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ORIGINAL INVESTIGATION

Assessment of lung ultrasound for early detection of respiratory complications in thoracic surgery

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Abstract

Background and objectives: To assess lung ultrasound for the diagnosis and monitoring of respiratory complications in thoracic surgery.
Methods: Prospective observational study in a University hospital, single institution. Adult patients scheduled for pulmonary resection surgery excluding pneumonectomy. An ultrasound follow-up was performed from the day before the surgery to the third day after surgery with calculation of B-line and lung score (reaeration and loss of aeration scores). Respiratory complications were collected throughout the hospitalization period.
Results: Fifty-six patients were included. Eighteen patients presented a respiratory complication (32%), and they presented significantly higher BMI and ASA scores. Patients operated by videothoracoscopy were less at risk of complications. At day 3, a reaeration score $\leq$ 2 on the ventilated side or $\leq$ -2 on the operated side, and a B-line score > 6 on the operated side were in favor of a complication.
Conclusion: Lung ultrasound can help in the diagnosis of respiratory complications following pulmonary resection surgery.

Introduction

Pulmonary resection surgery is a surgery associated with a high risk of complications (24 to 41%).[1] The most frequent

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complications are respiratory (13–28%), including acute respiratory failure, atelectasis, and pneumopathy.[2] The other complications encountered specific to this surgery are persistent air leak, diaphragmatic or recurrent paralysis, and more rarely, bronchopleural fistula. Moreover, the appearance of cardiac rhythm disorders such as atrial fibrillation, often transient, is frequent in the first postoperative days.

During pulmonary resection surgery, both lungs are subjected to multiple stress factors: mechanical ventilation in positive pressure, one-lung ventilation (OLV), surgical injuries on the operated lung, inflammatory reaction, compression of the ventilated lung by the block and the mediastinum. This stress and the pain following the surgery will lead to an increase in the respiratory work, restrictive syndrome, hypoxemia, and respiratory muscle dysfunction in the postoperative period.[2,3] This explains the high incidence of respiratory complications after pulmonary surgery.

Ultrasound has become an increasingly used tool in intensive care units.[4] Its performances for the diagnosis of respiratory distress are superior to those of radiography.[5] It can easily be performed at the patient's bedside. The pleuro-pulmonary ultrasound semiology has been well described,[5] particularly the B-lines which are correlated to the radiologic alveolo-interstitial syndrome. In addition, pleuro-pulmonary ultrasound has the advantage of having a rapid learning curve.[6,7] However, to our knowledge, pulmonary ultrasound has not yet been evaluated for complications following pulmonary resection surgery.

Our hypothesis was that the appearance of B-lines, potentially related to secondary trauma to surgery and unipolar ventilation, could make it possible to detect respiratory complications by analyzing the evolution of ultrasound scores.

The main objective of our study was to determine whether lung ultrasound monitoring in thoracic surgery would allow the diagnosis of postoperative respiratory complications. Secondary objectives were to describe the evolution of ultrasound scores and images after thoracic surgery and to determine the factors underlying respiratory complications.

Methods

Patients

The study received a favorable opinion from the Ethics Committee of the University Hospital (n°16-0315). Adult patients scheduled to undergo thoracic surgery for lung resection with one-lung ventilation were included. Oral consent was collected from the patients. Patients with pleural anomaly (pneumothorax, pleural effusion, or pleural adhesion) or pneumonectomy were excluded. Pregnant women, as well as adult patients under legal protection were also excluded.

Achievement of follow up by ultrasonography

An experienced anesthetist performed each lung ultrasound. The ultrasonograph used was a LOGIC™ e (GE Healthcare), with a 4 MHz round-tipped probe. Six regions in each lung were examined in longitudinal section: upper and lower parts of the anterior, lateral and posterior region of each lung. The patient was on the back for the exam of anterior and lateral regions, and in lateral decubitus position for the exam of posterior regions. The exam detected the number of B-lines, alveolar consolidation, pleural effusion, and lung sliding.

Five lung ultrasounds were performed on each patient: the first was the day before surgery; the second after the surgery and extubation in the recovery room; then, one lung ultrasound per day for 3 days.

The postoperative follow-up included a clinical examination and a daily thoracic radiography until discharge from the department.

Intraoperative management

The care was that usually provided in the unit. Paramedular analgesia was performed before general anesthesia. A spinal anesthesia (sufentanil 10–15 μg + morphine 3–5 μg.kg^{-1}) was performed and a paravertebral catheter inserted by the surgeon at the end of the intervention, in which ropivacaine (2 mg.mL^{-1}) was injected at 7 mL.h^{-1} during 48 hours; or thoracic epidural analgesia (level T4–T5) with sufentanil (2.5 μg.h^{-1}) and ropivacaine (10 mg.h^{-1}) during 48 hours was administered.

A prophylactic antibiotic treatment (amoxicillin and clavulanic acid) was given intravenously before general anesthesia.

Induction anesthesia was achieved with sufentanil (0.2–0.3 μ.kg^{-1}), and propofol (2–3 mg.kg^{-1}). After checking the feasibility of ventilating with a face mask, patients were curarized by injection of cisatracurium (0.15 to 0.2 mg.kg^{-1}).

After induction, patients were intubated with a double-lumen endotracheal tube intubation Rüsh Bronchopart (Teleflex Medical®, Athlone, Ireland) to permit one-lung ventilation during surgery. The choice of the size of intubation tube (35 to 41 French) was left to the discretion of the anesthetist, based on the gender and size of the patient. The placement of the double-lumen endotracheal intubation tube was controlled by auscultation and endoscopy.

During two-lung ventilation, a tidal volume of 8 mL.kg^{-1} predicted body weight [PBW], and plateau pressures < 30 cm H_2O were used. A positive end-expiratory pressure [PEEP] was associated, starting with 5 cmH_2O. Based on hemodynamic tolerance, plateau pressure, or appearance of hypoxemia, PEEP was adjusted.

During one-lung ventilation, tidal volume of 6 mL.kg^{-1} PBW was used; the same PEEP and plateau pressures < 30 cmH_2O were associated. Patients were positioned in lateral decubitus, on contralateral side to surgery. A pillow was placed under the chest, at the scapular apex.

During the surgery, if hypoxemia appeared, the correct position of the tube was checked by endoscopy. If hypoxemia persisted, recruitment maneuvers on the ventilated lung were performed (pressure at 30 cm H_2O for 30 seconds), PEEP was optimized, and oxygen was administered on the non-ventilated lung. If these operations were insufficient, the operated lung was ventilated for a few minutes.

At the end of surgery, the operated lung was manually ventilated under observation to verify the re-expansion and the absence of atelectasis while complying with plateau pressure < 30 cmH_2O. Two Monaldi chest tubes were placed by the surgeon and connected to the aspiration system (-20 cmH_2O) on arrival at the recovery room. Patients were extubated in the surgical or recovery room. Then, they were moved to the intensive care unit of thoracic surgery.

Data collection

Data collected during the hospitalization included: demographic, anesthetic and surgical data; preoperative spirometry, and ultrasound results. The chest X-ray was analyzed, with the aid of a radiologist, after the performance of the lung ultrasound. The time to onset, types of complications, and the duration of oxygen therapy were noted.

Respiratory complications were atelectasis, acute respiratory failure with need of intubation or non-invasive ventilation, pneumonia, and exacerbation of chronic obstructive pulmonary disease (COPD).

Study objectives

The primary objective of our study was to determine if a follow-up by ultrasonography through a lung ultrasound reaeration score and B-lines score could diagnose postoperative respiratory complications.

Secondary objectives were to describe the evolution of ultrasound scores after thoracic surgery, determine risk factors of respiratory complications, and observe postoperative length of stay and duration of oxygen therapy.

Calculating lung ultrasound scores

B-lines are long and hyperechoic lines called ''lung rockets'' erasing A-lines, arising from the pleural line, and moving in concert with lung sliding. In each lung region examined, the number of B-lines was noted, and for each hemithorax the numbers of the 6 regions were added to obtain the B-lines score.

The reaeration or loss of aeration score was calculated as described by Bouhemad. Lung ultrasound aeration (N, B1, B2, C) was measured in each of 6 regions by hemithorax during each lung ultrasound. N is a normal pattern; B1, ultrasound lung comets with well-defined and irregular spacing; B2, abutting ultrasound lung comets; and C, an alveolar consolidation. In our study, the lung ultrasound performed after surgery in the recovery room was considered as the reference. According to the evolution of the patterns, the lung aeration score was calculated for each region as described in Supplementary Table 1, and the 6 scores by hemithorax were added to obtain the final score for each lung. A positive score symbolizes a gain of aeration and a negative score a loss of aeration.

Statistical analysis

The population was divided into two groups: patients with or without respiratory complication.

There are several steps in our statistical analysis, such as descriptive statistics for continuous variables (median, 95% confidence interval) and qualitative variables (n, %) on the global population and on each group; comparison between the 2 groups by a non-parametric test (Mann Whitney) for continuous variables (age, surgical duration, etc.), and by Fisher's exact test for qualitative variables.

The study of the ROC-curve (Receiver Operating Characteristic) and areas under the curve (AUC) of each covariable according to the criteria ''respiratory complication,'' permit evaluation of the discriminating threshold. The most discriminating threshold was selected with the best Youden index. At the same time, the positive and negative predictive values (PPV and NPV), the sensitivity, and the specificity were calculated according to these thresholds. For each of the thresholds, one ''grey zone'', or zone of uncertainty, was determined by using the two-step procedure defined by Cannesson. These ROC-curves were compared to eliminate the least discriminating covariables.

In a last step, we evaluated the association between different covariables and the variable ''respiratory complications'' in multivariate analysis (logistic regression), by calculation of odds ratio (OR). We used a backward elimination: variables with $p < 0.02$ were included, then the non-significant variables were eliminated along the way. The model with the best goodness of fit was chosen thanks to the Hosmer–Lemeshow test (chi2 goodness of fit).

The study was performed using MedCalc® statistical software (Mariakerke, Belgium). Differences were significant with $p < 0.05$.

Results

Population

A total of 57 patients were included between April 2015 and March 2016. One patient was excluded from the statistical analysis due to a lack of ultrasound data for day 2 and day 3. Of the 56 patients included in the statistical analysis, day-3 ultrasound data were missing for 7 of them, 4 of whom were in the respiratory complication group.

Demographic and anesthetic characteristics are presented in Table 1. There was no significant difference between the two groups except for a high body mass index (BMI) and the ASA score greater than 2.

Surgical characteristics are presented in Table 2; videothoracoscopy compared to thoracotomy was associated with a lower risk of respiratory complication. A total of 50 lobectomies (89.2%), 5 atypical resections and 1 exploratory thoracotomy were performed.

Complications

Of the 56 patients included, 24 had a complication (42.8%), 18 of whom had a respiratory complication (32.1%). Of the 7 patients with acute respiratory failure, 3 had reintubation performed immediately, or after failure of noninvasive ventilation, and 4 benefited from noninvasive ventilation alone. No deaths occurred during the follow-up period. The respiratory complications observed were: atelectasis n = 4, acute respiratory failure n = 7, pneumopathy n = 5, and COPD exacerbations n = 4. They generally appeared between day 1 and day 3 with a median occurrence at day 2. Other complications were observed such as car-

Table 1 Demographic and anesthetic characteristics.

	Global population	No respiratory complication	Respiratory complication	$p < 0,05$
Age (years)	64 (61–68)	64 (58–68)	64 (59–67)	0.9371
Sex (M/W)	34/22	22/16	12/6	0.5727
IMC (kg.m^{-2})	25,8 (23.1–26.7)	24,9 (22.9–26.5)	27,9 (22,8–32,8)	0.0474[a]
ASA > 2	9 (16.1%)	3 (7.9%)	6 (33.3%)	0.0101[a]
Preoperative spirometry				
TV (% theoric value)	94.5 (91.2–98.3)	95.5 (92.8–100.3)	91.5 (81.2–99.0)	0.2613
FEV1 (% theoric value)	92 (87.3–99.6)	91 (88–103.6)	93 (74.0–100.9)	0.2800
Tiffeneau (%)	80 (73–83)	81 (74.4–85.5)	72.5 (67.0–85.7)	0.3482
Duration of surgery (min)	130 (120–180)	137 (120–180)	127 (111–180)	0.5201
Duration of global ventilation (min)	167 (150–210)	192 (150–215)	165 (150–216)	0.7921
One lung ventilation				
Duration (min)	120 (105–140)	120 (105–165)	115 (90–134)	0.4190
FiO2 (%)	85 (80–100)	80 (80–100)	95 (80–100)	0.5751
Pplat (cmH_2O)	23 (22,4–24,0)	23 (22–24)	24 (23,0–26,7)	0.2828
PEEP (cmH_2O)	5 (5–5)	5 (5–5)	5 (5–5)	0.9477
TV/BIW (mL.kg^{-1})	6.10 (5.86–6.32)	6.10 (5.92–6.39)	6.02 (5.57–6.43)	0.6233
Two-lung Ventilation				
FiO2 (%)	70 (60–80)	70 (60–80)	65 (60–80)	0.6098
Pplat (cmH_2O)	19 (17–20)	19 (17–20)	19 (15.5–22.4)	0.7717
PEEP (cmH_2O)	5 (5–5)	5 (5–5)	5 (5–5)	0.7595
TV/IBW (mL.kg^{-1})	6.95 (6.77–7.26)	6.87 (6.55–7.19)	7.16 (6.79–7.58)	0.2194
Duration of hospitalization (days)	6 (6–7)	6 (6–6)	9.5 (7.0–13.8)	0.0001[a]
Duration of hospitalization in Intensive Care (days)	3 (2–3.8)	2 (2–3)	4.5 (3.33–7.6)	0.0001[a]

M/W, Man/Woman; BMI, Body Mass Index; FEV1, forced expiratory volume in one second, Pplat, plateau pressure, PEEP, positive end-expiratory pression, TV, Tidal Volume, IBW, Ideal Body weight.

Table 2 Surgical characteristics.

	Global population	No respiratory complication	Respiratory complication	*p*
Surgical Approach				
Thoracotomy/Thoracoscopy	42/14	25/13	17/1	0.0232*
Operated Side				
Right/Left	34/22	24/14	10/8	0.7702
Pathology				
Adenocarcinoma	34 (60.7%)	23 (60.5%)	13 (72.2%)	0.5522
Epidermoid carcinoma	4 (7.1%)	2 (5.3%)	2 (11.1%)	0.5866
Neuro-endocrine tumor	6 (10.7%)	5 (13.2%)	1 (5.6%)	0.6522
Others	12 (21.4%)	8 (21.0%)	2 (11.1%)	

diovascular complications (12.5%): auricular fibrillation, pulmonary embolism, acute pulmonary edema, acute coronary syndrome; surgical complications (10.7%), or infectious complications (7.1%)

Sonographic scores

Regarding the sonographic scores, there was a significant difference between patients with a respiratory complication and patients who did not have a respiratory complication for the day 3 reaeration score on both the ventilated and excluded side, and for the day 3 B-line score on the excluded side. The day 3 reaeration score on the excluded side was -2 [-5; 0.1] in the ''respiratory complication'' group, versus 0 [-1; 1] in the ''non-respiratory complication'' group. The day 3 reaeration score on the ventilated side was -0.5 [-2; 4] in the ''respiratory complication'' group, versus 3 [1; 5] in the ''non-respiratory complication'' group. Finally, the day 3 B-line score on excluded side was 8 [4; 10] in the ''respiratory complication'' group versus 4 [3; 7.1] in the ''non-respiratory complication'' group. The ultrasound scores are presented in Tables 3 and 4.

The diagnostic performance of the ultrasound scores for the detection of respiratory complications is summarized in Table 5. The reaeration score on the ventilated side at D3 showed the best AUC (area under the ROC curve) with sensitivity of 71.4% and specificity of 70.5% for a threshold set at 2.

The Receiving Operator Characteristic (ROC) curves drawn from these data are represented in Figure 1.

Table 3 Lung ultrasound scores: re-aeration or loss of aeration score.

Reaeration score	No respiratory complication	Respiratory complication	p
Excluded lung			
Day 1	-1 [-1;0]	-0.5 [-1;1.6]	0.6839
Day 2	0 [-2;0.5]	-2 [-4;1.6]	0.4870
Day 3	0 [-1;1]	-2 [-5;0.1]	0.0297*
Ventilated lung			
Day 1	2 [0;3]	0.5 [0;3.6]	0.7312
Day 2	2.5 [1;4]	-1 [-2;3]	0.1040
Day 3	3 [1;5]	-0.5 [-2;4]	0.0124*

Table 4 Lung ultrasound scores: B-line score.

B-line score	No respiratory complication	Respiratory complication	p
Excluded lung			
Day - 1	0 [0;0]	1 [0;2]	0.0747
Day 0	2 [0;3]	6 [4;8.2]	0.6536
Day 1	2 [0;3]	6.5 [4;9.6]	0.8812
Day 2	2 [0;3]	7.5 [4;10.6]	0.4762
Day 3	2 [0;3]	8 [4;11]	0.0251*
Ventilated lung			
Day − 1	0 [0; 0]	0.5 [0;2]	0.1481
Day 0	8 [7;9]	5.5 [3;7.6]	0.0624
Day 1	5.5 [4;7]	3.5 [1.3;6.6]	0.0573
Day 2	5 [4;6]	4.5 [1.3;6.6]	0.7782
Day 3	3 [1;5]	3 [2.2;7]	0.1685

Table 5 Diagnostic performance of the ultrasound scores.

	AUC	Threshold	Se %	Sp %	PPV %	NPV %	Gray zone
Reaeration score on ventilated lung at Day 3	0.73 [0.58; 0.85]	≤ 2	71.4	70.5	50	85.7	[-1.6; 5.6]
Reaeration score on excluded lung at Day 3	0.70 [0.55; 0.82]	≤ -2	57.1	76.4	50	81.2	[-4.3; 1.6]
B-lines score on excluded lung at Day 3	0.702 [0.55; 0.82]	> 6	66.7	64.7	45.5	81.5	[1.5;8.9]

AUC, area under curve; Se., sensibility; Sp., specificity; PPV, positive predictive value; NPV, negative predictive value.

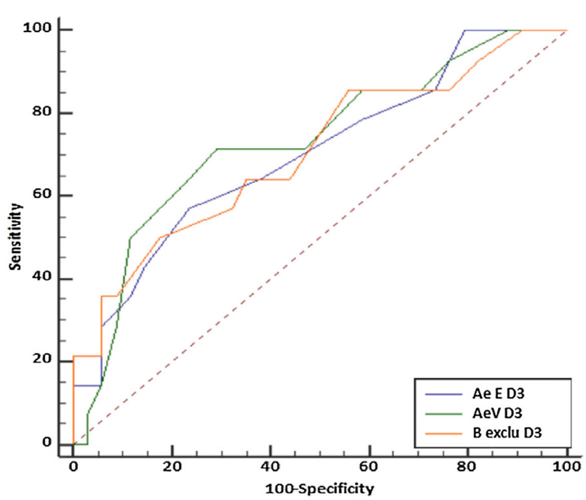

Figure 1 ROC curves of discriminative lung ultrasound scores. Ae E D3, Aeration score of excluded lung at Day 3; AeV D3, Aeration score of ventilated lung at Day 3; B exclu D3, B-line score of excluded lung at Day 3.

Evolution of lung ultrasound scores

The analysis of the reaeration scores curves (Supplementary Fig. 1) shows a global trend to a ventilation loss in both excluded and ventilated lungs. This trend is more pronounced in the ''non-respiratory complication'' group but without significant difference before day 3.

Supplementary Figure 2 shows the evolution of the B-line scores for groups ''respiratory complications'' and ''non-respiratory complication''. On the excluded side, the number of B-lines increases daily in the group ''respiratory complication'', whereas it decreases from day 2 in the group ''non-respiratory complication'', with a significant difference between the two groups at day 3. On the ventilated side, after a maximum reached on day-0, the B-line score decreases daily without there being any significant difference between the two groups. B-lines appeared as soon as day-0 in 47 patients (83.9%) on the excluded side, and in 52 patients (92.8%) on the ventilated side.

Therefore, these results show the appearance of B-lines in the majority of patients on the operated and ventilated

Table 6 Multivariate analysis.

Factors of respiratory complication	p	Odds ratio	IC95%
Reaeration score on ventilated lung at Day 3	0.0388	0.79	0.629–0.987
B-lines score on excluded lung at Day 3	0.0257	1.24	1.026–1.505
Videothoracoscopy	0.0814	0.10	0.007–1.334
AUC	0.84 (0.7--0.93)		
Hosmer-Lemeshow Test	0.7274		
Cases correctly classified	79.2%		

side. While there is a decrease of B-lines as early as day 1 on the ventilated side, the number of B-line tends to increase daily on the operated side, especially in patients with respiratory complication.

Multivariate analysis

A multivariate analysis was performed integrating the reaeration score on the ventilated side at day 3, and the B-line score on the excluded side at day 3 and completion of video thoracoscopy. The difference between the ''respiratory complication'' and ''non-respiratory complication'' groups remained significant for the reaeration score on the ventilated side at day 3 with an odds ratio (OR) of 0.79 for a score less than or equal to 2. It was also significant for the B-line score on the excluded side at day 3, with an OR of 1.24 for a score greater than 6. However, the difference was no longer significant between the two groups concerning thoracoscopy despite an OR of 0.10 ($p = 0.0814 > 0.05$), probably because of the small number of videothoracoscopies performed. These results are summarized in Table 6.

Discussion

These results show that lung ultrasound may be of help to diagnose respiratory complications. Indeed, a B-line score on the excluded side greater than 6, or a reaeration score on the ventilated side less than 2 were significantly correlated with the occurrence of a respiratory complication in multivariate analysis. This shows the interest of an ultrasound follow-up in the aftermath of pulmonary surgery.

As far as we know, ultrasound had never been assessed for the detection of respiratory complications following pulmonary surgery. Goudie et al. compared ultrasound to X-ray for the management of pleural drains after thoracic surgery.[8] They showed that X-rays remained indispensable for the detection of pneumothorax but focused on the search for pleural fluid or gases without studying the pulmonary parenchyma.

The B-lines observed by lung ultrasound may reflect either a thickening of the interstitial space or a loss of aeration of the pleural structures. Those are generally the result of inflammatory, fibrotic, lymphangitic phenomena, hydrostatic or lesion edema, or a ventilatory disorder (hypoventilation, microatelectasis).[9,10]

During pulmonary surgery, several factors contribute to the alteration of the pulmonary parenchyma. On the operated side, surgical stress, lung collapse and ischemia-reperfusion phenomena related to one-lung ventilation (OLV) are responsible for the observed parenchymal lesions.[3,11] On the ventilated side, barotrauma and volutrauma secondary to OLV, aggravated using the block, and the use of high FiO2s favoring oxidative stress are incriminated.[12,13] These factors explain that we observed B lines as soon as we left the operating room on both lungs.

For the calculation of the reaeration score, day-0 was chosen as a reference for several reasons. First, the calculation of the reaeration score was originally invented to measure the lung ultrasound evolution to evaluate the efficacy of therapeutic measures such as antibiotic therapy in ventilator acquired pneumonia[14] or PEEP level during ARDS.[15] It seemed more relevant to evaluate the lung's evolution after it had undergone the trauma of the operation, rather than performing a comparison before and after surgery knowing the anatomical changes that it entails.

The median plateau pressures measured during this study were 23 cmH_2O for a current volume based on the theoretical ideal body weight of 6.10 $mL.kg^{-1}$. There was no significant difference between the two groups in these parameters. Several authors have promoted the use of protective ventilation during one-lung ventilation[3,16] by analogy with what could be demonstrated in bipulmonary ventilation[17] and during ARDS. However, few prospective studies have compared high-volume ventilation (> 8 $mL.kg^{-1}$ without PEEP) with protective ventilation (low volume 4–6 $mL.kg^{-1}$ using PEEP 5–10 cmH_20) during one-lung ventilation. In a cohort study comparing morbidity and mortality before and after the introduction of a protective ventilation protocol, Lickers et al. found a decrease in the incidence of acute respiratory failure, atelectasis, admission to intensive care, and the duration of hospitalization after the introduction of such a protocol.[18] The use of protective ventilation does not benefit all patients, however. It may be a source of hypoxemia, particularly in patients with severe obstructive pulmonary disorder, with extrinsic PEEP adding to intrinsic PEP, and may lead to an increase in the shunt effect.[3] So, ventilatory assist can be responsible for various modifications of the lung parenchyma that could be observed by lung ultrasounds.

When performing postoperative ultrasounds, dressings, subcutaneous emphysema, or pain associated with mobilization may have interfered with image interpretation, especially on the operated side. This may have led to missed pleural effusions visible on the X-ray, or to underestimation of the B-line scores. Lung ultrasound remains an easily performed examination following thoracic surgery, but knowing its pitfalls and limits is necessary for a good interpretation. In our study, the appearance of ultrasound abnormalities was no earlier than the clinical diagnosis of the complication. This could be attributed to a lack of power.

In conclusion, lung ultrasound may be of help in the diagnosis of respiratory complications after thoracic surgery. However, the appearance of ultrasound signs does not precede the onset of clinical signs. It is interesting to note that most of patients have B-lines on both lungs after surgery. Therefore, in the context of thoracic surgery, lung ultrasound appears to us as complementary to radiography as a diagnostic aid, because it allows a better exploration of the pulmonary parenchyma, whereas radiography seems more effective, in this context, for the control of pleural tubes and the screening of pneumothorax. The development of a risk score for the occurrence of respiratory complications integrating clinical, radiographic, and ultrasound parameters determined as early as day 1 could make it possible to detect the patients most at risk of complication and to propose a strategy of detection and prevention of these complications.

Conflicts of interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:10.1016/j.bjane.2021.01.006.

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