than 5 ml/kg PBW, mean EFFi increased from 0.722 to 0.736, or by 1.8 ± 0.8% (mean ± SD). The exact value chosen for V_{ANA} appears not to be critical. Therefore, a moderate error in flow sensor calibration is of low importance. In future studies, EFFi should be compared with alternative parameters (e.g., V_{AE}/V_T proposed by Lucangelo and colleagues [10]).

Because EFFi and V_{Dphys}/V_T reflect uneven $\dot{V}/\dot{Q}$ among lung compartments, it was expected that they correlate closely. EFFi is easier to study, as it is noninvasive and may be continuously monitored.

The study is limited to small groups. However, at health, the results show a low degree of variation, as expected from absence of variability caused by disease. The total separation between health and ARDS indicates that, in mechanically ventilated patients, EFFi may be useful for monitoring of ARDS evolution. This aspect is strengthened by the fact that EFFi may automatically, continuously, and noninvasively be monitored in the individual patient, who then serves as his own standard of reference. EFFi merits further studies in broad materials covering ARDS and other diseases, performed with modern capnographic equipment. ■

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Björn Jonson, M.D., Ph.D.
Lund University
Lund, Sweden

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Training for Lung Ultrasound Score Measurement in Critically Ill Patients

To the Editor:

Bedside lung ultrasound is widely used in critically ill and emergency patients (1). Its role in pulmonary imaging was recently reviewed (2). A lung ultrasound score (LUS) based on examination of 12 regions of interest has been proposed to assess lung aeration changes after various therapeutic interventions in mechanically ventilated patients (3, 4). As shown in Figure 1, the LUS is based on the regional aeration of each examined region, which is graded between 0 and 3 depending on the degree of aeration loss. The LUS is a semiquantitative assessment of pulmonary aeration loss and can vary between 0 and 36.

In anesthetized patients scheduled for abdominal surgery, lung ultrasound detects intraoperative atelectasis and the LUS correlates with perioperative oxygenation impairment (5). In patients with acute respiratory distress syndrome, the LUS is correlated with disease severity and predicts mortality (6). It provides a comprehensive monitoring of regional lung aeration changes resulting from prone positioning (7), fluid loading (4), positive end-expiratory pressure (8), and drainage of large pleural effusions (9). In ventilated critically ill patients with ventilator-associated pneumonia, a rapid decrease in the LUS indicates successful antimicrobial therapy–induced lung reaeration, whereas an increase in the LUS indicates antibiotic failure (10). During weaning from mechanical ventilation, an LUS >13 measured at the end of a clinically successful spontaneous breathing trial is predictive of extubation failure (3).

Despite increased interest in the LUS, training methods to acquire the appropriate skills for LUS measurement vary among centers and are not codified. Based on clinical experience accumulated over 10 years of resident training, including the acquisition of skills in lung ultrasound, we hypothesized that 25 LUS determinations supervised by experts would be enough for trainees without expertise in lung ultrasound to appropriately assess the LUS. A multicenter, prospective, and educational study focusing on the acquisition of basic skills for bedside lung ultrasound was conducted in 10 ICUs in Brazil, China, France, and Uruguay. The training course started with a 2-hour video lecture. First, ultrasound patterns characterizing normal aeration, moderate aeration loss (interstitial syndrome, localized alveolar edema, and subpleural consolidations), severe aeration loss (diffuse alveolar edema), and complete aeration loss (consolidation) were described. Second, the method for assessing the LUS was carefully described. One of the objectives of the training program was to reach an agreement in LUSs between trainees and experts. Each trainee had to perform 25 bedside determinations of the LUS supervised by an expert. The experts who participated in the training protocol were staff members in critical care or emergency medicine with at least a 2-year daily lung ultrasound practice. After every five supervised lung ultrasound examinations, the trainee and the expert assessed the LUS in the same patient separately. Concordance was considered as clinically acceptable when the LUS assessment did not differ by more than 2 points between trainees and experts. A total of 610 comparative LUS measurements were

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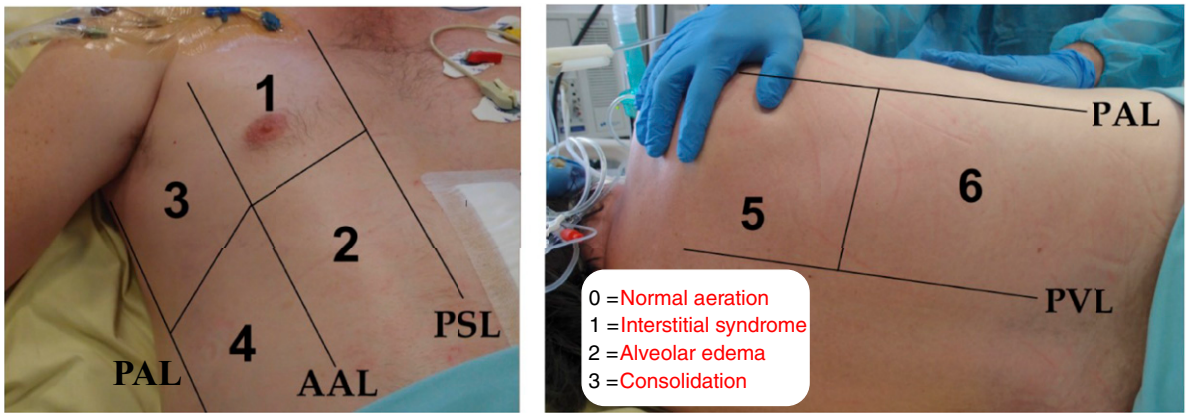

Figure 1. Lung ultrasound score (LUS) assessment. Six lung regions of interest (numbered in the figure), delineated by a parasternal line, anterior axillary line, posterior axillary line, and paravertebral line, are examined on each side. Each lung region is carefully examined in the longitudinal plane, and each intercostal space present in the region is examined in the transversal plane. The worst ultrasound pattern characterizes the region (regional LUS) using the following grading: 0 = normal aeration; 1 = moderate loss of aeration (interstitial syndrome, defined by multiple spaced B lines, or localized pulmonary edema, defined by coalescent B lines in less than 50% of the intercostal space examined in the transversal plane, or subpleural consolidations); 2 = severe loss of aeration (alveolar edema, defined by diffused coalescent B lines occupying the whole intercostal space); and 3 = complete loss of lung aeration (lung consolidation defined as a tissue pattern with or without air bronchogram). The LUS is calculated as the sum of the 12 regional scores. AAL = anterior axillary line; PAL = posterior axillary line; PSL = parasternal line; PVL = paravertebral line.

performed by 100 trainees and 18 experts in 233 mechanically ventilated and 137 spontaneously breathing critically ill patients. As shown in Figure 2, concordance between trainees and experts was obtained on the sixth evaluation.

The median (interquartile range) duration of training was 51 (23–69) days. At the end of the training, the median time required to measure LUS was 8 (3–14) minutes for experts and 10 (4–17) minutes for trainees.

This study shows that residents and senior physicians without expertise in lung ultrasound can acquire the skills required to measure the LUS after 25 supervised measurements. The training should include appropriate recognition of normal aeration, interstitial syndrome, alveolar edema, and lung consolidation—all of which have ultrasound patterns that are necessary to calculate the LUS. Two issues that could affect accurate determination of the LUS deserve specific comments. Alveolar edema, characterized by the presence of coalescent B lines, can remain localized, as in acute respiratory distress syndrome, or be diffuse, as in cardiogenic pulmonary edema. When an examined region is characterized by "focal" alveolar edema, corresponding to a "ground-glass area" on lung computed tomography, the loss of lung aeration is moderate, and the region should be graded 1. When the examined region is characterized by diffuse alveolar edema, the loss of lung aeration is severe, and the region should be graded 2. As recently recommended (11), when coalescent B lines occupy less than 50% of the intercostal space in the transversal plane, the grade should be 1, and when coalescent B lines occupy more than 50% of the intercostal space, the grade should be 2. Systematically grading "2" in the presence of coalescent B lines without considering their extension could lead to overestimation of the LUS and aeration loss. The same reasoning also applies for subpleural consolidations that characterize ventilator-associated pneumonia (12). These small subpleural consolidations, representative of foci of bronchopneumonia, have dimensions varying between 5 and 15 mm, are limited by spaced or coalescent B lines, and are associated with moderate loss of lung aeration (13). For this reason, regions characterized by subpleural consolidations should be graded 1 and not 3.

In conclusion, measurement of the LUS as a tool for monitoring lung aeration in critically ill patients requires a short and easy-to-implement training program based on 25 ultrasound examinations supervised by a physician with expertise in bedside lung ultrasound. ■

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Jean-Jacques Rouby, M.D., Ph.D.
Charlotte Arbelot, M.D.
La Pitié-Salpêtrière Hospital, Sorbonne University
Paris, France

Yuzhi Gao, M.D.
Mao Zhang, M.D., Ph.D.
Second Affiliated Hospital, Zhejiang University
Hangzhou, China

Jie Lv, M.D.
Youzhong An, M.D., Ph.D.
Peking University Health Science Center
Beijing, China

Wang Chunyao, M.D.
Du Bin, M.D., Ph.D.
Peking Union Medical College Hospital
Beijing, China

Carmen Silvia Valente Barbas, M.D., Ph.D.
Hospital Albert Einstein
São Paulo, Brazil

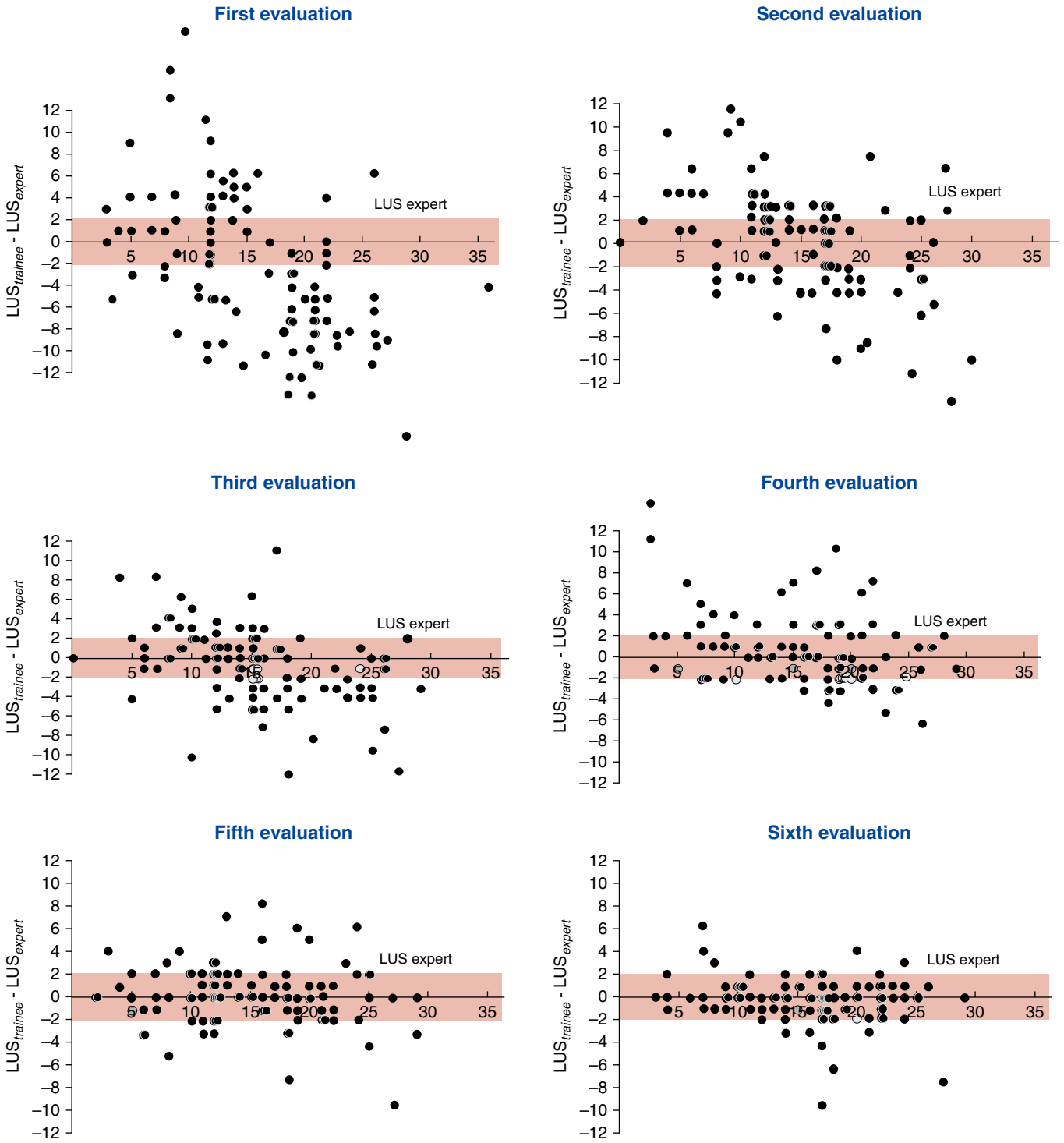

Figure 2. Difference between lung ultrasound scores (LUSs) measured by trainees and experts over six successive evaluations. The first evaluation was performed 2 hours after a lecture describing the method for measuring the LUS. Further evaluations were each separated by five ultrasound examinations performed by the trainee and supervised by the expert. The pink zone indicates the limit of agreement between trainees and experts.

Felippe Leopoldo Dexheimer Neto, M.D., Ph.D.
Hospital Ernesto Dornelles, Universidade Federal do Rio Grande do Sul
Porto Alegre, Brazil

Fabiola Prior Caltabeloti, M.D., Ph.D.
Das Clinicas Hospital, University of Sao Paulo
São Paulo, Brazil

Emidio Lima, M.D., Ph.D.
Hospital da Bahia
Salvador, Brazil
and
Santa Helena Hospital
Camaçari, Brazil

Andres Cebey, M.D.
Hospital de Clínicas Dr Manuel Quintela, Universidad de la Republica
Montevideo, Uruguay

Sébastien Perbet, M.D.
Jean-Michel Constantin, M.D., Ph.D.
CHU Estaing, University of Auvergne
Clermont-Ferrand, France

For the APECHO Study Group

The APECHO (Apprentissage de l'ECHOgraphie pulmonaire) Study Group members, listed according to their institution, include Charlotte Arbelot, Jean-Jacques Rouby, Hélène Brisson, Romain Deransy, Corinne Vezinet, Pierre Garçon, Nabil El Hadj Kacem, Denis Lemesle, Antoine Monsel, Qin Lu, and Olivier Langeron (Multidisciplinary Intensive Care Unit, Department of Anesthesiology and Critical Care Medicine, La Pitié-Salpêtrière Hospital, Assistance Publique Hôpitaux de Paris, Sorbonne University, Paris, France); Frédérick Gay (Department of Parasitology-Mycology, La Pitié-Salpêtrière Hospital, Assistance Publique Hôpitaux de Paris, Sorbonne University, Paris, France); Bruno Lucena, Luiz Malbouisson, and Maria José Carvalho Carmona (Surgical and Trauma Intensive Care Unit, Hospital Das Clinicas, University of São Paulo, São Paulo, Brazil); Julio Neves (Multidisciplinary Intensive Care Unit, Hospital da Bahia, Salvador, Brazil); Paulo de Tarso Roth Dalcin (Intensive Care Unit, Ernesto Dornelles Hospital, Hospital Moinhos de Vento and Programa de Pós Graduação em Ciências Pneumológicas, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil); Guilherme de Paula Pinto Schettino (Multidisciplinary Intensive Care Unit, Hospital Albert Einstein, São Paulo, Brazil); Alberto Biestro (Intensive Care Unit, Hospital de Clínicas Dr Manuel Qintela, Faculdade de Medicina, Universidad de la Republica, Montevideo, Uruguay); and Davi Cristovao and Jorge Salluh (Multidisciplinary Intensive Care Unit, Hospital Copa D'Or, Rio de Janeiro, Brazil).

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TREM-1 Response Signatures Common to Expression Profiles of Both Asthma Affection and Asthma Control

To the Editor:

It is an essential component of the scientific process to support a hypothesis by demonstrating the convergence of separate lines of evidence generated by independent research groups. In disease genomics, where high-dimensional data have many more features than samples ($p \gg n$), researchers must be especially sensitive to multiple-testing burdens and model overfitting. The case has been made in the *Journal* that gene expression profiling results in a particular need to be approached cautiously until confirmation can be made in other contexts (1, 2). To this end, we read with great interest the report by Bigler and colleagues, from the U-BIOPRED (Unbiased Biomarkers in Prediction of Respiratory Disease Outcomes) study, on the topic of whole-blood gene expression signatures of asthma severity (3). The authors noted that their severe asthma disease signature included three genes related to TREM-1 (triggering receptor expressed on myeloid cell-1) signaling (*CCL23* [C-C motif chemokine ligand 23], *OLIG* [oligodendrocyte transcription factor]-1, and *OLIG2*), which we recently identified as part of a signature of suboptimal asthma symptom control in the Asthma BRIDGE (Asthma Biorepository for Genomic Exploration) cohort (4). Given that the severe asthma disease signature was strongly present in mild and moderate asthma cases, it could also be viewed as a global signature of asthma affection (case) status, regardless of severity. We thus hypothesized that there was, in fact, even more substantive overlap

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