Anatomical and functional intrapulmonary shunt in acute respiratory distress syndrome*

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Objectives: **The lung-protective strategy employs positive end-expiratory pressure to keep open otherwise collapsed lung regions (anatomical recruitment). Improvement in venous admixture with positive end-expiratory pressure indicates functional recruitment to better gas exchange, which is not necessarily related to anatomical recruitment, because of possible global/regional perfusion modifications. Therefore, we aimed to assess the value of venous admixture (functional shunt) in estimating the fraction of nonaerated lung tissue (anatomical shunt compartment) and to describe their relationship.**

Design: **Retrospective analysis of a previously published study.**

Setting: **Intensive care units of four university hospitals.**

Patients: **Fifty-nine patients with acute lung injury/acute respiratory distress syndrome.**

Interventions: **Positive end-expiratory pressure trial at 5 and 15 cm H_2O positive end-expiratory pressures.**

Measurements and Main Results: **Anatomical shunt compartment (whole-lung computed tomography scan) and functional shunt (blood gas analysis) were assessed at 5 and 15 cm H_2O positive end-expiratory pressures. Apparent perfusion ratio (perfusion per gram of nonaerated tissue/perfusion per gram of total lung tissue) was defined as the ratio of functional shunt to anatomical shunt compartment. Functional shunt was poorly correlated to the anatomical shunt compartment (r^2 = .174). The apparent perfusion ratio at 5 cm H_2O positive end-expiratory pressure was widely distributed and averaged 1.25 ± 0.80. The apparent perfusion ratios at 5 and 15 cm H_2O positive end-expiratory pressures were highly correlated, with a slope close to identity (y = 1.10·x −0.03, r^2 = .759), suggesting unchanged blood flow distribution toward the nonaerated lung tissue, when increasing positive end-expiratory pressure.**

Conclusions: **Functional shunt poorly estimates the anatomical shunt compartment, due to the large variability in apparent perfusion ratio. Changes in anatomical shunt compartment with increasing positive end-expiratory pressure, in each individual patient, may be estimated from changes in functional shunt, only if the anatomical-functional shunt relationship at 5 cm H_2O positive end-expiratory pressure is known. (Crit Care Med 2008; 36:669–675)**

KEY WORDS: respiratory distress syndrome, adult; pulmonary gas exchange; computed tomography; positive-pressure respiration; regional blood flow

In acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), the physiologic rationale for using positive end-expiratory pressure (PEEP)—besides its effects on oxygenation—is to prevent regional increases in stress and strain within lung tissue obtained by distributing the tidal volume over a greater number of alveolar units, which are kept open at end-expiration (1), and by avoiding intratidal opening and closing (2).

This implies that the role of PEEP in the prevention of ventilator-induced lung injury relies on an anatomical phenomenon: regaining and maintaining aeration in previously nonaerated lung regions (3). Such anatomical lung recruitment is usually assessed, in clinical practice, by employing respiratory physiologic variables (functional lung recruitment); among them, the increase in the Pao_2/Fio_2 ratio and the decrease in Riley's shunt (4) are most commonly used (5).

Unfortunately, functional recruitment is a far more complex phenomenon than anatomical recruitment, since it implies not only the ventilation and perfusion of

***See also p. 983.**

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the newly anatomically recruited lung regions but also possible variations in the ventilation and perfusion of lung regions already open to gases (i.e., poorly and well-aerated lung regions).

We recently found (6), in a group of patients affected by ALI/ARDS, that respiratory physiologic variables, either *per se* or in combination, are quite disappointing predictors of anatomical lung recruitment, as measured with computed tomography (CT) scanning.

In the present study, by performing a further retrospective analysis of the data from that study, we investigate the relationship between anatomical recruitment (as assessed with CT scanning) and functional recruitment (as assessed with Riley's shunt).

Our main aim is to investigate to what degree of confidence variations in venous admixture with PEEP may be used to assess anatomical recruitment, the key issue in the lung-protective strategy.

METHODS

For the present analysis, we employed the database of a previously published study (6) in which lung recruitment was investigated in a population of ALI/ARDS patients. The study was approved by the institutional review boards of each hospital, and written informed consent was obtained according to the national regulations of each participating institutions. Briefly, 68 patients were enrolled in that study and underwent three whole-lung CT scans at 5, 15, and 45 cm H_2O. In 63 patients, a central venous catheter was in place. During the PEEP trial, a complete set of central venous blood gas data were available in 60 patients. Among them, one patient was excluded because of an unusual etiology (oil intoxication) (7). The remaining 59 patients, in whom it was possible to compute Riley's shunt, were included in the present analysis. Thirty-nine healthy subjects who underwent lung CT scanning for diagnostic purposes were included as a control group for the analysis of topographical lung mass distribution. Since our aim was to study the relationship between functional shunt and anatomical shunt compartment, only data recorded at 5 and 15 cm H_2O PEEP were used, because at these PEEP levels both functional and anatomical shunts were available. At 45 cm H_2O PEEP, in fact, no blood gases were collected.

Measurements

By using a quantitative CT scan analysis software (SOFT-E-FILM, University of Milan, Milan, Italy) we estimated, in each patient, sedated and paralyzed, the lung tissue weight, its density distribution (as measured in Hounsfield units, HU), and the fraction of aerated and nonaerated lung tissue. Nonaerated lung tissue was defined as the lung tissue with density >-100 HU, while aerated lung tissue was defined as the lung tissue with density <-100 HU. Arterial-venous oxygen content difference and Riley's shunt were computed with standard formulas using arterial and mixed venous blood, available in 19 patients, or, as a surrogate, central venous blood in the remaining 40 patients.

Statistical Analysis

Data were analyzed using SAS software, version 8.2 (SAS Institute, Cary, NC) and R-software (R-foundation for statistical computing, Vienna, Austria, http://www.R-project.org).

Comparisons between variables measured at 5 and 15 cm H_2O PEEP were performed using paired Student's *t*-test. Regression analysis was performed with the method of least square fitting. When comparing two groups of patients, unpaired Student's *t*-tests were used. Nonnormally distributed variables (e.g., the apparent perfusion ratio) were compared using Wilcoxon's test. Data are reported as mean ± SD, unless otherwise indicated. Statistical significance was defined as $p < .05$.

Assumptions

The relationship between the fraction of nonaerated lung tissue (defined throughout the article as intrapulmonary anatomical shunt compartment, i.e., nonaerated tissue [g]/total lung tissue [g]) and Riley's venous admixture (4) (defined as intrapulmonary functional shunt, $\dot{Q}s/\dot{Q}t$) may be expressed as

$$\frac{\dot{Q}s}{\dot{Q}t} = k \cdot \frac{\text{nonaerated tissue (g)}}{\text{total lung tissue (g)}} \qquad [1]$$

where k, the proportionality constant, may be defined as the perfusion ratio. In fact, according to Equation *1*,

$$k = \frac{\text{perfusion-per-gram of nonaerated tissue}}{\text{perfusion-per-gram of total lung tissue}} \qquad [2]$$

A perfusion ratio equal to 1 indicates that each gram of anatomical shunt compartment (i.e., of nonaerated lung tissue) is perfused as much as each gram of aerated lung tissue, since total lung tissue is the sum of aerated and nonaerated lung tissue. A perfusion ratio <1 indicates relative hypoperfusion of the anatomical shunt compartment, while a perfusion ratio >1 indicates its relative hyperperfusion. However, the validity of the relationship shown in Equation *1* holds only if the distribution of pulmonary edema is nearly homogeneous throughout the lung parenchyma (i.e., each gram of original lung tissue is associated with the same amount of edema fluid) and if the shunt flow ($\dot{Q}s$) perfuses only the anatomical shunt compartment. A preliminary discussion of these two assumptions is, therefore, necessary.

Assumption 1: Lung Edema Is Nearly Homogeneously Distributed. The entire lung parenchyma was divided into four subvolumes: two along the cephalocaudal axis (apical and basal), defined by a plane through 50% of lung cephalocaudal length, and two along the vertical axis (dependent and nondependent), defined by the plane through 50% of the vertical lung height. The ratio of the tissue mass of the basal subvolume to that of the whole lung was not different between ALI/ARDS patients and normal subjects (0.53 ± 0.06 vs. 0.52 ± 0.05, $p = .291$). This indicates a similar distribution of edema along the cephalocaudal axis. In contrast, the ratio of the dependent to total lung tissue mass was slightly but significantly greater in ALI/ARDS patients than that observed in normal subjects (0.66 ± 0.05 vs. 0.61 ± 0.04, $p < .001$), suggesting a preferential distribution of lung edema toward the dependent lung regions in ALI/ARDS patients, a downshift of the center of gravity of the lung due to the increased lung mass or the combination of the two phenomena.

The maximum possible error would occur if the uneven distribution of lung edema was entirely associated with the nonaerated lung tissue (i.e., anatomical shunt compartment). In this case, the perfusion ratio would be underestimated. In the worst scenario, where we attributed all of the excess of edema entirely to the anatomical shunt compartment, the error introduced in estimating the apparent perfusion ratio was on the order of 5%.

Indeed, our data suggest nearly homogeneous distribution of lung edema in ALI/ARDS, as already shown in humans (8) and in experimental settings (9, 10).

Assumption 2: Riley's Shunt Flow Perfuses the Nonaerated Lung Tissue. In the absence of low alveolar ventilation/perfusion ratio ($\dot{V}a/\dot{Q}$) lung regions, the ratio of computed Riley's venous admixture (in this case, true shunt) to the anatomical shunt compartment would exactly correspond to its perfusion ratio (Eq. *2*). If low-$\dot{V}a/\dot{Q}$ regions exist, besides true shunt, the calculated apparent perfusion ratio would tend to be overestimated.

Studies on ARDS patients ventilated with $F_{IO_2} > 60\%$ have consistently shown that low-$\dot{V}a/\dot{Q}$ areas are scarcely represented in ALI/ARDS patients (11–13). Similar results were obtained by Pesenti et al (14). However, in the patients ventilated with $F_{IO_2} < 60\%$, those authors found that the maldistribution accounted for a relevant fraction of the venous admixture (about 38%). Nonetheless, they observed that the oxygenation improvement due to PEEP increase was due uniquely to the reduction in true shunt while $\dot{V}a/\dot{Q}$ maldistribution remained constant. In our patient population, the average F_{IO_2} was 51% ± 15%.

Eighteen patients had an F_{IO_2} >60% and 48 patients had an F_{IO_2} <60%. In both subgroups, however, the apparent perfusion ratio was similar, while in the presence of relevant $\dot{V}a/\dot{Q}$ maldistribution it would had been greater in patients ventilated with lower F_{IO_2} (PEEP 5 cm H_2O, 1.09 ± 0.63 vs. 1.33 ± 1.00, $p = .36$; PEEP 15 cm H_2O, 1.08 ± 0.64 vs. 1.43 ± 1.22, $p = .28$, in the lower and higher F_{IO_2} subgroups, respectively).

CT Scan Threshold for the Anatomical Shunt Compartment. The computation of apparent perfusion ratio would require knowledge of the exact match between Riley's venous admixture and the lung CT scan anatomy. We do not know the degree of correspondence between possible low-$\dot{V}a/\dot{Q}$ regions and lung regions that are poorly aerated (i.e., those with a density >−500 HU). Therefore, we performed the whole analysis using four different thresholds for defining the anatomical shunt compartment. The thresholds we chose were 1) −100 HU, which is the most common threshold for noninflated tissue found in the literature; 2) −300 HU (i.e., a gas/tissue ratio <30%) as suggested by Richter et al. (15) using positron emission scanning; 3) −500 HU, including all poorly inflated tissue; and 4) an individualized threshold (i.e., either −500HU, −400HU, −300HU, −200HU, or −100HU) determined so as to minimize the possible discrepancy between anatomical and functional shunt.

Whichever was the applied threshold, the overall results did not change (data not shown). Therefore, we decided to use for the definition of the anatomical shunt compartment the most common threshold reported in the literature (i.e., −100 HU).

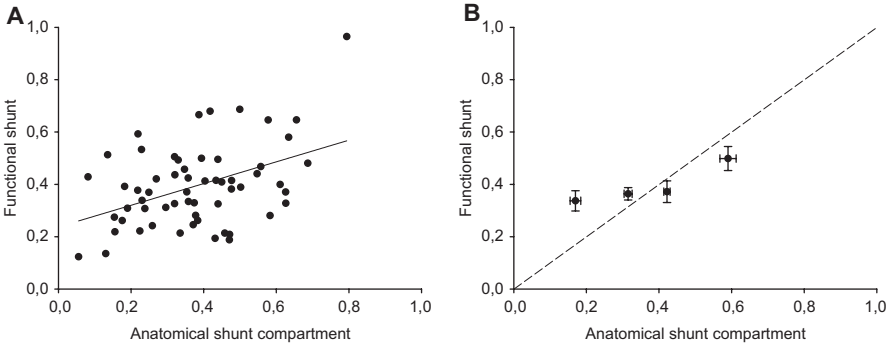

Figure 1. Baseline intrapulmonary functional shunt as a function of the anatomical shunt compartment. *A*, relationship in the overall population at 5 cm H_2O positive end-expiratory pressure (PEEP). *Solid line*, the regression line between the two variables ($y = 0.41 \cdot x + 0.24$, $p < .001$, $r^2 = .12$). *B*, relationship in the population as grouped into quartiles of baseline anatomical shunt compartment at 5 cm H_2O PEEP. *Dashed line*, the "identity" line (i.e., the isoperfusion line), whereby the apparent perfusion ratio is equal to 1.

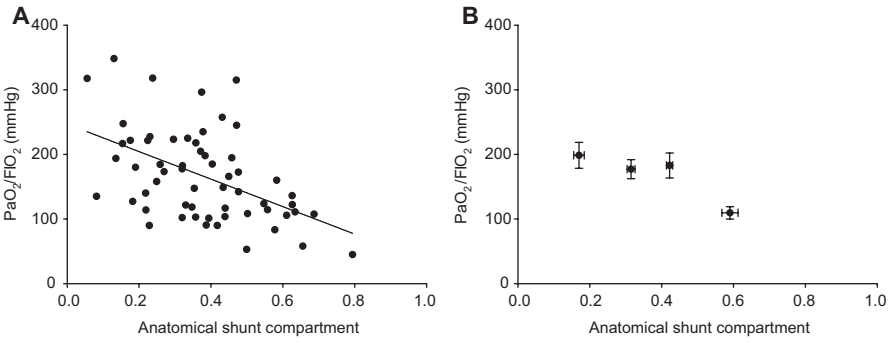

Figure 2. Baseline Pa_{O_2}/F_{IO_2} ratio as a function of the anatomical shunt compartment. *A*, relationship in the overall population at 5 cm H_2O positive end-expiratory pressure (PEEP). *Solid line*, the regression line between the two variables ($y = -213 \cdot x + 247$, $p < .001$, $r^2 = .23$). *B*, relationship in the population as grouped into quartiles of baseline anatomical shunt compartment at 5 cm H_2O PEEP. Data are reported as mean ± SEM.

RESULTS

Anatomical and Functional Shunt Relationship at Baseline

As shown in Figure 1*A*, the anatomical shunt compartment is poorly correlated to the functional shunt compartment ($r^2 = .17$, $p < .001$), accounting for the impossibility of predicting the anatomical shunt compartment when only the functional shunt is measured.

For clarity, the same data were grouped into quartiles according the anatomical shunt compartment (Fig. 1*B*). The identity line depicted in Figure 1*B* describes the relationship between the anatomical shunt compartment and the functional shunt that would be observed if the apparent perfusion ratio was equal to 1. Of note, it appears that the apparent perfusion ratio is likely to be >1 (relative hyperperfusion of the anatomical shunt compartment) when the anatomical shunt compartment is <∼35%, and <1 (relative hypoperfusion) when the anatomical shunt compartment is >∼35%.

Figure 2*A* shows the relationship between anatomical shunt compartment and the Pa_{O_2}/F_{IO_2} ratio at PEEP 5 cm H_2O; in Figure 2*B*, the same data are grouped into quartiles. As shown, the relationship is similar to the one observed with the functional shunt ($r^2 = .23$, $p < .01$).

Anatomical and Functional Shunt Relationship While Increasing PEEP

The PEEP effects on gas exchange and hemodynamic and lung mechanics are summarized in Table 1. To analyze the effects of increasing PEEP on the relationship between anatomical shunt compartment and functional shunt, the apparent perfusion ratio at 15 cm H_2O PEEP was estimated and compared with that observed at 5 cm H_2O PEEP. In the overall population, the apparent perfusion ratio at 15 cm H_2O did not differ from that recorded at 5 cm H_2O PEEP (1.25 ± 0.8 vs. 1.34 ± 1.01, $p = .18$, Table 1), suggesting the consistency of the anatomical-functional shunt relationship while increasing PEEP. This finding was confirmed in each patient, as highlighted by the correlation between the apparent perfusion ratio at PEEP 5 and 15 cm H_2O PEEP ($r^2 = .76$, $p < .001$, slope = 1.1, y-intercept = −0.03, Fig. 3*A*). This concept can also be shown by plotting both functional and anatomical shunts at 5 cm H_2O PEEP against the corresponding ones recorded at 15 cm H_2O PEEP. As shown, the slopes of the two regression lines were not different (0.74 vs. 0.80, respectively, $p = .36$) (Fig. 3*B*). All together, these data strongly indicate that each patient's own apparent perfusion ratio is maintained when PEEP is increased to 15 cmH_2O PEEP, no matter what its baseline value was.

The impossibility of predicting the changes in anatomical shunt by using the

Table 1. 5 cm H_2O positive end-expiratory pressure (PEEP) vs. 15 cm H_2O PEEP

Variable	PEEP		
	5 cm H_2O (n = 54)	15 cm H_2O (n = 54)	*p*
PaO_2, mm Hg	78 ± 23	107 ± 32	**<.001**
PaO_2/FIO_2, mm Hg	167 ± 70	225 ± 83	**<.001**
SaO_2, %	93.7 ± 4.4	96.6 ± 2.0	**<.001**
$PaCO_2$, mm Hg	41.7 ± 8.4	42.1 ± 8.5	.415
PvO_2, mm Hg	41 ± 6	44 ± 7	**<.001**
SvO_2, %	74.8 ± 6.6	76.9 ± 7.2	**.002**
$PvCO_2$, mm Hg	46.4 ± 8.1	47.6 ± 8.4	**.008**
pHa	7.39 ± 0.08	7.38 ± 0.08	**.004**
pHv	7.36 ± 0.07	7.35 ± 0.08	**.005**
$\Delta C(a\text{-}v)O_2$, mL_{O_2}/dL	2.64 ± 0.92	2.85 ± 1.02	**.001**
Apparent perfusion ratio	1.25 ± 0.80	1.34 ± 1.01	.180
Functional shunt	0.39 ± 0.16	0.31 ± 0.13	**<.001**
HR, beats/min	93 ± 20	92 ± 21	**.028**
MAP, mm Hg	84 ± 14	82 ± 15	.093
CVP, mm Hg	13 ± 4	14 ± 4	**<.001**
Paw, cm H_2O	11 ± 2	20 ± 2	**<.001**
P_{plat}, cm H_2O	20 ± 4	29 ± 3	**<.001**
P_{peak}, cm H_2O	29 ± 5	38 ± 5	**<.001**
C_{rs}, mL/cm H_2O	43.5 ± 18.9	42.9 ± 16.6	.584
Total lung weight, g[a]	1496 ± 516	1490 ± 513	.513
Anatomical shunt[a]	0.38 ± 0.16	0.30 ± 0.14	**<.001**

Bold, statistically significant; SaO_2, arterial blood oxygen saturation of hemoglobin; PvO_2, venous blood partial pressure of oxygen; SvO_2, venous blood oxygen saturation of hemoglobin; $PvCO_2$, venous blood partial pressure of carbon dioxide; pHa, arterial blood pH; pHv, venous blood pH; $\Delta C(a\text{-}v)O_2$, arteriovenous oxygen content difference; HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; Paw, mean airway pressure; P_{plat}, inspiratory plateau airway pressure; P_{peak}, inspiratory peak airway pressure; C_{rs}, respiratory system compliance.

[a]Data measured with quantitative computed tomography scanning analysis (42). Data presented as mean ± SD.

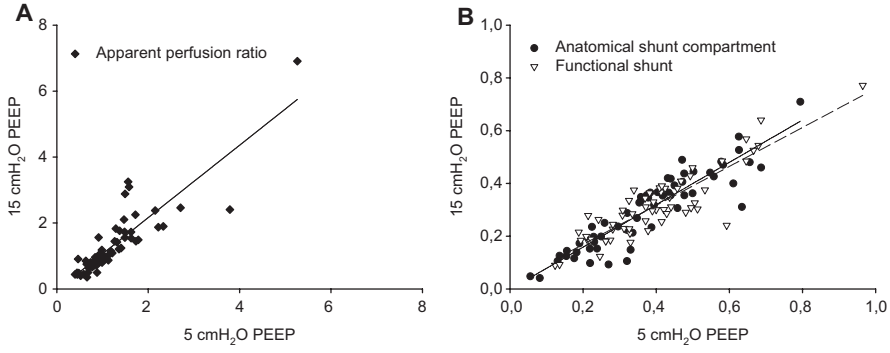

Figure 3. Similarity of apparent perfusion ratio, functional shunt, and anatomical shunt compartments between 5 and 15 cm H_2O positive end-expiratory pressure (PEEP). A, apparent perfusion ratio at 15 cm H_2O PEEP as a function of that estimated at baseline 5 cm H_2O PEEP (*diamonds*). *Solid line*, the regression line. *B*, functional shunt compartment (*open triangles*) and anatomical shunt compartment (*solid dots*) at 5 and 15 cm H_2O PEEP. *Solid and dashed lines*, regression lines for the functional shunt ($y = 0.74 \cdot x + 0.02$, $p < .01$, $r^2 = .79$) and for the anatomical shunt compartment ($y = 0.80 \cdot x - 0.001$, $p < .01$, $r^2 = .83$), respectively.

changes of physiologic variables is shown in Figure 4.

DISCUSSION

The approach used in our analysis may appear simplistic. However, it suffers from the same limitations but may share the same merits of Riley's approach to gas exchange, largely used since its description several decades ago. We applied Riley's rationale to the CT lung anatomy, defining two compartments, one ideal, aerated, and one degassed, the anatomical shunt. The link between the two models is the apparent perfusion ratio (Eq. *1*).

Anatomical and Functional Shunt at Baseline

In normal subjects, in supine position, the dependent regions of the lung are more perfused than the nondependent ones, because of gravity (16) and vascular configuration (17). These regions are those mainly transformed into anatomical shunt compartment in ALI/ARDS. In our patients, 87% ± 10% of the anatomical shunt compartment was located in the dependent lung regions. Indeed, any mechanism decreasing the apparent perfusion ratio would help preserve gas exchange, while any mechanism increasing the apparent perfusion ratio would further deteriorate gas exchange.

In our ALI/ARDS population, the apparent perfusion ratio was highly variable (Fig. 5). The different pathogenetic pathway (such as pulmonary vs. extrapulmonary injury) did not account for this variability, since the apparent perfusion ratio was similar in pulmonary and extrapulmonary ARDS. Other mechanisms, however, such as the size of lung injury, hypoxic pulmonary vasoconstriction, and global lung perfusion, may explain the large variability of perfusion ratio.

In experimental animals, Shuster and Marklin (18) showed that the greater the amount of the damaged portion of the lung, the lower is its perfusion (i.e., apparent perfusion ratio <1). Similarly, we found that in our patients, the size of the anatomical shunt compartment was inversely, but weakly, correlated with the apparent perfusion ratio (data not shown). Anatomical alterations in lung vasculature may account, in part, for this observation. Several studies (19, 20), using selective angiography, have clearly demonstrated filling defects of pulmonary vasculature during ARDS, possibly due to either microthrombi (21) or vessel compression. Perfusion defects have also been found using different techniques, such as perfusion lung scanning (22) and nuclear scanning (23), and, in general, appear to be rather the rule than the exception (22). We may speculate that such lesions are more frequent in the more severely injured patients and may contribute to explain the relative hypoperfusion of their anatomical shunt compartments.

Hypoxic pulmonary vasoconstriction is a key pulmonary reflex that preserves gas exchange by diverting pulmonary blood flow from the nonaerated to the aerated regions of the lung. The physiologic reflex, however, appears to be blunted in human ALI/ARDS (24). The lack of the vasoconstrictor response to hypoxic stimuli may be due to the inhibitory effects of cytokines (25), nitric oxide (26), leukotrienes (27, 28), and endotoxin (29, 30). Moreover, the physiologic stimulus for hypoxic vasoconstriction may ac-

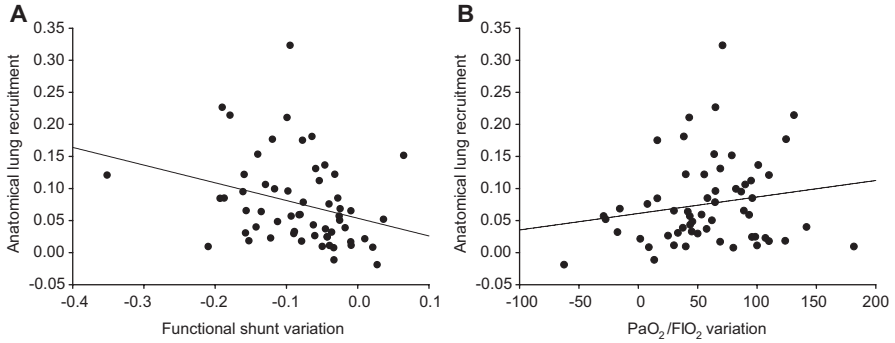

Figure 4. *A*, anatomical recruitment from 5 to 15 cm H_2O positive end-expiratory pressure (PEEP) (i.e., the fraction of nonaerated tissue at 5 cm H_2O PEEP minus fraction of nonaerated tissue at 15 cm H_2O PEEP) as a function of the shunt improvement (functional shunt at 15 cm H_2O PEEP minus functional shunt at 5 cm H_2O PEEP). Positive value on the *y*-axis indicates a decrease of nonaerated tissue (anatomical recruitment); negative values on the *x*-axis indicate the functional shunt reduction increasing PEEP. *Solid line*, the regression line ($y = -0.28 \cdot x + 0.05$, $p = .02$, $r^2 = .07$). *B*, anatomical lung recruitment as a function of the difference in Pao_2/Fio_2 ratio (i.e., Pao_2/Fio_2 at PEEP 15 cm H_2O minus Pao_2/Fio_2 at PEEP 5 cm H_2O). Positive values on *x*-axis indicate the improvement of oxygenation when PEEP is increased. *Solid line*, the regression line ($y = 0.0003 \cdot x + 0.06$, $p = .19$, $r^2 = .01$).

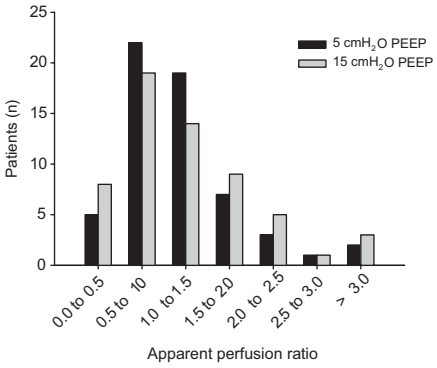

Figure 5. Frequency distribution of the apparent perfusion ratio measured at 5 (*black bars*) and 15 (*gray bars*) cmH_2O positive end-expiratory pressure (*PEEP*) in the overall study population.

tually be lacking in human ALI/ARDS. Such stimulus (Pso_2), according to Marshall and Marshall (31, 32), depends on mixed venous ($P\bar{V}o_2$) and alveolar (Pao_2) oxygen tensions ($Pso_2 = P\bar{V}o_2^{0.38} Pao_2^{0.62}$). In most ALI/ARDS patients, the Pso_2 is largely above its critical value (65–85 mm Hg, or 8.6–11.3 kPa), since cardiac output (and therefore Pvo_2) and the alveolar Po_2 (due to the high Fio_2 used) are frequently elevated. In our population, the Pso_2 averaged 146 ± 31 mm Hg (19.5 ± 4.1 kPa).

A third determinant of the apparent perfusion ratio is global lung perfusion. It has been firmly established by several studies on humans (33) and animal models (34, 35) that intrapulmonary functional shunt is directly associated with cardiac output, decreasing and increasing with decreases or increases in cardiac output, respectively. Several mechanisms are likely to contribute to this phenomenon, including mechanical recruitment of pulmonary vasculature as well as increases in oxygenation of venous blood perfusing the nonaerated lung regions, with a possible reduction of hypoxic vasoconstriction (36). Likewise, in our population, we found that the greater the global perfusion (as estimated by a lower arterial-venous oxygen content difference), the lower is the perfusion of aerated lung regions compared with that of nonaerated lung regions ($r^2 = .21$, $p < .001$).

Indeed, in our population, the interaction of different determinants of the apparent perfusion ratio, operating to different extents in each individual patient, may account for the weak correlation between the anatomical shunt compartment and the functional shunt.

Anatomical and Functional Shunt Relationship While Increasing PEEP

Different patterns of pulmonary blood flow redistribution with PEEP application have been described in acute lung injury. In some experiments, PEEP redistributes pulmonary blood flow toward the most injured lung regions (37). In normal subjects (38) and in experimental models of ARDS (39), PEEP did not change the distribution of blood flow, while variable and unpredictable responses have been described in human ARDS (11, 40). In our population the average apparent perfusion ratio at 15 cm H_2O PEEP was similar to that observed at 5 cm H_2O PEEP. Indeed, one may expect that the variations in functional shunt from 5 to 15 cm H_2O PEEP may accurately predict the variations in the anatomical shunt compartment. Unfortunately, prediction of the anatomical shunt compartment based on the functional shunt variations is not feasible. This does not occur due to the baseline apparent perfusion ratio. In fact, for instance, a change in functional shunt of 10% may be associated with an anatomical recruitment of either ~20%, if the apparent perfusion ratio is equal to 0.5, or only ~5%, if apparent perfusion ratio is equal to 2. Indeed, the estimate of anatomical shunt at 15 cm H_2O PEEP requires at least the knowledge of the apparent perfusion ratio at 5 cm H_2O PEEP.

Although a nearly unchanged apparent perfusion ratio appears to be a firm observation in the overall population, it may be the result of an averaging process on the values derived from the individual patients who may either slightly increase or decrease it. In fact, the application of PEEP has two opposite effects on apparent perfusion ratio. On one hand, the decrease in anatomical shunt compartment may be associated with an increase in its perfusion (increased apparent perfusion ratio) (24). On the other hand, the PEEP-induced decrease in global lung perfusion may be associated with a parallel decrease in functional shunt (decreased apparent perfusion ratio) (13).

Clinical Consequences

Whatever the mechanisms responsible for the discrepancy between anatomical and functional shunt, the clinical consequence is that gas exchange variation cannot be used with sufficient confidence to assess anatomical lung recruitment. As PEEP, according to the protective lung strategy, should be tailored according to lung recruitability, CT scanning or alternative methods should be implemented. However, adjusting PEEP according to lung recruitability, although physiologically sound (6), has not yet been proven to be beneficial. On the other hand, random application of higher PEEP compared with lower PEEP did not provide survival benefits (41). Indeed, the issue is still open. Although we routinely use CT scanning to assess lung recruitability for choosing higher or lower PEEP, we recognize that the available data, to date, are

insufficient to recommend a widespread use of this strategy (42).

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