Noninvasive Measurement of Carboxyhemoglobin: How Accurate Is Accurate Enough?

William H. Maisel, MD, MPH, Roger J. Lewis, MD, PhD

From the Medical Device Safety Institute, Beth Israel Deaconess Medical Center, Boston, MA (Maisel); and the Department of Emergency Medicine, Harbor-UCLA Medical Center, the Los Angeles Biomedical Research Institute, Torrance, CA, and the David Geffen School of Medicine at UCLA, Los Angeles, CA (Lewis).

SEE RELATED ARTICLE, P. 382.


Exposure to carbon monoxide (CO) is the leading cause of death by poisoning in industrialized countries. It accounts for hundreds of accidental deaths and thousands of intentional deaths annually in the United States. CO is a colorless, odorless gas that is easily absorbed through the lungs when inhaled. It competes with oxygen for binding to hemoglobin, but because hemoglobin has an affinity for CO that is 200 to 250 times greater than that for oxygen, CO poisoning leads to decreased hemoglobin oxygen-carrying capacity, impaired oxygen delivery, and tissue hypoxia.

Although timely diagnosis and treatment of CO poisoning are critical, diagnosis based on clinical presentation alone is difficult because symptoms are often nonspecific and can mimic the flu or other viral illness. Definitive diagnosis therefore relies on measurement of increased carboxyhemoglobin levels, which have traditionally been performed on blood samples by using a spectrophotometer. Because of the need to screen many patients with low likelihood of clinically important CO poisoning to ensure that all truly poisoned patients are identified and, further, because of the occasional need to screen large numbers of patients in the setting of a possible mass exposure, a rapid noninvasive diagnostic method would be clinically useful.

Although conventional oximeters are unable to distinguish carboxyhemoglobin from oxyhemoglobin and can mistakenly report a 100% oxygen saturation even in the presence of CO, the Rad-57 CO-Oximeter (Masimo Corporation, Irvine, CA) uses a noninvasive sensor to distinguish between oxygenated hemoglobin, deoxygenated hemoglobin, and carboxyhemoglobin. Data are obtained by passing various wavelengths of visible and infrared light through a capillary bed (typically the sensor is placed on a finger), taking advantage of the variable light absorption of the different hemoglobin species. Initial marketing clearance of the Rad-57 was granted by the Food and Drug Administration (FDA) in 2005 on the basis of company-submitted data comparing the noninvasive methodology with simultaneous invasive carboxyhemoglobin measurements in human volunteers over a carboxyhemoglobin range of 1% to 40%. According to the company Web site and FDA submission, the device has an accuracy of 3% (1 SD), although detailed data analysis has not been presented in a peer-reviewed journal or other public format.

In this issue of Annals, Touger et al provide contrasting data on the real-world performance of the Rad-57 CO-Oximeter. The authors studied 120 adult and pediatric patients presenting with suspected CO poisoning at a single medical center during a 16-month period. Noninvasive carboxyhemoglobin measurements by the Rad-57 were compared with laboratory carboxyhemoglobin measurements (performed with the Siemens Rapidlab TM 1200 blood gas analyzer) on simultaneously obtained blood samples. Several observations by Touger et al are noteworthy. Although the mean difference between the laboratory and noninvasive carboxyhemoglobin values was only 1.4%, suggesting a lack of systematic bias, occasional differences between the 2 test methods exceeded 10% carboxyhemoglobin. Of particular concern are individual readings that yielded widely disparate results. For example, in one case the laboratory carboxyhemoglobin value exceeded 30%, whereas noninvasive measurement by the Rad-57 was less than 5% (ie, a false-negative noninvasive measurement). In another case, the noninvasive carboxyhemoglobin value exceeded 20% and was more than 4 times the laboratory carboxyhemoglobin measurement, consistent with a false-positive reading. In total, more than 35% of the time, the noninvasive and laboratory carboxyhemoglobin measurements were discrepant by greater than 5% carboxyhemoglobin. Using a cutoff of greater than or equal to 15% carboxyhemoglobin, the Rad-57 had a sensitivity of 48% (correctly identifying only 11 of 23 patients with increased carboxyhemoglobin) and a specificity of 99% (correctly identifying 96 of 97 patients with carboxyhemoglobin levels below the cutoff).

Small previous studies have also evaluated the accuracy of the Rad-57 CO-Oximeter. For example, simultaneous noninvasive and laboratory carboxyhemoglobin measurements in 31 patients undergoing arterial blood tests showed reasonably good correlation, although the majority of carboxyhemoglobin saturations were less than 7%.

Simultaneous noninvasive and
laboratory carboxyhemoglobin in 10 healthy volunteers who breathed CO until their carboxyhemoglobin levels reached 15% resulted in a test accuracy of 2%.9

Other studies have evaluated the clinical utility of noninvasive CO oximetry in screening patients for possible CO poisoning. One investigation evaluated the utility of screening more than 10,000 patients presenting to an urban, academic emergency department and reported identifying 9 unsuspected cases of CO poisoning during a 3-month period by using the Rad-57 CO-Oximeter; cases identified with the noninvasive methodology were confirmed with subsequent laboratory blood analysis.10 The high specificity of the Rad-57 CO-Oximeter—found to be 99% in the analysis by Touger et al7—is critical to providing clinical utility for screening of patients to avoid a large number of false-positive tests. Similarly, the device has also been used to provide early diagnosis of CO poisoning by fire rescue personnel.11 However, the low sensitivity observed by Touger et al7 would suggest that the RAD-57 device cannot be used to reliably exclude CO poisoning in any patient with appreciable risk of being poisoned.

Multiple factors may have contributed to the inaccurate measurement of carboxyhemoglobin levels by the Rad-57 CO-Oximeter observed by Touger et al.7 Notably, several substances may interfere with the accuracy of noninvasive carboxyhemoglobin measurement, including increased levels of methemoglobin, very low arterial oxygen saturations, and increased levels of total bilirubin. Little information about these potential confounders is provided in the Touger report. In addition, although laboratory analysis of blood samples has long been considered the criterion standard for measuring carboxyhemoglobin, inaccuracies can result from inadequate maintenance or calibration of the machine.12

Virtually every diagnostic test used in medicine is susceptible to inaccuracies, false-negative and false-positive results, or a lack of sensitivity or specificity. Nonetheless, imperfect tests can still be highly useful when applied by physicians in the proper diagnostic setting. And although the clinical utility and diagnostic accuracy of the Rad-57 CO-Oximeter may be debated, informed discussions can occur only in the presence of validated data. The stark contrast between the Rad-57 performance under real-life, clinical circumstances as reported by Touger et al7 and its performance as reported by the manufacturer in data submitted to the FDA underscores the importance of providing public access to selected regulatory data to permit critical appraisal of diagnostic test performance. Recently, controversy has arisen over the adequacy of data used to support premarket device evaluation by the FDA, both evaluations obtained by the 510(k) mechanism used for the RAD-57 device and the more-stringent premarket approval process.13-15 The FDA has commissioned the Institute of Medicine to study the 510(k) premarket notification process; completion of the IOM review is expected in 2011.16,17 Ideally, premarket evaluation should describe and predict the clinical performance of diagnostic devices.

Accurate and reliable noninvasive measurement of CO would be an important clinical advance, providing the potential for faster diagnosis and earlier treatment of a clinically important diagnostic problem. However, because of its potential inaccuracies, the RAD-57 device should not be viewed as a substitute for laboratory measurement of carboxyhemoglobin. Efforts to develop a CO oximeter that is more accurate in practice should be undertaken.

Supervising editor: Lewis S. Nelson, MD

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article that might create any potential conflict of interest. The authors have stated that no such relationships exist. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement. Dr. Maisel is an FDA consultant. The article represents the opinions of the authors and does not necessarily represent the practices, policies, or positions of the FDA.

Reprints not available from the authors.

Address for correspondence: William H. Maisel, MD, MPH, Medical Device Safety Institute, Beth Israel Deaconess Medical Center, 185 Pilgrim Rd, Baker 4, Boston, MA 02215; 617-667-8800, fax 617-632-7620; E-mail wmaisel@bidmc.harvard.edu.

REFERENCES


Did you know?
Podcasts are available for almost every article in *Annals*. Visit http://www.annemergmed.com/content/podcast to find out more.