Intensive Care Med (1986) 12:137–142

Intensive Care Medicine

Morphological response to positive end expiratory pressure in acute respiratory failure. Computerized tomography study

L. Gattinoni [1], D. Mascheroni [1], A. Torresin [2], R. Marcolin [1], R. Fumagalli [1], S. Vesconi [1], G. P. Rossi [1], F. Rossi [1], S. Baglioni [1], F. Bassi [1], G. Nastri [3] and A. Pesenti [1]

[1] Istituto di Anestesiologia e Rianimazione, Università degli Studi di Milano, and [2] Servizio Fisica Sanitaria and [3] Servizio Radiologia – TAC, IRCACS, Ospedale Maggiore, Milan, Italy

Accepted: 1 November 1985

Abstract. Ten patients with acute respiratory failure (ARF), (4 pneumonia, 4 sepsis, 2 polytrauma), underwent computerized tomography (CT) of the lungs, (apex, hilum, base), at 5, 10, 15 cm H_2O positive end expiratory pressure (PEEP). The ARF lungs, on CT scan, appeared as a patchwork of normal and dense areas with generally well defined boundaries. Most of the densities were found in the dependent regions. The areas of density were correlated with PaO_2 ($r = 0.51$). The PEEP increase resulted in a significant expansion of total cross-sectional lung surface area. The dense areas decreased significantly at the hilum and base when increasing PEEP while the changes at the apex were not significant. The changes of density with PEEP were highly correlated with the changes in oxygenation ($r = 0.91$). In the individual patient, however, the modifications of gas exchange can not be entirely predicted from morphological changes, possibly due to a diversion of pulmonary blood flow.

Key words: Acute respiratory failure – PEEP – CT scan

Since the introduction of PEEP in the treatment of parenchymal acute respiratory failure (ARF) [2] several studies have attempted to elucidate its mechanisms of action; these have been recently reviewed [6].

There is a general agreement that PEEP acts by increasing the functional residual capacity through alveolar expansion and/or recruitment.

However, the effects of PEEP have been always inferred from gas exchange and/or modifications of pulmonary mechanics. The aim of this preliminary paper is to provide direct evidence of PEEP induced morphological modifications of lung parenchyma in a group of patients with ARF undergoing lung scanning by computerized tomography (CT).

Materials and methods

The study population consisted of 10 patients with ARF (6 males, 4 females mean age 40.5 ± 20 years, range 11–74). The etiology of lung injury, the oxygenation during standardized mechanical ventilation as well as the final outcome are summarized in Table 1.

Experimental procedure

All patients were already being mechanically ventilated, before the study and were paralyzed and anesthetized with i.v. drugs. After a chest X ray in the ICU (at the end of expiration, PEEP = 10 cm H_2O) the patients were transferred to the radiology department. Continuous monitoring and mechanical ventilation were provided in the CT room with identical instrumentation and care as in the ICU setting.

PEEP study

The mechanical ventilation (Servo B or C, Siemens) in the CT room was delivered in a volume controlled mode with the following parameters: $FiO_2 \geqslant 0.6$, tidal volume 10 ml kg^{-1}, respiratory rate 16–20 b.p.m., square wave form, inspiratory/expiratory ratio 1:1, end inspiratory pause = 0. In each patient, PEEP was applied at 5, 10 and 15 cm H_2O in randomized sequence, while all other parameters were kept constant. Each level of PEEP was maintained for at least 15 min before the CT scan.

CT scan

After obtaining a frontal tomogram covering the chest, three levels were selected for CT scanning: the first above the carina (apex) the second at the hilum (hilum) and the third 1–2 cm above the diaphragm (base), as described by Hedenstierna et al. [4] for

Table 1. ARF etiology, oxygenation, and outcome of the study population. The PaO_2 shown were recorded in ICU, before the CT scan, after 30 min of mechanical ventilation, with the patients paralyzed and anesthetized. Mechanical ventilation was delivered under the following conditions: Tidal volume 10 ml kg^{-1}, respiratory rate 16 – 20 bpm, PEEP = 10 cm H_2O, FiO_2 = 0.6

Patients	ARF etiology	PaO_2 (mm Hg)	Final outcome
1	Bacterial pneumonia in heroin addicted, rhabdomyolysis, multiple organ failure	67	Survivor
2	Viral pneumonia in kidney transplant recipient	94	Died
3	Peritonitis	104	Survivor
4	Bacterial pneumonia in encephalitis coma	158	Survivor
5	Blunt chest trauma	65	Survivor
6	Viral pneumonia	85.1	Survivor
7	Peritonitis, hypovolemic shock	43.7	Died
8	Polytrauma	82	Survivor
9	Bacterial pneumonia	52	Survivor
10	Pulmonary embolism, sepsis, renal failure	61	Survivor

anesthetized patients. With the CT scanner we used (Pfizer AS E0450) a single exposure lasted 5 s. The slice thickness was 9 mm. Every single exposure was taken with the patient in apnea at the selected PEEP level. Within the exposures the mechanical ventilation was delivered for about 1 min. The scan procedure for a given level of PEEP (three exposures for each level of PEEP) was then completed in about 5 min. The entire study lasted at least 60 min (three levels of PEEP, 9 exposures). No attempts were made to compensate for the possible displacement of lung structures due to increase or decrease of PEEP (i.e., diaphragm movements). At each level of PEEP, after the CT scan was completed, arterial blood was sampled and analyzed immediately for gases (IL 1312).

CT scan analysis

Total lung cross-sectional surface area. The transverse areas of the thorax were obtained planimetrically using the digital PDP 11/23/RT 11 operative system connected to the scanner. For each lung the external boundary was drawn manually along the inside of the ribs, the internal boundary along the edge of the mediastinal organs. The total cross-sectional lung surface area, for each exposure, was then obtained from the sum of each individual lung area.

Computation of pathological and normal areas. The "normal" areas within the lung surface were also determined manually by planimetry with a PDP/23 computer. The areas were considered normal when the mean of the absolute CT numbers of that area was $\leqslant -400$ Hounsfield (H) units (air = -1000 H, water = 0 H).

The pathological (density) areas were then computed by subtracting the normal areas (average CT number $\geqslant -400$ H) from the total cross-sectional lung surface areas.

The -400 H was chosen arbitrarily as discriminant after the observation of the biphasic frequency distribution of CT numbers in each individual image.

The percent density was computed, for each patient at the given PEEP as the ratio between the total density areas (apex + hilum + base) and the total cross-sectional lung surface areas (apex + hilum + base).

The planimetric method we used was validated by scanning a model of different materials of known areas. The variation coefficient in this case was within 0.3% and 1%.

In planimetry of the real CT images, with areas of different size and shape, the variation coefficient was within 1% – 7% (the higher the area the lower the error).

Statistics

Data are expressed as mean ± 1 SD. Significance of differences between results was tested by paired Student's t test. Correlation between variables was tested by linear regression analysis and multiple regression analysis using a dummy variable for each patient [1].

Results

On the CT scan the lungs in ARF appear as a patchwork of normal and dense areas, with generally well defined boundaries. All the patients had dense areas of variable size in the dependent part of the lungs, while the non dependent regions appeared normal. The apex was less compromised whilst the hilum and base were more affected.

The highest percentage area of density found was 90% of the total cross-sectional lung surface area.

The patchwork of dense and normal areas is less apparent on the standard chest X ray as shown in

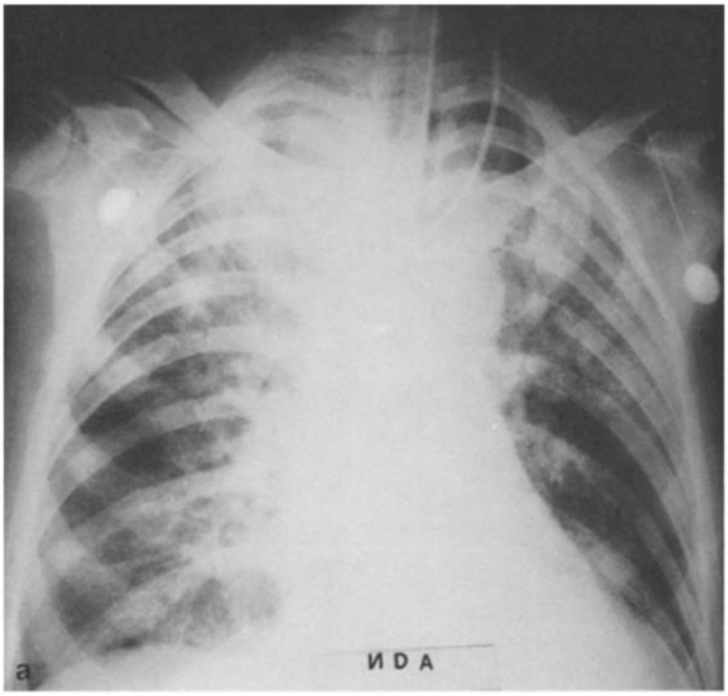
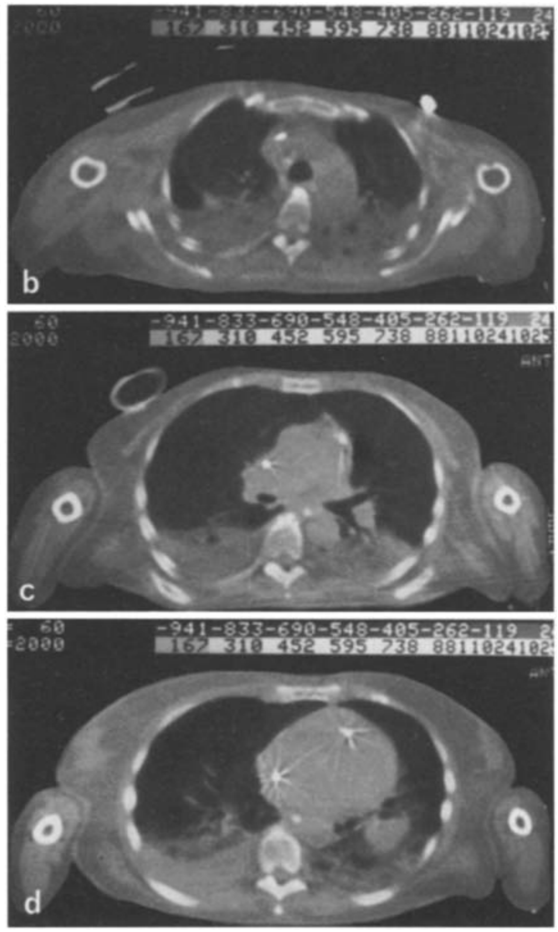



Fig. 1. **a** Chest X ray and **b** – **d** CT scan [apex (**b**), hilum (**c**) and base (**d**)] in ARF from sepsis. All the images were taken during apnea at 10 cm H_2O inflation. CT scan shows the typical gravity-dependence of the lung injuries

Figure 1. This discrepancy between chest X ray and CT images is further emphasized in Figure 2.

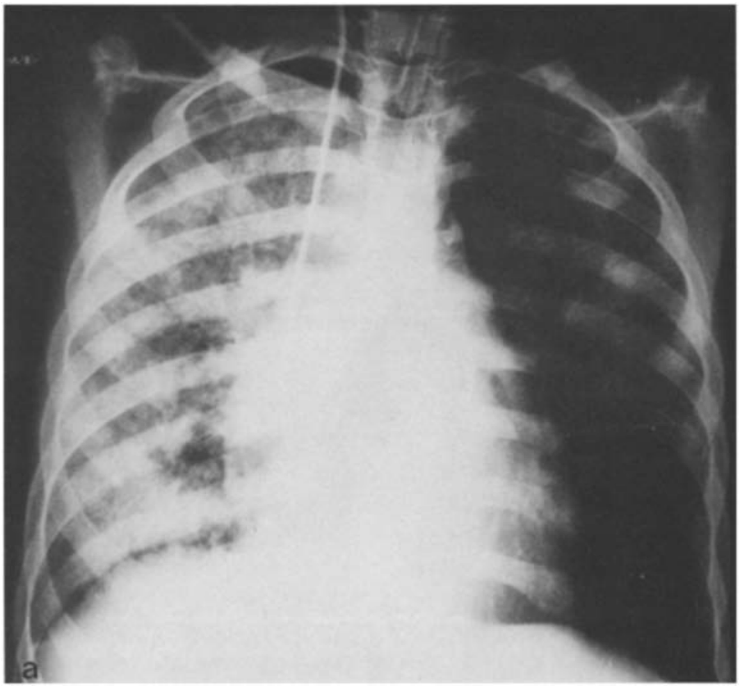
Pooling all the data, the percent of dense areas correlated with PaO_2 ($r = 0.51$) (Fig. 3). If the variability between patients is taken into account, the correlation coefficient rises to 0.91 (multiple regression analysis using a dummy variable for each patient) [1].

Figure 4 shows the morphometrical response to PEEP. Apex, hilum, and base areas significantly increase when increasing PEEP. PEEP decreased significantly the dense areas at the hilum and at the base but changes at the apex were not significant. Figure 5 shows the modification of CT images when increasing PEEP in two patients, of which one improved the gas exchange (lower panel) and one did not (upper panel).

Discussion

Rommelsheim et al. [5] were the first, to our knowledge, to report a CT scan study in ARF patients. As in the present study the gravity-dependency of the intraparenchymal densities was a major finding. Induction of anesthesia in normal subjects produces similar densities, though quantitatively smaller, in the dependent regions of both lungs [3]. These densities are not detected by the standard chest X ray. In our patients too the chest X ray does not entirely reflect the overall lung involvement as observed with CT scan images. Are the densities really areas of pathology? We have some indirect evidence of this since the percent of density correlated with the severity of gas exchange impairment ($r = 0.51$). Taking in account the variability between patients most of the oxygenation changes may be explained by changes of the densities ($r = 0.91$).

Unfortunately, we can not draw any inference about the pathological nature of these areas. Atelectasis, edema, consolidation, or a combination of these three kinds of lesion produce densities, which can not be discriminated by CT scan. The gravity-dependency, however, suggests that edema and atelectasis are the most likely causes of the densities that we observed. In a lung with 'leaking-capillaries', it seems reasonable to expect development of edema and, pos-



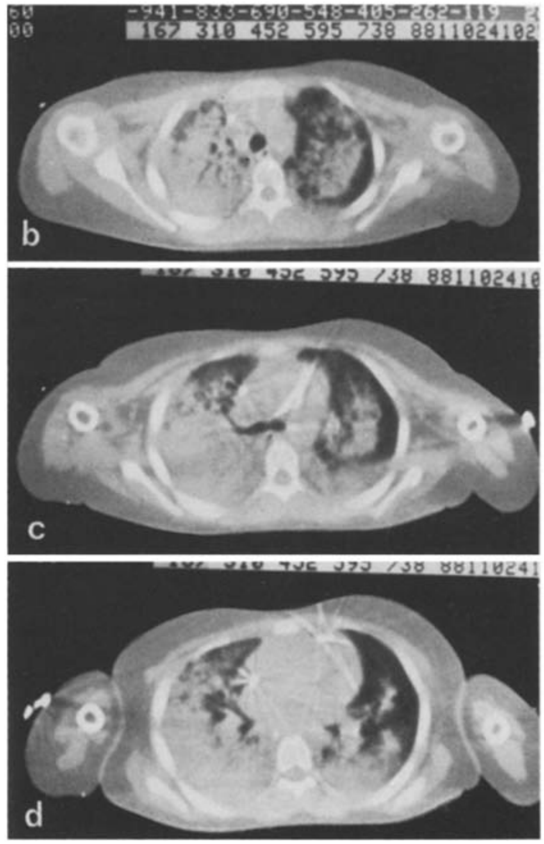


Fig. 2. **a** Chest X ray and **b – d** CT scans [apex (**b**), hilum (**c**) and base (**d**)] in ARF from viral pneumonia. All the images were taken at 10 cm H_2O inflation. While the chest X ray shows mainly a "unilateral" involvement, with hyperinflation of the left lung, the CT scan clearly demonstrates the parenchymal involvement of the left lung

sibly, of reabsorption atelectasis in the more dependent regions, where the capillary pressures are highest. In four of our patients, where we had evidence of consolidated pneumonia (diagnosed on the basis of chest X ray, bronchial cultures, and clinical signs) the consolidations were also observed in the dependent regions. However, pneumonia could have developed on a previous atelectasic area, or, alternatively, this finding could be of no significance with the limited number of observations.

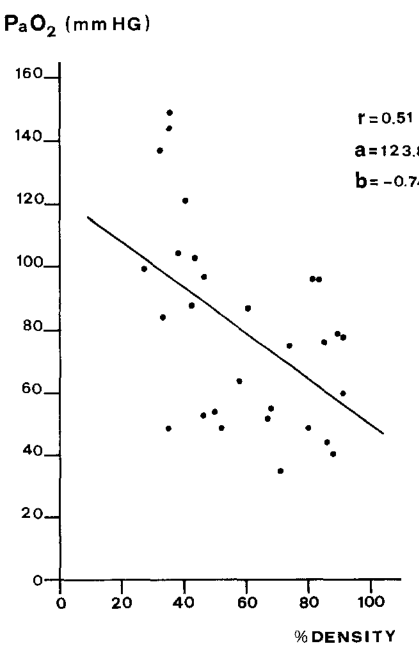


Fig. 3. PaO_2 as a function of percent of density areas ($p < 0.001$)

The application of PEEP induced two morphological changes: expansion of the total cross-sectional lung surface area and/or decrease of the intraparenchymal densities. In our patients a significant expansion was observed at every level of exposure (apex, hilum and base), when increasing PEEP, while a significant decrease of the densities occurred only at the hilum and at the base.

Considering Figure 4 it would be tempting to consider the total increase of lung cross-sectional surface area as the morphological equivalent of alveolar expansion, and the absolute decrease of the intraparenchymal densities as the morphological equivalent of alveolar recruitment. In a few instances we had complete clearing of the densities and in these, we are fully justified in considering most of the alveoli to be "recruited". However, when the intraparenchymal densities do not disappear completely, but only reduce in size, it is not possible to discriminate, with the methods of analysis we used, between real recruitment and

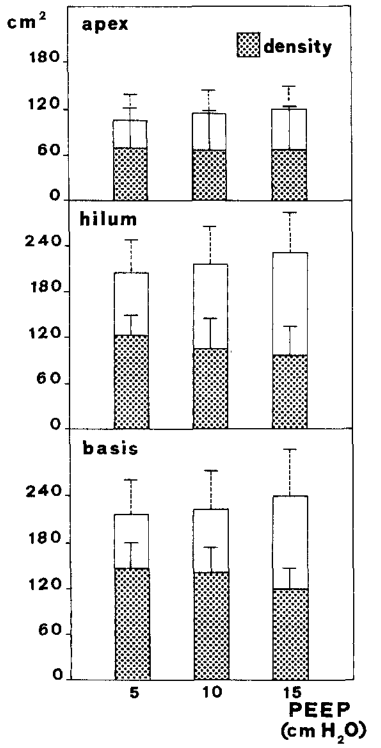


Fig. 4. Lungs cross-sectional surface areas at different PEEPs. The superimposed shaded areas represent the surface of the dense areas. All the changes of the lung cross-sectional surface areas when increasing PEEP are significant ($p<0.05$), but at the apex and at the base from 5 to 15 cm H_2O (NS). The dense area changes are significant only at the hilum (from 5 to 15 cm H_2O PEEP, $p<0.05$), and at the base (from 5 to 15 and 10 to 15 cm H_2O, $p<0.05$)

"compression" of the densities by "overexpansion" of previously open areas.

Most of the gas exchange modifications, while applying PEEP, may be explained by the changes in density. However, in the individual patient a decrease of density may be accompanied by a steady or even decreased PaO_2. This finding may suggest a concomitant diversion of pulmonary blood flow.

We conclude, from this study, that the lung injuries in ARF are mainly gravity-dependent, and that the application of PEEP causes both expansion of lung cross-sectional surface area and absolute decrease of the intraparenchymal densities. Decrease of the densities correlates with an increase of PaO_2, however, modifications of gas exchange are not entirely predictable from morphological changes, due to a possible diversion of pulmonary blood flow.

Acknowledgements. We thank Dr. G. Hedenstierna for his essential contribution in stimulating and discussing this work. The paper was supported in part by CNR grant 8402098.57-Rome, Italy.

References

1. Armitage P (1979) Metodi statistici per la ricerca in medicina. In: Statistica medica. Feltrinelli, Milan, p 316
2. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE (1967) Acute respiratory distress in adults. Lancet 2:320
3. Brismar B, Hedenstierna G, Lundquist H, Strandberg A, Svens-

PEEP: 5 cm H_2O **PEEP: 10 cm H_2O** **PEEP: 15 cm H_2O**

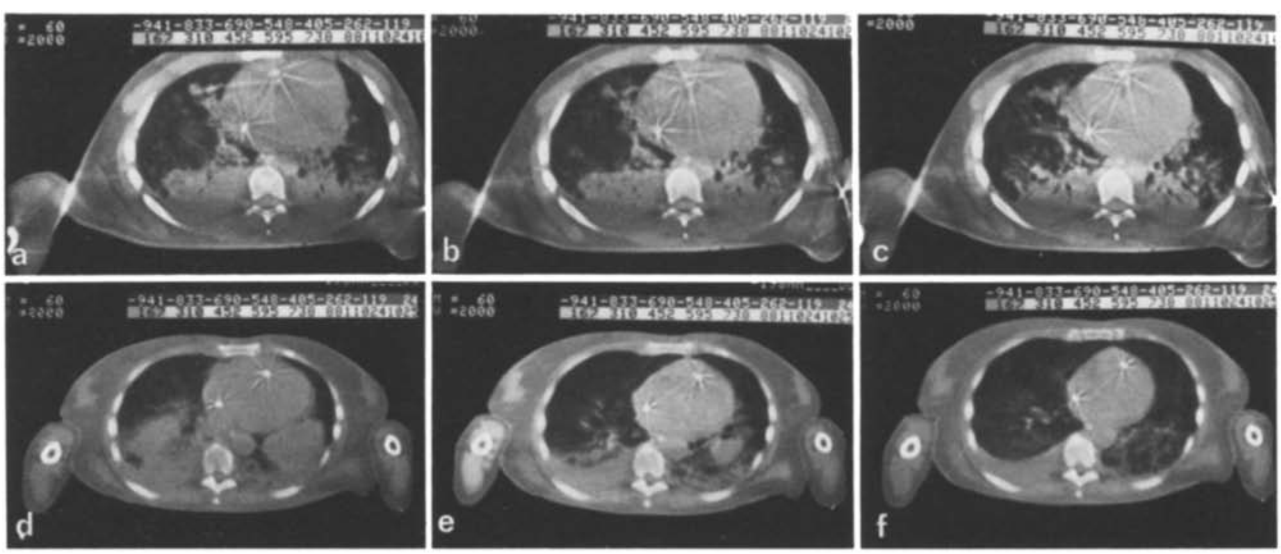


Fig. 5. **a – c** ARF from bacterial pneumonia (pt 1). CT scan of the base at 5, 10 and 15 cm H_2O PEEP. No changes in density and PaO_2 are observed: **a** PaO_2: 97 mm Hg, density 59%; **b** PaO_2: 103 mm Hg, density 56%; **c** PaO_2: 106 mm Hg, density 53%. **d – f** ARF from sepsis (pt 10). CT scan of the base at 5, 10 and 15 cm H_2O. Substantial clearing of the densities is accompanied by increase of PaO_2. **d** PaO_2: 34 mm Hg, density 70%; **e** PaO_2: 49 mm Hg, density 52%; **f** PaO_2: 121 mm Hg, density 32%

son L, Tockics L (1985) Pulmonary densities during anesthesia with muscular relaxation. A proposal of atelectasis. Anesthesiology 62:422
4. Hedenstierna G, Strandberg A, Brismar B, Lundquist H, Svensson L, Tockics L (1985) Functional residual capacity. Thoracoabdominal dimension and central blood volume, during general anesthesia with muscle paralysis and mechanical ventilation. Anesthesiology 62:247
5. Rommelsheim K, Lackner K, Westhofen P, Distelmaier W, Hirt S (1983) Das respiratorische Distress-Syndrom des Erwachsenen (ARDS) im Computertomogramm. Anasth Intensivither Noftallmed 18:59
6. Shapiro BA, Cane RD, Harrison RA (1984) Positive end-expiratory pressure therapy in adults with special reference to acute lung injury: a review of the literature and suggested clinical correlations. Crit Care Med 2:127

Dr. Luciano Gattinoni
Istituto di Anestesiologia e Rianimazione
Via Francesco Sforza 35
I-20122 Milano
Italy