Validation of measurements of ventilation-to-perfusion ratio inequality in the lung from expired gas

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Prisk, G. Kim, Harold J. B. Guy, John B. West, and James W. Reed. Validation of measurements of ventilation-to-perfusion ratio inequality in the lung from expired gas. J Appl Physiol 94: 1186–1192, 2003. First published October 25, 2002; 10.1152/japplphysiol.00662.2002.—The analysis of the gas in a single expirate has long been used to estimate the degree of ventilation-perfusion (V˙A/Q˙) inequality in the lung. West et al. (10) used this technique to measure the range of V˙A/Q˙ in the lung. For example, Prisk et al. (5) used this technique to measure the range of V˙A/Q˙ in anesthetized mongrel dogs under control conditions and after exposure to aerosolized methacholine. These measurements were then compared with arterial blood gases and with measurements of V˙A/Q˙ inhomogeneity obtained using the multiple inert gas elimination technique. The slope of the instantaneous respiratory exchange ratio (R slope) vs. expired volume was poorly correlated with independent measures, probably because of the curvilinear nature of the relationship due to continuing gas exchange. When R was converted to the intrabreath V˙A/Q˙ (iV˙/Q˙), the best index was the slope of iV˙/Q˙ vs. volume over phase III (iV˙/Q˙ slope). This was strongly correlated with independent measures, especially those relating to inhomogeneity of perfusion. The correlations for iV˙/Q˙ slope and R slope considerably improved when only the first half of phase III was considered. We conclude that a useful noninvasive measurement of V˙A/Q˙ inhomogeneity can be derived from the intrabreath respiratory exchange ratio.

single-breath tests; respiratory exchange ratio

THE ANALYSIS OF THE GAS in a single expirate has long been used to estimate the degree of inequality in the ventilation-to-perfusion ratio (V˙A/Q˙) in the lung. West and colleagues (10) showed that an index of V˙A/Q˙ inequality could be obtained in the lung by calculating the change in respiratory quotient in expired gas, provided mixed venous blood gas composition was assumed to be constant during the expiration. Later, Guy et al. (3) used computerized data acquisition to allow the calculation of the intrabreath respiratory exchange ratio (R) over the course of a single vital capacity expiration. In addition, the resulting plot of intrabreath R could then be compared with the theoretical behavior of a perfectly mixed lung model to provide an index of V˙A/Q˙ inhomogeneity that was less sensitive to ongoing gas exchange. As shown by West et al. (10), proportional changes in respiratory quotient could be converted to proportional changes in V˙A/Q˙ without knowledge of the exact mixed venous blood composition if this remained the same.

The technique has been applied to provide an index of the range of V˙A/Q˙ in the lung. For example, Prisk et al. (5) used this technique to measure the range of V˙A/Q˙ in subjects exposed to periods of weightlessness during spaceflight in Spacelab, and at the present time this technique is also in use on the International Space Station. Recently, Cremona et al. (1) used plots of intrabreath R to determine closing volume in subjects who may have high-altitude pulmonary edema, but they did not extend the measurements to determination of the range of V˙A/Q˙ in these subjects.

However, despite occasional use, the technique has never been validated against other known techniques for measuring V˙A/Q˙ inequality in the lung. We provide the first such validation by measuring the intrabreath V˙A/Q˙ range (iV˙/Q˙) in anesthetized dogs under normal conditions and after the inhalation of methacholine. The noninvasive measurements of intrabreath R and iV˙/Q˙, which are comparable to the previous method of West et al. (10), are compared with the range of V˙A/Q˙ in the same animals determined using arterial blood gases and also the multiple inert gas elimination technique (MIGET).

METHODS

Experimental details. The study was approved by the University of California, San Diego, Animal Subjects Committee. Nine mongrel dogs [18–24 (mean 20.6) kg body wt] were anesthetized with pentobarbital sodium (30 mg/kg iv) and paralyzed with pancuronium bromide (0.1 mg/kg iv). The level of anesthesia and relaxation was maintained by incremental administration of both drugs. A cuffed endotracheal tube (9 mm ID) was placed through a tracheostomy. Normal arterial blood gas tensions were maintained by adjusting the frequency of a Harvard mechanical ventilator set at a tidal volume of 15 ml/kg. A 7-Fr Swan-Ganz catheter was inserted via the right external jugular vein and advanced into the pulmonary artery by using direct pressure monitoring. The femoral artery was cannulated for sampling arterial blood (Fig. 1).

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Flow through the endotracheal tube was measured with a pneumotachograph (Fleisch no. 1) connected to a differential pressure transducer (Validyne MP-45). Before each study, the flowmeter was calibrated using a 1-liter precision syringe.

Gas concentrations were measured using a mass spectrometer (model MGA-1100, Perkin-Elmer) sampling from the midstream point of the proximal end of the endotracheal tube. The sample transit time was checked each day and was generally ~400 ms. This was later used to correctly align the gas concentration and flow signals before analysis. Airway pressure was measured via a Statham P23 ID transducer connected to a point 8 cm distal to the mass spectrometer sampling point. This position was selected to avoid sampling puffs of gas from the airway pressure catheter during major pressure changes.

Data were monitored on a strip-chart recorder (Gould-Brush Mark 200) and digitized at 30 Hz using a 12-bit analog-to-digital converter in a computer system.

Methacholine administration. We used aerosolized methacholine to induce bronchoconstriction and, thus, alter the distribution of ventilation. A 1% methacholine solution was aerosolized using a jet nebulizer (Acorn II, Marquest Medical Products) and administered via the ventilator circuit for 1 min. During this time, the respiratory rate was adjusted to maintain a normal end-tidal CO2. A short period was then allowed to obtain a new quasi-steady state, and the measurements after methacholine administration were performed. On average, postmethacholine measurements were made ~27 min after methacholine administration.

MIGET. MIGET was applied as described by Gale et al. (2). The inert gas solution (SF6, ethane, cyclopropane, enflurane, ether, and acetone) was prepared in 5% dextrose (2) and infused for ~20 min at ~10 ml/min before collection of the samples. The total volume of fluid infused over the course of the study (1–2 h) was ~1 liter.

Quadraplicate 15-ml samples of mixed expired gas and duplicate 6-ml samples of pulmonary and systemic arterial blood were obtained using gastight syringes under normal conditions (before the iV/Q measurements) and after the stabilization subsequent to methacholine administration (just before the iV/Q measurements). These samples were used to measure the steady-state concentrations of the six inert gases using a gas chromatograph (model 5890A, Hewlett-Packard, Wilmington, DE) (9). Va/Q distributions were calculated by using MIGET in the usual fashion. Solubilities, retentions (the ratio of arterial to mixed venous partial pressures), and excretions (the ratio of mixed expired to mixed venous partial pressure) for the inert gases were determined and corrected for body temperature, and Va/Q distributions were calculated from the inert gas data (8, 9).

The second moment of the perfusion distribution exclusive of intrapulmonary shunt (SDVq) and the second moment of the ventilation distribution exclusive of dead space (SDVv) were used as indicators of the degree of Va/Q inequality. Dispersion of retention (DispR), excretion (DispE), and retention minus excretion (DispR – E) were derived directly from the retention and excretion data (2). The residual sum of squares was used as an indicator of the adequacy of fit of the data to the 50-compartment model of the lung (9).

Blood gas measurements. Arterial samples (2 ml) were collected immediately after each inert gas sample and kept on ice until analyzed for PO2, PCCO2, and pH using a blood gas analyzer (model IL-1306, Instrumentation Laboratories, Lexington, MA). Alveolar-arterial PO2 difference was determined using the ideal alveolar PO2 calculated using the alveolar gas equation and measured arterial PCCO2 (PACO2) and R.

iV/Q test maneuver. For each test, the dogs were ventilated at a constant rate and tidal volume until stable end-tidal gas concentrations were obtained. Data were then collected for ~60 s to provide a measurement of O2 consumption and CO2 production. The technique described by Tomioka et al. (7) was used. At the end of a normal expiration, the airway was connected to a constant-pressure source of air at ~80 cmH2O pressure, and the animal was inflated to full lung volume. Inflation was via a flow restrictor limiting flow to ~0.1 l/s. On reaching maximum volume, the airway was connected to a constant-pressure source of ~80 cmH2O pressure and deflated (again via the flow restrictor at ~0.1 l/s) to minimum lung volume. The animal was then returned to normal ventilation.

iV/Q analysis. The slow vital capacity expiration was analyzed using the techniques described by Guy et al. (3). Gas concentration data were converted on a point-by-point basis to R using the standard alveolar gas equation (3)

$$ R = \frac{P_{ECO2}}{P_{I2O2}(P_{E2O2}/P_{IN2}) - P_{E2O2}}$$

where PECO2 is expired PCO2, PCCO2 and PICO2 are expired and inspired PO2, and PECO2 and PICO2 are expired and inspired PO2. The data were then plotted as a function of expired volume (Fig. 2). Because a perfectly homogeneous lung produces intrabreath R curves that are curvilinear as a result of
have only modest effects on the output. For example, a large gas exchange from the preceding period of quiet breathing residual volume, \( Q \) different \( V \) interpolation between the family of R isopleths calculated for straight-horizontal isopleths of \( iV \) opposed to the curvilinear R isopleths. Figure 2 shows a of \( V \) each individual isopleth describes the behavior of a lung, free supplied with blood of constant mixed venous concentration partment connected via a serial dead space to the mouth and calculated. The model comprises a single, perfectly mixed com- ing the same controlled vital capacity expiration was calcu-

\[ R = \frac{\dot{V}}{\dot{Q}} \]

These R isopleths form a scale for \( V \) free of any oscillations and a terminal rise (phase IV) can be clearly seen. Note curvilinear behavior of the R isopleths, which results from continu-

continuing gas exchange (4), it is difficult to separately determine the change in \( R \) caused by Va/Q inequality.

For this reason, the behavior of a theoretical lung perform-

Regarding the fit for the Va/Q model, often the second-order polynomial equation (4) is used to describe the behavior of the lung. This polynomial equation is fitted between these limits is indicated by the vertical lines, limits of phase III. Note abrupt rise in \( iV/Q \) as a function of volume (Fig. 2) we measured the slope of the curve using linear least-squares regression as a function of expired volume (\( iV/Q \) slope). We determined the range of \( iV/Q \) (\( iV/Q \) range) by measuring the maximum differences in \( iV/Q \) over the portion of the exhalation corresponding to phase III. Thus \( iV/Q \) range included any excursions in \( iV/Q \) beyond that of slope itself caused by cardiogenic oscillations and by any deviation from the least-squares fitted line. Figure 3 illustrates these parameters. Additionally, using the intrabreath R curve (Fig. 2), we measured the slope of \( R \) as a function of expired volume (\( R \) slope) over the same lung volume range and also used this as a possible index of inhomogeneity of gas exchange, reasoning that, although the isopleths were curvilinear, an index based on this curve alone would be easier to calculate than the \( iV/Q \)-based measurements.

**Statistical techniques.** Values are means ± SE. Two-way ANOVA was performed on the results where appropriate, and in cases with significant \( F \) ratios, post hoc pairwise comparisons were made using the Bonferroni adjustment (Systat version 5). To compare responses, linear regression was used (Excel 2002, Microsoft, Redmond, WA). Significance was accepted at \( P < 0.05 \).

**RESULTS**

**Gas exchange.** During control measurements performed before methacholine administration, arterial blood gases were essentially normal, with \( P_{aCO_2} \), of 34.5 Torr and arterial \( P_{aO_2} \) (\( P_{aO_2} \)) of 87 Torr (inspired \( O_2 \) fraction = 0.21 in all cases). Methacholine administration worsened gas exchange: \( P_{aCO_2} \) of 36.2 Torr and \( P_{aO_2} \) of 63 Torr (Table 1). Alveolar-arterial \( P_{aO_2} \) difference increased from 23 to 40 Torr after methacholine

From the plot of \( iV/Q \) as a function of expired volume (Fig. 3), we identified the onset of phase IV (airway closure) and measured the slope of the curve using linear least-squares regression as a function of expired volume (\( iV/Q \) slope). We determined the range of \( iV/Q \) (\( iV/Q \) range) by measuring the maximum differences in \( iV/Q \) over the portion of the exhalation corresponding to phase III. Thus \( iV/Q \) range included any excursions in \( iV/Q \) beyond that of slope itself caused by cardiogenic oscillations and by any deviation from the least-squares fitted line. Figure 3 illustrates these parameters. Additionally, using the intrabreath R curve (Fig. 2), we measured the slope of \( R \) as a function of expired volume (\( R \) slope) over the same lung volume range and also used this as a possible index of inhomogeneity of gas exchange, reasoning that, although the isopleths were curvilinear, an index based on this curve alone would be easier to calculate than the \( iV/Q \)-based measurements.
administration. Table 1 lists the average values for the gas exchange variables and other measurements for the control period and after methacholine administration.

**Multiple inert gas variables.** Methacholine administration resulted in a significant widening of the V/AQ distribution (Table 1), with SDQ increasing from 0.64 to 1.33 (Fig. 4). There were comparable increases in DispR, DispE, and DispR - E.

**Expired gas variables.** Neither iV/Q range nor R slope changed significantly as a result of methacholine administration (Table 1). iV/Q slope became steeper (more negative) as a result of methacholine administration, changing from −0.092 ± 0.021 to −0.245 ± 0.089 (P < 0.10; cf. Fig. 3 with Fig. 5).

Because there were often significant nonlinearities in the plot of R as a function of volume and iV/Q as a function of volume, we then considered R slope and iV/Q slope over the first and second halves of phase III by dividing that portion of the exhalation into two halves and repeating the slope measurements (Fig. 5). When the breath divided into the first and second halves of phase III was considered, the effect of methacholine on iV/Q slope was much greater over the first than over the second half of the breath. Over the first half of phase III, iV/Q slope significantly steepened from −0.020 ± 0.025 to −0.379 ± 0.108 (P < 0.05); over the second half of the breath, iV/Q slope changed from −0.149 ± 0.034 to −0.122 ± 0.076 (not significant). In contrast, R slope over the first half of the exhalation became considerably steeper after methacholine administration (−0.014 ± 0.017 vs. −0.190 ± 0.033, P < 0.05), but R slope over the second half of the breath was considerably flatter after exposure to methacholine (−0.325 ± 0.061 vs. −0.180 ± 0.028, P < 0.05). The major changes are shown in Fig. 6.

**Correlations between intrabreath R, iV/Q, and other measures of gas exchange.** iV/Q slope correlated strongly with several measures of gas exchange and V/AQ distribution. Table 2 lists the correlation coefficients between iV/Q and blood gas and inert gas variables. iV/Q slope was most strongly correlated with

![Image](http://jap.physiology.org/)

**Table 1. Gas exchange, inert gases, and iV/Q**

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 9)</th>
<th>Postmethacholine (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time, min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO₂, Torr</td>
<td>86.9 ± 2.7</td>
<td>62.8 ± 3.4*</td>
</tr>
<tr>
<td>AaO₂, Torr</td>
<td>23.3 ± 2.5</td>
<td>39.6 ± 2.5*</td>
</tr>
<tr>
<td>PaCO₂, Torr</td>
<td>34.5 ± 0.7</td>
<td>36.2 ± 1.0</td>
</tr>
<tr>
<td>SDQ</td>
<td>0.64 ± 0.07</td>
<td>1.33 ± 0.14*</td>
</tr>
<tr>
<td>SDV</td>
<td>1.10 ± 0.15</td>
<td>0.83 ± 0.07*</td>
</tr>
<tr>
<td>DispR</td>
<td>4.12 ± 0.56</td>
<td>11.81 ± 1.60*</td>
</tr>
<tr>
<td>DispE</td>
<td>5.50 ± 0.99</td>
<td>8.01 ± 1.00*</td>
</tr>
<tr>
<td>DispR - E</td>
<td>8.60 ± 1.32</td>
<td>17.28 ± 2.16*</td>
</tr>
<tr>
<td>R slope</td>
<td>−0.165 ± 0.036</td>
<td>−0.177 ± 0.029*</td>
</tr>
<tr>
<td>1st half of breath</td>
<td>−0.014 ± 0.017</td>
<td>−0.190 ± 0.033*</td>
</tr>
<tr>
<td>2nd half of breath</td>
<td>−0.325 ± 0.061</td>
<td>−0.180 ± 0.028*</td>
</tr>
<tr>
<td>iV/Q range</td>
<td>0.195 ± 0.032</td>
<td>0.239 ± 0.031</td>
</tr>
<tr>
<td>iV/Q slope</td>
<td>−0.092 ± 0.025</td>
<td>−0.245 ± 0.089†</td>
</tr>
<tr>
<td>1st half of breath</td>
<td>−0.020 ± 0.025</td>
<td>−0.379 ± 0.108*</td>
</tr>
<tr>
<td>2nd half of breath</td>
<td>−0.149 ± 0.034</td>
<td>−0.122 ± 0.017</td>
</tr>
</tbody>
</table>

Values are means ± SE. PaO₂ and PaCO₂, arterial PO₂ and PO₂; AaO₂, alveolar-arterial PO₂ difference; SDQ and SDV, log standard deviations of perfusion (Q) and ventilation (V) distributions; DispR, DispE, and DispR - E, dispersion of retention, excretion, and retention minus excretion; R slope, slope of respiratory exchange ratio as a function of volume over phase III; iV/Q range, range of intrabreath ventilation-to-perfusion ratio (iV/Q) over phase III; iV/Q slope, slope of iV/Q as a function of volume over phase III. *P < 0.05; †P < 0.10 compared with control.
blood gases and with the indexes of MIGET associated with pulmonary perfusion, DispR and SDQ.

Not surprisingly, iV/Q slope over the first half of the breath correlates strongly with iV/Q slope over the entire breath (r² = 0.85, P < 0.05). However, iV/Q slope over the first half of the breath is much less strongly correlated with iV/Q slope over the second half of the breath (r² = 0.28), supporting the observation of significant non-linearities in iV/Q slope. The change in iV/Q slope over the first half of phase III was the most strongly correlated with all other variables measured in these dogs, showing significant correlations with all measures of Vₐ/Qinhomogeneity, with the exception of SDQ. Correlations with iV/Q slope over the second half of the breath were much weaker (Table 2).

Similarly, R slope over the first half of phase III was strongly correlated with other measures of gas exchange. In general, R slope over the first half of the breath correlated with the same variables as did iV/Q slope over the first half of the breath, and the correlations were of similar strength (Table 2). As was the case with iV/Q slope, R slope over the second half of the breath was poorly correlated with other measures of gas exchange.

**DISCUSSION**

**iV/Q slope.** The correlations between iV/Q slope and independent measures of Vₐ/Qinhomogeneity before and after methacholine administration (Table 2) suggest that iV/Q slope provides a useful index of gas exchange disruption. In particular, in this circumstance, it appears that the administration of aerosolized methacholine resulted in different behavior of the lung when the gas expired from the lung in the first half of the breath was compared with the gas expired from the lung in the second half of the breath. When we considered iV/Q slope calculated from only the first half of the exhalation, we obtained better correlations with independent measures of Vₐ/Qinhomogeneity (Table 2). Although calculation of iV/Q slope is somewhat complex, iV/Q slope has the advantage of being a completely non-invasive measurement and relatively simple to perform experimentally.

Necessary assumptions in the calculation of iV/Q are the concentrations of O₂ and CO₂ in the mixed venous blood entering the lungs. We used an estimate of these based on O₂ consumption, CO₂ production, and assumed Q (the Fick principle). West et al. (10) showed that although the value of iV/Q corresponding to a particular value of R is sensitive to the composition of the mixed venous blood, the fractional change in calculated iV/Q is very insensitive. Errors in O₂ and CO₂ concentration in opposite directions (such as those arising from an error in metabolic rate or Q) result in very small errors in iV/Q. A 10% error of this nature results in changes in iV/Q of <1%, which, when coupled with the previous observations of West et al., shows that conversion from R to iV/Q is robust.

**Effect of methacholine.** We used methacholine to induce bronchoconstriction and, presumably, uneven ventilation, thus disrupting gas exchange. We wished to induce gas exchange lesions of varying intensity to test the usefulness of the change in iV/Q slope over a range of gas exchange defect severity. PaO₂, was be-
between 93 and 44 Torr (between 93 and 69 Torr for control condition and between 83 and 44 Torr after methacholine), which shows that we were successful in inducing a range of severity of the gas exchange defect between different animals. Similarly, calculated alveolar-arterial Po$_2$ difference rose from 23 to 40 Torr after methacholine administration. That iV/Q slope (and especially iV/Q slope over the first half of the exhalation) correlates well with the change in PaO$_2$ and with alveolar-arterial Po$_2$ difference (Table 2) is a good indication that the measurement is a useful noninvasive means by which to determine the severity of a gas exchange defect. The change in the distribution of Va/Q distributions from MIGET (Fig. 4) is similar to that reported in previous studies. In particular, an increase in the inhomogeneity of ventilation resulting from bronchoconstriction in dogs results in a widening of the distribution of perfusion (an increase in SD$_Q$) through the appearance of a low Va/Q mode (6).

**Intrabreath changes in Va/Q**. There were significant differences in iV/Q slope measured over the first and second halves of phase III of the vital capacity expiration, in particular, in those tests after methacholine administration (Table 1). Although it might be tempting to compare the first and second halves of the breath, such a comparison is almost certainly invalid when attempting to compare the data before and after methacholine administration. Although after methacholine administration the portion of the lung that empties first exhibits a greater degree of Va/Q inhomogeneity than does the portion that empties last, there is no means to determine whether these correspond to the same lung regions measured before methacholine administration.

To investigate the degree of Va/Q inequality in the entire lung, it is important to consider data only from phase III. The onset of phase IV represents the point at which airway closure occurs somewhere in the lung. Thus, after that point, exhaled gas is a reflection of only those regions still contributing to the exhalate. However, it is not generally possible to determine which lung regions close, especially in abnormal lungs, such as those exposed to methacholine. Although the iV/Q data from phase IV may provide insight into other aspects of Va/Q inhomogeneity, they are likely not useful in comparing iV/Q with whole lung measures such as MIGET.

It is important to recognize that the model used to generate the R isopleths, from which iV/Q is calculated, is not intended to represent an actual lung. Rather, it is used to provide a series of reference lines describing how a perfect lung, following the same lung volume history as the test lung, would behave. The data from the test lung are then interpreted using this scale “as if” the test lung were a collection of such perfect lungs following the same volume history. Although the gas arising from a particular lung unit with a given Va/Q may well have significant phase III slopes of O$_2$ and CO$_2$, there is no corresponding effect on the phase III slope for R (and, hence, for iV/Q). This is because, on the O$_2$-CO$_2$ diagram, the value of R is the slope of the line joining the inspired point and the alveolar point. Thus any factor that contributes to variable mixtures from these sources produces no change in R (the obvious example being the lack of effect of dead space admixture, which has a big effect on the O$_2$ and CO$_2$ trace, especially in the first half of expiration). Thus, with changes in R (and iV/Q), we are measuring the effects of different lung regions with different Va/Q ratios emptying at different points in the breath. The causes of such differences in emptying cannot be inferred from these measurements. However, it is clear from these data, and from those of West et al. (10) and Guy et al. (3), that the patterns that result are strikingly different between normal and abnormal lungs.

**Using R slope instead of iV/Q slope.** We also attempted to determine whether the slope of the R plot vs. expired volume (R slope) could be used instead of the computationally more demanding iV/Q plot. As the data in Table 2 illustrate, there were virtually no significant correlations between R slope and the independent measures of Va/Q inhomogeneity, nor did R slope change as a result of methacholine administration (Table 1). We were not entirely surprised by this finding. As Fig. 2 illustrates, even a perfectly mixed lung (the model lines in Fig. 2) produces curvilinear R plots. Attempting to measure a slope from a curvilinear plot such as that shown in Fig. 2 introduces consider-
able error into the resulting slope unrelated to a V\textsubscript{A}/Q defect. This is reflected in the poor correlation performance (Table 2).

R slope over the first half of phase III produced correlations with independent measures of gas exchange that were almost as strong as those from iV/Q slope measured over the first half of phase III. This measurement may provide a more easily calculated surrogate to iV/Q slope, albeit at the expense of not having a scale that is as easily interpretable. The degree of curvilinearity (which results from continuing gas exchange as the exhalation proceeds) depends largely on lung volume and expired flow rate, with smaller lung volumes and lower flow rates exhibiting greater curvilinearity. These effects are smallest over the first half of phase III. Thus measurements of R slope over the first half of phase III in adult humans in which exhalation is kept to less than \sim 10 s may be less prone to the curvature artifact. In that case, a stronger correlation between the independent measures of V\textsubscript{A}/Q inhomogeneity and R slope might result.

Other expired gas measurements of V\textsubscript{A}/Q inhomogeneity. The most informative expired gas measurements of V\textsubscript{A}/Q inhomogeneity in this study were iV/Q slope and R slope over the first half of phase III. We attempted to use the range of iV/Q, which also includes any contribution from cardiogenic oscillations. It might be expected that the magnitude of the cardiogenic oscillations would be an indicator of the range of V\textsubscript{A}/Q inhomogeneity in the lung. If this is the case, then it might be thought that including this component in the measurement by measuring the range (as opposed to the slope, which averages out any component due to cardiogenic oscillations) would improve the noninvasive estimation of V\textsubscript{A}/Q inhomogeneity. However, on the basis of the much less robust correlations in Table 2, this appears not to be the case.

In conclusion, in anesthetized dogs exposed to methacholine, measurements of iV/Q slope provide a useful index of the degree of V\textsubscript{A}/Q disruption in the lung. The changes in iV/Q slope correlate well with more direct measurements of V\textsubscript{A}/Q range obtained using MIGET and also with changes in arterial blood gas variables. The degree of correlation is improved when only gas from the first half of exhalation is considered. Because iV/Q slope can readily be measured noninvasively, this may prove useful in future studies of disruption to gas exchange, especially in humans in remote environments where noninvasive techniques are often desirable.

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