Ref: Ro Med J. 2021;68(Suppl5)
DOI: 10.37897/RMJ.2021.S5.19

Use of lung ultrasound and and aEEG patterns to predict the need for mechanical ventilation and the readiness for extubation in neonates with respiratory distress

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ABSTRACT

Objective. The aim of the study was to establish if lung ultrasound findings could anticipate the need for intubation and mechanical ventilation in neonates with respiratory distress and if lung ultrasound and aEEG criteria could be used in appreciation of the readiness for extubation of the neonatal patients resulting in a decrease of the rate of extubation failure.

Material and method. There were analysed the cases of 50 late preterm and early term neonates presenting with respiratory distress. Lung ultrasound was performed during the first 4 hours after delivery in all the neonates and then as clinically indicated in the case of ventilated patients. A lung ultrasound was performed in all the ventilated patients before extubation. 12 of the 25 ventilated patients were also monitored by aEEG. The decisions regarding the intubation and mechanical ventilation and the moment of extubation of the patients were taken by the clinicians in accordance with the local and international guidelines. The extubation failure was defined as the need to re-intubate the patient in the first 24 hours after the extubation. The lung ultrasound pattern was considered as normal if the image was consisting of A lines with rare B lines or "double lung point" as in the case of the delayed absorption of fetal lung fluid and abnormal in the case of "white lung" appearance (coalescent B lines) or an image of consolidation. A normal aEEG was defined as the presence of a continuous normal voltage pattern with sleep-wake cycles present and an abnormal aEEG as either discontinuous normal voltage, burst-suppression, low voltage or flat background patterns. The lung ultrasound patterns in the first hours of life were compared between patients that needed intubation and those that did not need mechanical ventilation. The lung ultrasound and aEEG patterns before extubation were compared between the patients that did not need re-intubation and those with extubation failure.

Results. An abnormal image on lung ultrasound was significantly associated with the risk of intubation ($p < 0.001$) (sensitivity 84%, specificity 100%, positive predictive value 100% and negative predictive value 86.2%) An abnormal lung ultrasound pattern before extubation was associated with a significant risk of extubation failure ($p < 0.049$) (sensitivity 75%, specificity 85%, positive predictive value 50%, negative predictive value 94.7%). In the case of the subset of patients in which aEEG was performed, an abnormal aEEG pattern was significantly associated with extubation failure ($p < 0.034$)

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Article History:
Received: 4 November 2021
Accepted: 29 November 2021

(sensitivity 100%, specificity 88%, positive predictive value 75%, negative predictive value 100%). In the case of association of the two parameters (lung ultrasound and aEEG pattern) there was again a statistically significant association between the abnormal patterns and extubation failure.
Conclusions. An abnormal lung ultrasound during the first hours of life is a strong predictor for the need of intubation and mechanical ventilation in the neonates with respiratory distress. The normal lung ultrasound pattern just before extubation is predictive of a good evolution without the need for re-intubation of the patient. A normal aEEG pattern at the same time is associated also with a decreased risk of extubation failure.

Keywords: lung ultrasound, aEEG, intubation, mechanical ventilation, neonates, respiratory distress

BACKGROUND

Respiratory distress is the most frequent diagnosis for admission in the neonatal intensive care unit and the amount of respiratory support needed is one of the most difficult decisions a neonatologist has to take (1). Also, the decision if the patient is ready for extubation is a very difficult one, weaning and extubation being more subjective rather than based on objective criteria (2).

Objective criteria are established for intubation both of term neonates (3,4) and preterm infants (5), in order to avoid both not offering the appropriate support and get to the deterioration of the status of the patient and unnecessary ventilating patients that could improve with less invasive ventilatory support. There are clinical criteria (Silverman Score) (6), blood gas criteria (3-5) and radiologic criteria (3).

In the case of the extubation, the decision is more subjective. In order for a patient to be ready for extubation and spontaneous breathing, several conditions must be fulfilled: the lung has to be prepared for gas exchange, the respiratory muscles should work properly, the patient should not get tired from breathing and the respiratory drive should function (i.e. the patient should have spontaneous, conscious breathing). There are means to identify these conditions before extubation, though the predictive value of these is not satisfactory yet (2).

During the last decades, lung ultrasound has emerged as an adjuvant method in monitoring neonates with respiratory distress (7-9). There are established protocols for examination (8-10) and normal and pathologic images for all the neonatal diagnoses (11-15). Lung ultrasound is a good tool to assess the status of the neonatal lung and to confirm normal lung status (7-9).

aEEG (amplitude integrated EEG) represents a method of cerebral function monitoring of both term and preterm neonates (16). AEEG allows long term monitoring and an estimation of the status of the neonatal brain based on the background patterns (16,17). A classification system of the background patterns is in place, allowing a good correlation with the normal brain function and the pathologic conditions that affect brain function (17).

AIM

The aim of our study was to establish if lung ultrasound findings could anticipate the need for intubation and ventilation in neonates with respiratory distress and if lung ultrasound and aEEG criteria could be used in appreciation of the readiness for extubation of the patients resulting in a decrease of the rate of the extubation failure.

MATERIAL AND METHODS

There were analysed the cases of 50 late preterm (34-46 weeks gestational age) and early term (37-38 weeks + 6 days) (19) neonates born between January 1 2019 and October 30 2021 in the Neonatology unit at Life Memorial Hospital Bucharest presenting with respiratory distress. The demographic data of the patients are presented in Table 1.

TABLE 1. Characteristics of the study sample

Variable	Ventilated	Not ventilated	Significance
Birth weight (mean (SD) grams	3,240 (± 350)	3,310 (+ 450)	NS*
Gestational age (mean) (weeks)	37 and 3 days (33-38 and 6 days)	37 and 4 days (33-38 and 6 days)	NS
Corticoids used before delivery (number of cases)	21/25	20/25	NS
Maternal diabetes (number of cases)	5/25	6/25	NS

** not significant*

Indications for intubation and extubation

The indications for intubation and mechanical ventilation were those established by the current guidelines in Romania i.e.

- Severe apnea (unresponsive to stimulation or bag and mask ventilation)
- PaO2 < 50 mmHg or SpO2 < 90% at an FiO2 > 40%*
- PaCO2 > 50 mmHg**, pH< 7.25
- Not responding to CPAP with a PEEP > 9 cm H2O
- - Increase in respiratory effort (worsening retractions, continuous respiratory grunting, nasal flaring) (18)

* different from local guidelines (>50%)
** different from local guidelines (> 55-60%)
The criteria for extubation were as follows

- FiO2 <30%
- Respiratory rate of the ventilator < 20/min
- Presence of spontaneous breathing
- MAP < 7 cmH2O (18)

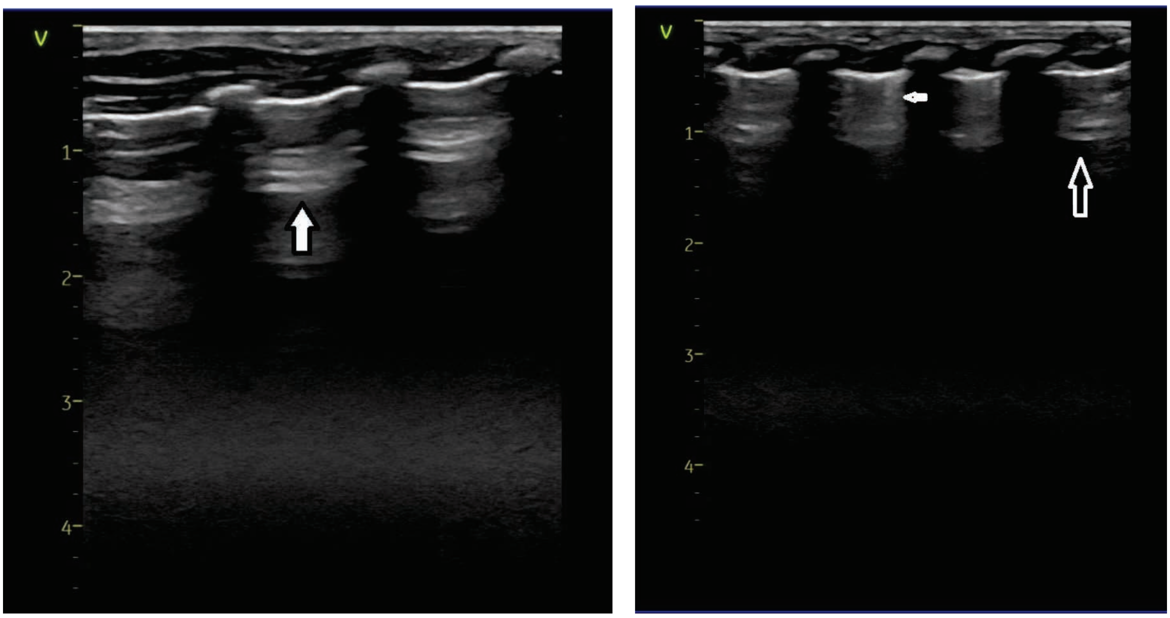
Extubation failure was defined as the need to re-intubate and mechanically ventilate the patient during the first 24 hours after extubation.

The decisions regarding intubation or extubation of the patients were the responsibility of the clinicians. Lung ultrasound or aEEG findings did not influence the decisions.

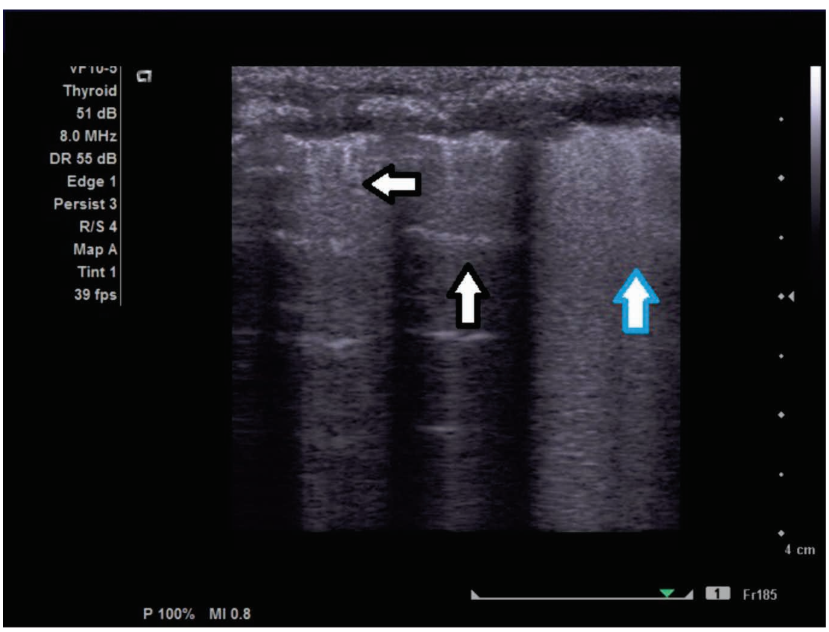
Lung ultrasound

A lung ultrasound was performed in all the cases in the first 4 hours after delivery and then as clinically indicated in the case of the ventilated patients. An ultrasound was performed in all the ventilated patients before extubation.

During the time interval of the study we used 2 types of ultrasound machines: Siemens X300 and General Electric Vivid S60. There were used linear

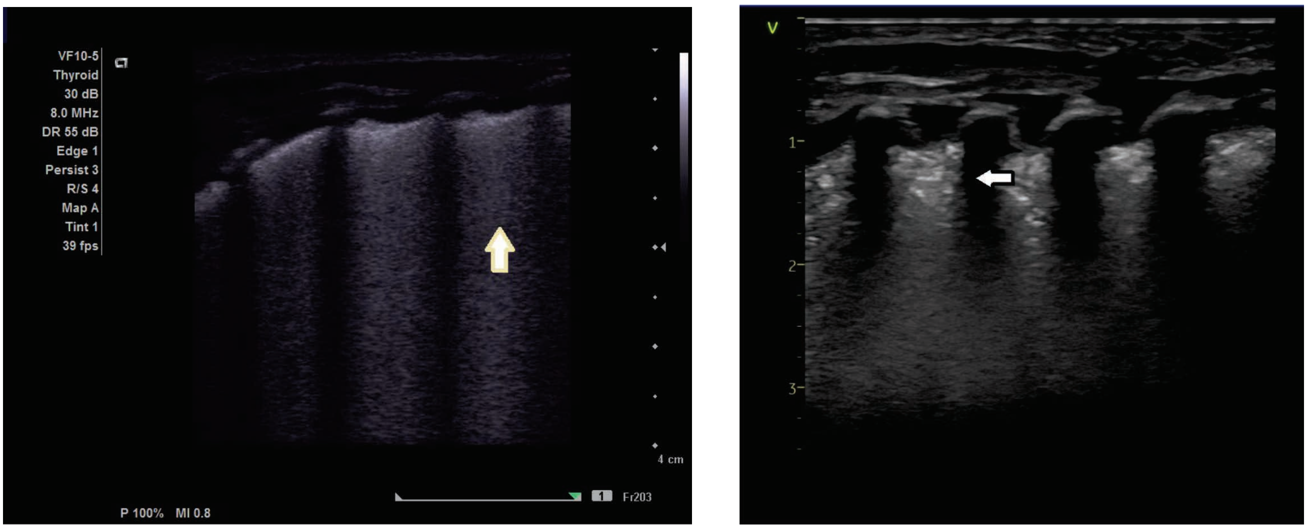


a. b.



c.

FIGURE 1
a. Normal lung ultrasound pattern. Horizontal A lines – arrow – reflexions of the pleura
b. Normal lung ultrasound pattern. Horizontal A lines – vertical arrow and rare B lines – interstitial fluid in small amounts (<3 lines) – horizontal white arrow
c. Normal lung ultrasound pattern – double lung point – delayed absorption of lung fluid – two types of patterns in the same image – horizontal A lines (vertical white arrow) + vertical B lines (horizontal white arrow) and “white lung” (coalescent B lines) – white arrow with blue margins



a. b.

FIGURE 2. a. Abnormal lung ultrasound pattern. "White lung" – coalescent B lines – arrow – fluid in the interstitium and alveoli; b. Abnormal lung ultrasound pattern – Consolidation – White round images close to the pleura – horizontal arrow.

probes with frequencies of 7-12 Hz. The examinations were performed by two of the members of the team, with competency and experience in the method (AT, IC).

The examination protocol was according to the current guidelines and medical practice (7-9). There were examined both lungs and all the lung fields as described by Brat (upper anterior, lower anterior and lateral) (7). The normal lung pattern was defined as the presence of a normal appearance (A lines and rare B lines and presence of lung sliding) (Figure 1a, Figure 1b) or the presence of a "double lung point" as defined in the reference (11). as a diagnostic criteria for delayed absorption of the lung fluid (Figure 1c). The abnormal appearance was defined as the presence of coalescent B lines – "white lung" (Figure 2a) or the presence of consolidation or air bronchogram (Figure 2b). The worst pattern was noted for each patient. For the purpose of the study, there were analysed the lung ultrasound patterns in the patients with respiratory distress at the first ultrasound during the first 4 hours after delivery and the pattern in the ventilated patients before extubation.

aEEG

aEEG monitoring was performed in 12 of the 25 ventilated patients. The tracings were interpreted daily by a pediatric neurologist with experience in aEEG (AT). There was noted the pattern before extubation. The tracing was considered as normal if a Continuous Normal Voltage with established sleep wake cycles according to the patients' gestational age was present (Figure 3a) or abnormal in the case a discontinuous normal voltage, burst supression, low voltage or flat background pattern was noted (Figure 3 b-e). The aEEG was performed using a BrainZ monitor. The tracing before extubation was analysed and noted.

Comparation of the samples

The lung ultrasound patterns were compared between the patients that needed intubation and the patients that did not need mechanical ventilation.

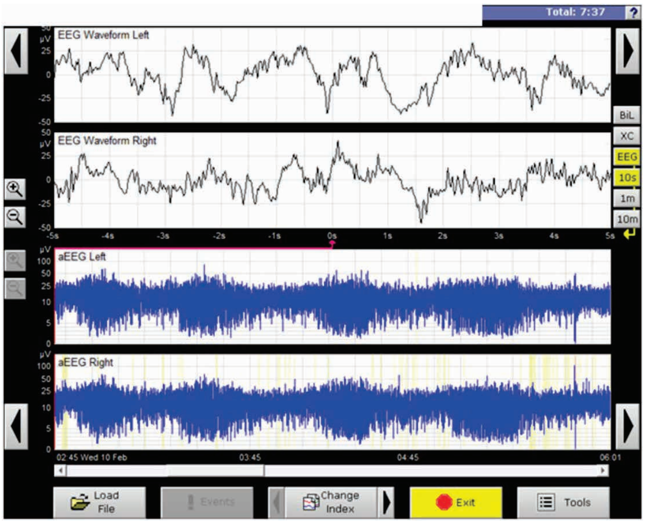
In the case of extubation readiness, the lung ultrasound patterns and aEEG patterns were compared between the group of patients that needed re-intubation and those that did not need re-intubation and mechanical ventilation. First, the comparison was performed for each variable. Then, the comparison was performed for the combined variables (both lung ultrasound and aEEG patterns).

The Chi-Square test was used to assess the significance of the findings, with a p value < 0.05 considered statistically significant. Sensitivity, specificity, positive and negative predictive values were calculated for the lung ultrasound pattern predicting the need for intubation and for the lung ultrasound and aEEG patterns in predicting the extubation failure.

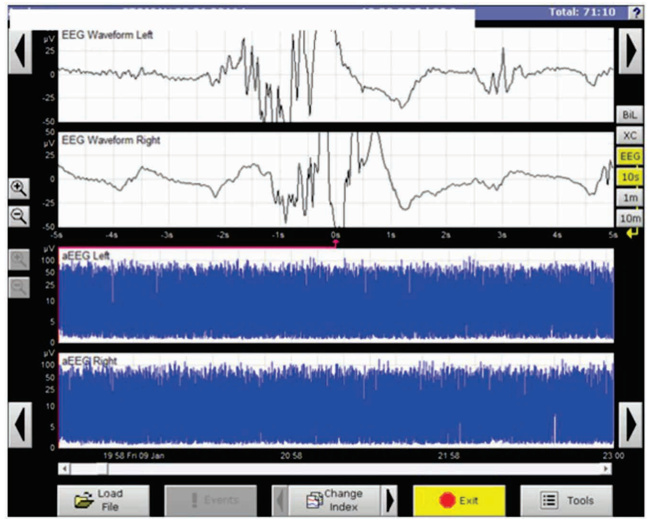
RESULTS

Risk of intubation and mechanical ventilation

An abnormal image on lung ultrasound (white lung or consolidation) was significantly associated with the need for intubation ($p < 0.001$) (Table 2). There were very good sensitivity (84%), specificity (100%), positive predictive value (100%) and negative predictive value (86.2%) (i.e. an abnormal lung ultrasound pattern correctly predicted the need for intubation and a normal pattern was predictive of decreased risk for mechanical ventilation).



a.



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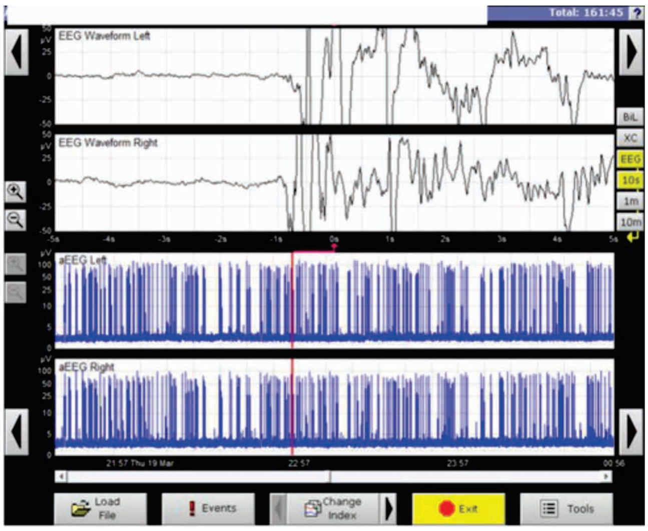

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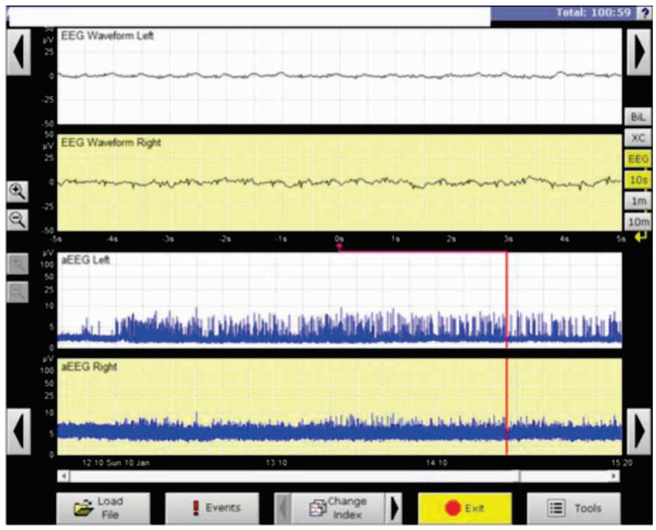

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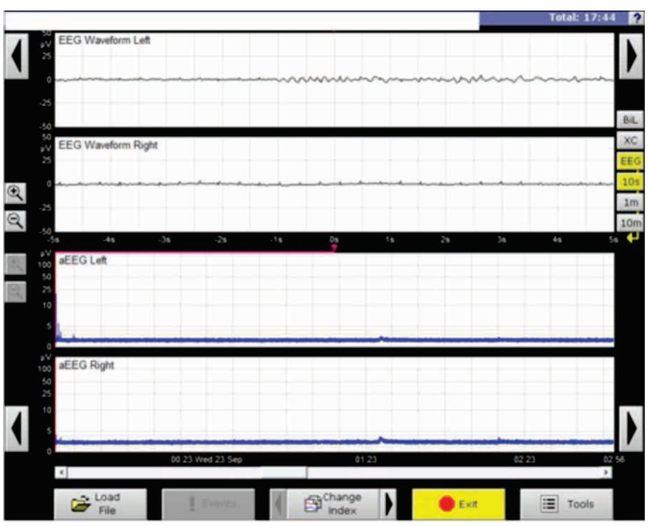

e.

FIGURE 3

a. Normal a EEG pattern – Continuous normal voltage – continuous activity with the lower amplitude around 5-7-10 µV and maximum amplitudes 10-25 – 50 µV and ciclicity (sleep/wake cycles)

b. Abnormal a EEG pattern – Dinscontinuous normal voltage - discontinuous activity with minimum amplitude variable, but mainly below 5 µV and maximum amplitude over 10 µV

c. Abnormal a EEG pattern – Burst suppression - discontinuous activity with minimum amplitude without variability 0-1-2 µv and amplitude > 25 – 50 µV

d. Abnormal a EEG pattern – Low voltage - continuous activity of very low amplitude (around or below 5 µV)

e. Abnormal a EEG pattern – Flat tracing: mainly inactive background (electrocerebral inactivity) below 5 µV

Risk of extubation failure

An abnormal lung ultrasound pattern (as described in the section above and Figure 2 was significantly associated with a significant risk of extubation failure ($p< 0.049$) (Table 3). The sensitivity and specificity were acceptable: sensitivity 75%, specificity 85% and there was a good negative predictive value (94,7%) (i.e. a normal lung ultrasound pattern was a very good predictor of successful extubation) but a poor positive predictive value (50%) (i.e. an abnormal lung ultrasound pattern was associated in 50% of the cases with extubation failure).

TABLE 2. Risk of endotracheal intubation and mechanical ventilation related to an abnormal lung ultrasound pattern

Lung ultrasound pattern	Intubation/mechanical ventilation		Total
	Ventilated	Not ventilated	
Abnormal	21 (84%)	0 (0%)	21 (42%)
Normal	4 (16%)	25 (100%)	29 (58%)
Total	25 (50%)	25 (50%)	50 (100%)

χ^2 = 36.41 p < 0.001 Estimated risk = 7.25 (IC95%: 2.92-18.01)

TABLE 3. Risk of extubation failure related to an abnormal lung ultrasound pattern

Lung ultrasound pattern	Extubation failure		Total
	Failure (re-intubated)	Successful extubation	
Abnormal	3 (75%)	3 (14.3%)	6 (24%)
Normal	1 (25%)	18 (85.7%)	19 (76%)
Total	4 (16%)	21 (84%)	25 (100%)

χ^2 = 3.87 p = 0.049 Estimated risk = 9.50 (IC95%: 1.20-75.19)

In the case of the subset of patients in which aEEG was performed, an abnormal aEEG pattern was significantly associated with extubation failure (p < 0.034) (Table 4) (sensitivity 100%, specificity 88%, positive predictive value 75%). The correlation was though stronger for the normal pattern – if the patient had a normal aEEG pattern, the risk of extubation failure was 0 (negative predictive value 100%).

TABLE 4. Risk of extubation failure related to an abnormal aEEG background pattern

A EEG background pattern	Extubation failure		Total
	Failure (re-intubated)	Successful extubation	
Abnormal	3 (100%)	1 (11%)	4 (33%)
Normal	0 (0%)	8 (89%)	8 (67%)
Total	3 100%	9 (84%)	12 (100%)

χ^2 = 4.50 p = 0.03

When ultrasound pattern was added to the above mentioned subset of cases, the results were the same (abnormal lung ultrasound was found in the same cases as abnormal aEEG pattern (Table 5). So, the association between lung ultrasound and aEEG had good sensitivity, specificity, positive predictive value and negative predictive value to estimate the extubation failure.

TABLE 5. Risk of extubation failure related to an abnormal lung ultrasound and abnormal a EEG

Lung ultrasound and aEEG background pattern	Extubation failure		Total
	Failure (re-intubated)	Successful extubation	
Abnormal	3 (100%)	1 (11%)	4 (33%)
Normal	0 (0%)	8 (89%)	8 (67%)
Total	3 100%	9 (84%)	12 (100%)

χ^2 = 4.50 p = 0.034

DISCUSSIONS

Our study is the first one to investigate the role of both lung-ultrasound images and the aEEG patterns in the prediction of a successful extubation in neonates with respiratory distress. This is one of the strong points of our study. The other strong points are represented by the unity of practice in the study (lung ultrasounds performed by the same physicians) and the unity of practice related to decisions regarding neonatal ventilation. Also, the calculation of the sensitivity, specificity, positive and negative predictive value of the parameters utilized allowed considerations about the value of normal and abnormal patterns in predicting the need for intubation or the extubation failure

The main weak point of the study is the small number of cases included. Another weak point is the absence from the study sample of the small premature infants (gestational ages less than 30 weeks). Regarding the latter, the inclusion in the study sample of only late preterm and early term neonates has been an attempt to have a homogenous population from the point of view of the pathology.

The fact that we did not use a lung score[7] could be considered a weakness of the study design. Though, our aim has been to find a very simple mean to anticipate the outcome and it seems more physiological to use an image and not a number.

We found a very good correlation between an abnormal lung ultrasound pattern (”white lung” or an image of consolidation) during the first 4 hours of life and the need for mechanical ventilation. There was a very good positive predictive value (precision) of the case 100% – an abnormal lung ultrasound image always predicted the need for intubation. This result has been found also in other studies (9) and it makes sense, because the ”white lung” appearance in all the lung fields is an ultrasound marker of the respiratory distress syndrome (7,12), a condition that is associated with the need for mechanical ventilation. Also neonatal pneumonia is a severe condition at this age and is related to a severe evolution and the need for respiratory support. The actual significance of the”white lung” pattern is fluid in both alveoli and interstia (8), so the actual status of the gas-exchange surface is poor, with fluid impending the good gas exchange and decreasing the lung compliance.

The neonates that did not need ventilation had always a normal lung ultrasound pattern (specificity 100%). This is also a logic result, because a normal ultrasound pattern as indentified in our study signifies a normal lung with no fluid or minimal interstitial fluid. It is worth to mention the cases of the patients with”double lung point” image (11). This image is a marker for the delayed absorption of fetal lung fluid (11), a condition less severe than respiratory distress syndrome. This is in our opinion the reason for which the patients in this category did not need all mechanical ventilation.

Another point to be discussed in the case of prediction of intubation is the situation of the false negatives (sensitivity 84%, negative predictive value 86.2%). Even if the number of false negative is small, it is worth to mention that different from the abnormal lung ultrasound pattern that was always related to the need for intubation, a normal lung ultrasound did not occur always in non-ventilated babies. The explanation for this could be the fact that there are other conditions than the status of the lungs that indicate the need for ventilation (persistent lung hypertension of the neonate being one of them) and a normal lung (as described by our ultrasound pattern) does not imply always a normal gas exchange surface or a normal respiratory centre.

Lung ultrasound has been investigated in 2 recent studies as a predictor of the readiness for extubation in neonates (20,21). Both studies found a good association between LUS scores and successful weaning from ventilator (20,21). Our research focused, as previously stated, more on patterns than on the lung score. The normal lung ultrasound pattern has been highly predictive of successful extubation and absence of extubation failure (negative predictive value 94.7%). We consider that the reason of this finding is that the normal ultrasound pattern reflects a normal lung with a good compliance and gas exchange and absent of fluid or edema in the interstitium and alveoli (7,8,9,11,12). The positive predictive value for a successful extubation was not so good (50%), i.e. half of the patients with abnormal lung ultrasound pattern could be successfully extubated. The explanation for this is that the intra-alveolar fluid is resorbing slowly and the abnormal ultrasound image was noted to persist for a period of time after the restore of the normal lung function in the case of the neonates with RDS (12). So, an abnormal ultrasound lung pattern could not be considered a good predictor for extubation failure.

The sensitivity of the method in detecting the patents with extubaton failure is also lower than the sensitivity for predicting the risk for intubation. In order to explain this, we must remember that conditions for a successful extubation are: a lung prepared for gas exchange, but also good respiratory muscles that have a good respiratory effort, a good respiratory drive and a good airway (2,22). There have been studies in the adult that assessed the readiness for extubation using combined lung and diaphragmatic ultrasound (lung readiness and muscle readiness) and EEG to assess the capacity of EEG to detect the conscious breathing (23,24).

It has been demonstrated that the aEEG correlates well with the awake state after the anaesthesia in neonates and small children (25) and the presence of continuous normal voltage with sleep-wake cycles is associated with the awake state (16,17) and the weaning of the effects of sedatives and anaesthetics (26). Breathing is an automated phenomenon paced by the respiratory centre in the medulla and pons. Though, respiration can become a conscious act controlled by the brain in the case of breathing difficulty and this situation could be identified also by EEG (24).

Considering the above-mentioned facts, the explanation of our findings about the value of aEEG in establishing extubation readiness and a decreased risk for re-intubation is as follows: all the patients in the subgroup with extubation failure had an abnormal aEEG pattern, i.e. the patient has not regained full consciousness, he was either sleeping or under the effect of the sedatives, so he could not ”take over” the breathing in case of problems of adaptation). On the opposite, the normal aEEG pattern has been associated always with the successful extubation and no extubation failure – the neonate was conscious, the effect of sedatives was gone and the baby was prepared to take control of the respirations in case of problems of adaptation.

When associated in the subset of patients, aEEG and lung ultrasound had the same effect – 100% sensitivity and negative predictive value – the abnormal patters predicted the extubation failure and the normal patterns a successful extubation. Considering both parameters in the decision for readiness to extubation is in agreement with the physiology of weaning and breathing spontaneously because in this way we could look assess both the lung and its integrity and function and at the neurologic respiratory control of the patient, two of the parameters that we need for a successful transition from assisted to spontaneous breathing.

As further directions of study, our aim is both to replicate the use of lung ultrasound and aEEG to assess extubation readiness in a larger cohort on both term and preterm infants (including a subgroup of patients of less than 30 weeks gestational age) and to add to the list of parameters followed the ultrasound of the diaphragm that could add information about the readiness of the respiratory muscles to sustain spontaneous breathing.

CONCLUSIONS

An abnormal lung ultrasound during the first hours of life is a strong predictor for the need of intubation and mechanical ventilation in the neonates with respiratory distress. Also, a normal lung ultrasound pattern is predictive of a good evolution of the respiratory distress in the neonatal patients, without the need of intubation and mechanical ventilation.

Related to the intubation failure, the normal lung ultrasound pattern just before extubation is predictive of a good evolution without the need for re-intubation of the patient. A normal aEEG pattern at the same time is associated also with a decreased risk of extubation failure. Associating the two techniques is increasing the accuracy of prediction of successful extubation.

Considering all these findings we advise for the use of lung ultrasound and aEEG neuro-monitoring as adjuvants in the decisions related to mechanical ventilation and readiness for extubation in the neonates with respiratory distress.

Conflict of interest: none declared
Financial support: none declared

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