, FTCD, but not CDS-5, was significantly associated with raw saliva cotinine concentration and log-transformed saliva cotinine adjusted for partners' smoking ($N = 353/476$, 74%).

Smoking Status at Follow-up

Table 4 presents the logistic regressions predicting smoking status 2 weeks after the quit date, controlling for treatment. Neither the CDS-5, FTCD, nor any other smoking-related measure predicted smoking status 2 weeks after the quit date (all $P > .09$). We found that treatment was not a significant predictor of abstinence (chi-square = 0.00, $P = 1.00$). Excluding treatment from the analyses did not alter the outcome of any logistic regression analysis.

Figure 1 depicts the outcomes of the receiver operating characteristic analyses of the optimized classification models. FTCD and CDS-5 were poor discriminators of smoking and abstinence 2 weeks after quit date in pregnant smokers. Area under the curve was 0.56 for FTCD compared with 0.57 for CDS-5. Accordingly, FTCD and CDS-5 were poor discriminators of smoking and abstinence 2 weeks after the quit date in pregnant smokers.

Discussion

The current study compared the internal consistency reliability and concurrent validity of the CDS-5 to those of the FTCD among pregnant smokers. Consistent with Etter et al.,⁶ the CDS-5 had higher internal consistency than FTCD. However, Cronbach's alphas for both measures were substantially lower than their published estimates and fell far below the 0.70–0.90 range of acceptable values.^{33,34} These findings are consistent with research indicating less than adequate internal consistency for the FTCD^{8,35} and borderline adequacy in a treatment population for the CDS-5.⁷

In addition, the reliability estimates showed a substantial amount of measurement error in FTCD and CDS-5 scores ($1 - 0.55^2 = 0.70$ and $1 - 0.62^2 = 0.61$, respectively). Factors such as the number of

items and dimensionality affect alpha.³⁶ The CDS-5 had lower reliability compared with CDS-12 in several investigations,^{6,7,35} suggesting researchers may opt for the longer version of the CDS. Several researchers^{37–40} also have identified more than a single factor in the FTCD, suggesting the multidimensionality of the questionnaire.

The coefficient of determination (0.76^2) indicated that nearly 58% of the FTCD can be explained by the variation in CDS-5 and vice versa. This is not unexpected given that the measures have two items in common, “how many cigarettes do you smoke per day” (CPD) and “time to first cigarette after awakening”. CPD and time to first cigarette have consistently been valid indicators of tobacco dependence.^{41,42} Given the redundancy in CDS-5 and FTCD, a brief measure of cigarette dependence using only those two items (eg, see the Heaviness of Smoking Index) strongly associated with plasma/saliva cotinine,⁴³ might provide an alternative in pregnant smokers. The predictive value of Heaviness of Smoking Index should be tested independently of FTCD because, Heaviness of Smoking Index is part of FTCD.

Both FTCD and CDS-5 were associated with CPD, suggesting they are also measures of baseline consumption.^{1,44–46} Both scales were strongly associated with craving and to less extent with withdrawal scores. This is not surprising for CDS-5 given that the most specific symptom of tobacco withdrawal in the CDS-5 is the “irresistible urge to smoke” item.⁶ Conceivably, the modest correlations between MNWS withdrawal might be attributable to general symptoms of unease (eg, sadness/anxiety) as opposed to nicotine withdrawal. Nevertheless, FTCQ-12 craving and MNWS withdrawal are also strongly correlated at baseline in treatment seekers,²⁷ and pregnant smokers have elevated levels of craving and withdrawal prior to smoking cessation.^{47,48}

Table 4. Results of the Individual Logistic Regressions Predicting Smoking Status 2 Weeks After the Quit Date, Controlling for Treatment

	Odds ratio	Standard error	–95% CI	+95% CI	Wald's chi-square	P
Fagerström Test for Cigarette Dependence (FTCD)	0.10	0.09	–0.07	0.27	1.32	.25
Five-item Cigarette Dependence Scale (CDS-5)	0.07	0.06	–0.05	0.19	1.38	.24
Saliva cotinine	0.05	0.05	–0.06	0.15	0.70	.40
Cigarettes smoked per day (CPD)	0.48	0.41	–0.34	1.29	1.33	.25
Age initiated regular smoking	0.13	0.57	–1.00	1.26	0.05	.82
Previous quit attempts	–0.47	0.26	–0.98	0.04	3.27	.07
FTCQ-12 general craving score	0.02	0.02	–0.01	0.05	1.04	.31
MNWS total withdrawal score	0.19	0.18	–0.16	0.54	1.11	.29

CI = Confidence interval; FTCQ-12 = French Tobacco Craving Questionnaire; MNWS = Minnesota Nicotine Withdrawal Scale.

Table 3. Multiple Regression Summary With Fagerström Test for Cigarette Dependence (FTCD) and Five-Item Cigarette Dependence Scale (CDS-5) Predicting Saliva Cotinine Adjusted for Partner's Smoking

Model	B ^b	Standard error of B	Beta ^c	t (473)	P-level
Saliva cotinine (raw concentration) ^a					
Intercept	78.576	24.967		3.147	.002
CDS-5	1.045	1.767	0.040	0.592	.554
FTCD	12.118	2.537	0.322	4.777	.000
Saliva cotinine (log transformed) ^a					
Intercept	1.82	0.0913		19.604	.000
CDS-5	0.007	0.006	0.071	1.057	.291
FTCD	.039	0.009	0.286	4.323	.000

^aDependent variable.

^bParameter estimate (nonstandardized coefficient).

^cStandardized coefficient.

Figure 1. Receiver operating characteristic (ROC) analyses of the optimized classification models (abstinent vs. nonabstinent) for Fagerström Test for Cigarette Dependence (FTCD) and five-item Cigarette Dependence Scale (CDS-5) among treatment-seeking pregnant smokers 2 weeks after quit date.

As stated by the Society for Research on Nicotine and Tobacco (SRNT) Subcommittee on Biochemical Verification of tobacco use and cessation, “cotinine appears to be the best marker to gauge the severity of dependence”.⁴⁹ We therefore used saliva cotinine concentration as the biomarker most likely associated with cigarette dependence. We found that FTCD was strongly associated with saliva cotinine concentration and CDS-5 was not, suggesting that it is a better measure of cigarette dependence in pregnant smokers than the CDS-5. We also found that FTCD, CDS-5, saliva cotinine, and all smoking-related measures did not predict smoking status 2 weeks after the quit date. Other studies involving nonpregnant smokers and direct comparisons of the CDS-5 and FTCD examining point-prevalence abstinence at 7 days, 14 days, 1 month, and approximately 45 days also have yielded nonsignificant results.^{6,7} Vaz et al.²⁵ reanalyzed data of the SNAP trial (Smoking, Nicotine, and Pregnancy)⁴⁷ and found that at 1 month, cessation rate was greater with more education and lower when saliva/blood cotinine was higher; no other characteristic predicted cessation at 1 month. FTCD, MNWS, or a measure of craving to smoke in predicting cessation at 1 month were not reported. The current findings complete those of Vaz et al.²⁵ with the difference that cessation was assessed at Week 2 and not at 1 month. However, abstinence at 1 month after quit date may better differentiate smoking status than that assessed at 2 weeks, which can explain that baseline cotinine concentration predicted 1-month but not 2-weeks abstinence.

One of the shortcomings of this study is that the randomization visit was scheduled after the grace period, which made it impossible to analyze 2 weeks postquit day data on an intention to treat basis using all included participants. Participants who were included but not randomized started regular smoking at an earlier age, and experienced a greater intensity of withdrawal at enrollment than those who were randomized, factors that had no significant effect on 2-week postquit abstinence assessment. There was no treatment group difference in the FTCD and CDS-5 predictive effect for postquit day abstinence at week 2, suggesting that an intent-to-treat analysis including all included women would have resulted in the same outcomes as we observed here. In addition, Rohsenow et al.⁷ utilized intent-to-treat analyses and obtained similar results.

Similarly, in the initial CDS reliability and validity study,⁶ neither CDS predicted smoking abstinence at follow-up.

In the current study, Area under the curves for 2-weeks smoking status were similar (ie, very low) to those reported by Courvoisier and Etter.¹⁰ However, they found that both CDSs were significant predictors of smoking abstinence at 8-day follow-up and only FTCD was a significant, although poor, predictor of abstinence at the 31-day endpoint. Inconsistent findings across the studies are likely attributable to sample differences, methods of data collection, or a true lack of predictive value of cigarette dependence scales. In both studies,^{6,10} only current cigarette smokers were invited to respond to the internet survey or spontaneously visited the website. Indeed, participants in both samples were more dependent on cigarettes, better educated, and more motivated to quit than smokers in the general population.¹⁰

Pregnant smokers differ in many aspects from the general population of smokers. Despite knowing that smoking during pregnancy is associated with negative pregnancy and birth outcomes, continuing to smoke might indicate increased tobacco dependence. Pregnant smokers might have different frequency and/or intensity of craving to smoke and withdrawal symptoms in response to a quit attempt, either as a consequence of increased nicotine metabolism, or of other pregnancy-related physiological (eg, hormonal), obstetrical, familial, and societal factors. Replication of the present findings is needed to assess the predictive value of these cigarette dependence scales for both short and long-term abstinence among pregnant smokers.

No repeated measurements were collected for the FTCD and CDS-5, thus we were unable to assess test-retest correlations and conditions. Future research should utilize a prospective, longitudinal design to determine whether changes in CDS-5 and FTCD scores are more accurate predictors of smoking status than baseline scores. The sample also reflects populations of French smokers, limiting generality. Although Etter et al.⁶ studied French language smokers in their CDS-5 and FTCD comparisons, results need confirmation using independent samples from other countries, nationalities, languages, and ethnicities to determine generality across clinical populations.

In summary, among treatment-seeking pregnant smokers, FTCD and CDS-5 were correlated as shown in other population of

smokers. Both dependence measures were most strongly related to cigarettes per day, which was not surprising given that CPD makes up a considerable portion of the variance in the measures themselves. The FTCD, but not CDS-5, was significantly associated with saliva cotinine concentration. However, low reliability and failure to predict short-term smoking outcome calls into question the merit of using either measure to investigate obstacles and barriers to smoking cessation in pregnant smokers. Replications are needed and further studies are needed to identify predictors of smoking cessation in this special subpopulation.

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Declaration of Interests

None declared.

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IB and EGS had full access to the data and take responsibility for the data and accuracy of the data analysis. Acquisition of data was done by IB. Study concept and design was provided by IB, EGS, SJH. IB, EGS, and SJH analyzed and interpreted the data. IB, EGS, and SJH drafted the manuscript.

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