ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Research letter

Real world diffusing capacity simulation data - how well do they fit current ERS/ATS acceptability criteria?

Jeffrey M. Haynes, Gregg L. Ruppel, David A. Kaminsky

Please cite this article as: Haynes JM, Ruppel GL, Kaminsky DA. Real world diffusing capacity simulation data - how well do they fit current ERS/ATS acceptability criteria?. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00626-2022).

Title Page

Manuscript Type: Research Letter

Title: Real World Diffusing Capacity Simulation Data - How Well Do They Fit Current ERS/ATS Acceptability Criteria?

Authors:

Jeffrey M. Haynes RRT RPFT
Pulmonary Function Laboratory
Elliot Health System
Manchester, NH, USA

Gregg L. Ruppel RRT RPFT
Division of Pulmonary, Critical Care and Sleep Medicine
St. Louis University
St. Louis, MO, USA

David A. Kaminsky MD
Division of Pulmonary and Critical Care Medicine
University of Vermont College of Medicine
Burlington, VT, USA

Correspondence:

Jeffrey M. Haynes RRT RPFT
Pulmonary Function Laboratory
Elliot Health System
185 Queen City Avenue
Manchester, NH, USA, 03101
jhaynes@elliot-hs.org
1-603-663-2332

Conflicts of Interest:

Jeffrey Haynes	Consultant, Morgan Scientific Inc, Honoraria from the American Association for Respiratory Care, and the Washington, Pennsylvania, and Ohio Respiratory Care Societies. Member of the National Board for Respiratory Care Board of Trustees
Gregg Ruppel	Consulting fees, National Board for Respiratory Care. Honoraria, MGC Diagnostics
David Kaminsky	Royalties, UptoDate, Inc. Honoraria, MGC Diagnostics

Summary/Take Home Message

The ERS/ATS D_{LCO} standards recommend acceptability ranges for weekly D_{LCO} simulation testing performed with a 3L syringe. On some devices the ERS/ATS limits may exceed or not fit a 3SD range, in which case simulation ranges based on 3SD may be appropriate.

To the Editor:

Diffusing capacity of the lungs for carbon monoxide (D_{LCO}) is an important pulmonary function test for the diagnosis and management of obstructive, restrictive and pulmonary vascular disease. The 2017 ERS/ATS standards for single-breath carbon monoxide uptake in the lungs recommend that a weekly D_{LCO} simulation test be performed with a calibrated 3L syringe.[1] This type of simulation provides quality control values for both D_{LCO} and alveolar volume (V_A). According to ERS/ATS standards, an acceptable simulated D_{LCO} is <0.5 ml/min/mmHg and an acceptable simulated V_A is 3±0.3L, under ambient temperature, pressure, dry (ATPD) conditions.[1] The ERS/ATS D_{LCO} standards document states that the simulated V_A should be reported under BTPS conditions; however, in this type of simulation, volumes should be reported under ATPD conditions.

We previously reported a case from a single system where the simulated V_A were 8-11 standard deviations (SD) above the measured mean due to a leak in a gas sampling collection bag, yet all of these values were within the ERS/ATS limits of acceptability.[1-2] We suggested that D_{LCO} and V_A simulation limits based on actual performance rather than fixed arbitrary values may provide better quality control of D_{LCO} devices. The purpose of this study is to analyse D_{LCO} and V_A simulation data from multiple devices and laboratories and compare the performance of these devices against the ERS/ATS recommended simulation limits.

We analysed D_{LCO} and V_A simulation data collected from three different types of D_{LCO} systems: Medisoft BodyBox™ (3 devices) and SpiroAir™ (1 device), Sorinnes Belgium, ComPAS™ software, Morgan Scientific, Haverhill MA, USA; Platinum Elite™ (9 devices), MGC Diagnostics Corporation, St. Paul MN, USA. The Medisoft devices are classical systems that use plastic bags for the collection of discrete gas samples (referred to as "expiratory bag" in this letter), whereas the MGC devices were equipped with either a rapid gas analyser (RGA; 6 devices) or gas chromatograph (GC; 3 devices). Data were collected from four clinical laboratories (St. Louis University, St. Louis MO, USA; University of Vermont, Burlington VT, USA; Elliot Health System, Manchester NH, USA; St. Joseph Hospital, Nashua, NH, USA). Data were collected between 2017 and 2021.

D_{LCO} and V_A simulations were performed with a 3L calibration syringe with a current accuracy certification according to each laboratory's protocol. The Medisoft/Morgan Scientific devices perform the D_{LCO} simulation with a full syringe of test gas in patient testing mode while the MGC devices perform the D_{LCO} simulation with 1L of air mixed with 2L of test gas in a simulation test mode. Consecutive measurements performed on different days were retrospectively collected from each device. D_{LCO} or V_A simulation values identified as statistical outliers that would likely prompt corrective action were excluded. Data from each type of device were compared to the 2017 ERS/ATS limits,[1] and then to each other. Following individual comparisons, the data from all devices were pooled and compared to the 2017 ERS/ATS limits.[1] The use of 3SD limits (common in laboratory medicine)[3] were considered in comparison to the fixed limits as recommended by the ERS/ATS standards.

Commercially available software was used to perform statistical analysis (Prism, version 4.0, GraphPad Software, San Diego CA, USA). Grubb's test was applied to identify statistical

outliers. Mean and SD were calculated for each type of device, differences between device types was assessed with the Kruskal-Wallis (one-way analysis of variance) test and Dunn's multiple comparison post-test if necessary. A p-value <0.05 was considered significant.

A total of 4 D_{LCO} measurements (2 expiratory bag, 2 GC) and 5 V_A measurements (1 expiratory bag, 2 RGA, 2 GC) were removed from analysis after being identified as outliers. Following outlier removal, 1,157 D_{LCO} (expiratory bag = 286; RGA = 707; GC = 164) and 1158 V_A (expiratory bag = 287; RGA = 706; GC = 165) simulation tests were analysed. The mean D_{LCO} and V_A values from different devices and when pooled collectively were within the ERS/ATS simulation limits (Figure). The left panel of the figure shows the pooled D_{LCO} and V_A simulation data in comparison to the ERS/ATS limits. There were some differences between devices. If a 3SD range is used, the high end of the D_{LCO} range marginally exceeds the ERS/ATS limit (<0.5 ml/min/mmHg) for the expiratory bag (.58 ml/min/mm Hg), RGA (.81 ml/min/mm Hg) and for the pooled data (.75 ml/min/mm Hg).

The measured 3SD V_A range for the RGA, GC, and pooled data matched the ERS/ATS recommended variance of ±0.3L, and were 10.4%, 10.3%, and 10.3% of the mean, respectively. However, the 3SD V_A range for the RGA, GC, and pooled data were offset below the ERS/ATS fixed range (3±0.3L) because the mean V_A for these devices were below 3L: 2.89L, 2.92L, and 2.91L, respectively.

The measured 3SD range for the expiratory bag devices (±0.15 L, 5% of the mean 2.98L) was tighter than the ERS/ATS range. Using the ERS/ATS V_A range for these devices would create acceptability boundaries of -5.6 and +6.4SD from the measured mean. Using a ±3SD range may be more appropriate than the fixed ERS/ATS V_A range for devices with less variance.

Comparison of DL_{CO} and V_A simulation data between device types revealed statistically significant differences between all device types (see the right panel of the figure). While it is unclear if these differences are clinically important, they may be important with regards to establishing acceptable ranges for V_A simulation.

Our data support the limits of acceptability for D_{LCO} simulation (<.5 ml/min/mmHg) as recommended by the ERS/ATS D_{LCO} standards. However, a potential limitation of this recommendation is that there is no consideration of limits on negative D_{LCO} values which may indicate gas analyser malfunction. Indeed, all 4 D_{LCO} outliers that were removed from this study were negative values (expiratory bag: -.32, -.32; GC: -.34, -.30), but satisfy the ERS/ATS single-sided limit of <.5 ml/min/mmHg. While a V_A range of ±0.3L perfectly fit the 3SD range for the RGA, GC, and pooled data, the mean V_A were below 3L resulting in an offset of the 3SD range from the ERS/ATS range. However, the 3SD V_A range from the expiratory bag devices were significantly tighter than the ERS/ATS recommended ranges.

It is possible that a methodologic difference might be responsible for the varying results between devices. For example, the expiratory bag devices performed the D_{LCO} simulation with a full syringe of test gas in patient testing mode while the RGA and GC devices used in this study performed the D_{LCO} simulation with 1L of air mixed with 2L of test gas in a simulation test mode. Factors that might cause the simulated V_A to be less than 3L include the volume of dead space correction applied to either the syringe or the D_{LCO} system, as well as the mechanism supplying the inspired gas (e.g., reservoir bag or demand valve). Manufacturers must perform these simulations on their equipment and provide guidance for their customers to achieve ERS/ATS-compliant simulation data.

Performing a weekly D_{LCO} simulation test, or whenever a problem is suspected, provides a quick means for troubleshooting a complex system. Any simulation data outside of the acceptability limits should prompt users to take the system out of service until the problem can be resolved. This requires that the acceptability limits accurately represent the performance of the D_{LCO} system under normal operating conditions. Subtle D_{LCO} system malfunctions may escape detection by calibration procedures so failure to perform weekly D_{LCO} simulation and biologic control testing risks reporting inaccurate patient data. Because D_{LCO} thresholds are used in many clinical scenarios, inaccurate data may have serious consequences for patients.[4-5]

Our data, collected from 13 devices and 4 clinical laboratories under real world conditions, indicate that the ERS/ATS acceptability limits for D_{LCO} simulation are appropriate. However, a limit on negative values should be added. For many of the devices we examined the absolute V_A ranges fit the ERS/ATS recommendation but were offset below 3±0.3L because the mean V_A was offset below 3L. Unfortunately, our study is limited to a few devices, additional research on other D_{LCO} systems and the cause of the mean V_A offset is needed. Manufacturers must ensure that their systems produce simulation data that fit the ERS/ATS targets. A V_A range ±3SD may be more appropriate for devices with a measured range tighter than ±0.3L. Based on the data presented, we suggest that future ERS/ATS D_{LCO} technical standards recommend a D_{LCO} target that accounts for negative values and a V_A target of 3L±0.3L or ±3SD, whichever is smaller.

The authors would like to thank Kevin Hodgdon, Vanessa Gall, and Teresa Goodwin for assisting with data collection.

References

1. Graham BL, Brusasco V, Burgos F, et al. 2017 ERS/ATS standards for single-breath carbon monoxide uptake in the lung. Eur Respir J. 2017;49(1):1600016.

2. Haynes JM, Ruppel GL, Kaminsky DA. Should diffusing capacity quality control be treated like other laboratory devices? Eur Respir J. 2021;58(6):2102642.

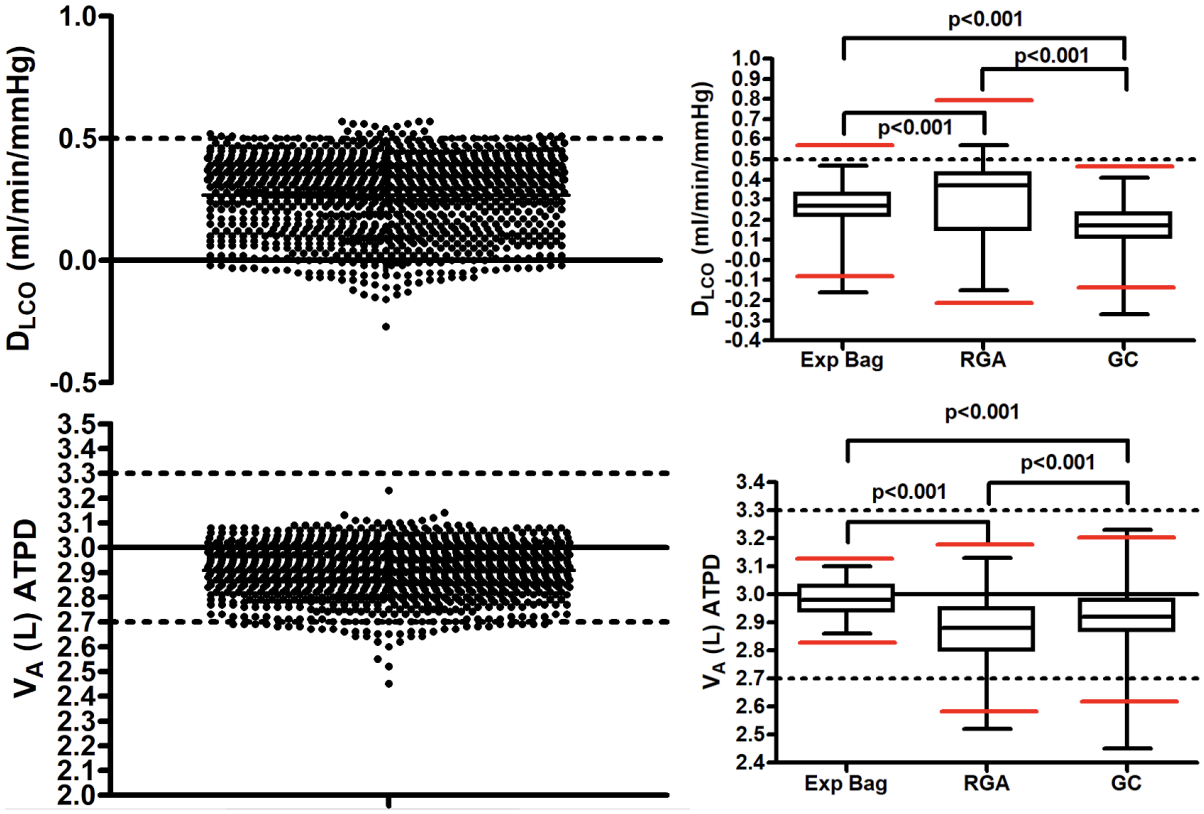
3. Westgard JO. Internal quality control: planning and implementation strategies. Ann Clin Biochem. 2003;40(Pt 6):593-611.

4. Neder JA, Berton DC, Muller PT, O'Donnell DE. Incorporating lung diffusing capacity for carbon monoxide in clinical decision making in chest medicine. Clin Chest Med. 2019;40(2):285-305.

5. Neder JA, Berton DC, O'Donnell DE. The lung function laboratory to assist clinical decision-making in pulmonology: evolving challenges to an old issue. Chest. 2020;158(4):1629-1643.

Figure Legend

Fig. The left panel shows pooled diffusing capacity (D_{LCO}) and alveolar volume (V_A) simulation data from multiple devices and laboratories compared to ERS/ATS acceptability ranges. The right panel shows box-and-whisker plots of D_{LCO} and V_A simulation data from different devices assessed with the Kruskal-Wallis (one-way analysis of variance) test and Dunn's multiple comparison post-test. The red lines in the right panels represent the measured 3 standard deviation range. The solid lines in the lower panels represent the V_A simulation target and the dotted lines in all panels represent the ERS/ATS acceptability ranges. ATPD = gas conditions at atmospheric temperature, pressure, dry; Exp Bag = expiratory bag; RGA = rapid gas analyser; GC = gas chromatograph.


1.0
0.5
0.0
-0.5
D_{LCO} (ml/min/mmHg)
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
V_A (L) ATPD
p<0.001
p<0.001
p<0.001
D_{LCO} (ml/min/mmHg)
Exp Bag
RGA
GC
p<0.001
p<0.001
p<0.001
V_A (L) ATPD
Exp Bag
RGA
GC