# Ultrasound assessment of antibiotic-induced pulmonary reaeration in ventilator-associated pneumonia*

Bélaïd Bouhemad, MD, PhD; Zhi-Hai Liu, MD; Charlotte Arbelot, MD; Mao Zhang, MD; Fabio Ferarri, MD, PhD; Morgan Le-Guen, MD; Martin Girard, MD; Qin Lu, MD, PhD; Jean-Jacques Rouby, MD, PhD

***Objectives:*** **To compare lung reaeration measured by bedside chest radiography, lung computed tomography, and lung ultrasound in patients with ventilator-associated pneumonia treated by antibiotics.**

***Design:*** **Computed tomography, chest radiography, and lung ultrasound were performed before (day 0) and 7 days following initiation of antibiotics.**

***Setting:*** **A 26-bed multidisciplinary intensive care unit in La Pitié-Salpêtrière hospital (University Paris–6).**

***Patients:*** **Thirty critically ill patients studied over the first 10 days of developing ventilator-associated pneumonia.**

***Interventions:*** **Antibiotic administration.**

***Measurements and Main Results:*** **Computed tomography reaeration was measured as the additional volume of gas present within both lungs following 7 days of antimicrobial therapy. Lung ultrasound of the entire chest wall was performed and four entities were defined: consolidation; multiple irregularly spaced B-lines; multiple abutting ultrasound lung "comets" issued from the pleural line or a small subpleural consolidation; normal aeration. For each of the 12 regions examined, ultrasound changes were measured between day 0 and 7 and a reaeration score was calculated. An ultrasound score >5 was associated with a computed tomography reaeration >400 mL and a successful antimicrobial therapy. An ultrasound score <–10 was associated with a loss of computed tomography aeration >400 mL and a failure of antibiotics. A highly significant correlation was found between computed tomography and ultrasound lung reaeration (Rho = 0.85, $p < .0001$). Chest radiography was inaccurate in predicting lung reaeration.**

***Conclusions:*** **Lung reaeration can be accurately estimated with bedside lung ultrasound in patients with ventilator-associated pneumonia treated by antibiotics. Lung ultrasound can also detect the failure of antibiotics to reaerate the lung. (Crit Care Med 2010; 38:84–92)**

**KEY WORDS: ventilator-associated pneumonia; lung ultrasound; alveolar recruitment**

In critically ill patients with acute lung injury, pulmonary aeration may be reliably assessed using bedside lung ultrasound (LUS) (1). Normal aeration is detected as the visualization of the pleural line with its characteristic lung sliding and artifactual horizontal A-lines (2). Pulmonary interstitial syndrome, which induces a moderate decrease in lung aeration caused by the thickening of interlobular septa, is detected as the presence of multiple and regularly spaced vertical B-lines (comet tails), at least 7 mm apart (3). Alveolar-interstitial edema resulting from the irruption of liquid within the alveolar space corresponds to the computed tomography (CT) entity of ground glass and is detected as abutting comet tails <3 mm apart (3). Lung consolidation appears as a tissue structure whose dimensions do not vary with respiratory movements and which contains white points characterized by an inspiratory reinforcement, corresponding to persisting aeration of distal bronchioles (4).

CT is the reference method for measuring lung aeration and its variations (5, 6). CT requires the transportation of the patient outside the intensive care unit (7) and exposes the patient to high radiation exposure (8), two limitations that preclude that routine use of CT in clinical practice. In addition, quantitative analysis of lung aeration is time consuming and requires much training. As different ultrasound patterns correspond to different degrees of aeration loss, therapeutic interventions aimed at increasing lung aeration, such as positive end-expiratory pressure or antimicrobial therapy for treating ventilator-associated pneumonia (VAP), should result in LUS changes. If the whole lung is examined, LUS might be accurate enough to quantify lung reaeration.

A prospective study was undertaken to compare the accuracy of bedside chest radiography (CRx) and LUS for measuring lung reaeration resulting from the administration of antibiotics in patients

***See also p. 308.**

From the Réanimation Polyvalente Pierre Viars, Department of Anesthesiology and Critical Care, Hôpital de la Pitié-Salpêtrière Assistance Publique Hôpitaux de Paris, Paris, France; Université Pierre et Marie Curie Paris-6 (BB, FF, ML, CA, MG, QL, JJR), Paris, France; and Department of Emergency Medicine (ZH, MZ), Second Affiliated Hospital, Zhejiang University, School of Medicine, Hangzhou, China.

Fabio Ferarri is a research fellow with the Department of Anesthesiology, Faculdade de Medicina da Universidade Estadual Paulista Julio de Mesquita Filho, Botucatu, Brazil, and recipient of a postdoctorate award from CNPQ-Brasil/Processo 201023/2005-9. Martin Girard is a Research Fellow with the Department of Anesthesiology and Critical Care, Centre Hospitalier de l'Université de Montréal, Canada, and recipient of a scholarship from the Royal College of Physicians and Surgeons of Canada.

Presented, in part, at the 19th Annual Congress of the European Society of Intensive Care Medicine, Barcelona, Spain, September 24–27, 2006.

The authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: jean-jacques.rouby@psl.aphp.fr



**DOI: 10.1097/CCM.0b013e3181b08cdb**

with VAP. CT of the whole lung served as gold standard for measuring lung reaeration.

## METHODS

*Patients.* After gaining approval of the ethical committee of La Pitié-Salpêtrière hospital and obtaining written informed consent from patients' next of kin, we prospectively included 30 consecutive patients with VAP proven by clinical, radiologic, biological, and microbiological criteria (9). For each patient, the diagnosis of VAP was established according to two criteria: a clinical pulmonary infection score $\geq$6 (10) and a positive lower respiratory tract specimen obtained from a fiberoptic nonprotected bronchoalveolar lavage (BAL) or a protected minibronchoalveolar lavage (mini-BAL) (11). A positive sample was defined as $\geq 10^4$ colony-forming units/mL for nonprotected BAL and $\geq 10^3$ colony-forming units/mL for protected mini-BAL (10, 12, 13). In each patient, a transesophageal echocardiography was performed to rule out systolic and diastolic left ventricular dysfunction causing cardiogenic pulmonary edema. Subcutaneous emphysema and thoracic dressings were exclusion criteria.

*Lung Ultrasound.* LUS was performed using an HP-SONOS 5500 (Hewlett-Packard, Andover, MA) and a 2- to 4-MHz round-tipped probe. As previously described (1), all intercostal spaces of upper and lower parts of anterior, lateral, and posterior regions of left and right chest wall were examined, and videos were stored on magneto-optical disks. Each region of interest was extensively examined, and the worst ultrasound abnormality detected was considered as characterizing the region examined. The mean duration of a complete ultrasound exam was around 10 mins.

Four ultrasound patterns were defined: 1) normal aeration (no bronchopneumonia): presence of lung sliding with A-lines and, occasionally, an isolated B-line (2); 2) loss of lung aeration resulting from scattered foci of bronchopneumonia or interstitial pneumonia: presence of multiple well-defined and irregularly spaced ultrasound lung "comets" issued from the pleural line or a small subpleural consolidation; 3) loss of lung aeration resulting from confluent bronchopneumonia: multiple abutting ultrasound lung comets issued from the pleural line (Fig. 1 *A*) or a small subpleural consolidation (Fig. 1*B*); 4) lung consolidation characterizing extensive bronchopneumonia (Fig. 1*C*): presence of a tissue pattern (14) containing hyperechoic punctiform images representative of air bronchograms (15).

An ultrasound lung reaeration score was calculated from changes in the ultrasound pattern of each region of interest between day 0 and day 7. The method of calculation is summarized in Table 1. Intra- and interobserver reproducibility of the lung ultrasound score was performed by analyzing patient's lung ultrasound data stored in video files either by two different investigators blinded to each other's evaluations and to CT and CRx or by the same investigator twice at different time intervals.

*Bedside Chest Radiography.* Anterior portable radiographs were obtained by using an AMX4 (General Electric, Kawasaki, Japan) with high voltage (120–130 kV) with standardized exposure time, focus-film distance, and degree of exposure. Lung parenchyma was di-

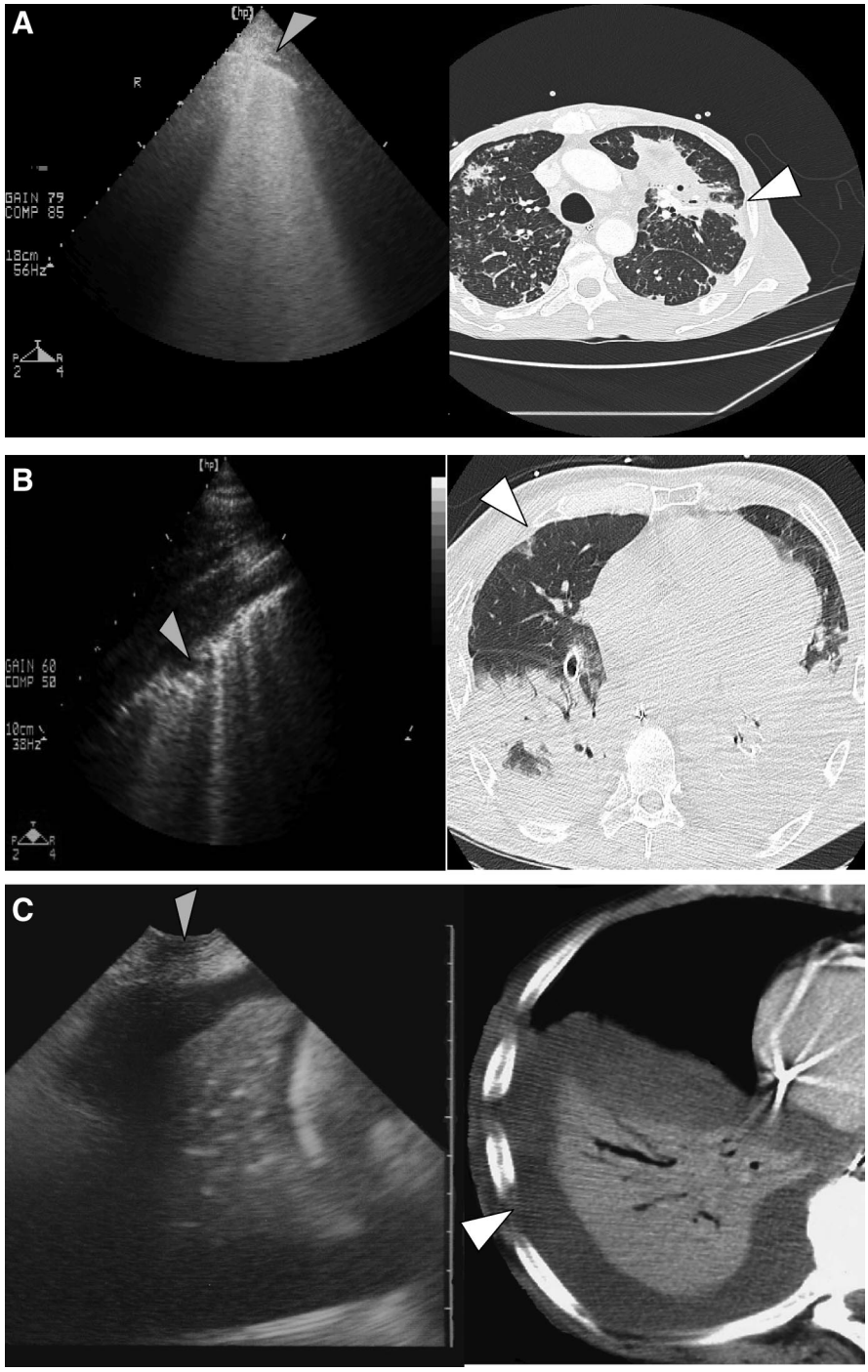


**Figure 1.** Computed tomography (CT) section and corresponding ultrasound pattern in a patient with ventilator-associated pneumonia characterized by multiple rounded CT attenuations and consolidation. A, confluent CT attenuations of the left upper lobe (*white arrow*) correspond to abutting ultrasound lung comets arising from the pleural line (*gray arrow*). B, a subpleural and intraparenchymal rounded CT attenuation of the right upper lobe (white arrow), corresponding to irregularly spaced and abutting ultrasound lung comets arising from a subpleural consolidation (*gray arrow*). C, consolidation of right lower lobe with parapneumonic pleural effusion. The white and gray arrows indicate position of the probe.

vided into 12 regions by cephalocaudal midclavicular and transversal hilar lines. Upper lung regions were defined as lung regions delineated by the apex, midclavicular, mediastinal, and hilar lines. Upper and lower lateral lung regions were defined as lung regions delineated by the external limit of the chest wall, midclavicular line, and apex (upper) or diaphragm (lower). Upper and lower posterior lung regions were defined as lung regions with radiologic signs erasing the mediastinum border (silhouette sign) and delineated by the mediastinum, midclavicular line, hilar line, and apex (upper) or diaphragm (lower). Pleural effusion, alveolar consolidation, and alveolar-interstitial syndrome were defined according to the terminology recommended by the Nomenclature Committee of the Fleischner Society (16). The extent of lung injury was assessed as the number of lung regions with radiologic signs suggestive of alveolar consolidation or alveolar-interstitial syndrome.

*Thoracic CT.* Lung scanning was performed from the apex to the diaphragm without injection of contrast material during a 15-sec apnea. Contiguous axial CT sections 10 mm thick were reconstructed from the volumetric data (17) and recorded on an optical disk. On each CT section, lung parenchyma was manually delineated. As previously described (18) using

**Table 1.** Lung ultrasound reaeration score aimed at evaluating the effects of antibiotics on lung aeration

| Quantification of Reaeration | | | Quantification of Loss of Aeration | | |
|---|---|---|---|---|---|
| 1 point | 3 points | 5 points | −5 points | −3 points | −1 point |
| B1 → N | B2 → N | C → N | N → C | N → B2 | N → B1 |
| B2 → B1 | C → B1 | | | B1 → C | B1 → B2 |
| C → B2 | | | | | B2 → C |

B1, ultrasound lung comets with well-defined and irregular spacing; B2, abutting ultrasound lung comets; C, alveolar consolidation; N, normal pattern. First, ultrasound lung aeration (N, B1, B2, and C) was measured in each of the 12 regions of interest before (day 0) and after antibiotic administration (day 7). Second, the score of lung reaeration was calculated as the sum of each score characterizing each region of interest according to the scale table.

**Table 2.** Computed tomography (CT) lung morphology at day 0 (before antibiotic administration) in the 30 patients with ventilator-associated pneumonia

| Patients, No. | Left Upper Lobe | Right Upper Lobe | Left Lower Lobe | Right Lower Lobe |
|---|---|---|---|---|
| Four patients with disseminated rounded CT attenuations | | | | |
| 1 | Normal | Normal | Rounded CT attenuations | Normal |
| 1 | Normal | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations |
| 1 | Rounded CT attenuations | Normal | Rounded CT attenuations | Rounded CT attenuations |
| 1 | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations |
| Three patients with lobar consolidations | | | | |
| 1 | Normal | Normal | Normal | Consolidation |
| 1 | Normal | Normal | Consolidation | Consolidation |
| 1 | Consolidation | Normal | Consolidation | Consolidation |
| 23 patients with disseminated rounded CT attenuations and lobar consolidations | | | | |
| 5 | Rounded CT attenuations | Rounded CT attenuations + consolidation | Rounded CT attenuations | Rounded CT attenuations + consolidation |
| 2 | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations + consolidation | Rounded CT attenuations + consolidation |
| 1 | Rounded CT attenuations + consolidation | Rounded CT attenuations | Rounded CT attenuations + consolidation | Rounded CT attenuations |
| 1 | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations + consolidation | Rounded CT attenuations + consolidation |
| 1 | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations + consolidation | Rounded CT attenuations |
| 1 | Rounded CT attenuations | Rounded CT attenuations | Consolidation | Rounded CT attenuations + consolidation |
| 2 | Rounded CT attenuations | Rounded CT attenuations | Consolidation | Consolidation |
| 1 | Consolidation | Rounded CT attenuations + consolidation | Consolidation | Consolidation |
| 1 | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations + consolidation | consolidation |
| 1 | Rounded CT attenuations | Rounded CT attenuations | Rounded CT attenuations | consolidation |
| 1 | Normal | Normal | Rounded CT attenuations | Consolidation |
| 1 | Normal | Rounded CT attenuations + consolidation | Rounded CT attenuations + consolidation | Rounded CT attenuations |
| 1 | Normal | Rounded CT attenuations + consolidation | Rounded CT attenuations | Rounded CT attenuations |
| 1 | Rounded CT attenuations | Normal | Consolidation | Rounded CT attenuations |
| 1 | Rounded CT attenuations | Normal | Rounded CT attenuations | consolidation |
| 1 | Rounded CT attenuations | Normal | Rounded CT attenuations + consolidation | Normal |
| 1 | Rounded CT attenuations | Normal | Rounded CT attenuations + consolidation | Rounded CT attenuations |

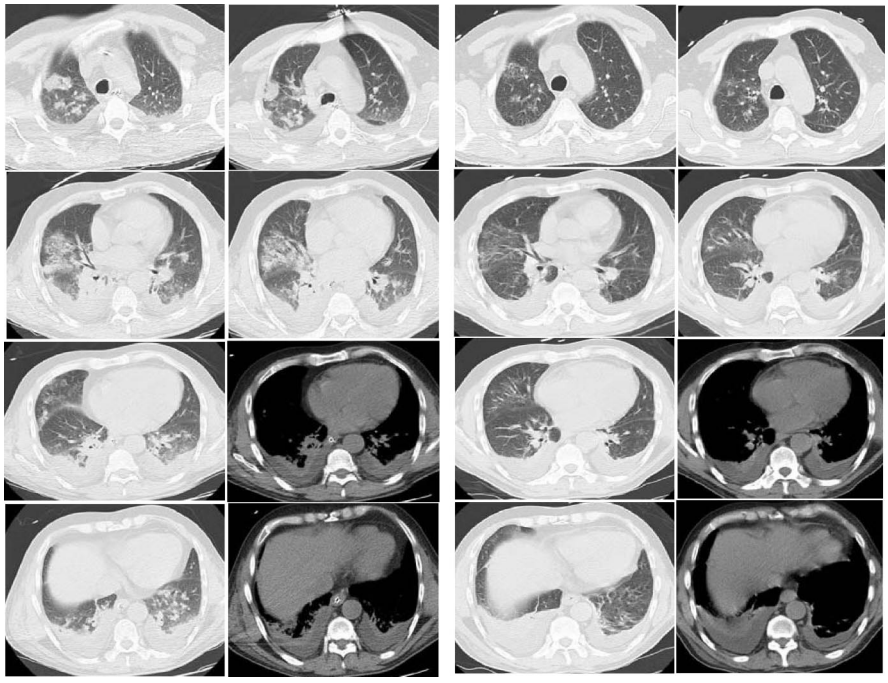

**Figure 2.** Computed tomography (CT) sections of a patient with ventilator-associated pneumonia characterized by multiple rounded CT attenuations disseminated within right upper lobe and lower lobes. The right image corresponds to day 0 and the left image to day 7. CT at day 0 and 7 are obtained at the same anatomical level according to anatomical landmarks. There is an obvious CT lung re-aeration attesting the efficacy of antimicrobial therapy and characterized by a quasi-complete regression of rounded CT opacities, persisting small pleural effusion and the apparition of a small consolidation in posterior segments of right lower lobe

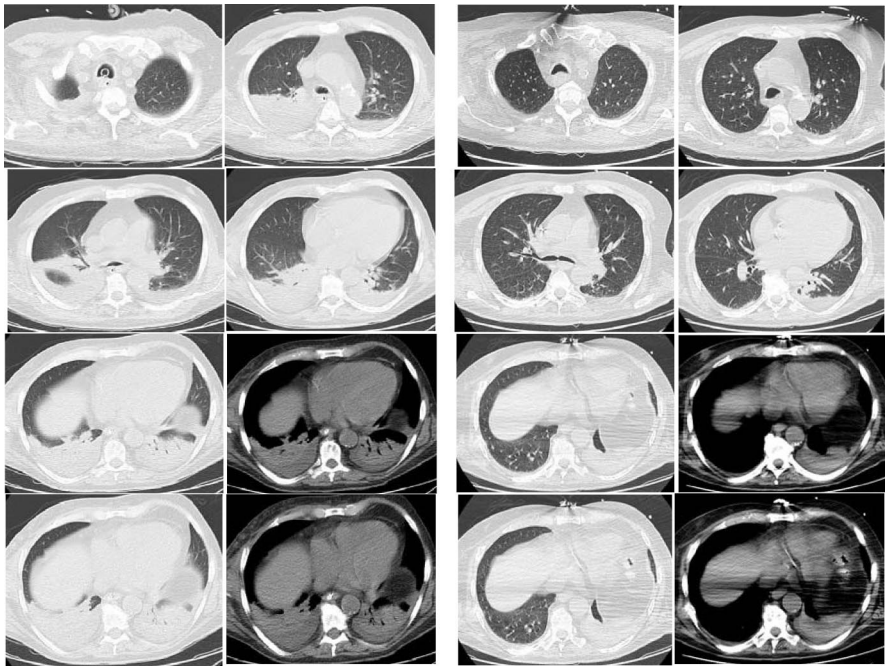

**Figure 3.** Computed tomography (CT) sections of a patient with ventilator-associated pneumonia characterized by bilateral consolidations of upper and lower lobes. The right image corresponds to day 0 and the left image to day 7. CT at day 0 and 7 are obtained at the same anatomical level according to anatomical landmarks. There is an obvious CT lung re-aeration attesting the efficacy of antimicrobial therapy and characterized by a quasi-complete regression of consolidations of right upper, middle and lower lobes and posterior segments of left lower lobes with a persisting small left pleural effusion.

the software Lungview (Institut National des Telecommunications, Evry, France) (19), the total volume of gas was computed as (–CT/1000) × total volume (total number of voxels), where CT is the CT attenuation of voxels with a CT number $<0$. Lung reaeration resulting from antibiotics administration was defined as the additional volume of gas present within both lungs following 7 days of antimicrobial therapy.

*Protocol.* To provide similar conditions of measurements at day 0 and day 7, a time at which nearly half of the patients were spontaneously breathing, CRx, LUS, and CT were consecutively performed in the supine position at zero end-expiratory pressure. Each exam was separated by a time interval $\geq$2 hrs, allowing the reestablishment of positive end-expiratory pressure to avoid prolonged derecruitment in mechanically ventilated patients. The posterior zone was examined in the supine position using a short probe pointed "to the sky" and placed between the back and the bed as far as possible toward the spine. Accuracy of CRx for detecting lung reaeration was performed as follows: Radiographies obtained at day 0 and 7 were blinded, and two independent radiologists unaware of the clinical, biological, ultrasound, and CT findings stated whether CRx at day 7 was identical, improved, or deteriorated compared with day 0. Lung aeration was assessed by comparing the extension of consolidation and alveolar-interstitial syndrome at day 0 and 7. Intra- and inter-observer reproducibility of CRx assessment was performed. After 7 days of antimicrobial therapy, clinical, radiologic (CRx and CT), biological, and microbiological variables were measured again. Nonprotected BAL or protected mini-BAL was performed at days 1, 3, and 7. VAP was considered as successfully treated by antimicrobial therapy if three criteria were met: 1) decrease in clinical pulmonary infection score; 2) CT reaeration corresponding to partial or complete regression of consolidations and rounded CT attenuations; and 3) either extubation between day 4 and 7 or negative mini-BAL in patients remaining ventilated at day 7.

*Statistical Analysis.* Normality of data distribution was assessed by a Kolmogorov-Smirnov test. Data with normal distribution are expressed as mean $\pm$ SD. Data without normal distribution are expressed as median and interquartile range. Inter- and intra-observer agreements in lung reaeration score (Table 1) determined for each region of interest were assessed using the kappa coefficient test (20). Correlations between ultrasound lung reaeration score and CT reaerations were tested using Spearman correlation rank analysis. The amount of statistical uncertainty was assessed by reporting the 95% confidence interval. Statistical analysis was performed using NCSS 2004 software (NCSS, Statistical & Power Analysis Software, Kaysville, UT), and statistical significance level was fixed at .05.

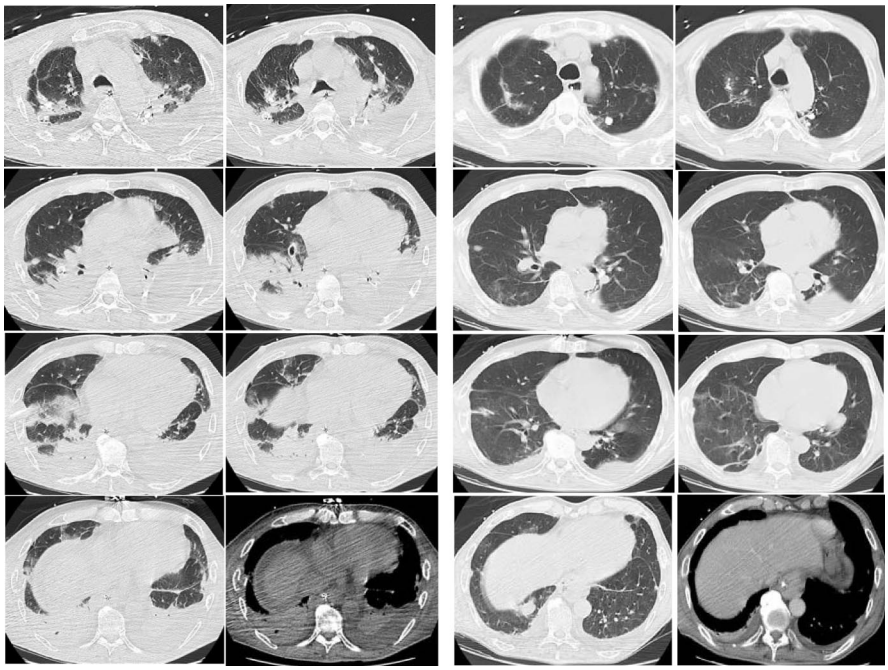

**Figure 4.** Computed tomography (CT) sections of a patient with ventilator-associated pneumonia characterized by bilateral consolidations of lower lobes and rounded CT attenuations disseminated within upper lobes. The right image corresponds to day 0 and the left image to day 7. CT at day 0 and 7 are obtained at the same anatomical level according to anatomical landmarks. There is an obvious CT lung re-aeration attesting of the efficacy of antimicrobial therapy and characterized by a regression of rounded CT opacities, pleural effusion and consolidation.

## RESULTS

*Patients.* Forty one consecutive surgical patients with VAP were prospectively screened for inclusion and 30 included in the study. Ten were excluded because of the presence of large thoracic dressings and one for the presence of subcutaneous emphysema. Mean age was 58 ± 18 yrs. Initial etiology was major vascular surgery (n = 14), multiple trauma (n = 10), digestive or urologic surgery (n = 5), and cardiac surgery (n = 1). At inclusion in the study, the mean Severity Acute Physiologic Score was 34 (median, 36; interquartile range, 24–42), Lung Injury Severity Score (21) was 2.0 ± 0.5, and mean Clinical Pulmonary Infection score was 8.0 (median, 8.0; interquartile range, 7.0–9.0) (10). Mortality rate was 7%. Ten patients had early VAP, caused by sensitive bacteria of the oropharyngeal flora in three and by sensitive *Pseudomonas aeruginosa* in seven. Twenty patients had late VAP caused by *P. aeruginosa* that was multidrug resistant in three patients. All patients were treated by a combination of antibiotics during a 7-day period. In 22 patients, VAP was considered as successfully treated by antimicrobial therapy on the following arguments: a) the mean Clinical Pulmonary Infection Score had decreased to 4.7 at day 7 (median, 4.5; interquartile range, 3.0–5.0); b) a significant CT reaeration was observed at day 7 together with a partial regression or a complete disappearance of consolidations and round CT attenuations that were present at day 0; c) 14 patients were extubated between day 4 and 7; d) mini-BALs performed in the eight patients who remained ventilated were negative at day 7. In eight patients, VAP was considered as unsuccessfully treated by antimicrobial therapy on the following arguments: a) the mean Clinical Pulmonary Infection score remained at 5.7 ± 1.6 (median, 5.0; interquartile range, 5.0–6.0); b) in four patients, no significant CT reaeration was observed at day 7, corresponding to persisting consolidations and round CT attenuations present at day 1; c) in four patients, no significant CT reaeration was observed at day 7, corresponding to new consolidations and round CT attenuations whereas consolidations and round CT attenuations present at day 0 had partially disappeared; d) the eight patients were still on mechanical ventilation at day 7; and e) mini-BALs performed in the eight patients were all positive at day 7. Therapeutic failure was related to lack of eradication of causative microorganism in four patients and to secondary lung infection by another microorganism resistive to the antimicrobial therapy in four patients.

*Lung Morphology Characterizing VAP.* As shown in Table 2, in four patients (12%), VAP was exclusively characterized by intraparenchymal and subpleural rounded CT attenuations disseminated within upper and/or lower lobes (Fig. 2). In three patients (10%), VAP was exclusively characterized by consolidations of lower lobes associated or not with consolidation of upper lobes (Fig. 3). In 23 patients (78%), VAP was characterized by an association of consolidations affecting one or several lobes with intraparenchymal and subpleural rounded CT attenuations disseminated within upper and/or lower lobes (Fig. 4). Rounded CT attenuations were either isolated or confluent, forming more or less extended ground glass areas. Their size ranged between 1 and 15 mm, and many of them were subpleural, surrounded by normally aerated lung parenchyma.

*Accuracy of Bedside CRx for Measuring Lung Reaeration After 7 Days of Antibiotic Administration.* CRx was poorly accurate for detecting changes in lung aeration following antimicrobial therapy. Among the 22 patients whose VAP was successfully treated by antimicrobial therapy, CRx remained unchanged in three, improved in nine, and deteriorated in eight. Among the eight patients whose VAP was unsuccessfully treated by antimicrobial therapy, CRx remained unchanged in three, improved in two, and deteriorated in three.

*Diagnostic Accuracy of Ultrasound for Quantifying Antibiotic-Induced Lung Reaeration.* As shown in Figure 5, a highly statistically significant correlation was found between CT and ultrasound lung reaeration, considering both or each lung separately. As shown in Figure 6, LUS was accurate for detecting significant variation of aeration. A loss of aeration (failure of antibiotics to treat lung infection) >400 mL was detected by a lung ultrasound score <–10, and a reaeration >400 mL (success of antibiotics to treat lung infection) was detected by a lung ultrasound score ≥5. Lung ultrasound score was less effective for detecting smaller changes of lung aeration. Intra- and interobserver agreements for estimating antibiotic-induced changes in lung aeration were good as attested by kappa coefficients of 0.75 and 0.70, respectively.

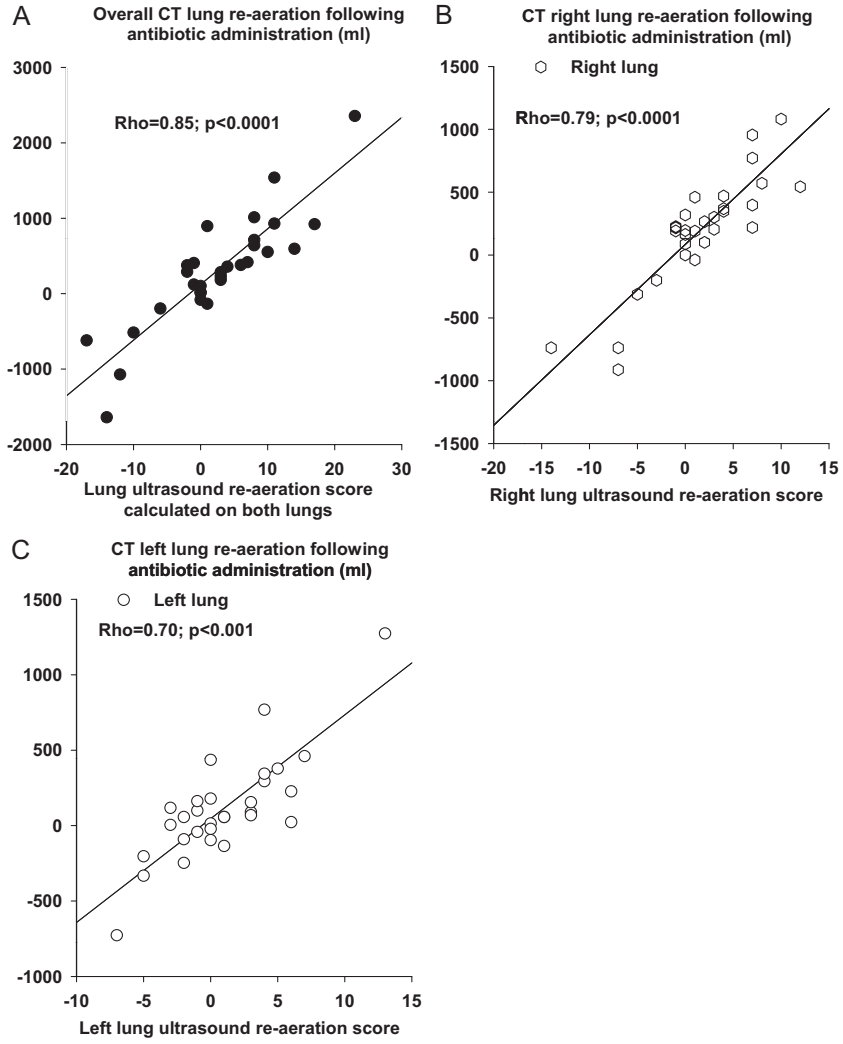


Figure 5. Correlations between lung ultrasound reaeration score and computed tomography (*CT*) measurement of lung reaeration in 30 patients with ventilator-associated pneumonia treated by antibiotics during 7 days. *A*, Correlation between overall CT lung re-aeration following antibiotic administration (mL) and lung ultrasound reaeration score calculated on both lungs. *B*, Correlation between CT right lung reaeration following antibiotic administration (mL) and right lung ultrasound reaeration score calculated on the right lung. *C*, Correlation between CT left lung reaeration following antibiotic administration (mL) and left lung ultrasound reaeration score calculated.

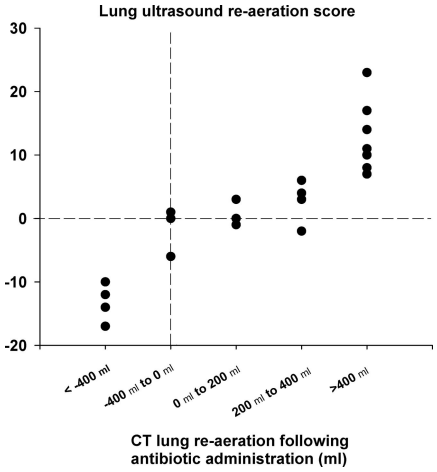


Figure 6. Accuracy of lung ultrasound re-aeration score for quantifying changes in lung aeration following antibiotic administration in 30 patients with ventilator-associated pneumonia. Each closed circle represents an individual patient. *CT*, computed tomography.

*Characteristics of Lung Reaeration Following Antibiotic Administration.* A total of 248 lung regions of interest were examined before and after antimicrobial therapy. As shown in Figure 7, ultrasound lung reaeration following antibiotic administration was predominantly caused by disappearance or growing infrequency of ultrasound lung comets (61%) and also by transformation of ultrasound consolidation into ultrasound lung comets. Inversely, failure of antibiotics to treat lung infection was characterized by the new appearance of ultrasound lung comets (87%) and, less frequently, by the appearance of consolidation (3%) or the transformation of ultrasound lung comets into consolidation (7%). Such patterns corresponded to CT changes: Success of antimicrobial therapy was characterized by predominant disappearance of rounded opacities, whereas antibiotic failure was mainly characterized by new rounded opacities disseminated within both lungs.

## DISCUSSION

This study demonstrates that bedside lung ultrasound is more appropriate than bedside chest radiography for quantifying lung reaeration in patients with ventilator-associated pneumonia who are successfully treated by antibiotics. The comparison between CT lung morphology and corresponding ultrasound patterns observed in VAP provides a solid rationale for understanding this result of potential clinical relevance.

*Correlations Between Changes in CT Aeration and Lung Ultrasound Reaeration Score.* Until now, the value of LUS for assessing change in pulmonary aeration has been reported in a few studies. Tsubo et al (22) reported that positive end-expiratory pressure-induced reaeration of a consolidated left lower lobe can be assessed using transesophageal echocardiography. As shown in Figure 6 of the article by Tsubo et al, the ultrasound tissue pattern characteristic of lung consolidation was replaced by abutting ultrasound lung comets following positive end-expiratory pressure, indicating partial reaeration. Agricola et al (23, 24) showed that an ultrasound score based on the total number of comet tails correlates with extravascular lung water and pulmonary artery occlusion pressure measured in cardiac patients and pigs with oleic acid-induced lung injury (25). Since increased extravascular lung water is associated with loss of lung aeration, these studies suggest that LUS can accurately detect aeration changes.

*Comparison Between CT Lung Morphology and Corresponding LUS Patterns Characterizing VAP.* The infected lung is characterized by tissue inflammation extending to lung periphery, predominating in lower lobes, and is associated with various degrees of aeration loss, depending on the severity and extension of pneumonia (26, 27). At early stages, a few infected alveoli surrounding an infected

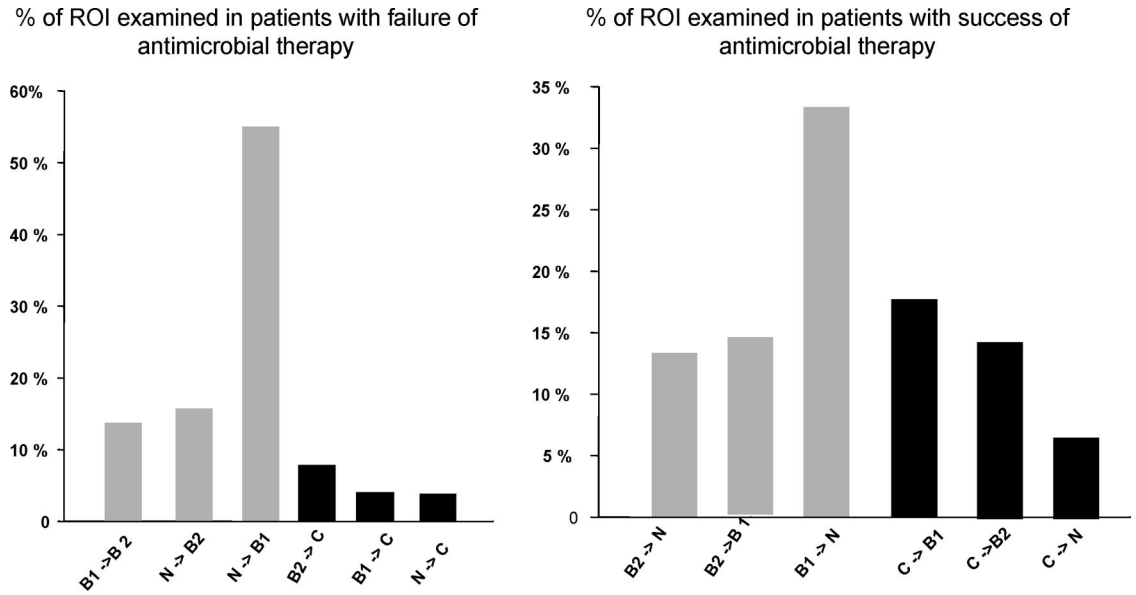


**Figure 7.** Changes of ultrasound pattern characterizing 324 regions of interest (*ROI*) examined in 30 patients with ventilator-associated pneumonia before and 7 days following antibiotic administration (36 ROI could not be examined because of lack of adequate visualization of lung parenchyma). The left figure shows changes of ultrasound pattern characterizing ROI in the eight patients with antimicrobial therapy failure. The right figure shows changes of ultrasound pattern characterizing ROI in the 22 patients with antimicrobial therapy success. C = Alveolar consolidation; B1 = ultrasound lung comets with well defined and irregular spacing; B2 = multiple abutting ultrasound lung comets; n = normal aeration. The second symbol after each arrow indicates ultrasound pattern following 7 days of antimicrobial therapy. In light gray, changes in lung aeration of ROI characterized by partial aeration loss are represented. In black, changes in lung aeration of ROI characterized by complete aeration loss are represented.

bronchiole coexist with normally aerated acini (26, 28). We hypothesize that the abnormal interface between gas and inflammation produces multiple vertical ultrasound lung comets, characterized by well-defined and irregular spacing, arising from the pleural line or a small subpleural consolidation, two characteristics that differentiate them from 7-mm apart vertical B lines observed in hemodynamic interstitial edema and arising exclusively from the pleural line (Fig. 8). Previous reports have outlined the value of ultrasound lung comets for diagnosing lung infection (29–31). We could not confirm, however, that ultrasound comet tails characteristic of lung infection are often associated with the abolition of lung sliding (29, 31).

Recently, Reissig and Kroegel (32) reported the value of LUS for diagnosis and follow-up of community-acquired pneumonia. Ultrasound diagnosis was based on the detection of multiple consolidations characterized by air bronchogram and frequently associated with pleural effusion. Interestingly, irregularly spaced, multiple ultrasound lung comets were not reported in the study as evocative of pneumonic lesions. Resolution of pneumonia was characterized by a decrease or disappearance of the hypoechoic, irregularly shaped parenchymal pneumonic lesion, as measured by dimensions of ultrasound consolidation. To understand the different approach considered in the present study, radiologic and histologic differences between community-acquired pneumonias and VAP should be highlighted. In patients on mechanical ventilation, lung infection results from continuous bacterial seeding of the tracheobronchial tree by microorganisms colonizing upper respiratory tract. Therefore, pneumonic lesions are disseminated within lung parenchyma, are centered on infected bronchioles, and involve all pulmonary segments even though they predominate in dependent lung regions (26, 28). In spontaneously breathing patients, community-acquired pneumonia is rather characterized by infection of contiguous pulmonary segments resulting into lobar pneumonia (33). Reissig and Kroegel (32) referred exclusively to the detection and dimensions of ultrasound consolidations for the diagnosis and follow-up of community-acquired pneumonia, a method that may not be appropriate for VAP. In fact, we set up a score based on the ultrasound detection not only of large consolidations but also of multiple nodular lesions of various sizes, appearing as multiple irregularly spaced or abutting ultrasound lung comets arising from the pleural line or a small subpleural consolidation. Assessment of lung reaeration following infection resolution was based on the rarefaction or disappearance of previously existing ultrasound lung comets as well as on the transformation of consolidations into ultrasound lung comets attesting of a partial reaeration. Therefore, we did not measure consolidations' dimensions and their changes during the administration of antibiotics as described by Reissig and Kroegel.

Multiple vertical B-lines have been described in acute respiratory distress syndrome (3), cardiogenic pulmonary edema (23, 31), lung contusion (34), and interstitial lung disease (35) and, therefore, are not specific of VAP. Furthermore, isolated B-lines can be also detected in up to one third of patients with normal lungs (3, 35, 36). In patients with VAP, however, the presence of vertical ultrasound artifacts with irregular spacing likely corresponds to early stages of infection corresponding to small foci of bronchopneumonia surrounded by normally aerated noninfected areas (37, 38). As shown in Figures 4 and 8, multiple abutting ultrasound comet tails are representative of more severe aeration loss and extension of lung infection, whereas lung consolidation, present in 93% of cases of VAP, likely indicates confluence of lung infection. Correlations between aeration and ultrasound patterns have been demonstrated in patients with acute respiratory distress syndrome: Comet tails 7 mm

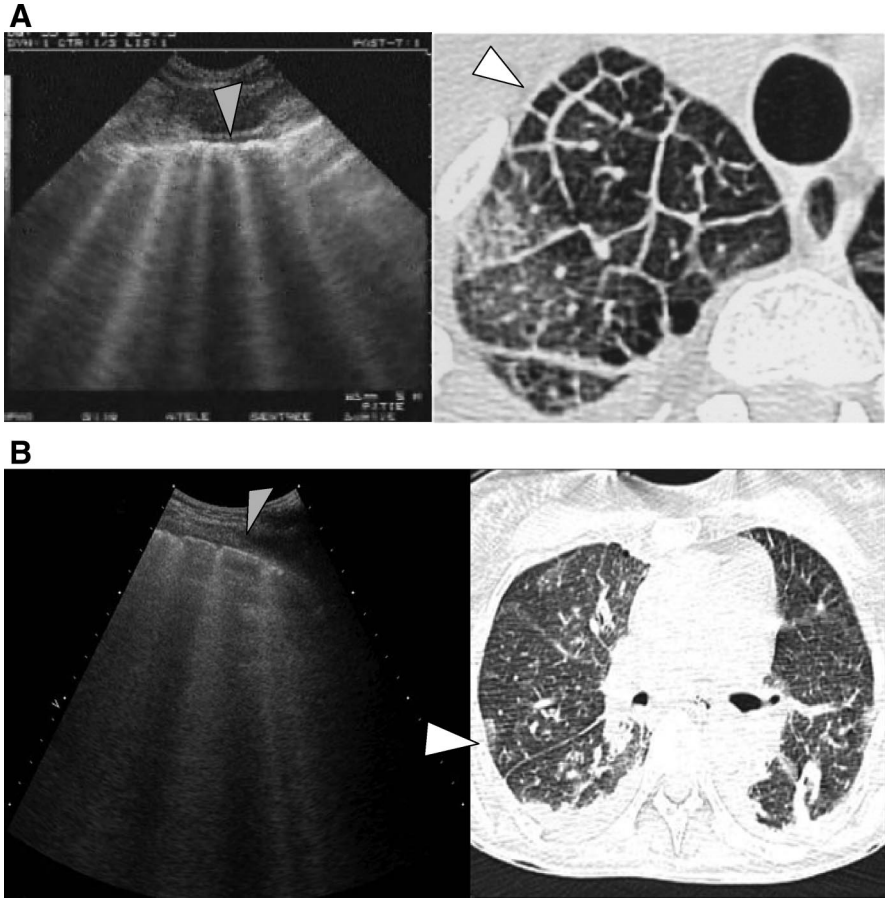


**Figure 8.** Significance of ultrasound lung comets with regular and irregular spacing. A, 7-mm apart ultrasound lung comets representative of interstitial edema (thickened interlobular septa) and recorded in a patient with cardiogenic pulmonary edema. B, ultrasound lung comets with well-defined and irregular spacing representative of small foci of bronchopneumonia and recorded in a patient with ventilator-associated pneumonia. The white and gray arrows indicate position of the probe.

apart correspond to thickened alveolar septa, whereas comet tails ≤3 mm apart correspond to ground glass attenuation areas (3, 39, 40). In VAP, if antibiotic administration results in the transformation of abutting ultrasound lung comets into ultrasound lung comets with well-defined and irregular spacing, it can be reasonably assumed that infection of lung parenchyma has been reduced. Similarly, the replacement of consolidation by vertical ultrasound lung comets indicates partial reaeration resulting from regression of lung infection. The transformation of ultrasound lung comets into normal aeration likely indicates eradication of focal bronchopneumonia and reaeration of the lung. The fact that antibiotic success or failure induces predominantly the appearance or disappearance of ultrasound lung comets consolidates the hypothesis that ultrasound lung comets are representative of foci of bronchopneumonia. As a matter of fact, small infectious pulmonary lesions clear up more rapidly than extended areas of parenchymal infection under antimicrobial therapy. Conversely, extension of VAP despite antimicrobial therapy manifests itself as the appearance of additional foci of infection that later join to form large areas of consolidation (Fig. 4).

*Limitations.* Bedside LUS has some limitations. First, subcutaneous emphysema causes vertical B-lines that are not issued from the pleural line and should not be confounded with vertical ultrasound lung comets representative of bronchopneumonia (39). Second, thoracic dressings preclude the examination of subjacent lung regions. Third, gain of gas in normally aerated lung regions and mechanical ventilation-induced pulmonary hyperinflation, a frequent issue in severe bronchopneumonia (37, 41), cannot be detected by LUS. Fourth, the use of lung ultrasound requires the knowledge and skills necessary to interpret ultrasound images (42). As previously pointed out (4), operator dependence, which is always a salient issue with general and echocardiography, is minimal with LUS.

Finally, lung ultrasound detects exclusively pulmonary infection extending to the visceral pleura. With antimicrobial therapy, foci of bronchopneumonia are reduced in size and in numbers (32) and do not extend to the visceral pleura, thereby explaining the disappearance or the rarefaction of ultrasound lung comets. Remaining pneumonia, however, cannot be detected by lung ultrasound. The fact that an excellent correlation was found between changes of lung ultrasound score and antibiotic-induced lung reaeration strongly suggests that changes at the lung periphery are representative of changes of the whole lung.

One possible limitation concerns the clinical interest and applicability of LUS for the follow-up of VAP. Is it superior to the follow-up of fever, $Pa_{O_2}/F_{IO_2}$ ratio, and clinical pulmonary infection score, as previously reported (43). A previous study (44) demonstrated that radiologic infiltrates are poor indicators of pneumonia resolution at day 7. The present study confirms this finding and demonstrates that LUS is much more accurate than bedside CRx for assessing antibiotic-induced lung reaeration. We believe that the technique has a promising future in the care of critically ill patients, and we hope that further studies by other groups will confirm our statement.

Lung ultrasound appears to be an accurate diagnostic tool for assessing the respiratory effects of antimicrobial therapy in patients with VAP. Since ultrasound is noninvasive and easily repeatable at the bedside, it allows the early detection of antibiotic-induced lung reaeration or the extension of lung infection in cases of antimicrobial therapy failure.

## ACKNOWLEDGMENT

We thank Jean-Louis Golmard, MD, PhD, Biostatistical Unit, Pitié-Salpêtrière Hospital, Paris, France, for statistical advice.

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