# Multi-Wavelength Pulse Oximeter Is Not Suitable for Adjusting $D_{LCO}$ Measurements

Gregg L Ruppel MEd RRT RPFT FAARC, Holly A Wilson RPFT, Vanessa K Gall RRT CPFT, and John A Hempkens BSRT RRT

**BACKGROUND: Diffusing capacity of the lung for carbon monoxide ($D_{LCO}$) can be affected by abnormal hemoglobin (Hb) or carboxyhemoglobin (COHb) levels. Predicted $D_{LCO}$ can be adjusted to reflect abnormal Hb or COHb levels. Until recently, blood sampling was required to determine Hb and COHb levels, but a new pulse oximeter, the Masimo RAD-57, can measure Hb and COHb noninvasively. We hypothesized that there would be no significant difference between the invasive and noninvasive Hb and COHb measurements for adjusting $D_{LCO}$. METHODS: In patients referred to our university hospital for $D_{LCO}$ testing, we simultaneously took arterial blood gas samples and measured Hb and COHb with the RAD-57 (SpHb and SpCOHb, respectively). We analyzed the paired values and the Hb-adjusted and COHb-adjusted predicted $D_{LCO}$ values with *t* tests and Bland-Altman plots. We compared the differences in predicted $D_{LCO}$ to a clinical threshold of 3 mL/min/mm Hg. RESULTS: SpHb differed from Hb measured via arterial blood analysis (12.1 ± 2.4 g/dL vs 13.3 ± 2.1 g/dL, $P < .001$). SpCOHb did not differ significantly from COHb (ie, measured via arterial blood analysis) (2.1 ± 4.0 vs 2.5 ± 2.3, $P = .25$), but there was wide variability. There were small but statistically significant differences in the adjusted predicted $D_{LCO}$, depending on whether blood or pulse oximetry values were used. Predicted $D_{LCO}$ adjusted for both Hb and COHb was 22.5 ± 4.8 mL/min/mm Hg measured with the RAD-57 and 23.5 ± 4.5 mL/min/mm Hg via arterial blood analysis ($P < .001$). The limits of agreement for pulse oximetry adjusted $D_{LCO}$ exceeded the clinical threshold of 3 mL/min/mm Hg for Hb adjustments and combined Hb + COHb. Predicted $D_{LCO}$ values differed by > 3 mL/min/mm Hg in 17% of patients. CONCLUSIONS: Pulse oximetry may be of limited usefulness for adjusting either predicted or measured $D_{LCO}$ values, but might be useful to screen patients for invasive testing, particularly if the $D_{LCO}$ is close to the lower limit of normal.** *Key words: diffusing capacity; pulse oximetry; arterial blood analysis; hemoglobin; carboxyhemoglobin; predicted values; lung function tests.* [Respir Care 2011; 56(8):1115–1121. © 2011 Daedalus Enterprises]

## Introduction

Diffusing capacity of the lung for carbon monoxide ($D_{LCO}$) can be affected by the patient's hemoglobin (Hb) concentration and by back-pressure from carbon monoxide in the blood and an "anemia" effect of CO bound to Hb (carboxyhemoglobin [COHb]) at the time of testing.[1] The American Thoracic Society/European Respiratory Society guidelines for $D_{LCO}$ testing with the single-breath method recommend adjusting all reported $D_{LCO}$ for the effects of Hb and COHb, for interpreting the results.[2] Earlier guidelines suggested adjusting the measured $D_{LCO}$ with the equations of Cotes et al[3] for Hb and an empirical equation that

Mr Ruppel, Ms Wilson, and Ms Gall are affiliated with the Pulmonary Function Laboratory, Pulmonary, Critical Care, and Sleep Medicine Department; and Mr Hempkens is affiliated with the Respiratory Care Department, St Louis University Hospital, St Louis, Missouri.

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Correspondence: Gregg L Ruppel MEd RRT RPFT FAARC, Pulmonary Function Laboratory, Pulmonary, Critical Care, and Sleep Medicine Department, Saint Louis University Hospital, 3635 Vista Avenue, St Louis MO 63110-0250. E-mail: ruppelgl@slu.edu.

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increases $D_{LCO}$ in proportion to the elevation of COHb above 2%.[2] The 2005 guidelines suggest adjusting the predicted $D_{LCO}$ as a more appropriate method to gauge the effects of abnormal Hb or COHb levels on diffusing capacity. These adjustments, whether applied to the measured or predicted $D_{LCO}$, require an accurate Hb and COHb measurement from arterial or venous blood obtained near the time of $D_{LCO}$ testing.

A new multi-wavelength pulse oximeter, the RAD-57 (Masimo, Irvine, California) can noninvasively measure total Hb (SpHb) and carboxyhemoglobin (SpCOHb). We investigated the use of SpHb and SpCOHb for adjusting $D_{LCO}$, which could obviate drawing blood and the associated risks and discomfort. We hypothesized that there would be no significant differences between the Hb and COHb values from the RAD-57 and from arterial blood analysis.

## Methods

This study was approved by the institutional review board of St Louis University.

### Patients

We enrolled consecutive patients referred to our university hospital pulmonary function laboratory for pulmonary function studies with $D_{LCO}$ and arterial blood gas measurement. All subjects gave informed consent. We recorded age, height, and sex, and used the equations of Gaensler and Wright to calculate predicted $D_{LCO}$.[4]

### Arterial Blood Sampling and Analysis

Blood samples were obtained via radial artery puncture, with the patient seated in a blood drawing chair. Each blood specimen was analyzed within 5 minutes (RapidPoint 405, Siemens Healthcare Diagnostics, Deerfield, Illinois). The blood gas analyzer was monitored daily with 3 control levels, which included oximetry values. We report total Hb in g/dL, and COHb as a percentage of Hb.

### Pulse Oximetry

Pulse oximetry measurements were made with the Masimo RAD-57. We purchased 18 new RAD-57s for clinical use in our center, and randomly selected 3 of them for this study. Because separate sensors are required for measurement of SpHb and SpCOHb, we used 2 RAD-57s simultaneously: one with an Hb sensor, and one with a COHb sensor. The third RAD-57 was kept as a back-up, and the 3 RAD-57s were used interchangeably. The sensors were applied to 2 fingers of the opposite hand from which the blood sample was obtained. The oximetry readings were allowed to stabilize, and SpHb and SpCOHb were recorded at the time the arterial sample was obtained. The RAD-57 reports SpCOHb as an integer percentage. We observed for and recorded pulse oximeter warnings, failure to display data, and patient conditions (eg, nail polish) that might compromise the oximetry measurements.

### $D_{LCO}$ Adjustments

Each patient's predicted $D_{LCO}$ was adjusted with the following equations:

Hemoglobin:

Male: Adjusted predicted $D_{LCO}$ = Predicted $D_{LCO} \times (1.7\ Hb/(10.22 + Hb))$

Female: Adjusted predicted $D_{LCO}$ = Predicted $D_{LCO} \times (1.7\ Hb/(9.38 + Hb))$

Carboxyhemoglobin:

Adjusted predicted $D_{LCO}$ = Predicted $D_{LCO} \times (102\% - COHb\%)$

### Data Analysis

We compared the Hb and COHb values to the SpHb and SpCOHb values with paired *t* tests and Bland-Altman difference plots.[5,6] Bias was defined as the mean difference between the measurements, and error (precision) was defined as the standard deviation of the differences. We defined the limits of agreement between the measurement methods as $\pm$ 1.96 SD around the mean difference. *P* values $< .05$ were considered significant. We also used Bland-Altman plots to compare the predicted $D_{LCO}$ values adjusted with arterial blood analysis (Hb and COHb) to the $D_{LCO}$ values adjusted with the RAD-57 values (SpHb and SpCOHb). If a pulmonary function technologist comment suggested questionable data (eg, low perfusion alarm, no result displayed), the result was considered an outlier and not included in the data analysis. We considered it a clinically important difference if the difference between the arterial-blood adjusted and pulse-oximetry adjusted predicted values was $>$ 3 mL/min/mm Hg.

## Results

Table 1 describes the 149 subjects. Data from 10 subjects were excluded as outliers because of pulse oximeter warnings, or failure of the pulse oximeter to stabilize and display data. Table 2 shows the total Hb, COHb, and adjusted predicted $D_{LCO}$ values. There was a small but significant (via paired *t* test) difference between Hb and SpHb. The difference between COHb and SpCOHb was not significant because of the wide variability of the measurements. Figures 1 and 2 show the scatter of values for Hb and SpHb, and COHb and SpCOHb, respectively. When

Table 1. Subjects

| | |
|---|---|
| Patients, no. | 139* |
| Age (y) | 56 ± 11 |
| Male (%) | 64 |
| White (%) | 76 |
| Unadjusted predicted $D_{LCO}$ (mL CO/min/mm Hg) | 24.3 ± 4.4 |

± values are mean ± SD.
* Ten patients were excluded because of pulse oximeter warning or failure to display data.
$D_{LCO}$ = diffusing capacity of the lung for carbon monoxide

Table 2. Hemoglobin, Carboxyhemoglobin, and Adjusted Predicted $D_{LCO}$ Values

| | Arterial Blood Analysis (mean ± SD) | RAD-57 Measurement (mean ± SD) | *P** |
|---|---|---|---|
| Total Hb (g/dL) | 13.4 ± 2.1 | 12.1 ± 2.4 | < .001 |
| COHb (%) | 2.5 ± 2.3 | 2.1 ± 4.0 | .25 |
| Predicted $D_{LCO}$ (mL/min/mm Hg) | | | |
| Hb adjusted | 23.6 ± 4.6 | 22.5 ± 4.6 | < .001 |
| COHb adjusted | 24.2 ± 4.4 | 24.3 ± 4.7 | .07 |
| Hb + COHb adjusted | 23.5 ± 4.5 | 22.5 ± 4.8 | < .001 |

* Via 2-tailed paired *t*-test.
$D_{LCO}$ = diffusing capacity of the lung for carbon monoxide
Hb = hemoglobin
COHb = carboxyhemoglobin

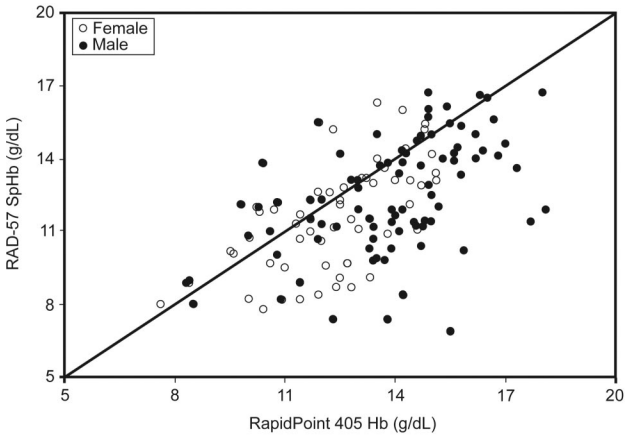


Fig. 1. Scatter plot of hemoglobin (Hb) measured with the RapidPoint 405 blood analyzer versus the RAD-57 pulse oximeter (SpHb). The solid line is the line of identity.

the predicted $D_{LCO}$ was adjusted with the 2 methods, there were small but significant differences for the Hb and combined Hb + COHb adjusted values (see Table 2).

Table 3 shows the bias, error (precision), and limits of agreement for the Hb, COHb, and adjusted predicted $D_{LCO}$ values. There was a slight negative bias for both Hb and

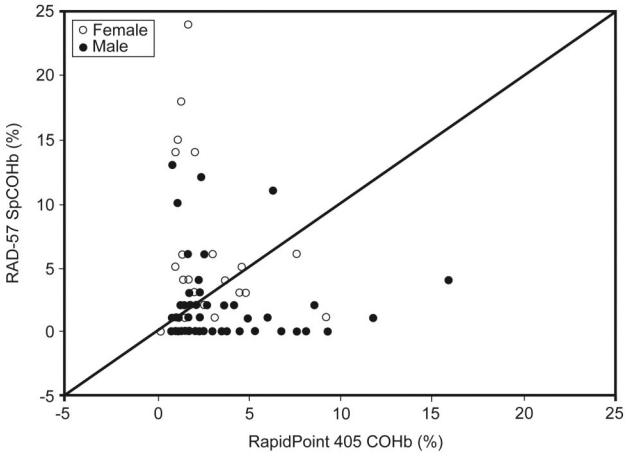


Fig. 2. Scatter plot of carboxyhemoglobin (COHb) measured with the RapidPoint 405 blood analyzer versus the RAD-57 pulse oximeter (SpCOHb). The solid line is the line of identity.

Table 3. Bias, Error, and Limits of Agreement

| | Bias | Error | Limits of Agreement |
|---|---|---|---|
| Hb vs SpHb (g/dL) | –1.26 | 2.15 | 2.95 to –5.48 |
| COHb vs SpCOHb (%) | –0.39 | 3.98 | 7.41 to –8.20 |
| Predicted $D_{LCO}$ (mL/min/mm Hg) | | | |
| Hb adjusted | –1.11 | 2.01 | 2.82 to –5.04 |
| COHb adjusted | 0.14 | 0.88 | 1.86 to –1.58 |
| Hb + COHb adjusted | –0.95 | 2.20 | 3.37 to –5.26 |

Hb = hemoglobin
$D_{LCO}$ = diffusing capacity of the lung for carbon monoxide
SpHb = hemoglobin measured with the Masimo RAD-57 oximeter
COHb = carboxyhemoglobin
SpCOHb = carboxyhemoglobin measured with the Masimo RAD-57 oximeter

COHb (arterial blood analysis > pulse oximetry). Figures 3 and 4 show the Bland-Altman plots of the differences between the RAD-57 and RapidPoint 405 measurements versus the averages of the 2 instruments. Figures 5, 6, and 7 show the bias and limits of agreement between the 2 methods when $D_{LCO}$ was adjusted for Hb, COHb, and Hb + COHb. The shaded areas in Figures 5, 6, and 7 represent the clinical threshold of 3 mL/min/mm Hg centered around a difference of zero. For Hb adjustments the upper limit of agreement was within the clinical threshold, but the lower limit exceeded the threshold by approximately 2 mL/min/mm Hg. The results were similar for the combined Hb + COHb adjustments. The limits of agreement were well within the ± 3 mL/min/mm Hg threshold when the predicted $D_{LCO}$ was adjusted only for COHb.

Of the 139 patients, 23 (17%) had adjusted $D_{LCO}$ values that differed by > 3 mL/min/mm Hg when the RAD-57

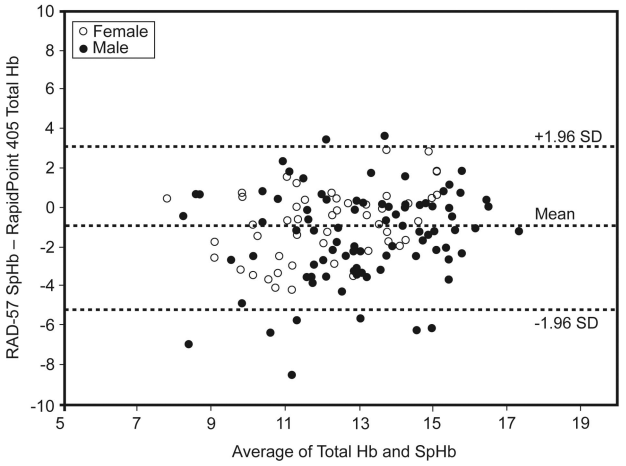


Fig. 3. Bland-Altman plots of hemoglobin (Hb) measured with the RapidPoint 405 blood analyzer versus the RAD-57 pulse oximeter (SpHb). The dashed lines represent the mean and limits of agreement (± 1.96 SD).

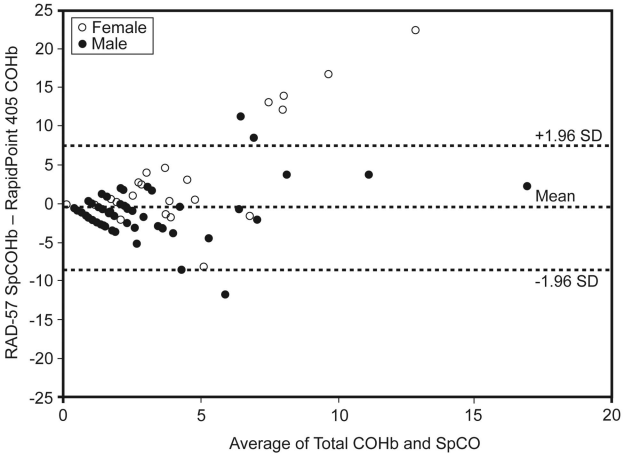


Fig. 4. Bland-Altman plots of carboxyhemoglobin (COHb) measured with the RapidPoint 405 blood analyzer versus the RAD-57 pulse oximeter (SpCOHb). The dashed lines represent the mean and limits of agreement (± 1.96 SD). The RAD-57 reports SpCOHb values as integer percentages, which fall along straight lines when plotted against the COHb values, which are reported to one decimal place.

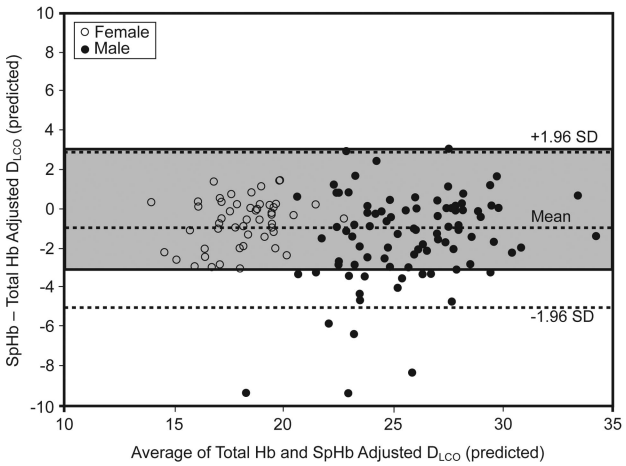


Fig. 5. Bland-Altman plot of diffusing capacity of the lung for carbon monoxide ($D_{LCO}$) adjusted with hemoglobin (Hb) values from the RapidPoint 405 blood analyzer versus the RAD-57 pulse oximeter (SpHb). The dashed lines represent the mean and limits of agreement (± 1.96 SD). The shaded area represents our defined threshold of clinical importance (± 3 mL/min/mm Hg).

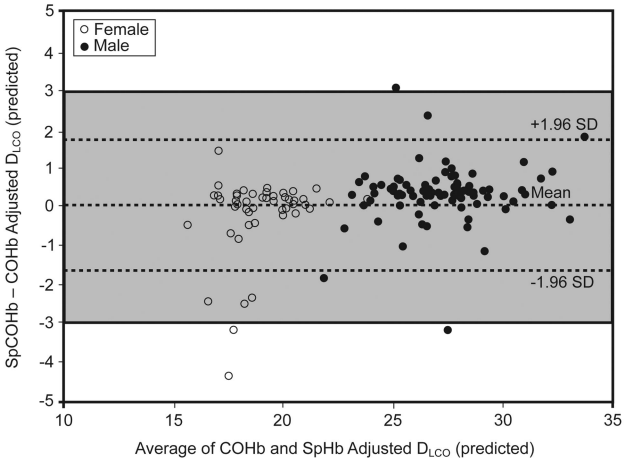


Fig. 6. Bland-Altman plot of diffusing capacity of the lung for carbon monoxide ($D_{LCO}$) adjusted with carboxyhemoglobin (COHb) values from the RapidPoint 405 blood analyzer versus the RAD-57 pulse oximeter (SpCOHb). The dashed lines represent the mean and limits of agreement (± 1.96 SD). The shaded area represents our defined threshold of clinical importance (± 3 mL/min/mm Hg).

value was used (Table 4). Of these, 19 (14%) differed because of Hb, and 4 (3%) differed because of COHb.

## Discussion

There was a small but statistically significant difference when the predicted $D_{LCO}$ was adjusted with the RAD-57 values, compared to the arterial blood analysis values. For the Hb measurements there was a small negative bias (arterial blood analysis > pulse oximetry) in addition to significant error, expressed as the SD of the differences. There was poor correlation between Hb measured by the RAD-57 versus via arterial blood analysis (see Fig. 1). The COHb and SpCOHb measurements were not statistically different, but there was wide variability (see Fig. 2).

When the Hb and SpHb measurements were used to adjust the predicted $D_{LCO}$, the RAD-57 underestimated the adjusted value by approximately 1 mL/min/mm Hg. The limits of agreement between the 2 methods, however, were approximately 4 mL/min/mm Hg, which is slightly greater than the clinical threshold of 3 mL/min/mm Hg, based on the acceptable within-session variability for $D_{LCO}$.[2] Ad-

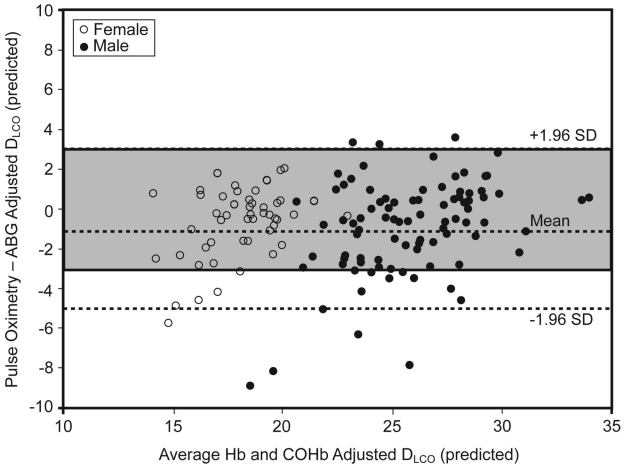


Fig. 7. Bland-Altman plot of diffusing capacity of the lung for carbon monoxide ($D_{LCO}$) adjusted with both hemoglobin (Hb) and (COHb). The dashed lines represent the mean and limits of agreement (± 1.96 SD). The shaded area represents our defined threshold of clinical importance (± 3 mL/min/mm Hg).

Table 4. Subjects in Whom Adjusted Predicted $D_{LCO}$ Differed by > 3 mL/min/mm Hg ($n$ = 139)

| $D_{LCO}$ Adjusted With | No. | Percent |
|---|---|---|
| Hb | 19 | 14 |
| COHb | 4 | 3 |
| Hb + COHb | 23 | 17 |

$D_{LCO}$ = diffusing capacity of the lung for carbon monoxide
Hb = hemoglobin
COHb = carboxyhemoglobin

justments to predicted $D_{LCO}$ based on the COHb measurements were similar despite some large differences between individual samples. This is partly explained by the equation used for COHb adjustment (see the Methods section). The limits of agreement for adjusting the predicted $D_{LCO}$ for COHb were approximately one half of the clinical threshold of 3 mL/min/mm Hg.

When predicted $D_{LCO}$ was adjusted for both Hb and COHb, there was a negative bias (arterial blood analysis > pulse oximetry) and the limits of agreement were approximately 4 mL/min/mm Hg, due primarily to the Hb differences. This suggests that the noninvasive measurement may not be a suitable alternative for adjusting $D_{LCO}$, if a threshold of 3 mL/min/mm Hg is considered clinically important. Some statisticians suggest that the limits of agreement should be ≤ 0.5 times the coefficient of variation.[7] Of the 139 subjects, 23 (17%) had a difference > 3 mL/min/mm Hg between their predicted $D_{LCO}$ values. These results suggest that our null hypothesis should be rejected.

Jou et al[8] reported (in abstract) a mean ± SD bias of 0.18 ± 1.10 g/dL in a comparison of the RAD-57 and the i-STAT handheld blood gas analyzer. Lamhaut et al[9] reported (in abstract) a mean ± SD bias of 0.26 ± 1.11 g/dL in a comparison of the RAD-57 and an unnamed laboratory blood gas analyzer. Torp et al[10] reported (in abstract) a mean ± SD bias of 0.2 ± 0.8 g/dL in a comparison of the RAD-57 and a laboratory blood gas analyzer that incorporates oximetry (Nova Biomedical). Each of those investigations considered the utility of trend versus intermittent monitoring as well as the accuracy and precision of the device.

Chung and co-workers[11] compared the RAD-57 to a laboratory spectrophotometer and found a correlation coefficient of 0.814 for 217 paired samples, but they did not calculate the bias or precision (error), as is usually recommended for method comparisons. Allard et al[12] reported (in abstract) the results of 335 paired samples in subjects whose Hb levels were experimentally reduced with phlebotomy. They found a bias of −0.15 g/dL (pulse oximeter vs laboratory analysis) and an error of 0.92 g/dL. Our results in the present study show a higher bias and error, perhaps related to the comparative method we used (ie, the RapidPoint 405).

Carbon monoxide poisoning is the most common type of fatal poisoning in the United States, with an estimated 500 unintentional deaths and 15,000 emergency department visits annually.[13] Not all hospitals in the United States have the ability to measure COHb via arterial blood analysis. Several authors have reported the utility of monitoring CO via pulse oximetry in the emergency department. Piatkowski et al[14] reported a mean error of 3.15% in patients who had CO poisoning when the pulse oximeter was compared to arterial blood analysis. In their patients whose COHb was > 10%, the bias and error (precision) were 3.4% and 2.4%, respectively. That error was only slightly greater than when different blood gas analyzers were compared. Coulange et al[15] reported a bias of 1.5% for COHb (pulse oximeter > arterial blood analysis) in a cohort of emergency department patients with suspected CO poisoning. Barker et al studied induced carboxyhemoglobinemia in a small group of healthy volunteers and found a bias of −1.22% and a precision of 2.19% with the RAD-57.[16] In a letter to the editor, O'Malley[17] reported a high rate of false positive findings (pulse oximetry > arterial blood analysis), and terminated a prospective study because of the inconsistencies. The present study found a somewhat smaller bias (0.50%), but with an error of 3.43%. However, the manufacturer's specifications for accuracy are ± 3% for COHb levels from 1% to 40%.

When considering whether one method can be substituted for another, both the bias and error (precision) must be considered. If the bias is constant (ie, does not change with the magnitude of the measurement), it may be cor-

Table 5. Example of Adjusting Measured Versus Predicted $D_{LCO}$*

| | Measured | Predicted | % Predicted |
|---|---|---|---|
| Unadjusted $D_{LCO}$† | 21.0 | 30.0 | 70 |
| Measured $D_{LCO}$ adjusted | 23.3 | 30.0 | 78 |
| Predicted $D_{LCO}$ adjusted | 21.0 | 27.0 | 78 |
| Difference | 2.3 | 3.0 | 8 |

* In a male patient with a hemoglobin (Hb) of 11.5 g/dL.
† $D_{LCO}$ = diffusing capacity of the lung for carbon monoxide, reported in mL/min/mm Hg.

rected by addition or subtraction. Of somewhat greater importance is whether the limits of agreement (1.96 × SD of the differences) exceed a clinically acceptable threshold. We defined the threshold as 3 mL/min/mm Hg, and deemed that reasonable because it is also the within-session limit of variability for $D_{LCO}$ measurements. Any factor (such as Hb or COHb adjustment) that might change the predicted value by > 3 mL/min/mm Hg could be considered clinically important. Changes of this magnitude would be of greatest concern when the patient's $D_{LCO}$ is near the lower limit of normal and hemoglobinopathies need to be ruled out.

Applying Hb or COHb adjustment factors to a patient's measured $D_{LCO}$ produces the same result when expressing the variable as a percent of predicted. Table 5 shows an example, in which the patient has an unadjusted $D_{LCO}$ of 70% of predicted. In this example the patient is a moderately anemic male (Hb 11.5 g/dL), so an adjustment factor of 0.90 might be used, as a multiplier to adjust the predicted value, or as a divisor to adjust the measured value. In either case the patient's percent-of-predicted $D_{LCO}$ becomes 78%. However, in terms of an absolute change, the measured value changed by < 3 mL/min/mm Hg. We derived the limits of agreement from adjustments applied to the predicted value as a more conservative comparison to the fixed clinical threshold of 3 mL/min/mm Hg.

## Limitations

The RAD-57 SpHb sensor requires several minutes to stabilize and produce a reading. In some instances, the pulse oximeter reading was changing as the arterial blood sample was being obtained. It is possible that a longer stabilization period might have given a different bias and error. The SpCOHb sensor stabilized much more quickly. We used several different sensors and 3 RAD-57s (one for SpHb, one for SpCOHb, and one as a back up), which probably reflects what would happen in clinical practice, but the bias and error values we found reflect the characteristics of those 3 RAD-57s and might not be generalizable to all instruments. The comparison instrument (RapidPoint 405) was evaluated on each measurement day, with 3 levels of blood gas controls, that included oximetry. And the RapidPoint 405 performed acceptably on 2 proficiency testing challenges during the data-collection period. Other comparison blood oximeters or Hb analyzers might produce slightly different results.

## Conclusions

Although our findings suggest that pulse oximetry should not be used in place of invasive measurements, there may be clinical utility in checking SpHb and SpCOHb in the context of $D_{LCO}$ testing. Noninvasive screening for extreme Hb or COHb values may be useful to guide whether a blood sample is needed. For patients who have abnormal screening results, an invasive measurement can be performed to allow appropriate adjustments for interpretive purposes. Clinically important differences in the predicted $D_{LCO}$ for most adults require an Hb 3–4 g/dL higher or lower than normal, or a markedly elevated COHb.

Clinically important differences in the measurement of Hb and COHb by the RAD-57 limit its usefulness for adjusting predicted $D_{LCO}$ values. However, there may be a role for noninvasive Hb and COHb measurement in screening for extreme values that indicate a need for invasive sampling.

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