**Title:** The use of ultrasound as a tool to evaluate pulmonary disease in cystic fibrosis

**Supplementary Material 1**

**Methods**

**Lung ultrasound (Supplementary table 1)**

The areas indicated by International Consensus on lung ultrasound: anterior superior, anterior basal, lateral superior and lateral basal and those zones delimited by parasternal and axillary lines (anterior and posterior); concomitantly, dorsal regions (posterior, superior and basal) and those delimited by paravertebral and parascapular lines were also used.20,21

Ultrasound was performed in the Toshiba Aplio 500 device (Canon Medical Systems, Michelle Drive, Tustin, USA), with the linear transducer of high frequency 10 MHz. We established a depth of four focused on the pleural line and hold the pleural assessment of the parties at 34 fps. During the exam, the transducer was positioned in the chest with the marker turned to the cephalic region to obtain cross-sections of costal arches, the two acoustic shadows of the ribs being the images of interest. A cross-sectional evaluation with the transducer positioned in parallel to the costal arches was also held.23,28

**A-lines pattern:** normal pleural sliding and regular echogenicity of pleural line with predominance of A-lines artefacts. When positioning the transducer longitudinally regarding the trunk, we get the cross section of costal arches – oval-shaped hypoechoic image, with hyperechoic line in its anterior margin and posterior acoustic shadow. The area of contact between the parietal and visceral pleura corresponds to horizontal hyperechoic line between two costal arches – pleural line. Above the pleural line there is the chest wall and below it, the lung parenchyma. In a healthy lung, sound waves disperse to reach the air medium, preventing the formation of direct images of the lung parenchyma. However, one can observe horizontal and equidistant hyperechoic lines corresponding to reverberation artefacts of the pleural line – A-lines that indicate the presence of air above the pleural line. However, in some diseases such as pneumothorax, the presence of A-lines is common. This way, there is need to assess the pleural line to verify sliding between parietal and visceral pleurae. In the 2D mode, it is possible to observe the dynamic change of the pleural line during the respiratory movement of the rib cage, as a healthy lung features A-lines and positive pleural sliding.

**B-lines pattern – interstitial syndrome:** the physical and anatomical nature of B-lines is not completely understood. However, its occurrence is associated with fluid in the lung interstitial of hydrostatic or inflammatory origin.20 B-lines, also known as comet tail artifacts, feature linear hyperechoic aspect of vertical presentation originated in the pleural line, moving according to the pleural sliding, erasing the A-lines artifacts during its trajectory. The presence of multiple regions of interstitial involvement bilaterally suggests interstitial syndrome.

Interstitial syndrome can be caused by: pulmonary edema, interstitial pneumonia and diffuse lung parenchymal disease. In addition to the situations described, the presence of B-lines is common along with lung damage caused by pneumonia, atelectasis, pulmonary infarction or contusion, pleura diseases, neoplasia and acute respiratory distress syndrome.20 In this study, a minimum of three artefacts (B-lines) per region/zone was considered as B-lines pattern.

**Consolidation:** the pathological process of substitution of the air in the alveoli with fluids allows the observation of consolidations in the lung ultrasound from a subpleural hypoechoic area with irregular margin and heterogeneous texture, with hyperechoic imaging in its inside (static or dynamic air bronchogram). It can present comet’s tail artifact (B-line) adjacently to its posterior margin or similar aspect to hepatic parenchyma.22

Several diseases present lung consolidation (pneumonia, atelectasis, embolism, contusion and neoplasia) and the only required condition for imaging consolidation is the need for the image to extend up until the pleura. On the other hand, the attenuation sound waves by air can prevent its observation. However, in around 98.5% of adults with pneumonia, pleural involvement occurs contributing to the evaluation of lung ultrasound.22 It is believed that this range is higher among children due to their lower lung volume and thinner chest wall.23-26

**Pleural effusion:** is represented by an anechoic image between the visceral and parietal pleura due to the atelectasis caused by the extrinsic compression of liquid around the lung. The movement of lung parenchyma during the respiratory cycle can be seen.

The septations can be observed as a linear hyperechogenic image within the effusion, often reaching the pleura. Hyperechoic points in motion can indicate the presence of free debris. Consolidation in the lung foundation can be diagnosed as pleural by chest radiogram imaging in the supine position. In these cases, lung ultrasound can carry out this distinction almost as accurately as HRCT. In addition, it is possible to evaluate the cavity content regarding its fluid aspect (homogeneous and heterogeneous) and the presence of septation. The evaluation of pleural effusion must be carried out at the diaphragmatic line (thoracic-abdominal transition), near the middle and posterior axillary line.

**Modified** **Bhalla score**

The modified Bhalla score is a computed tomography scan score to assist the assessment of pulmonary involvement, therapeutic effect and selection for transplant. The total score value is obtained by the sum of the points, considering the severity and/or extension of each one of these morphological alterations. The score value ranges from zero (absence of abnormalities) to up to 37 points (severe alterations in all parameters) (**Supplementary table 2**).

**Spirometry**

For the test, participants had to remain standing using a nasal clip and were requested to make vigorous and prolonged expiratory maneuver to achieve the reproducibility criterium of the FVC maneuver. The equipment was calibrated immediately after the completion of the first morning exam, and the parameters evaluated were (% of predicted):

(i) FVC: volume difference between maximum inspiration and full expiration, performed at the mouth level, very quickly and with maximum effort, being measured in liters. Obtained by asking the individual to conduct maximum inspiration up until its total lung capacity, followed by a quick and intense expiration, with prolonged duration up until exhaling all air.

(ii) FEV1%: exhaled air volume, in liters, during the first second of FVC, being obtained after the strategy to obtain FVC.

(iii) relation between FEV1 and FVC (FEV1/FVC);

(iv) FEF25–75%: airflow eliminated during the central part of FVC, measured in liters per second (L/sec).

**Reference**

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| **Supplementary table 1.** Descriptive and comparative analysis between different evaluative methods of structural lung damage. |
| **Datum** | **Thorax ultrasound** | **X-ray** | **High resolution computed tomography** | **Magnetic Resonance** |
| What does it evaluate? | Diagnoses [pleural effusion (and volume quantification), pneumothorax, pleura solid lesions], differentiates transudate from exudate, guides invasive procedures | Diagnoses or evaluates treatment response of numerous diseases, including cystic fibrosis. | Detects and classifies lung abnormalities accurately (mainly interstitial ones) by the presence of alterations, such as thickening, nodule, consolidation, increase or decrease of the parenchyma density, bronchiectasis | Serves for staging of lung tumor, lung vascular disease, especially in patients who should not be exposed to radiation, including those with cystic fibrosis |
| Limitation | Edema in soft parts, subcutaneous emphysema or obesity can affect image quality Limited data interpretation | It prevents the detailed evaluation of lung parenchyma | High exposure to ionizing radiation | Cost and technical limitation due to need of generating image in fabric with high volume of air. In addition, dispersion and movement occurs between the layers of tissue/air, lungs being the organ with greater difficulty for the use of such technique |
| Cost per exam | Low | Low | High | High |
| Cost of the equipment | Low | Low | High | High |
| Use of radiation | No | Yes | Yes | No |
| Exam time | Medium | Fast | Medium | High |
| Team’s need | No | Yes | Yes | Yes |
| Need for specific location  | No | Yes | Yes | Yes |
| Ambulatorial use | Yes | No | No | No |
| Age indicated in cystic fibrosis | Every age group | Under clinical criterion | ~ 2 years | No consensus  |
| Time between exams (interval) | In each consult, if necessary | Under clinical criterion | Every two years |  |
| Use to evaluate exacerbation | Yes | Yes  | No (depending on time) | Yes |
| Use to evaluate disease progression | Yes | Yes | Yes | Yes |
| Reproducibility | Yes | Yes | Yes | Yes |
| Most common findings | B-line pattern/consolidation | Hyperinflation/bronchial wall thickening/atelectasis/cyst/pneumothorax | Bronchiectasis/mucoid impaction/tree-in-bud/mosaic perfusion | Signal difference between transudate and exudate (simple, infectious and malignant). Difference between parenchymal disease and tumor |

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| The modified Bhallacomputed tomography scoring system reproduced equally to Folescu and collaborators.29,\*  |
|  | **Score** |
| **HRCT scan parameter** | **0** | **1** | **2** | **3** |
| Severity of bronchiectasis | Absent | Luminal diameter slightly greater than that of the adjacent blood vessel | Luminal diameter 2-3 times greater than that of the adjacent blood vessel  | Luminal diameter 3 times greater than that of the adjacent blood vessel |
| Bronchial wall thickening | Absent | Airway wall thickness equal to the diameter of the adjacent blood vessel | Airway wall thickness greater than and up to twice the diameter of the adjacent blood vessel | Airway wall thickness > 2 times the diameter of the adjacent blood vessel  |
| Extent of bronchiectasis (no of bronchopulmonary segments) | Absent | 1-5 | 6-9 | > 9 |
| Extent of mucus plugging (no of bronchopulmonary segments) | Absent | 1-5 | 6-9 | > 9 |
| Sacculations/abscesses (no of bronchopulmonary segments) | Absent | 1-5 | 6-9 | > 9 |
| Generations of bronchial division involved [bronchiectasis/mucous plugging] | Absent | ≤ 4th generation | ≤ 5th generation | ≤ 6th generation and distal |
| Number of bullae | Absent | Unilateral | Bilateral (≤ 4) | > 4 |
| Emphysema (no of bronchopulmonary segments) | Absent | 1-5 | > 5 |  |
| Collapse/consolidation | Absent | Subsegmental | Segmental/lobar |  |
| Mosaic attenuation/perfusion pattern | Absent | 1-5 | > 5 |  |
| Air trapping | Absent | 1-5 | > 5 |  |
| Acinar nodule | Absent | Subsegmental/segmental | Lobar | Diffuse (>1 lobe) |
| Intralobular septal thickening | Absent | Subsegmental/segmental | Lobar |  |
| Ground-glass infiltrate | Absent | Subsegmental/segmental | Lobar | Diffuse (>1 lobe) |

\*, complete reference citation: Folescu TW, Marques Ede A, Boechat MC, Daltro P, Higa LY, Cohen RW. High-resolution computed tomography scores in cystic fibrosis patients colonized with *Pseudomonas aeruginosa* or *Staphylococcus aureus*. J Bras Pneumol 2012;38(1):41-49.