



occupational and environmental lung disease

Indirect and Direct Gas Exchange at Maximum Exercise in Beryllium Sensitization and Disease*

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Study objectives: To determine whether pulse oximetry accurately estimates arterial blood gas measurements during exercise in the assessment of chronic beryllium disease (CBD) and beryllium sensitization (BeS).

Design: Participants underwent maximal exercise physiology testing in a clinical-practice setting. Oxygen saturation in the blood was measured through an indwelling arterial line and by pulse oximetry.

Setting: All exercise physiology tests were performed in the pulmonary physiology unit of the National Jewish Medical and Research Center (NJMRC) between December 1985 and November 1998.

Patients: We analyzed the exercise physiology data for 168 individuals who were referred to NJMRC for evaluation of possible CBD and underwent exercise testing. On evaluation, they subsequently received diagnoses of either CBD or BeS.

Results: In BeS subjects, the percentage of oxygen saturation as measured by pulse oximetry (SpO_2) often underestimated the percentage of arterial oxygen saturation (SaO_2) (mean $[\pm SD]$ underestimation, $0.88 \pm 4.6\%$) at maximum exercise and showed no significant correlation ($r = -0.13$; $p = 0.3$). The use of SpO_2 misclassified 14.9% of BeS subjects as having abnormal gas exchange levels ($< 90\%$) that were normal by arterial blood gas measurement. In contrast, SpO_2 and SaO_2 values correlated at maximum exercise in CBD subjects ($r = -0.55$; $p = 0.0001$) without exhibiting SpO_2 underestimation of SaO_2 , and misclassification occurred in only 5.9%.

Conclusions: These data suggest that pulse oximetry cannot be used reliably to distinguish between CBD and BeS and, thus, is not an adequate substitute for arterial blood gas analysis with exercise.

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Key words: arterial blood gas measurements; beryllium sensitization; chronic beryllium disease; pulse oximetry

Abbreviations: BeLPT = beryllium lymphocyte proliferation test; BeS = beryllium sensitization, sensitized; CBD = chronic beryllium disease; NJMRC = National Jewish Medical and Research Center; P(A-a) O_2 = alveolar-arterial oxygen pressure difference; SaO_2 = arterial oxygen saturation; SpO_2 = pulse oxygen saturation; $\dot{V}O_2$ = oxygen uptake; $\dot{V}O_{2max}$ = maximum oxygen uptake; WLM = workload level at maximum exercise

While the noninvasive pulse oximetry measurement is quick and convenient during an exercise physiology test, it has been shown to be unreli-

able in certain clinical conditions.¹⁻⁵ Although maximal exercise testing is considered to be an important indicator of early physiologic abnormalities in patients with interstitial lung disease, there are limited published data addressing the variability of pulse oximetry in clinical practice.^{1,2,6,7} Even less is known about the merits of pulse oximetry in testing for early physiologic derangements due to granulomatous lung disorders.⁸⁻¹⁰

Chronic beryllium disease (CBD) is a lung disorder which produces interstitial granulomas and mononuclear cell infiltrates similar to those seen in other granulomatous lung diseases such as sarcoidosis.¹¹ CBD is preceded by beryllium sensitization

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(BeS), in which individuals display a cellular immune response to beryllium in the blood but no lung abnormality. Specifically, individuals with BeS who have no coexisting lung disorders have normal results for chest radiographs, pulmonary function testing, and exercise tolerance and have no evidence of lung BeS. To determine the relationship of pulse oximetry to arterial blood gas analysis in the clinical setting of granulomatous disease, we studied a population of CBD and BeS subjects, 82% of whom were at stages of early disease, having been identified through workplace surveillance programs. We obtained simultaneous oxygen saturation measurements during an exercise test from each subject both through an arterial line and a pulse oximeter placed on the patient's ear.

We hypothesized that pulse oximetry would accurately estimate and correlate with arterial blood gas measurements of oxygen saturation at rest and at maximum exercise. The purpose of this study was to (1) compare the oxygen saturation measurements taken from an indwelling arterial line to the measurements taken from a pulse oximeter, and (2) to evaluate how arterial blood gas analysis changes during exercise can be used to assess the severity of CBD and potentially differentiate between CBD and BeS.

MATERIALS AND METHODS

Study Population

All subjects were referred to the National Jewish Medical and Research Center (NJMRC) for evaluation of possible CBD. Most of the study population (82%) was identified through the blood beryllium lymphocyte proliferation test (BeLPT) as a part of a workplace medical surveillance program for beryllium-exposed workers. The remainder were referred for clinical evaluation based on respiratory symptoms or abnormal chest radiographs and history of beryllium exposure. On evaluation, subjects subsequently received diagnoses of either CBD or BeS. The CBD subjects were defined as having abnormal results of BAL BeLPTs and histologic evidence of disease in the form of noncaseating granulomas or mononuclear cell infiltrates found on lung biopsy specimens. The BeS subjects were defined as having abnormal results for two blood BeLPTs, but with no confirming abnormal results of BAL BeLPTs and no evidence of granulomas found in biopsy specimens.¹² We excluded only those CBD and BeS patients who were unable to complete an exercise physiology test to maximum exercise and, thus, had no data available. These study subjects originally were evaluated for the purpose of clinical diagnosis and subsequently reevaluated for purposes of both clinical follow-up and research. Some have been subjects of previous publication.^{8,11,12}

Demographic and Smoking Information

We obtained demographic information through a self-administered standardized questionnaire, the results of which are summarized in Table 1. We defined never-smokers, in accordance with the American Thoracic Society standardized respiratory questionnaire,¹³ as having smoked < 20 packs of cigarettes or 12 oz of tobacco in

Table 1—Demographic Information for CBD and BeS Subjects*

Characteristics	BeS (n = 67)	CBD (n = 101)
Age, yr	53 (27–80)	51 (31–78)
Gender		
Male	58	79
Female	9	22
Race		
White, non-Hispanic	57 (85)	83 (82)
White, Hispanic	6 (9)	11 (11)
African American	2 (3)	6 (6)
Asian American	2 (3)	1 (1)
Smoking status†		
Current	19 (28)	12 (12)
Former	22 (33)	43 (43)
Never	26 (39)	46 (45)
Pulmonary characteristics		
DLCO uncorrected	34.3 ± 7.6	31.9 ± 8.6
FEV ₁ , L	3.2 ± 0.9	3.2 ± 0.8
FVC, L	4.3 ± 1.0	4.2 ± 1.1
Abnormal CXR‡	4 (6.4)	44 (44.4)

*Values given as No. (range), No. (%), or mean ± SD.

DLCO = diffusing capacity of the lung for carbon monoxide; CXR = chest radiograph.

†p = 0.026.

‡p < 0.0001.

their lifetime or having smoked < 1 cigarette a day per year. Individuals who exceeded this amount but who stopped at least 1 month prior to the exercise physiology testing were considered to be former smokers. Smoking habits differed between CBD and BeS individuals (p = 0.026). Current tobacco use was more prevalent in BeS individuals, while former and never-smoking habits are more prevalent in CBD individuals.

Pulmonary Characteristics

A complete clinical evaluation was performed of each individual after informed consent was obtained. The basic pulmonary characteristics of the study population are presented in Table 1. Details of testing methods have been previously described.⁸ FVC and FEV₁ were measured with a recording spirometer or pneumotachograph. There were no significant differences in these measures between BeS and CBD subjects. The diffusing capacity of the lung for carbon monoxide was measured using the single-breath method of Ogilvie and coworkers¹⁴ and was not significantly different between BeS and CBD subjects. A certified B reader (a physician who is certified by the National Institute of Safety and Health to read radiographs for changes related to pneumoconiosis according to the International Labour Organization classification system for pneumoconiosis radiographs¹⁵) scored standard posteroanterior chest radiographs. Only 4 of the BeS subjects (6.4%) had chest radiograph abnormalities that potentially were due to Be, while 44 of the CBD subjects (44.4%) had abnormal chest radiograph results that potentially were due to Be exposure (p < 0.0001).

Exercise Physiology Evaluation

After obtaining informed consent approved by our institutional review board, subjects underwent a complete exercise physiology examination using a standard protocol. Exercise physiology tests

were performed in the pulmonary physiology unit at NJMRC between December 1985 and November 1998. Currently, the unit uses a cycle ergometer (Vmax 29; SensorMedics Corporation; Yorba Linda, CA). An indwelling radial arterial line was inserted prior to the exercise test. Baseline measurements were obtained after the patient mounted the bike just before pedaling began. Subjects began pedaling at 60 revolutions per minute with no additional workload for 3 min. Work was then added incrementally every minute with the intent of reaching the subject's maximal exercise capacity within 6 to 12 min.

Arterial blood was withdrawn from the arterial line at baseline and after each minute during exercise. Immediately following the exercise testing, the blood gas samples were analyzed on a blood gas analyzer and a co-oximeter (from 1985 to 1990: Radiometer ADL2 and 282 co-oximeter; Instrumental Laboratory; Lexington, MA; from 1990 to 1998: 1620 pH Blood Gas Analyzer and 682 Co-oximeter; Instrumental Laboratory). The analyzers were calibrated the morning of the test using a two-point calibration sequence control (Instrumental Laboratory). The blood gas analyzer measured PaO₂, which then was used to calculate the alveolar-arterial oxygen pressure difference (P[A-a]O₂) using the alveolar gas equation based on the measured PaO₂, the barometric pressure, and the calculated respiratory quotient.⁸ The co-oximeter measured the percentage of arterial oxygen saturation (SaO₂). In this study, we compared the SaO₂, PaO₂, and P(A-a)O₂ values from arterial blood gas to the oximetry measurements (from 1985 to 1993: model 3740 Bioximeter; Ohmeda; Madison, WI; from 1993 to 1998: Sat-Trak Pulse Oximeter; SensorMedics) and the percentage of oxygen saturation as measured by pulse oximetry (SpO₂), with the oximeter placed on the subject's earlobe after a few seconds of rubbing to improve perfusion to the earlobe.

Statistical Analysis

Pearson correlation coefficients were used to compare the SpO₂ measurements to the arterial blood gas measurements in this cross-sectional analysis. We compared baseline values, maximum exercise values, and the differences between baseline and maximum values for SpO₂, SaO₂, PaO₂, and P(A-a)O₂. Regression analysis was used to compare SpO₂ and SaO₂ values at baseline and at maximum exercise. This line was tested against the identity line (slope = 1; intercept = 0).^{4,6} The methods developed by Bland and Altman¹⁶ also were used to assess the agreement between SaO₂ and SpO₂. The demographic information was compared using either a χ^2 test or Fisher's Exact Test for small sample sizes. An independent Student's *t* test with prior testing for equal variances was performed to assess whether exercise parameters or blood gas analyses differed between CBD and BeS subjects. We used computer software (SAS statistical software package; SAS Institute; Cary, NC) for the analyses. A *p* value of < 0.05 was used to assess statistical significance for all tests. All tests were two-sided.

RESULTS

Pulse Oximetry Compared to Arterial Blood Gas Analysis

Table 2 summarizes the Pearson correlation coefficients for invasive and noninvasive gas exchange variables at baseline and at maximum exercise and the difference between baseline and maximum exercise values by study groups. As expected, SaO₂ correlated with PaO₂ at baseline and at maximum

Table 2—Correlation Among Measures of Gas Exchange in CBD and BeS Subjects*

Variables	SaO ₂ vs PaO ₂	SpO ₂ vs SaO ₂	SpO ₂ vs PaO ₂	SpO ₂ vs P(A-a)O ₂
CBD				
Baseline	0.77†	0.41†	0.39†	-0.24‡
Maximal exercise	0.91†	0.55†	0.52†	-0.51†
Difference§	0.87†	0.55†	0.53†	-0.49†
BeS				
Baseline	0.64†	0.43	0.63†	-0.44
Maximal exercise	0.71†	-0.13	-0.15	-0.07
Difference	0.78†	0.03	-0.15	-0.05

*Values given as correlation coefficients.

†*p* = 0.0001.

‡*p* < 0.05.

§Difference = baseline - maximal exercise.

||*p* < 0.001.

exercise for both CBD subjects (*r* = 0.77 and *r* = 0.91, respectively) and BeS subjects (*r* = 0.64 and *r* = 0.71, respectively). While baseline and maximum exercise SpO₂ measurements for CBD subjects correlated less well with SaO₂ (*r* = 0.41 and *r* = 0.55, respectively), both values are statistically significant (*p* = 0.0001). Similar results were seen for BeS subjects at baseline (*r* = 0.43; *p* = 0.0003), but at maximum exercise BeS subjects showed no correlation between SpO₂ and SaO₂ (*r* = -0.13; *p* = 0.3).

The corresponding regression lines are displayed in Figures 1 and 2. The regression lines for CBD subjects (Fig 1) at baseline and at maximum exercise

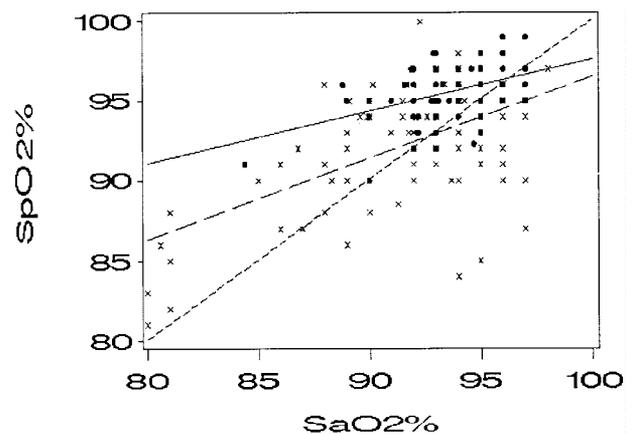


FIGURE 1. Relationship between SaO₂ and SpO₂ at baseline and at maximum exercise for CBD subjects. Solid dot = baseline data point; x = maximum exercise data point. The solid line is a regression line at baseline (SpO₂ = 0.326 × SaO₂ + 65.0; *n* = 101; *p* = 0.0001). The dashed line is the regression line at maximum exercise (SpO₂ = 0.52 × SaO₂ + 44.71; *n* = 101; *p* = 0.001). Both regression lines are significantly different from the dotted identity line (*p* = 0.0001). Due to overlapping data points, a single point may represent between one and nine observations.

both had positive slopes, indicating that although SpO₂ rises as SaO₂ rises, they do not agree with and were significantly different from the line of identity (p = 0.0001). The regression line for BeS subjects (Fig 2) at baseline also had a positive slope that was significantly different from the identity line. The regression line at maximum exercise for BeS subjects had a negative slope. This may, in part, have been a reflection of variability in the data, but it also indicated that pulse oximetry measurements at maximum exercise for BeS subjects resulted in an underestimation of the arterial saturation measurements. In fact, 34 of 67 BeS subjects (50.7%) had SpO₂ measurements that underestimated SaO₂ levels. Among these 34 subjects, the average underestimation at maximum exercise was 4.42%, ranging from 0.2 to 14.0%. Only 37 of 101 CBD subjects (36.6%) had pulse oximetry measurements that underestimated arterial saturation measurements. Among this subgroup, the average underestimation at maximum exercise was 3.53%, ranging from 1 to 13.6%. A plot of the difference between SaO₂ and SpO₂ against their mean, a method developed by Bland and Altman,¹⁶ also was used, and the results agreed with the regression results we have reported above.

Clinical Misclassification Caused by Using SpO₂ Measurements

As a matter of clinical practices, physicians commonly define patients as having abnormal oxygen saturation when their SpO₂ level is < 90%.¹⁷ In our study, by these criteria, 10 of 67 BeS individuals (14.9%) would be considered as having abnormal levels at maximum exercise when in fact all 10 subjects had normal SaO₂ levels of > 90%. Misclassification occurred in only 5.8% of the CBD subjects (p = 0.05).

Possible Confounding Factors

Additional analyses were undertaken excluding smokers and those with abnormal baseline SaO₂ measurements. To determine whether tobacco use contributed to the variable SpO₂ measurements at maximum exercise for BeS subjects, we excluded the current smokers from analysis. The SpO₂ values underestimated SaO₂ at maximum exercise by an average (± SD) of 2.175 ± 4.45% at maximum exercise and still displayed large variability (p = 0.3936). Excluding the 10 BeS subjects with abnormal baseline SaO₂ measurements also did not substantially change the results of the analysis.

Exercise Level

We hypothesized that the SpO₂ underestimated the SaO₂ at maximum exercise for BeS subjects because they achieved a higher level of exercise than did CBD subjects. To evaluate the relationship between exercise level and the underestimation of SaO₂ by SpO₂, we compared their workload levels at maximum exercise (WLMs) and oxygen uptake at maximum exercise ($\dot{V}O_{2max}$) (Table 3). WLM values were higher in BeS subjects (p = 0.10). On average, BeS subjects tended to have higher $\dot{V}O_{2max}$ levels compared to CBD subjects (p = 0.10). The percent predicted of $\dot{V}O_{2max}$ was significantly lower in CBD subjects compared to BeS subjects (p = 0.02). We analyzed efficiency, as defined by the WLM divided by the $\dot{V}O_{2max}$,¹⁸ and found that CBD subjects were slightly less efficient than BeS subjects while also having a lower respiratory quotient at maximum exercise (data not shown). In BeS subjects, SpO₂ at maximum exercise underestimated SaO₂ at maximum exercise (p = 0.08). This underestimation became statistically significant after the BeS-abnormal group was excluded from the analysis (p = 0.003). Regardless of disease status, those individuals who would be misclassified by their SpO₂ results (*ie*, SpO₂ < 90% while SaO₂ > 90% or vice versa) tended to have higher $\dot{V}O_{2max}$ values and had significantly higher WLM values (p = 0.03).

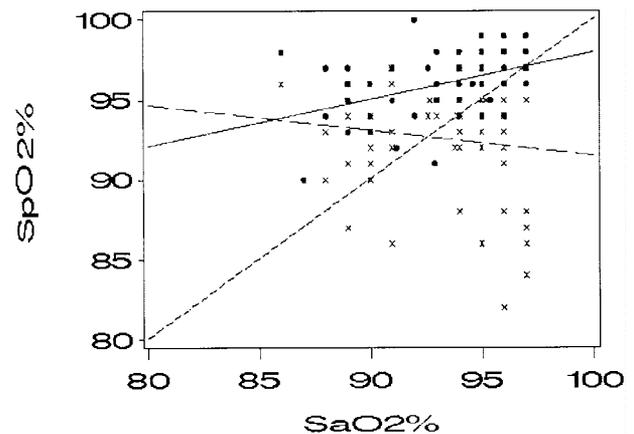


FIGURE 2. Relationship between SaO₂ and SpO₂ at baseline and at maximum exercise for BeS subjects. Solid dot = baseline data points; x = maximum exercise data points. The solid line is regression line at baseline (SpO₂ = 0.294 × SaO₂ + 68.54; n = 67; p = 0.0003). The dashed line is the regression line at maximum exercise (SpO₂ = -0.11 × SaO₂ + 83.34; n = 67; p = 0.2856). Both regression lines are significantly different from the dotted identity line (p = 0.0001). Due to overlapping data points, a single point may represent between one and five observations.

Table 3—Exercise Level of CBD vs BeS Subjects*

Variables	CBD (n = 101)	BeS (n = 67)	p Value†
SpO ₂			
Baseline	95.5 ± 1.6	96.1 ± 1.9	0.06
ME	92.3 ± 3.9	92.6 ± 3.4	0.66
SaO ₂			
Baseline	93.7 ± 2.0	93.5 ± 2.8	0.59
ME	92 ± 4.0	93.5 ± 2.8	0.009
PaO ₂			
Baseline	73.4 ± 6.7	73.7 ± 7.6	0.84
ME	71.7 ± 11.6	77.8 ± 9.3	0.0004
P(A-a)O ₂			
Baseline	7.9 ± 5.0	7.3 ± 5.2	0.45
ME	20.8 ± 10.6	15.3 ± 7.1	< 0.0001
WLM, W	160 ± 55	174 ± 48	0.1
VO ₂ max			
mL/min	1,889 ± 530	2,032 ± 563	0.1
% predicted	79.98 ± 18.7	86.94 ± 20.4	0.02

*Values given as mean ± SD, unless otherwise indicated.
ME = maximum exercise.

†p values indicate independent *t* test result with prior testing of equal or unequal variances (CBD vs BeS).

Use of Maximum Exercise to Determine Extent of Disease Severity

We tested the hypothesis that a change in arterial blood gas measurements between baseline and maximum exercise can be used to differentiate between CBD and BeS subjects (Table 4). The CBD subjects demonstrated a mean decrease in SaO₂ of 1.7 ± 3.4%, which was significantly different (*p* = 0.0001) from the change exhibited by BeS subjects with exercise (mean, 0.07 ± 1.4%). The PaO₂ tended to increase for BeS subjects, as it often does in individuals without disease,^{19–24} while CBD subjects did not exhibit the same increase (*p* = 0.0001). The CBD subjects had a wider P(A-a)O₂ at maximum exercise than did BeS subjects (*p* = 0.0001). However, no difference was detected by pulse oximetry between CBD and BeS (*p* = 0.65).

DISCUSSION

Pulse oximetry is commonly used to estimate SaO₂. However, little is known about the degree to which

such indirect measures reflect arterial blood gas results in subjects with granulomatous lung disorders in clinical practice. We observed only moderate correlation between SpO₂ and direct arterial blood gas measurements in CBD subjects. Furthermore, we found that pulse oximetry underestimated the measured SaO₂, is highly variable in BeS subjects, and often misclassifies a subject as having abnormal (*ie*, < 90%) gas exchange when in fact they do not. We found that maximum exercise testing differs in subjects with early stages of CBD and those with BeS who do not have disease. Specifically, BeS subjects tend to achieve higher WLMs and VO₂max, and have blood gas changes with exercise much like healthy individuals.^{19–24}

In a meta-analysis, Jensen et al¹ considered 169 trials comparing SpO₂ measurements to those for SaO₂ and used 74 of those studies in which the study subjects ranged from ICU patients to high-performance athletes. The studies that analyzed the relationship of SpO₂ to arterial blood gas measurements using correlation coefficients found that the lowest weighted correlation was 0.760. Another study⁴ found correlations consistently of > 0.90. These correlations are notably higher than any found in our study. There may be several explanations for this discrepancy. Our data were collected from patients in a clinical hospital setting not in an experimental, controlled setting. The majority of the published literature on this subject has been based on prospective controlled data collection.¹ Thus, our experience suggests that measures of SpO₂ in clinical practice do not reflect SaO₂ values as accurately as those in controlled prospective experiments. By convention, we picked each patient's first exercise physiology test at NJMRC in order to create a cross-sectional design for data analysis purposes. The 168 subjects in our study were tested over a long period of time (December 1985 to November 1998). Over this period, our center has updated equipment and changed personnel, as might be expected in a clinical setting. We found no obvious changes in our data corresponding in time to specific facility or equipment changes, suggesting that over time our exercise

Table 4—Gas Exchange From Baseline to Maximum Exercise in CBD and BeS Subjects*

Variables	CBD (n = 101)	BeS (n = 67)	BeS, SaO ₂ ≥ 90% (n = 57)	p Value†
Arterial line measurements				
SaO ₂	1.7 ± 3.4	0.07 ± 1.4	0.2 ± 1.4	0.0001
PaO ₂	1.8 ± 10.4	-4.1 ± 7.4	-4.3 ± 7.8	0.0001
P(A-a)O ₂	-12.9 ± 9.0	-8.0 ± 6.3	-8.1 ± 6.25	0.0001
Pulse oximetry measurement				
SpO ₂	3.2 ± 3.9	3.5 ± 3.4	3.8 ± 3.4	0.65

*Values given as mean ± SD, unless otherwise indicated.

†p value indicates independent *t* test result with prior testing of equal or unequal variances (CBD vs BeS).

physiology tests were performed uniformly. While a high degree of correlation can be achieved under ideal experimental conditions, in clinical practice, SpO₂ may not prove to be as reliable.

The limits of exercise in healthy individuals and highly trained athletes are determined by the ability of the cardiovascular system to continue to provide oxygen to the tissue, which commonly results in reduced peripheral perfusion.^{2,5,21} Reduced perfusion has been shown to cause pulse oximetry readings to underestimate arterial blood gas measurements.^{1,3,5,24} Because BeS subjects were in better cardiovascular condition with higher raw and percent predicted $\dot{V}O_{2\max}$ values, we speculated that the variability and underestimation seen in BeS subjects at peak exertion may be the result of decreased peripheral perfusion, as has been demonstrated in individuals who are capable of reaching such exercise levels.^{1,5} BeS subjects not only have increased $\dot{V}O_{2\max}$ percent predicted and workloads but also show a decreased ability to increase $\dot{V}O_{2\max}$ with increasing workloads, suggesting a cardiovascular, not a ventilatory, limitation to exercise.^{2,19,24,25} We speculate that our BeS subjects are more likely than CBD subjects to experience reduced perfusion at maximum exercise, which would explain the underestimation.

Because all of our subjects exercised on a cycle ergometer, we used an ear probe for pulse oximetry analysis. In the meta-analysis referred to earlier, it was concluded that finger oximetry may be superior to ear oximetry when poor perfusion is anticipated.¹ Problems with the pulse oximeter during decreased perfusion states might be avoided by placing the oximeter on the patient's finger; however, the finger probe often gets in the way during exercise on an ergometer.⁶ While correlations between SpO₂ measurements and direct measures of arterial blood gases might be better when finger oximeters are used, our data cannot be used to directly test this hypothesis.

Since many of our CBD subjects and BeS subjects were detected through medical surveillance, we are evaluating them in the very earliest stages of CBD and BeS.⁸ It is often necessary to have such individuals undergo exercise testing in order to detect early physiologic differences in the clinical evaluation of patients with CBD and BeS.⁸⁻¹⁰ These results are consistent with those of previous articles on CBD.^{8,26} However, to our knowledge, this is the first report to show that exercise physiology may help to distinguish BeS from CBD. Much like in healthy individuals, arterial blood gas measurements did not decrease significantly during exercise in our BeS subjects.^{22,23} Their oxygen saturation at baseline is 93.52%, and at maximum exercise it is 93.45%. Our 101 CBD

subjects, however, exhibit a decline in saturation of nearly 2% on average (range, 93.73 to 92.04%) and a fall in PaO₂ and a rise in P(A-a)O₂ during exercise, which is consistent with other reports^{8,14,18,25} of exercise physiology for individuals with restrictive and/or obstructive pulmonary diseases. However, pulse oximetry cannot be used to distinguish between CBD and BeS subjects in our data ($p = 0.65$). Due to the high variability in pulse oximetry measurements with exercise and to the risk of misclassification, arterial blood gas measurements are preferred in assessing CBD and BeS subject status.

While tobacco smoking can affect the accuracy of pulse oximetry, Brown et al⁵ have suggested that differences between pulse oximetry and arterial blood gas analysis in smokers should be consistent, regardless of workload. Although our BeS subjects were more likely to be current smokers, tobacco use among BeS subjects did not appear to play a role in this underestimation. When we analyzed the non-smoking BeS subjects alone, we showed an even greater negative slope, again indicating that the healthiest individuals are the ones contributing to the poor correlations seen at maximum exercise. In addition, the 70 CBD and levels in BeS subjects in whom SpO₂ underestimated SaO₂ did not differ in their smoking status ($p = 0.29$). In fact, only 13% of those whose values were underestimated were current smokers, compared to 18.5% for the entire cohort.

In conclusion, while pulse oximetry is a convenient way of estimating oxygen saturation, these data must be interpreted with caution. In clinical practice, the correlations of SpO₂ with direct measures of PaO₂ and SaO₂ are less robust than previously reported and may lead to significant underestimates and variable results. On clinical evaluation, the use of SpO₂ risks misclassifying levels in BeS subjects as abnormal (*ie*, SpO₂ < 90%), when, in fact, their arterial blood gas levels are normal. While the risk of clinical misclassification is lower in the CBD group, if clinicians rely solely on SpO₂, they can mistakenly tell patients that they are hypoxemic when they are not. However, arterial blood gas results in exercise testing are useful in assessing BeS and CBD and may differentiate the two conditions. Patients with disease show poorer gas exchange and exercise tolerance. In conclusion, we would not recommend replacing arterial blood gas measurements during exercise with finger pulse oximetry.

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