Impact of Recruitment on Static and Dynamic Lung Strain in Acute Respiratory Distress Syndrome

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ABSTRACT

Background: Lung strain, defined as the ratio between end-inspiratory volume and functional residual capacity, is a marker of the mechanical load during ventilation. However, changes in lung volumes in response to pressures may occur in injured lungs and modify strain values. The objective of this study was to clarify the role of recruitment in strain measurements.

Methods: Six oleic acid–injured pigs were ventilated at positive end-expiratory pressure (PEEP) 0 and 10 cm H_2O before and after a recruitment maneuver (PEEP = 20 cm H_2O). Lung volumes were measured by helium dilution and inductance plethysmography. In addition, six patients with moderate-to-severe acute respiratory distress syndrome were ventilated with three strategies (peak inspiratory pressure/PEEP: 20/8, 32/8, and 32/20 cm H_2O). Lung volumes were measured in computed tomography slices acquired at end-expiration and end-inspiration. From both series, recruited volume and lung strain (total, dynamic, and static) were computed.

Results: In the animal model, recruitment caused a significant decrease in dynamic strain (from [mean ± SD] 0.4 ± 0.12 to 0.25 ± 0.07, $P < 0.01$), while increasing the static component. In patients, total strain remained constant for the three ventilatory settings (0.35 ± 0.1, 0.37 ± 0.11, and 0.32 ± 0.1, respectively). Increases in tidal volume had no significant effects. Increasing PEEP constantly decreased dynamic strain (0.35 ± 0.1, 0.32 ± 0.1, and 0.04+0.03, $P < 0.05$) and increased static strain (0, 0.06 ± 0.06, and 0.28 ± 0.11, $P < 0.05$). The changes in dynamic and total strain among patients were correlated to the amount of recruited volume. An analysis restricted to the changes in normally aerated lung yielded similar results.

Conclusion: Recruitment causes a shift from dynamic to static strain in early acute respiratory distress syndrome. **(Anesthesiology 2016; 124:443-52)**

LUNG parenchyma is subjected to mechanical loads in each breath. This stress may be augmented beyond the lung tolerance level, leading to tissue injury, under different circumstances. Patients with acute respiratory distress syndrome (ARDS) subjected to mechanical ventilation can suffer excessive airway pressures, decreased lung compliance, and inhomogeneous gas distribution.[1] Therefore, preinjured lungs under positive-pressure ventilation are prone to develop further damage due to an excessive stretch. In these conditions, lung tissue may develop a biological response, including activation of the inflammatory response. All these phenomena are framed in the concept of ventilator-associated lung injury (VALI).[2]

Limitation of VALI has been the main target of the so-called protective-ventilatory strategies. In fact, the majority of therapeutic strategies that have shown a survival benefit in ARDS patients have been those aimed to reduce the mechanical load by reducing tidal volume[3,4] or improving lung homogeneity by turning the patient prone.[5] Even the benefits of the use of neuromuscular-blocking agents in this population[6] could be related to a decrease in mechanical

What We Already Know about This Topic

- Mechanical strain in the injured lung depends on its rest volume, overinflation of previously aerated areas, and the cyclical deformation in each breath. As positive end-expiratory pressure can modify all these factors, its effects on strain are uncertain.

What This Article Tells Us That Is New

- Positive end-expiratory pressure decreased dynamic (cyclical) strain and increased static strain in an animal model (six pigs; oleic acid lung injury) and in a study of six patients with acute respiratory distress syndrome.

Submitted for publication March 18, 2015. Accepted for publication October 14, 2015. From the Servicio de Medicina Intensiva, Hospital Universitario Central de Asturias, Oviedo, Spain (E.G.-P., D.P.-R., G.M.A.); Critical Care Center, Hospital de Sabadell, I3PT, Corporació Sanitaria Parc Taulí, Universitat Autònoma de Barcelona, Sabadell, Spain (J.L.-A., L.B.); Centro de Investigación Biomédica en Red (CIBER)-Enfermedades Respiratorias, Instituto de Salud Carlos III, Madrid, Spain (J.L.-A., L.B., G.M.A.); Area de Gestión Clínica de Medicina Intensiva, Hospital Valle del Nalón, Langreo, Spain (L.A.-R.); and Departamento de Biología Funcional, Instituto de Oncología del Principado de Asturias (IUOPA), Universidad de Oviedo, Oviedo, Spain (L.A.-R., I.L.-A., J.B.-P., G.M.A.).

 Anesthesiology 2016; 124:443-52

<zdoi;10.1097/ALN.0000000000000946>

stretch caused by inhibition of patients' efforts, which have been linked to mortality.[7]

In this setting, optimization of mechanical ventilation is a major goal. Different respiratory mechanics parameters have been used to guide ventilator settings. It has been proposed that plateau pressures should not exceed certain levels in the 28 to 30 cm H_2O range.[8] However, this parameter may be modified by several factors including not only positive end-expiratory pressure (PEEP) level and tidal volume but also chest wall compliance.[9] Different approaches based on lung mechanics have also been proposed to set PEEP level, but none of them has reached a significant consensus.

Recently, it has been highlighted the role of lung strain as a marker of the amount of mechanical load during mechanical ventilation.[10] Strain has been defined as the ratio between end-inspiratory and rest lung gas volumes. In the case of mechanically ventilated patients, total strain is the sum of dynamic and static strain as follows[11]:

$$\text{Strain} = \text{Strain}_{dyn} + \text{Strain}_{st} = \frac{V_T}{FRC} + \frac{V_{PEEP}}{FRC} = \frac{V_T + V_{PEEP}}{FRC},$$

where V_T is tidal volume, V_{PEEP} is the increase in volume caused by PEEP, and FRC is the functional residual capacity. Different experimental studies have shown that the amount of dynamic strain (or derived parameters) is well correlated with the inflammatory response within the lung.[11–13]

As the FRC is decreased in patients with ARDS,[14] the influence of PEEP in strain is unclear. On one side, PEEP increases the gas volume of previously aerated areas (increases in aeration), thus increasing the static strain. However, the recruitment of nonventilated areas can also contribute to the restoration of the FRC. If this is the case, dynamic strain should decrease. We hypothesized that an increase in recruitment could decrease the strain in spite of a concomitant increase in aeration. Unfortunately, increases in aeration cannot be easily distinguished from recruited volume and requires measurements in different conditions or with specific techniques such as the quantitative analysis of computed tomography (CT) scan images. To test our hypothesis, we studied both an animal model of lung injury and patients with ARDS. By using different ventilatory strategies and measurement techniques, lung aeration, recruited volume, and strain were quantified and compared to characterize the net effects of the changes in lung volumes.

Materials and Methods

Experimental Model of Acute Lung Injury

The experimental protocol was approved by the Animal Ethics Committee of the Hospital de Sabadell (Sabadell, Spain). Six male pigs were anesthetized with azaperone (5 mg/kg), metomidate (4 mg/kg), and atropine (0.04 mg/kg), intubated, and connected to a mechanical ventilator (Servo 900C; Siemens, Sweden). After muscle paralysis (0.1 mg/kg pancuronium), a jugular vein and a carotid artery were catheterized. Additional doses of anesthesia and muscle relaxation were administered as needed during the protocol. Airway pressure, flow, and tidal and lung volumes were registered.[15] In brief, airway pressures and flows were measured using differential pressure transducers connected to a signal recorder and stored for later analysis. The FRC was measured after lung injury by multiple breath helium dilution, and changes in lung volume were followed using respiratory inductance plethysmography (Respitrace, NIMS, USA). These volumes were added to the FRC to calculate the end-expiratory lung volume (EELV). Signals from the plethysmograph were calibrated using tidal volumes measured by flow integration.[16]

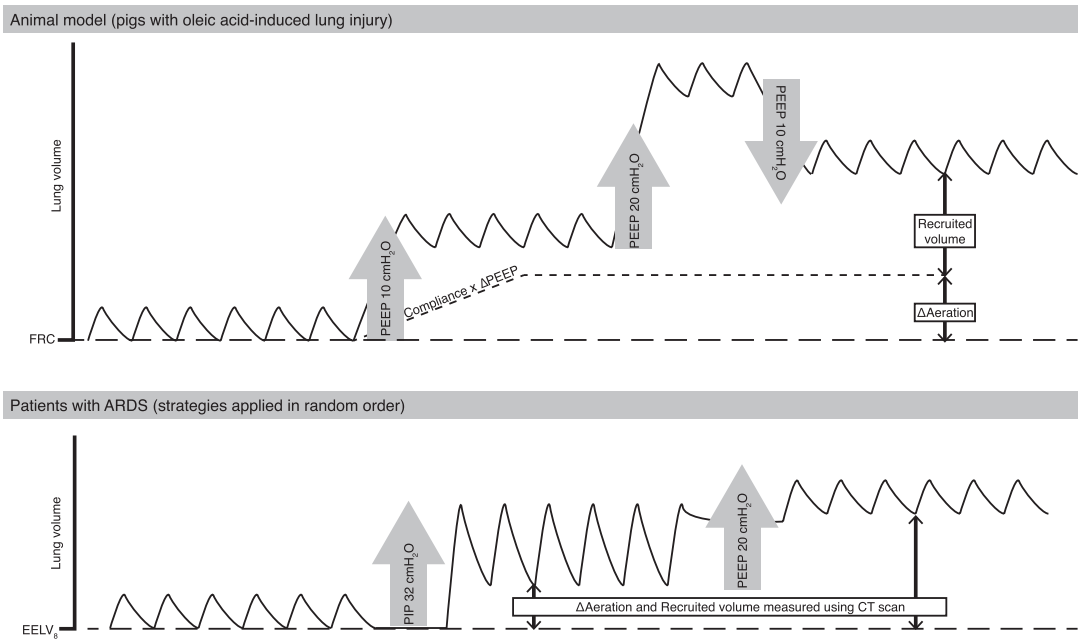
Animals were ventilated in volume-controlled mode (inspired oxygen fraction [F_{IO_2}], 0.8; tidal volume, 8 ml/kg; respiratory rate, 20 breaths/min; and PEEP 2 cm H_2O). An infusion of oleic acid (0.09 ml/kg) was administered by the jugular catheter to induce lung injury. After 90 min, the severity of injury was established. Then, PEEP was decreased to 0 cm H_2O (zero end-expiratory pressure), and blood gases, tidal volume, airway pressures, and the FRC were measured. Afterward, PEEP was increased to 10 cm H_2O and a new set of measurements was obtained. Finally, PEEP was increased to 20 cm H_2O and then decreased to 10 cm H_2O to promote lung recruitment. Again, data were collected in this final stage. Changes in PEEP were done only after stabilization of EELV. This protocol is depicted in figure 1.

Ventilatory Protocol and Data Acquisition in Patients

Six consecutive patients meeting ARDS criteria[17] were enrolled and studied within the first 72 h after diagnosis. Exclusion criteria were as follows: younger than 18 yr, more than 5 days of prior mechanical ventilation, presence of chronic respiratory diseases, air leaks, or severe hemodynamic instability. As all the patients were deeply sedated, informed consent was obtained from patients' next of kin. The protocol was reviewed and authorized by the regional ethics committee (Comité Ético de Investigación Clínica, Principado de Asturias, Spain).

After inclusion, demographic and clinical data were collected, including age, sex, weight, height, diagnoses, severity (using the second version of the Acute Physiology and Chronic Health Evaluation-II score), and baseline blood gases. Lung injury score[18] was computed. Patients, under sedation and muscle paralysis, were transferred to the CT scan ward and connected to an Evita 4 ventilator (Drager, Germany). Airway pressure, flow, volume, and exhaled P_{CO_2} were collected from the ventilator using the VentView software (Drager) and stored for subsequent analysis.

Under pressure-controlled ventilation, three different ventilatory settings were applied in random order: peak inspiratory pressure (PIP) 20 cm H_2O with PEEP 8 cm H_2O, PIP 32 cm H_2O with PEEP 8 cm H_2O, and PIP 32 cm H_2O with PEEP 20 cm H_2O. These settings were chosen to compare a "low-pressure" baseline (the 20/8 group) against high dynamic or high static strain conditions, respectively.



	Animal study		Patients
	Baseline	After recruitment	
Static strain	0	$\frac{\Delta\text{Aeration}}{\text{FRC+Recruited volume}}$	$\frac{\Delta\text{Aeration (above EELV}_8\text{)}}{\text{EELV}_8\text{+Recruited volume}}$
Dynamic strain	$\frac{\text{Tidal volume}}{\text{FRC}}$	$\frac{\text{Tidal volume}}{\text{FRC+Recruited volume}}$	$\frac{\text{CT-derived tidal volume}}{\text{EELV}_8\text{+Recruited volume}}$
Total strain	$\frac{\text{Tidal volume}}{\text{FRC}}$	$\frac{\Delta\text{Aeration+Tidal volume}}{\text{FRC+Recruited volume}}$	$\frac{\Delta\text{Aeration+CT-derived tidal volume}}{\text{EELV}_8\text{+Recruited volume}}$

Fig. 1. Schematic representation of the different ventilatory strategies applied in the animal model and in patients with acute respiratory distress syndrome (ARDS). Aeration in animals was computed as the product of compliance and an increase in positive end-expiratory pressure (PEEP, 10 cm H_2O), resulting in the predicted increase in volume above functional residual capacity (FRC) due to the increase in airway pressure (*dashed line*). Therefore, the additional increase up to end-expiratory lung volume (EELV) is recruited volume. In patients, all the measurements were done above the EELV at a PEEP of 8 cm H_2O ($EELV_8$). Equations used for strain measurements are presented. CT = computed tomography; PIP = peak inspiratory pressure.

Respiratory rate was modified to keep minute ventilation constant, avoiding air trapping. After an equilibrium time of 15 min, once provided that end-tidal carbon dioxide and tidal volume were in a steady state, an arterial blood sample was drawn for gas analysis. Then, end-inspiratory and end-expiratory pauses were performed to measure plateau pressure and total PEEP. Finally, six CT scan slices (1 mm thick, 120 kV, 335 mA/s) were acquired during the prolonged end-expiratory and end-inspiratory pauses. Voxel volume was 0.42 μl. All these measurements were repeated for each ventilatory setting.

Respiratory Mechanics and Gas Exchange

Compliance was computed from the stored tracings of pressure and volume as the ratio between tidal volume and driving pressure (plateau pressure – total PEEP). Alveolar dead space fraction was computed as the ratio as follows:

$$\frac{V_{D_{alv}}}{V_T} = \frac{Pa_{CO_2} - P_{ETCO_2}}{Pa_{CO_2}},$$

where Pa_{CO_2} and P_{ETCO_2} are arterial blood and end-tidal partial pressures of carbon dioxide, respectively.

CT Scan Analysis

Each CT scan slice was stored in DICOM (Digital Imaging and Communications in Medicine) format and analyzed using the ImageJ software.[19] The lung contour was manually drawn and a 16-bit histogram obtained. According to its density in Hounsfield units (HU), four lung compartments were defined: hyperinflated (–1,000 to –900 HU), normally

aerated (−899 to −500 HU), poorly aerated (−499 to −100 HU), and nonaerated (−100 to +100 HU). The total volume of each compartment was computed. The gas volume was also calculated by multiplying each voxel by its gas fractional content. No CT scan was acquired at the FRC due to the strong recommendations of maintaining a certain level of PEEP in ARDS patients. Therefore, the volume of lung gas present at a PEEP level of 8 cm H_2O during ventilation with a PIP equal to 20 cm H_2O was considered the baseline level in patients (represented as $EELV_8$ in fig. 1).

Strain Measurements

To distinguish between the increase in volume caused by changes in aeration or recruitment, we took advantage of our ventilatory protocol (fig. 1). In the animal model, the increase in aeration was quantified as the increase in EELV predicted by the increase in PEEP and the baseline compliance, as proposed by Dellamonica *et al.*[20] The additional increase in EELV at PEEP 10 cm H_2O obtained after the recruitment maneuver was considered recruited volume.

In patients, all the volumes were quantified using the gas content of the CT scan slices. CT scan–derived tidal volumes were computed as the difference in gas volume between end-inspiration and end-expiration. Recruited volume was measured as the gain in normally aerated lung volume at a given pressure after a recruitment maneuver (such as increasing driving pressure or PEEP). Therefore, recruited volume during ventilation with PIP 32/PEEP 8 was measured as the increase in normally aerated lung volume at end-expiration compared with ventilation with PIP 20/PEEP 8 (*i.e.*, at the same airway pressure of 8 cm H_2O). Similarly, recruited volume during ventilation with PEEP 32/PEEP 20 was measured as the difference in normally aerated lung volume between end-inspiration during ventilation with PIP 20/PEEP 8 and end-expiration with PEEP 20 cm H_2O (therefore, in both cases at an airway pressure of 20 cm H_2O).

Increases in aeration were calculated in each ventilatory strategy as the difference between the total volume gain and recruited volume. Once these increases were quantified, static, dynamic, and total strain were calculated as depicted in figure 1.

Statistical Analysis

Sample sizes were chosen based on previous experience, trying to minimize the number of animals and patients at risk. Data are presented as mean ± SD. Differences among ventilatory strategies were studied using a repeated-measurements ANOVA. When significant, pairwise comparisons were performed using Holm correction. Correlation analyses were performed using a random-effects linear model. A two-tailed *P* value of less than 0.05 was considered significant. All the statistical analyses were performed using the R 3.0.2 statistical package.[21]

Results

Recruitment Modifies Strain in an Animal Model

Six oleic acid–treated pigs were studied to characterize the potential impact of recruitment on lung strain. After injury, the FRC was 381 ± 114 ml. After increasing PEEP to 10 cm H_2O, measured EELV was 657 ± 270 ml. The estimated increase in aeration was 110 ± 15 ml. After the recruitment maneuver (temporary increase in PEEP to 20 cm H_2O), EELV further increased to 770 ± 356 ml, rendering a mean recruited volume of 224 ± 95 ml (P = 0.041 for the changes in EELV among the three interventions). Pao_2/Fio_2 increased from 186 ± 106 mmHg (at zero end-expiratory pressure) to 342 ± 137 mmHg (PEEP 10 cm H_2O, before the recruitment maneuver) and 390 ± 107 mmHg (PEEP 10 cm H_2O, after the maneuver, P = 0.038 in the ANOVA).

The changes in strain induced by recruitment are shown in figure 2. Total strain did not change after PEEP increments (fig. 2A). As hypothesized, the increase in recruited volume was related to a significant decrease in dynamic strain (fig. 2B) and an increase in static strain (fig. 2C).

Strain Is Modified by Recruitment in ARDS Patients

To translate these findings to the clinical setting, six patients were studied. All of them completed the ventilatory protocol without adverse events. Demographical and clinical data are presented in table 1. There was a significant improvement in Pao_2 during ventilation with PEEP 20 cm H_2O. Regarding ventilation, the different combinations of plateau and end-expiratory pressures yielded significant differences in tidal volumes, with a significant increase during ventilation with a driving pressure of 24 cm H_2O over a PEEP of 8 cm H_2O. In spite of respiratory rate adjustments, $Paco_2$ decreased during this stage. However, there were no significant differences in respiratory system compliance or alveolar dead space ratio. There were significant increases in EELV among the different ventilatory strategies, due to changes in both aeration and recruited volume. These data are presented in table 2.

Strain was computed using the changes in lung air content in six CT scan slices. Interestingly, there were no significant differences in total strain among the three ventilatory strategies (fig. 3A). This absence of differences was caused by a trade-off between dynamic and static strain. There were no significant differences in dynamic strain when increasing driving pressure, keeping constant the PEEP level. However, increasing PEEP to 20 cm H_2O caused a significant decrease in dynamic strain (fig. 3B). Static strain showed an opposite behavior. There were no significant differences in static strain when driving pressure was increased but increased when PEEP was increased up to 20 cm H_2O (fig. 3C).

Cyclic changes in aeration of the normally aerated lung are a major determinant of its metabolic response.[13] Therefore, we repeated the strain measurements using only changes in the gas content of this normally aerated compartment. The results are shown in figure 4. Dynamic strain was almost

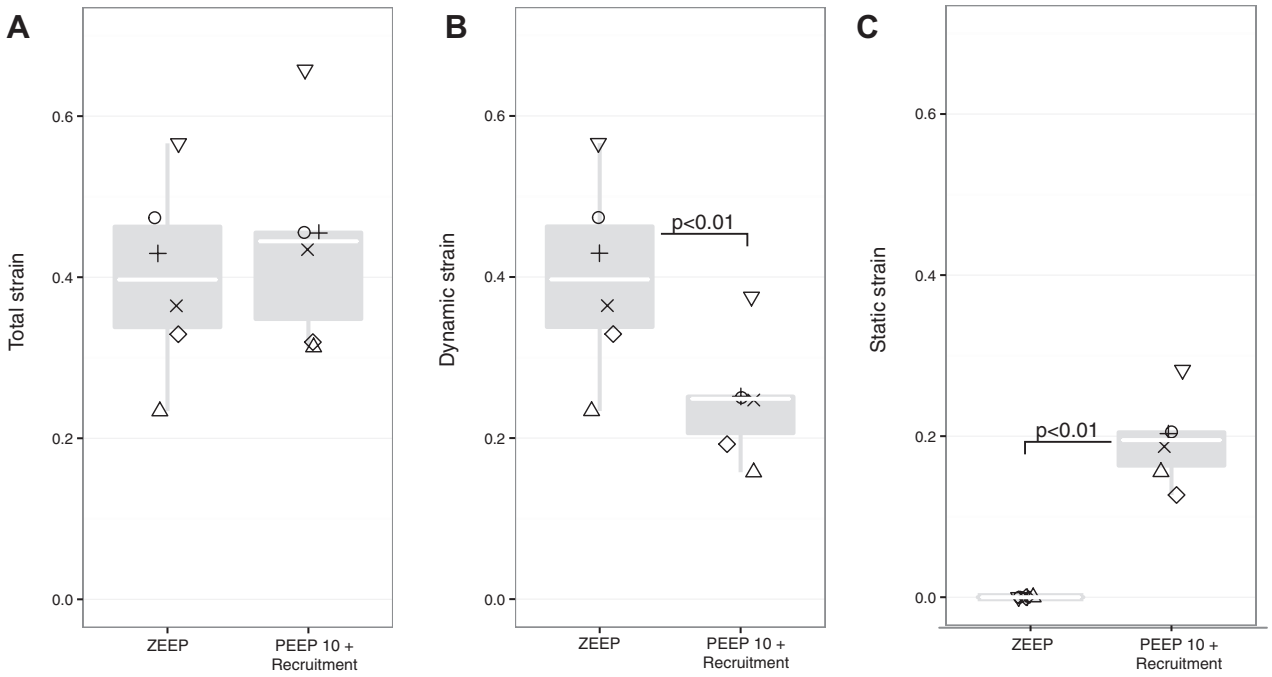


Fig. 2. Results from the animal study. In oleic acid–injured animals, increasing positive end-expiratory pressure (PEEP) did not modify total strain (*A*), but decreased dynamic strain (*B*) and increased static strain (*C*). Each *symbol* represents one animal. Significant differences are shown. ZEEP = zero end-expiratory pressure.

Table 1. Characteristics of the Sample

Patient No.	Sex	Age (yr)	Cause of ARDS	APACHE-II	LIS	Pao_2/FIo_2	Outcome
1	F	62	Septic shock	14	3.5	153	S
2	F	51	Pneumonia	26	3.25	152	D
3	M	56	Polytrauma	14	3.25	180	D
4	M	40	Alveolar hemorrhage	22	3.25	63	D
5	F	74	Pancreatitis	18	3.5	118	S
6	F	36	Pneumonia	29	2.75	205	S
Mean ± SD		53 ± 14		21 ± 6	3.25 ± 0.27	145 ± 50	

APACHE-II = Acute Physiology and Chronic Health Evaluation-II score, version 2; ARDS = acute respiratory distress syndrome; D = dead; F = female; FIo_2 = fraction of inspired oxygen; LIS = lung injury score; M = male; Pao_2 = partial pressure of the oxygen in arterial blood; S = survivor.

Table 2. Gas Exchange (Pao_2 and $Paco_2$), Tidal Volume, Crs, Alveolar Dead Space Fraction ($V_{D_{alv}}/V_T$), CT-derived Values of Tidal Volume, and EELV for the Different Ventilatory Settings Applied

	PIP 20/PEEP 8	PIP 32/PEEP 8	PIP 32/PEEP 20
Pao_2 (mmHg)	127 ± 48	150 ± 58	242 ± 70*†
$Paco_2$ (mmHg)	58 ± 14	41 ± 8*	57 ± 13†
Tidal volume (ml)	365 ± 155	707 ± 290*	320 ± 111†
Crs (ml/cm H_2O)	26 ± 10	29 ± 11	25 ± 7
$V_{D_{alv}}/V_T$	0.49 ± 0.13	0.47 ± 0.14	0.55 ± 0.06
CT-derived V_T (ml per three slices)	3.9 ± 1.8	4.9 ± 1.2*	1.9 ± 1†
EELV (ml per three slices)	11.8 ± 4	14.6 ± 5.4*	24.2 ± 7.7*†
Aeration (ml per three slices)	—	0.8 ± 1.1	4.9 ± 1.6†
Recruitment (ml per three slices)	—	1.9 ± 1.6	7.5 ± 3†

* $P < 0.05$ in *post hoc* test compared with PIP 20/PEEP 8. † $P < 0.05$ in *post hoc* test compared with PIP 32/PEEP 8.

Crs = respiratory system compliance; CT = computed tomography; EELV = end-expiratory lung volume; $Paco_2$ = partial pressure of carbon dioxide in arterial blood; Pao_2 = partial pressure of oxygen in arterial blood; PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure; $V_{D_{alv}}/V_T$ = alveolar dead space/tidal volume.

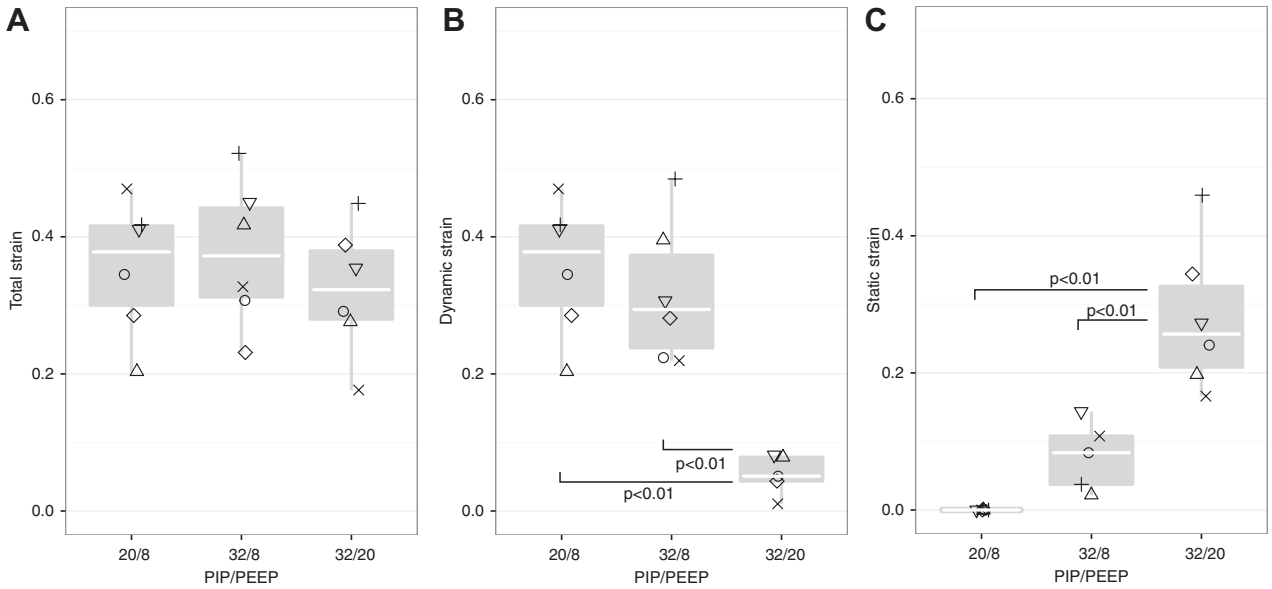


Fig. 3. Differences in total (*A*), dynamic (*B*), and static (*C*) strain among the three ventilatory strategies applied to patients. Each *symbol* represents one patient. Significant differences in *post hoc* tests are drawn. PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure.

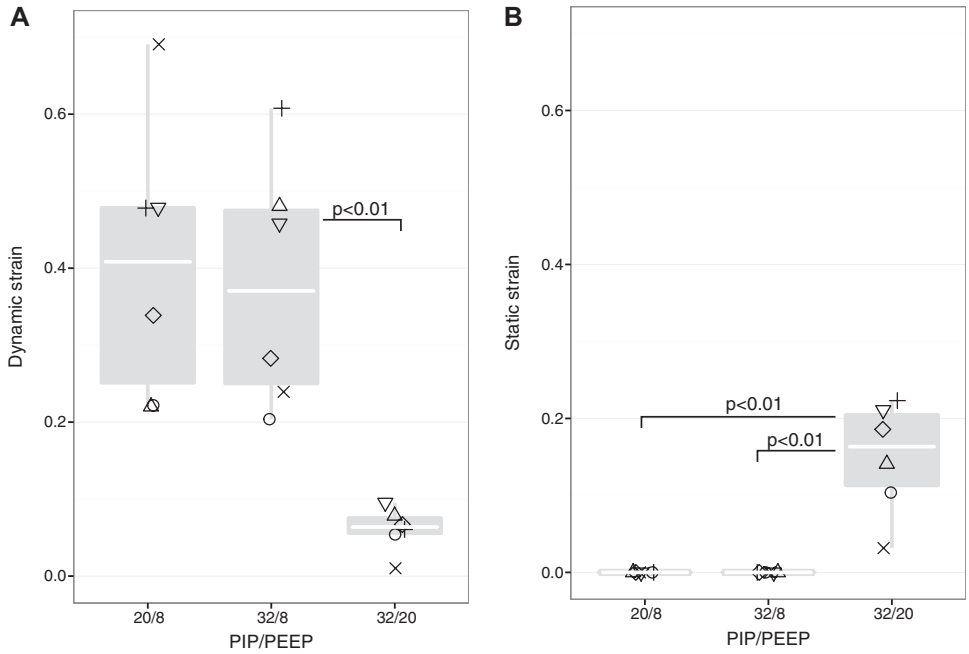


Fig. 4. Differences among the three ventilatory strategies in dynamic (*A*) and static (*B*) strain of normally aerated lung tissue. Each *symbol* represents one patient. Significant differences in *post hoc* tests are drawn. PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure.

abolished (fig. 4A) with a PEEP of 20 cm H_2O, whereas static strain increased with PEEP increments (fig. 4B).

Finally, in order to clarify the role of recruitment in the strain measurements, we performed a correlation analysis. There was a significant correlation between recruited volume and changes in total strain (R^2 = 0.25, P = 0.024; fig. 5A) or changes in dynamic strain (R^2 = 0.61, P = 0.006; fig. 5B). There was no significant correlation between recruited volume and changes in static strain (R^2 = 0.38, P = 0.159; fig. 5C).

There were no significant relations between strain and other measured parameters including oxygenation, ventilation, alveolar dead space, or respiratory system compliance (data not shown).

Discussion

Our results demonstrate that PEEP changes in experimental and human ARDS have a major impact on the strain

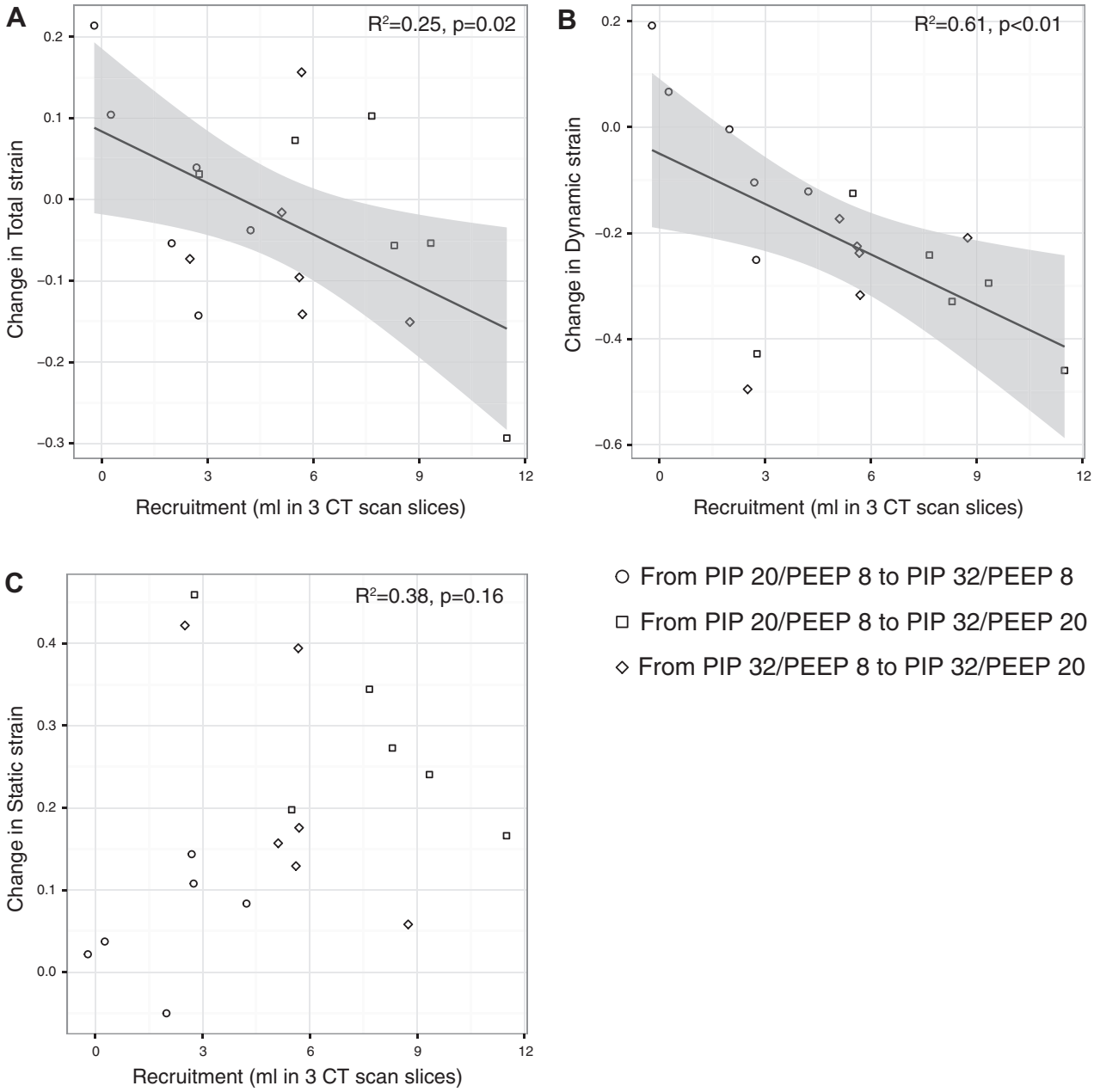


Fig. 5. Correlation of recruited volume measured in the three computed tomography (CT) scan slices and changes in total (*A*), dynamic (*B*), and static (*C*) strain among the different ventilatory strategies tested. *Shaded areas* represent the 95% CI of the regression line. PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure.

imposed by the ventilator to the lung parenchyma. Globally, increasing PEEP induces a shift from dynamic to static strain, while preserving gas exchange and compliance. The mechanism responsible for these changes is the increased lung rest volume due to recruitment of previously nonaerated areas.

Limitation of VALI is a major goal in the contemporary management of ARDS.[2] Reduced tidal volume and a certain level of PEEP are part of this strategy. However, there are no clear guidelines on which are the best ventilatory settings for a specific patient. Moreover, widely accepted protocols (such as those tested in the Acute Respiratory Distress Syndrome Network [ARDSNet] clinical trials) may have beneficial or harmful effects in different patients.[22,23] Different parameters derived from respiratory mechanics have been proposed to individually optimize the ventilatory management at the bedside.[24] Among these, plateau pressures have been tested as a marker of alveolar overstretching. Nevertheless, there are many factors that influence this measurement. In fact, randomized trials testing two different PEEP levels yielded different plateau pressures with no differences in outcomes between groups.[25,26] Similarly, respiratory system

compliance is modified by many factors such as ongoing recruitment and overdistension and, therefore, is not a reliable guide.[27] Even more complex global measurements, such as pressure–volume curves, face similar problems.[28]

In this setting, measurement of lung strain has been recently proposed as a better marker of the superimposed mechanical load to the lung parenchyma. The original definition of strain assumes that after an increase in PEEP, the lung is exposed to both continuous and cyclic mechanical loads, resulting in the partitioning in static and dynamic strain.[11] However, only the cyclical changes in aeration or pressure were correlated with lung injury in experimental models of ventilator-induced lung injury, including cell[29] and animal studies.[11,30] In patients, the ratio between tidal volume and EELV, a surrogate marker of the ratio between static and dynamic strain, has been related to the lung inflammatory response.[12,13] Moreover, recent analyses suggest that reduction in driving pressure, also a marker of dynamic lung strain, is related to an improved survival in ARDS patients.[31] Therefore, reduction in dynamic strain could be a relevant clinical goal to minimize further lung damage in ventilated ARDS patients.

Our results demonstrate that increasing PEEP is related to a decrease in dynamic strain, keeping constant total strain. This is due to the achieved recruitment that increases the lung volume available for ventilation. In the same sense, increasing driving pressure (and thus tidal volume) may also cause recruitment due to the high end-inspiratory pressure reached.[32] This phenomenon can explain the absence of an increase in dynamic strain in the group with the highest driving pressures. Previous studies have measured the changes in strain after PEEP changes or different recruitment strategies.[20,33,34] However, no data on dynamic strain were provided. Of note, our measurements of recruited volumes were conservative, as we did not consider the gas volume in poorly aerated areas (in patients) or tidal recruitment (in both series). If this additional volume is taken into account, the effects of high PEEP levels on dynamic strain could be even more pronounced. On the other side, helium dilution may not include areas with low ventilation or trapped air, which could contribute to the recruited volume after increasing PEEP or tidal volumes. The relevance of these zones to the distribution of mechanical loads in the remaining parenchyma has not been clarified. In spite of the marked effect of PEEP on dynamic strain, it must be recognized that high PEEP levels may have other undesired effects, such as severe hemodynamic impairment and right ventricle overload[35] or overstretching of aerated alveoli.[36] These factors could explain the lack of benefits of high PEEP levels in clinical trials.

We did not observe a correlation between recruited volume and static strain. The changes in static strain depend not only on recruited volumes but also on increases in aeration. As the relation between these two phenomena can be highly variable, due to the different potential of recruitment among patients,[37] this lack of association is not surprising. In the same sense, other variables, such as respiratory system compliance, alveolar dead space, or $Pa_{O_2}/F_{I_{O_2}}$, were not related to changes in strain. This could be due to the changes in recruited volume, aeration, and regional blood flow driven by airway pressures, resulting in mixed changes in the regional mechanics and in the distribution of ventilation/perfusion ratios along the parenchyma. In other words, the complexity of local changes cannot be summarized using the average values of global changes.[38]

The major limitation of the current study is the small number of patients included. The potential for recruitment in ARDS lungs can be highly variable,[37] thus determining different responses in strain. Increasing tidal volume had mixed effects on total, dynamic, and static strain. However, increasing PEEP systematically increased static and decreased dynamic strain in all patients, mimicking the animal model. Moreover, the close correspondence between animal and human data reinforces the idea that the underlying mechanism that explains the different responses in strain is recruitment (either induced by tidal volume or maintained by PEEP). With these results, increasing the sample size would not lead to a significant change in the conclusions. Another limitation comes from the study of only three CT scan slices instead of the whole lung. This strategy aims to reduce the radiation dose received by the patient. Although there could be some discrepancies between these regional measurements and the whole lung,[39] reflected by the nonlinear change in CT scan–derived tidal volumes, as FRC, the computation of regional strain remains valid as aeration and recruitment were measured in the same slices.

In conclusion, our series show how recruitment has a large influence on strain in the injured lung. Therefore, focusing in strain as a relevant target aimed to reduce VALI implies the need for an accurate measurement of recruited volume.

Acknowledgments

Supported by Consejería de Economía, Principado de Asturias, Oviedo, Spain (GRUPIN14-089). Dr. Albaiceta is the recipient of a grant from the Instituto de Salud Carlos III, Madrid, Spain (INT14-00062).

Competing Interests

The authors declare no competing interests.

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