Charles University

1st Faculty of medicine

UNIVERZITA KARLOVA
1. lékařská fakulta

Autoreferát disertační práce

Imaging methods in monitoring organ function of critically ill patients with an emphasis on lung ultrasound

MUDr. Masego Candy BUDKA MOKOTEDI

Prague, 2024

Doktorské studijní programy v biomedicíně
Univerzita Karlova a Akademie věd České republiky

Obor: Zobrazovací metody v lékařství

Předseda oborové rady: doc. MUDr. Andrea Burgetová, Ph.D., MBA

Školicí pracoviště: Klinika anesteziologie,resuscitace a intenzivní mediciny, 1. Lékařská fakulta, Univerzita Karlova a Všeobecná fakultní nemocníce Praha.

Školitel: doc. MUDr. Martin Balík, Ph.D., EDIC

Disertační práce bude nejméně pět pracovních dnů před konáním obhajoby zveřejněna k nahlížení veřejnosti v tištěné podobě na Oddělení pro vědeckou činnost a zahraniční styky Děkanátu 1. lékařské fakulty.

Contents

Abstract

There are different methods monitoring thoracic organ function in the critically ill by using various imaging methods (chest x-ray, computed tomography, magnetic resonance, and the newly popular lung ultrasound as a stand-alone method or combined with echocardiography). The disadvantages of these methods make lung ultrasound in this group of patients an exquisite bed side imaging tool to assess and diagnose a myriad of lung pathologies, gauge therapeutic interventions and ultimately assess the diaphragm, extradiaphragmatic apparatus and cardiopulmonary changes during weaning of mechanical ventilation and as thus predict its potential failure or success. Furthermore, lung ultrasound has also proved to be extremely useful during the COVID-19 pandemic in assessing COVID-19 pneumonia and its complications with a resultant reduction in potential cross- contamination of staff and patients due to transport to and from the radiology department for imaging. Moreover, vital information can be attained on the hemodynamics of a patient when lung ultrasound is combined with vascular assessment and echocardiography.

This doctoral thesis delved into evaluating chest drain positioning on chest x-ray using several simple parameters (chest drain inclination, tortuosity of the chest drain and its foreshortening) and we further sought to locate a chest drain on lung ultrasound post drainage. These investigations into chest drain positioning help in the diagnosis of chest drain malposition which can potentially lead to residual/occult pneumothoraces which further can have dire implications in mechanically ventilated patients. We also challenged the established method of quantifying pleural fluid volume on lung ultrasound wherein this method could give erroneous pleural fluid estimates in patients with consolidated lungs and lastly, we sought the impact of serial imaging with the growing popularity of lung ultrasound on the intensive care unit outcome of patients with COVID-19 acute respiratory distress syndrome treated with extracorporeal membrane oxygenation.

Keywords: Lung ultrasound, chest x-ray, computed tomography, pneumothorax, pulmonary consolidation, pleural effusion, pulmonary edema, COVID- 19 pneumonia, acute respiratory distress syndrome, pulmonary embolism, fluid loading, extravascular lung water, proning, weaning failure, diaphragm dysfunction

Abstrakt

Existují různé metody monitorování funkce hrudních orgánů u kriticky nemocných pacientů pomocí různých zobrazovacích metod (rentgen hrudníku, počítačová tomografie, magnetická rezonance a nově populární ultrazvuk plic jako samostatná metoda nebo v kombinaci s echokardiografií). Nevýhody těchto metod dělají z ultrazvuku plic u této skupiny pacientů vynikající zobrazovací metodu vyšetření na lůžku k posouzení a diagnostice mnohých plicních patologií, k provedení terapeutických intervencí a dále k posouzení dysfunkce bránice, extradiafragmatického aparátu a kardiopulmonálních změn během odvykání od umělé mechanické ventilace a eventuální predikce jeho úspěchu či potenciálního selhání. Kromě toho se ultrazvuk plic také ukázal jako mimořádně užitečná metoda během pandemie COVID při hodnocení COVID pneumonie a jejích komplikací s výsledným snížením potenciální křížové kontaminace personálu a pacientů v důsledku transportu na radiologického oddělení za účelem vyšetření. Kromě toho lze získat důležité informace o hemodynamice pacienta, v případě, když je ultrazvuk plic kombinován s vaskulárním vyšetřením a echokardiografií.

Tato disertační práce se ponořila do hodnocení umístění hrudního drénu na rentgenu srdce a plic pomocí několika jednoduchých parametrů (sklon hrudního drénu, tortuozita hrudního drénu a jeho zkrácení) a dále jsme hledali umístění hrudního drénu po drenáži. Tato vyšetření umístění hrudního drénu pomáhají při diagnostice malpozice hrudního drénu, která může potenciálně vést k reziduálním/okultním pneumotoraciím, které dále mohou mít vážné důsledky u mechanicky ventilovaných pacientů. Zpochybnili jsme také metodu kvantifikace objemu pleurální tekutiny na ultrazvuku plic, kde by tato metoda mohla poskytnout chybné odhady objemu pleurální tekutiny u pacientů s konsolidovanými plícemi, a nakonec jsme hledali dopad sériového zobrazování s rostoucí popularitou ultrazvuku plic na výsledky léčby pacientů na jednotce intenzivní péče se syndromem akutní dechové tísně při COVID-19 léčených pomocí mimotělního oběhu.

Klíčová slova: Ultrazvuk plic, rentgen srdce a plic, počítačová tomografie, pneumotorax, plicní konsolidace, pleurální výpotek, plicní edém, COVID- 19 pneumonie, syndrom akutní dechové tísně, plicní embolie, tekutinová zátěž, extravaskulární plicní voda, pronační poloha, selhání odvykání/weaning, dysfunkce bránice.

1 Introduction

Chest imaging is pivotal in the diagnosis and management of patients with respiratory pathologies, especially in the intensive care unit (ICU). There are different imaging methods available for imaging the chest being: chest x-rays (CXR), lung ultrasound (LUS), computed tomography (CT) and magnetic resonance imaging (MRI).
The limitations brought on by the aforementioned methods with the exception of LUS, make LUS the go to method of assessing critically ill patients, and when paired with echocardiography, LUS is a force to be reckoned with, with diagnostic capabilities similar to CT.

LUS helps to evaluate the dynamics of pulmonary consolidation, pneumothoraces (PNOs), and pleural effusions (PEs) and is also excellent in guiding thoracentesis. This reduces serial mobilised bedside chest X-rays, and as thus, a reduction in unnecessary radiation exposure of patients (for reference, one non-contrast chest CT (effective dose of 8mSv) equals about 400 chest postero-anterior (PA) chest x-ray examinations and 1 chest x-ray has an effective dose of about 0.02mSv), and the side effects of contrast administration notably contrast induced nephropathy (CIN) and a potential allergic reaction to contrast media.
LUS has also been an incredible tool in the recent and ongoing COVID-19 pandemic whereby it is used for triage and in assessing COVID-19 pneumonia and its complications while reducing potential cross contamination of patients and staff caused by transport to and from the radiology department (Mokotedi et al., 2023).

The bedside CXR is particularly lackluster in diagnosing discrete pulmonary consolidations, small to moderate pleural effusions (PEs), pneumothoraces (PNOs) or eventually an alveolar interstitial syndrome (Engdahl et al., 1993; Bouhemad et al., 2007) due to technical complications that arise when a bedside CXR is performed. The spatial resolution of the CXR is compromised by the fact that the patient can't do a breath hold, as thus, there is movement of the thorax, furthermore, due to film cassette positioning (between the bed and the patient) the x-ray beam is shortened because of shorter acquisition distance. This leads to suboptimal images that can be particularly challenging to interpret accurately. (Bouhemad et al., 2007)

In critically ill patients who are closely monitored by various invasive devices, CT scanning is not only cumbersome, transporting these patients to the CT suite and positioning of such patients in the gantry is a task in itself, with the potential for significant respiratory and haemodynamic derangements (Peris et al., 2010). In the morbidly obese patients, CT scanning is not possible to obtain as the table itself has a weight limit and the gantry itself is only so big. Another important factor is the potential for contrast induced nephropathy, which further complicates care of the already critically patient, as is a potential allergic reaction to contrast, if unknown. Furthermore, unless ICU related complications arise, or in cases where CT scanning is imperative, substituting CT imaging by CXR, LUS in combination with echocardiography confers a financial benefit (Balik et al., 2023).

This is where, in particular, LUS shines- it can be performed at the bedside when needed and waiting for a radiology report is eliminated as clinical information is acquired in a matter of a few seconds if not minutes. LUS as a portable mobile imaging tool does not have a steep learning curve in contrast to echocardiography and other imaging modalities; however, the combination of LUS coupled with echocardiography is extremely valuable not only in the evaluation of lung pathology, but also in the evaluation of hemodynamics of a patient.

For our dissertation work we evaluated chest drain (CD) positioning on CXR using several simple parameters (CD inclination, tortuosity of the CD and its foreshortening) and we further sought to locate a CD on lung ultrasound post drainage. These investigations into CD positioning help in the diagnosis of CD malposition which can potentially lead to residual/occult pneumothoraces which further can have dire implications in mechanically ventilated patients. We also challenged the established method of quantifying pleural fluid volume (PEv) on lung ultrasound wherein this method could give erroneous pleural fluid estimates in patients with consolidated lungs and lastly, we sought the impact of serial imaging with the growing popularity of lung ultrasound on the intensive care unit outcome of patients with COVID-19 acute respiratory distress syndrome (ARDS) treated with extracorporeal membrane oxygenation (ECMO).

2 Aims and hypotheses

2.1 Aims

- To show and demonstrate that some novel CXR indicators can be utilized to assess the positioning of CDs.

- To evaluate how CD positioning, assessed via LUS and CXR, may be associated with a residual or occult pneumothorax.

- To explore the correlation between the absence of CD detection and signs of a residual pneumothorax on LUS

- To determine if there is a prediction error when using the established gold standard method for ascertaining pleural fluid volume on LUS.

- To ascertain whether there is a causal relationship between the number of bedside serial antero-posterior supine CXRs and CT scans performed and the ICU outcomes in patients with severe COVID-19 ARDS treated with ECMO

2.2 Hypotheses

Due to the above-mentioned aims, our hypotheses were as follows:

- A CD that has changed its position on a CXR should prompt further evaluation on LUS to exclude a residual pneumothorax that is occult on CXR.

- The absence of CD detection between the ventral pleural layers on the bedside LUS may be associated with signs of a residual pneumothorax.

- The established gold standard to quantify pleural effusion volume on LUS underestimates pleural fluid volume in patients with consolidated lungs, therefore, multiple pleural separation measurements may be more useful to provide an accurate quantification of pleural fluid in these patients.

- The frequency of CXRs and CTs might not relate to ICU outcome in patients with severe COVID-19 ARDS treated with ECMO

3 Investigations

Our work presented in this dissertation thesis is constituted of two retrospective studies (Study 1 and Study 3) and two prospective studies (Study 2 and Study 4).

This dissertation thesis will therefore be divided into three parts: Part one will be evaluating CD positioning on CXR and LUS and residual/occult PNOs, part two will be challenging the established method of quantifying pleural fluid volume on LUS, and the last part, part three will be delving into the impact of serial imaging with the growing popularity of LUS on the ICU outcome of patients with COVID-19 ARDS treated with ECMO.

3.1 Part 1: Studies evaluating CD positioning on CXR and LUS

3.1.1 Study 1 - X-ray indices of chest drain malposition after insertion for drainage of pneumothorax in mechanically ventilated critically ill patients

Hypothesis: A CD that has changed its position on a CXR should prompt further evaluation on LUS to exclude a residual pneumothorax that is occult on CXR.

Methods

We carried out this study between May 2015 and June 2017 in a 20-bed intensive care unit in a tertiary non-trauma centre. It was approved by the Institutional Review Board and informed consent was waived due to the retrospective design of the study.

The inclusion criteria were: (I) the presence of a CD in the pleural space inserted for PNO drainage from the safe triangle; (II) mechanical ventilation; (III) CXR and CT scan with the drainage performed less than 24 hours apart. The exclusion criteria were: (I) all anatomical CD malpositions (extrathoracic, intraparenchymal, interlobar); (II) mid-clavicular access.
The study included a total of 28 patients. These patients were divided according to the position of the CD on CT into two groups: group A with the tip of the CD anterior to the mid-axillary line (correct placement, n=24) and group B with the tip of the CD at the level of or posterior to the mid-axillary line (incorrect placement, n=4).

The parameters measured on CT and CXR are listed in **Table 3.1.1 - 1**. The foreshortening of the CD was calculated as the distance of the CD from chest entry to its tip in the coronal plane (ignoring the anteroposterior dimension) divided by its true length obtained by 3D measurement. The angle of inclination of the CD above the horizontal line at chest entry was measured on CXR (**Figure 3.1.1 - 1**). CD tortuosity was determined as the ratio of a straight distance of the CD from chest entry of to its tip and the length of the CD in the patient measured on CXR (**Figure 3.1.1 - 1**). CT and CXR measurements were performed by a board-certified radiologist with >10 years of experience in thoracic imaging.

Table 3.1.1 - 1 - Parameters measured and calculated on CT and CXR.

Measured and calculated parameters on CT and chest radiographs (CXR)

Parameter	Group A: correct placement (n=24)	Group B: incorrect placement (n=4)	P	Test
CT scan (CT)				
CD entry: intercostal space	3 [2–5]	3 [3–7]	0.82	MW
CD length in the thoracic cavity (mm)	99±24	158±53	0.001	T
CD entry to tip distance (mm)	93±21	135±46	0.005	T
CD entry to tip distance in the coronal plane (ignoring the anteroposterior dimension) (mm)	88±19	118±49	0.033	T
CD foreshortening in the coronal plane (CD entry to tip distance ignoring the anteroposterior dimension/CD entry to tip length) (%)	90±10	75±13	0.015	T
Chest radiograph (CXR)				
Entry angle (angle of inclination above the horizontal) (°)	29 (IQR 29)	53 (IQR 22)	0.042	MW
Tortuosity (entry to tip distance/entry to tip length of the CD measured on a CXR) (%)	0.99 (IQR 0.03)	0.84 (IQR 0.5)	0.16	MW

CD, chest drain; T, *t*-test, MW, Mann-Whitney test; IQR, interquartile range.

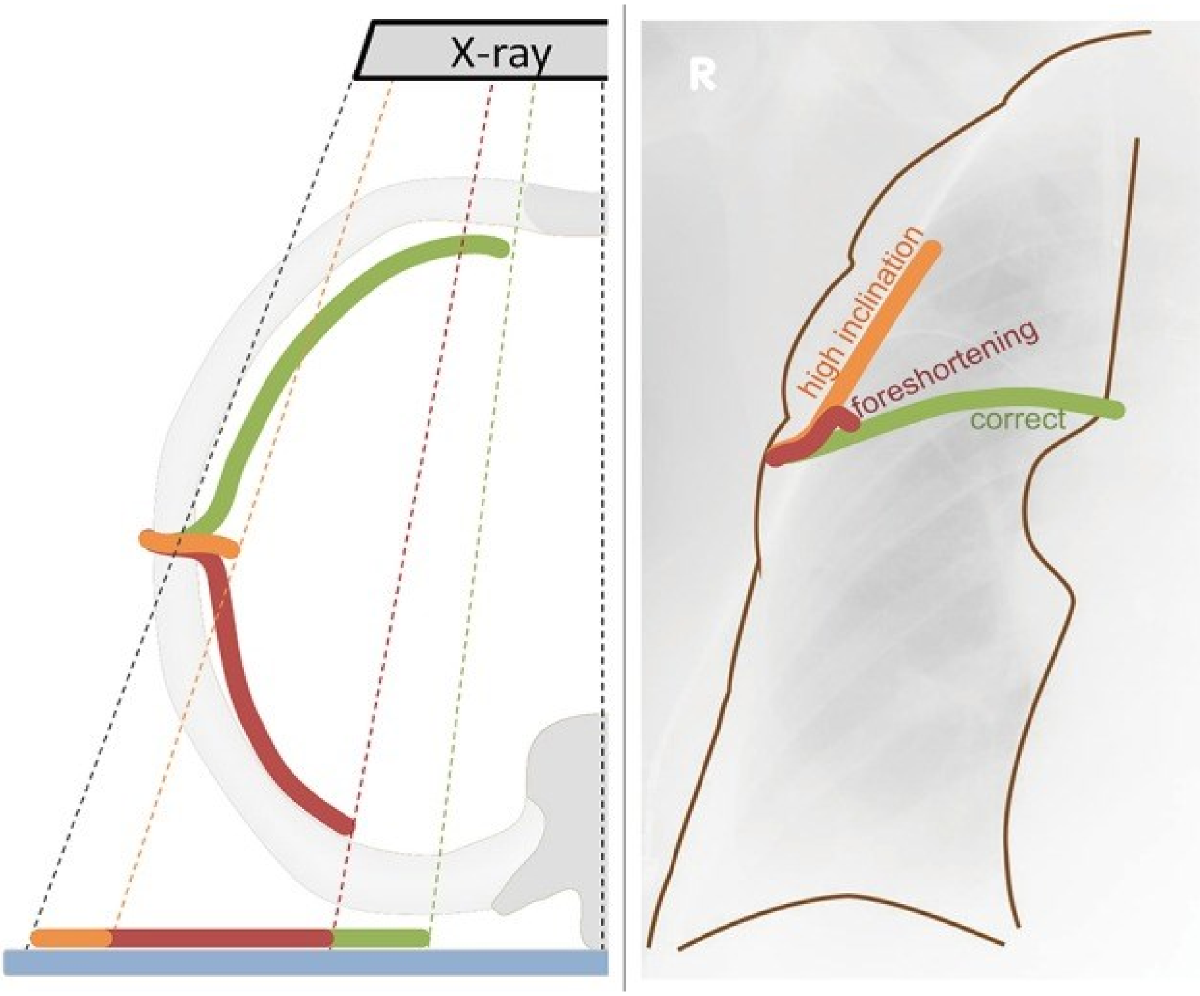

Figure 3.1.1 - 1 - Schematic drawing of the principle of foreshortening and cranial angulation (inclination) of a CD on a CXR due to its position and divergence of X-rays (dashed lines). The green CD shows the correct position; the orange CD shows lateral migration, and the red CD shows dorsal migration.

We analysed the data using GraphPad Prism (GraphPad Software, La Jolla, USA). We then tested the normality of the data by using the D'Agostino & Pearson omnibus test, whilst the statistical significance between the groups was tested by the *t*-test or the Mann-Whitney test as appropriate with a subsequent ROC analysis. A P value below 0.05 was considered significant.

Results

The patients were 59.5±15 years old and 78% were males. All patients were mechanically ventilated with APACHE II 23±6, SOFA 8.9±2.5. The causes of the PNO were postsurgical (n=10), ventilator related in pneumonia (n=7), ventilator related in ARDS requiring ECMO (n=6), postprocedural (n=3), and spontaneous on intermittent positive pressure ventilation (IPPV, n=2).

The parameters measured on CT and CXR are presented in **Table 3.1.1 - 1**. *Greater CD foreshortening was the best clue of a misplaced CD* with an AUC of 0.93 (95% CI: 0.83–1.0, P=0.0071), 100% sensitivity and 88% specificity for a cut-off value of 82% (**Table 3.1.1 - 1**, **Figure 3.1.1 - 2**). The angle of inclination of the CD was greater in patients with a misplaced CD with AUC of 0.83 (95% CI: 0.63–1.0, P=0.039), 75% sensitivity, and 92% specificity for a cut-off value of 50 degrees (**Figure 3.1.1 - 2**). There was no significant difference in CD tortuosity on CXR between the groups with an AUC of 0.69 (95% CI: 0.34–1.0, P=0.22).

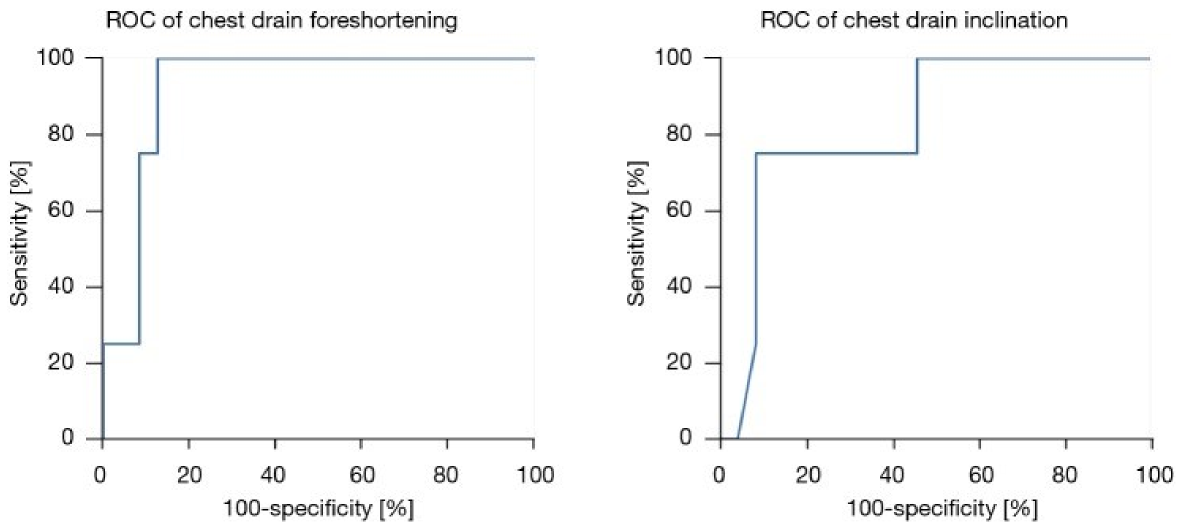

Figure 3.1.1 - 2 - ROC of CD foreshortening and inclination as a clue of a misplaced CD with an AUC of 0.93 and 0.83, respectively. ROC, receiver operating characteristic; AUC, area under the curve.

Three of the four patients with migrated CDs had a residual ventral PNO on the CT scan. The median time between the CXR and CT examinations was 5.4 hours (IQR 3.1).

The aforementioned hypothesis (a CD that has changed its position on a CXR should prompt further evaluation on LUS to exclude a residual PNO that is occult on CXR) was thus confirmed.

3.1.2 Study 2 - Interpleural location of chest drain on ultrasound excludes pneumothorax and associates with a low degree of chest drain foreshortening on the antero-posterior chest x-ray

Hypothesis: The absence of CD detection between the ventral pleural layers on the bedside LUS may be associated with signs of a residual pneumothorax.

Methods

We prospectively evaluated all patients between March 2020 and February 2022 with COVID-19 ARDS and with a concomitant PNO for the presence of a residual PNO on LUS, the detection of a CD between the pleural layers on LUS, and finally, for the CD foreshortening and angle of inclination of the CD both taken from the bedside CXR. All patients with a large subcutaneous emphysema or with anatomical drain malpositions were excluded.

The drainages were performed by intensivists using 16-20F CDs (Portex, UK) and utilising the blunt forceps technique in the safe triangle (Havelock et al., 2010). All CDs were connected to a closed suction system with a negative pressure of −20 cmH_2O. A PNO was diagnosed on LUS according to the current standards (Volpicelli et al., 2012) using a linear transducer (6–10 MHz, Vivid S6, VividS60 or Vivid I, General Electric).
Foreshortening was estimated as a decrease in the chest drain index (CDI), which should ideally be close to 1. The CDI is equal to the length of the CD in the chest measured on an antero-posterior CXR divided by the depth of insertion read directly on a CD scale plus 5 cm, which is the distance from the first drainage orifice to the tip of the CD. The angle of inclination of the CD was measured as the angle between the horizontal line and the CD at pleural space entry on the CXR. The angle of inclination of the CD was judged to be higher or lower than 50° (Mokotedi et al., 2018).

We analysed the data using Statistica v.12 software. Normality of the data was tested using the Kolmogorov–Smirnov test and the statistical significance between the groups was tested using the Mann–Whitney U test for the numerical variables and with the Chi-square test for categorical data. The numerical data is reported as medians and interquartile ranges. The risk ratio for a PNO on LUS was calculated in relation to the CXR findings. A p-value below 0.05 was considered significant.

Results

116 PNO drainages (75 on the right, 41 on the left) were performed and monitored in 88 patients (31 females, age 56.2 ± 19, APACHE II 22 ± 4, SOFA 9 ± 2.2). 10 patients were excluded due to significant subcutaneous emphysema.

The aetiologies of the PNO were spontaneous on mechanical ventilation in 79 (74%), post-cannulation or due to thoracocentesis in 25 (24%) and after transbronchial biopsy in 2 (2%).

The results in groups with and without residual post-drainage PNO are given in **Table 3.1.2 – 1**. Among the 80 cases with full lung expansion on LUS (no PNO in the six zones of each hemithorax), the CD was located by LUS after drainage in 69 (86%). The median CDI was 0.99 (0.88–1.06), and the steep angle of inclination of the CD on CXR (> 50°) was found in 10 patients (12.5%).

Table 3.1.2 - 1 - Comparison of the novel observed categorical parameters (CD location in %, its steep course in %, presence of an air leak in %) and continuous parameters (depth of CD insertion in cm, length of CD in chest in cm, CDI, all * medians and interquartile ranges) between groups with full lung expansion on LUS (PNO excluded in all lung fields) and groups with a residual PNO on LUS.

Pneumothorax $n = 106$	**Full lung expansion on post-drainage CUS ($n = 80$, 75%)**	**Residual pneumothorax on post-drainage CUS ($n = 26$, 25%)**
Drain located on CUS	69 (86%)	8 (31%), (p˂0.0001)
Depth of drain insertion on CD scale (cm)*	12 (10–14)	12 (12–16), (n.s)
Length of CD in chest on antero-posterior CR (cm)*	16.1 (14.2–17.9)	13.3 (11.4–16.5), (n.s.)
CDI*	0.99 (0.88–1.06)	0.76 (0.6–0.93), (p˂0.01)
Steep ascending drain in chest on CR	10 (12.5%)	6 (23%), (n.s.)
Continued air leak from the drain	19/80 (24%)	14/26 (55%), (p˂0.003)

26 cases had a residual PNO after drainage (24.5%), the CD was located by LUS in 8 of those (31%), the median CDI was 0.76 (0.6–0.93), $p < 0.01$, the steep angle of inclination of the inserted CD on CXR was observed in 6 patients (23%).

Of the 106 patients included, the CD was located in between the pleural layers in 77 patients, and 8 of those had a residual PNO. In contrast, the CD was not located in 29 patients, of which 18 still had a post-drainage PNO. The risk ratio for a PNO in a patient with a CD that is not visible in the interpleural space on LUS ($n = 29$) and an associated low CDI on CXR was 5.97, 95% CI [2.92–12.21], p<0.0001, NNT 1.94.

For the 16 patients with a steep angle of inclination of the CD on CXR greater than 50°, the risk ratio for a PNO was not significant (RR 1.68, 95% CI [0.80–3.54], $p < 0.17$, NNT 6.55). For the 33 patients with a continued air leak from the CD post drainage, the risk of a residual PNO is significant (RR 2.27, 95% CI [1.33–3.85], $p = 0.003$, NNT 3.32).

The aforementioned hypothesis (the absence of CD detection between the ventral pleural layers on the bedside LUS may be associated with signs of a residual pneumothorax) was thus confirmed.

3.2 Part 2 - Challenging the established method of quantifying pleural fluid volume on LUS in patients with consolidated lungs

3.2.1 Study 3 - Pulmonary consolidation alters the ultrasound estimate of pleural fluid volume when considering chest drainage in patients on ECMO

Hypothesis: The established gold standard method to quantify pleural effusion volume on LUS underestimates PEv in patients with consolidated lungs, therefore multiple pleural separation measurements may be more useful to provide an accurate quantification of PE in these patients.

Methods

In this study we prospectively collected pleural drainage data in patients with severe cardiorespiratory failure treated with ECMO for a period of 3 years (2019–2021). In addition to the presence of a PE, severe lung consolidations with a lung score of 3 in the basal lung regions and no better than a lung score of 2 in the anterior regions were diagnosed by applying a complex LUS protocol in six regions on both right and left hemithorax (Via et al., 2012). Patients were supine with the trunk elevated at a 15° angle to the horizontal, corresponding to the original method described by the authors in 2006 (Balik et al., 2006). The key measurements were taken in expiration with transducer scanning in the transverse plane above the base of the lung in the posterior axillary line at the planned drainage spot.

All drainages were performed by intensivists using the blunt forceps technique and the CDs were pulled from the trocar into the pleural cavity. Patients with pleural separations of less than 10 mm on the initial scan and/or with an absence of extensive lung consolidations (lung score 2 to 3) were excluded, as well as patients with incomplete PE aspiration on post-drainage ultrasound.

After we excluded three effusions (5.7%) for incomplete drainage, a total of 50 PEs were evaluated and drained in 42 patients (27 males and 15 females), (age 44 ± 17 years, APACHE II 25.8 ± 6.8, SOFA 11 ± 2.5, height 174 ± 7 cm, body weight 87 ± 20 kg). Twenty-eight patients were on veno-venous ECMO, four on veno-arterio-venous ECMO and ten on veno-arterial ECMO. The calibres of the CDs were 12F ($n = 33$), 16F ($n = 3$), 20F ($n = 7$), 24F ($n = 1$), 28F ($n = 2$), 32F ($n = 2$). The main character of the PE was exudate ($n = 25$), clear transudate ($n = 12$), sanguinolent ($n = 8$) and haemothorax ($n = 5$). The overall incidence of drainage-related bleeding or iatrogenic PNO was zero. All ECMO patients were on a pulmoprotective ventilation (BIPAP, $n = 30$, 60%; PSV, $n = 20$; 40%) with plateau pressures up to 24–26 cmH_2O and PEEP 8–12 cmH_2O.

Results

The PEv and pleural separations showed normal distributions according to the Kolmogorov–Smirnov test. The maximum pleural separation (Msep) was 24 ± 7 mm, correlating (all Pearson's correlation) with separation at the dorsal chest wall (Dsep, 21 ± 9 mm, $r = 0.88$, $p = 0.0001$). The paravertebral (Psep) and lateral (Lsep) separations were 17 ± 8 mm and 17 ± 7 mm, respectively.

The classic method of PE estimation (Balik et al., 2006) produced a mean underestimation error of 359 ± 187 ml, while the mean drained volume was 837 ± 206 ml. The Msep value correlated significantly with the drained volume ($r = 0.47$, $p = 0.001$); however, the best correlation was found for the Lsep ($r = 0.61$, $r^2 = 0.37$, $p = 0.0001$).
The volume of PE can be estimated with equation ***V[ml] = 540 + 17*Lsep[mm],*** resulting in a mean prediction error of 129 ± 98 ml. Similarly, the sum (Ssep) of the basal, lateral, and ventral pleural separations (mean 55 ± 18 mm) correlated with the drained volume ($r = 0.54$, $p = 0.0001$), showing a mean prediction error of 144 ± 95 ml. Only for the classic method, the prediction bias for the volume estimate was significantly different from zero (Bland–Altman, $p = 0.0001$).

Comparison of the right and left pleural effusions did not show a significantly better correlation of Lsep of the right hemithorax ($n = 30$, $r = 0.66$, $p = 0.0001$) compared to the left hemithorax ($n = 20$, $r = 0.52$, $p = 0.02$; $p = 0.49$ for comparison, Fischer´s z-transformation).

The aforementioned hypothesis (the established gold standard method to quantify pleural effusion volume on LUS underestimates pleural fluid volume in patients with consolidated lungs, therefore multiple pleural separation measurements may be more useful to provide an accurate quantification of pleural fluid in these patients) was confirmed.

3.3 Part 3 - The impact of serial imaging with the growing popularity of LUS on the ICU outcome of patients with COVID-19 ARDS treated with ECMO.

3.3.1 Study 4 Prognostic Impact of Serial Imaging in Severe Acute Respiratory Distress Syndrome on the Extracorporeal Membrane Oxygenation

Hypothesis: The frequency of CXRs and CTs might not relate to ICU outcome in patients with severe COVID-19 ARDS treated with ECMO.

Methods

Here, we retrospectively analysed patients with severe ARDS due to COVID-19 according to the Berlin 2011 criteria (Ferguson et al., 2012) admitted to a single high-volume ECMO centre between March 2020 and March 2022 was performed. We sought to determine the impact of the number of antero-posterior CXRs and CT scans on the resultant ICU outcome.

The requirements for imaging were stratified according to the body mass index (BMI), i.e., obese (BMI > 30) and non-obese (BMI ≤ 30) patients, and patients managed with and without ECMO. The exclusion criteria included all patients with mild ARDS and/or the absence of a weighted bed for BMI measurement. We retrieved the data from the hospital information system and included demographic characteristics, patients' histories, clinical data—body mass index (BMI), initial status at ICU admission, and severity scores [Acute Physiology and Chronic Health Evaluation (APACHE IV), Sequential Organ Function (SOFA)]. Imaging examinations were retrieved from an existing and already published dataset (Balik et al., 2022).

Statistical Analysis

After verifying the distribution of data, continuous data is expressed as the median and interquartile range (IQR), and the differences between the groups were tested with the Mann-Whitney U test. The categorical data is expressed as the number of probands, and percentage of a given group and evaluated using the Fischer's exact test. The Rank correlation with Spearman's coefficient is utilized for correlation analysis of the number of radiographic (RTG) records with the length of stay and outcome in the ICU. The design of the regression analysis followed the original method published previously (Balik et al., 2022), now with added data on imaging. The linear regression analysis and the Mantel-Haenszel test was performed in order to determine the odds ratio of a particular complication and its relationship to the frequency of RTG imaging. Cox proportional hazards regression analysis was used to test the various risk factors and their relationships to the outcomes. A *p*-value below 0.05 was considered significant.

Results

Chest X-ray

A total of 292 patients with severe ARDS were included in the analysis. Their median age was 57 years (IQR 48–69), with men comprising a total of 194 (66.4%). Out of the 292 patients, 173 were treated conservatively, and 119 (40.8%) were treated with ECMO. The characteristics of the patients relevant to chest imaging, including outcome data, are summarised in **Table 3.3.1 - 1**. The patients were divided into the obese group (*n* = 171, 58.6%) and the non-obese group (*n* = 121, 41.4%).

Table 3.3.1 - 1 - Patient characteristics.

	BMI > 30 (*n* = 171)	**BMI ≤ 30 (*n* = 121)**	***p*-Value**
Age (years)	56 (48–65)	61 (51–68)	**0.013**
Weight (kg)	110 (100–120)	82 (75–90)	**<0.001**
Height (m)	1.74 (1.68–1.8)	1.77 (1.7–1.8)	**0.024**
BMI	35.1 (32.1–40.1)	26.3 (24.8–27.8)	**<0.001**
Gender (males)	63.7% (109)	70.2% (85)	0.246
APACHE IV	87 (77–100)	90 (77–100)	0.371
SOFA	10 (8–12)	11 (8–12)	0.480
PaO_2/FiO_2 (at admission)	75 (62–101)	75.5 (60–105)	0.883
Orotracheal intubation on admission	95.9% (164)	94.2% (114)	0.505
NIV/HFNO (days)	2 (1–4)	2 (0–5)	0.702
Tracheostomy	75.4% (129)	69.4% (84)	0.254
MV parameters (at admission)			
PEEP	12 (10–14)	11 (8–14)	**0.048**
driving pressure	18 (15–20)	16 (12–18)	**<0.001**
plateau pressure	30 (26–34)	28 (24–30)	**0.002**
Prone position	62% (106)	59.5% (72)	0.623
VV ECMO	45% (77)	34.7% (42)	0.087
Pneumothorax	18.1% (31)	19.8% (24)	0.749
Pneumothorax in ECMO patients	26% (20)	33.3% (14)	0.404
Pneumomediastinum	8.8% (15)	9.9% (12)	0.763
Pneumomediastinum in ECMO patients	18.2% (14)	19% (8)	1.00
ICU LOS (days)	13 (7–22)	13 (6–20)	0.432
Hospital LOS (days)	27 (14–51)	27 (13–66)	0.639
ICU mortality	36.8% (63)	33.9% (41)	0.578
Hospital mortality	49.7% (85)	48.8% (59)	0.873
90-day mortality	48.5% (83)	45.5% (55)	0.603

Serial CXRs were indicated for the evaluation of respiratory apparatus (45%) and periprocedural related complications, for example, due to central line or CD placement (55%). The median number of CXRs per patient was eight (IQR 4–14) in all BMI classes. The univariate Mann–Whitney test did not find a significant relationship between the number of CXRs and ICU outcome, which was relevant for both obese (BMI > 30) and non-obese (BMI ≤ 30) patients (**Table 3.3.1 - 2**).

Table 3.3.1 - 2 - Comparison between the number of CXRs (median, IQR) of surviving and deceased patients in the ICU.

Parameter	Surviving (Median, IQR)	Dead (Median, IQR)	*p*-Value
ICU outcome	7 (4; 14), *n* = 187	8 (5; 15.5), *n* = 104	0.23
ICU outcome BMI > 30	8 (5; 14.8), *n* = 107	8 (5; 13), *n* = 62	0.69
ICU outcome BMI ≤ 30	7 (3.5; 12), *n* = 80	8.5 (5; 17), *n* = 42	0.21

The number of CXRs strongly correlated with the length of stay of both the survivors and the deceased in the ICU (r = 0.87, $p < 0.0001$, r = 0.83, $p < 0.0001$, respectively, **Figure 3.3.1 - 1**).

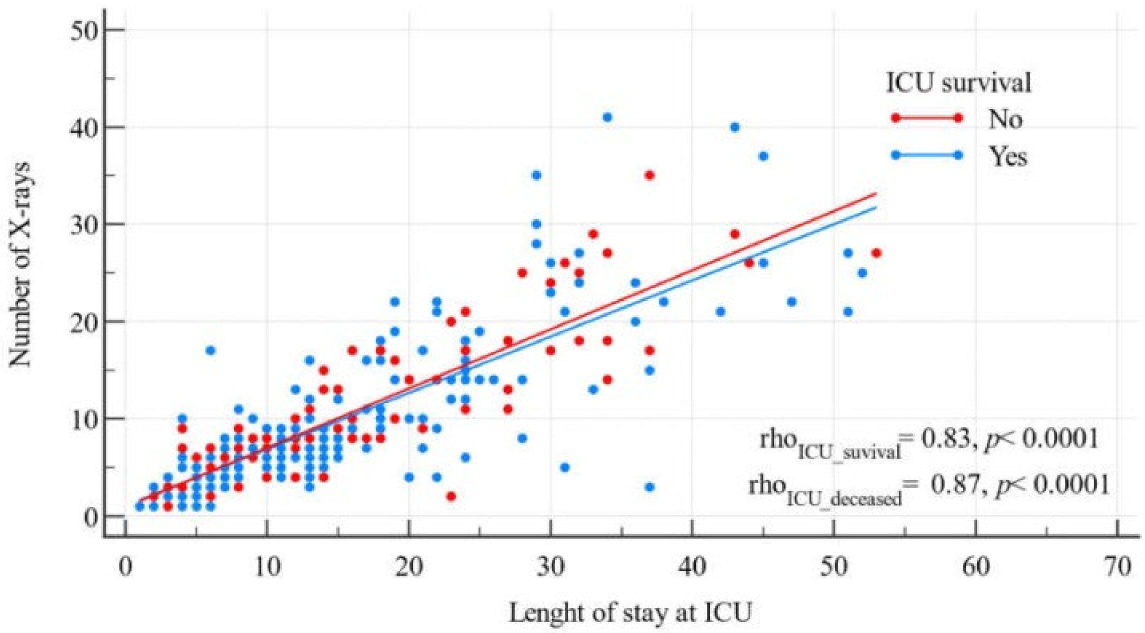

Figure 3.3.1 - 1 - A scatter diagram showing the relationship between the number of CXRs and the length of stay in the ICU. Blue line is for ICU deceased, red line for ICU survival.

The relationship between the length of stay and ICU survival was not significant ($p = 0.54$). Furthermore, to eliminate the effect of the length of stay in the ICU, the mean number of CXRs per day in the ICU unit was analysed for relationship to outcome. The mean number of CXRs per day in the ICU was 0.7 ± 0.32 and did not show a significant relationship with the ICU outcome ($p = 0.37$). The odds ratio (OR) for the number of CXRs per day in the ICU for the ICU outcome was 1.2 (0.57–2.49; $p = 0.63$). In addition, we analysed the multivariable combination of selected clinical factors and the mean number of CXRs per day in the ICU by multivariable logistic regression (**Table 3.3.1 - 3**). The relationship was not significant ($p = 0.45$).

Table 3.3.1 - 3 - Multivariable logistic regression for selected complications, adverse outcome, and mean number of CXRs per day in the ICU (BMI body mass index, DM diabetes mellitus, HT hypertension, and IHD chronic intermittent haemodialysis). The significant *p*-values below 0.05 are in bold.

Variable	Odds Ratio	95% CI	*p* Value
Age > 50	2.59	1.22–5.09	**0.006**
Gender male	1.25	0.7–2.22	0.44
BMI > 30	1.16	0.64–2.08	0.63
ECMO yes	2.11	1.13–3.94	**0.02**
DM yes	1.39	0.73–2.62	0.32
HT yes	0.96	0.54–1.69	0.88
IHD yes	1.18	0.53–2.64	0.68
Chronic immunosuppressive therapy yes	1.71	0.69–4.21	0.25
Imunosupression > 8 mg Dexamethasone or 40 mg Methylprednisolone yes	1.31	0.67–2.56	0.43
Pneumothorax	1.26	0.63–2.51	0.51
Barotrauma yes	0.42	0.16–1.12	0.08
Major bleeding event yes	2.1	1.01–4.37	**0.046**
Number of X-rays per day in the ICU	1.35	0.61–2.98	0.45

Computed Tomography

The median number of CT scans per patient was zero (IQR 0–1) because only 26.5% of patients with a BMI of 18–40 had at least one CT scan per ICU stay. A total of 145 CT scans were ordered for 77 patients with severe ARDS from the entire cohort of 291 patients. The rates of CT scanning were 26–33% across the classes of BMI, except for the morbidly obese patients (BMI > 40) who required a CT scan in 14% of the cases. The highest BMI of a patient with a CT scan was 44.2. The median number of CT scans in those who had at least one CT scan was one (IQR 1–2).

The indications for CT scans were mainly CT of the brain for a suspected intracranial pathology (74 scans), CT angiography indicated typically for a suspected pulmonary embolism (50 scans), and CT of the trunk obtained mostly to search for the source of sepsis or abdominal pathology (21 scans).
The relationship between the number of CT scans and the ICU outcome was evaluated with respect to the BMI (18–44.2) and ECMO therapy. The study did not find any differences in outcomes related to the presence of a CT scan performed, ECMO therapy, or the length of stay in the ICU (**Table 3.3.1 - 4**).

Table 3.3.1 - 4 - Comparison of CT scan rates (percentage, numbers) between survivors and deceased in the ICU.

Parameter	% CT among Surviving (No. of Probands)	% CT among Dead (No. of Probands)	*p*-Value
ICU outcome	29% (49)	25.8% (25)	0.67
ICU outcome ECMO	42.9% (24)	30.6% (15)	0.23
ICU outcome without ECMO	22.3% (25)	20.8% (10)	1.0
ICU LOS (days)	12 (6–19)	12 (8–20)	0.45

The ICU outcome of all patients treated with ECMO who required a CT scan (only patients with BMI < 45) was not different (49% rates of ECMO in the surviving vs. 60% in the deceased, $p = 0.46$). The absence of a CT scan in patients on ECMO, however, predicted the prognosis of patients (29.1% in survivors vs. 47.4% in deceased in the ICU, $p = 0.01$). The odds ratio (OR) for survival associated with ordering a CT scan (Cox analysis) for ECMO patients was 0.48, p= 0.01.

To evaluate the impact of selected diagnostic and therapeutic factors in relation to the purchased CXRs, CT scans, and ICU outcome, we performed the Mantel-Haenszel analysis, which calculated the OR for the presence of a particular complication. For the analysis, we used the mean CXR number per day in the ICU as a cut-off value (**Figure 3.3.1 - 1**). CT scanning was shown to be not statistically significant in relation to the length of stay in the ICU and an adverse outcome. The Mantel-Haenszel analysis showed a total effect of the various selected clinical factors on the impact of less or more frequent radiographic imaging close to one (0.9, $p = 0.15$), which was not significant.

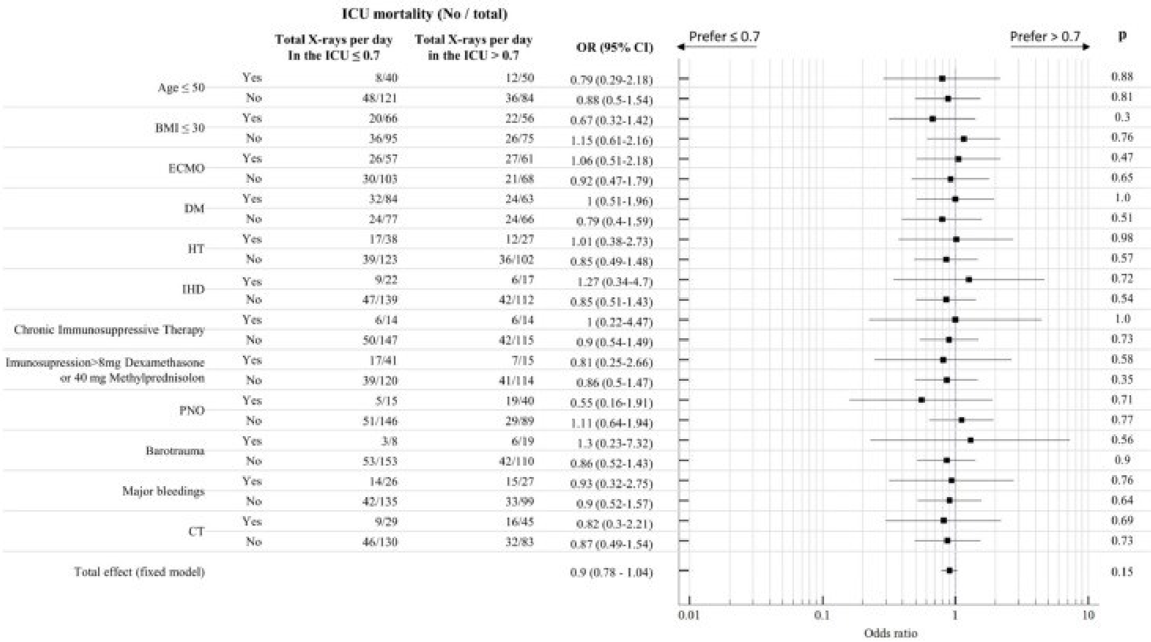

Figure 3.3.1 - 1 - Mantel–Haenszel analysis of factors tested for their relationship to the adverse outcome (death in the ICU) - the mean CXR number per day in the ICU and ICU outcome. The total effect of 0.9 represents the impact of selected variables on the impact of imaging on the patient's outcome.

Financial analysis of our data calculated an average cost of EUR 459 for a whole-body CT scan and EUR 304 for a head or chest CT. With CT scan rates in our cohort being 27%, the estimated savings on 292 patients with severe ARDS was EUR 98.685 if a CT had been ordered in all 100% cases over two years, compared to only 27% of the patients in whom the CT scans were indicated.

The aforementioned hypothesis (the frequency of CXRs and CTs might not relate to ICU outcome in patients with severe COVID-19 ARDS treated with ECMO) was confirmed.

4 Discussion

LUS has cemented itself in the area of critical care as the workhorse of critical care imaging. Our work which has been presented herein investigated 3 aspects: CD positioning on CXR and LUS, challenging the established method of quantifying PEv on LUS in patients with heavily consolidated lungs and the impact of serial imaging with the growing popularity of LUS on the ICU outcome of patients with COVID-19 ARDS treated with ECMO.

The detection of malposition of CD inserted for PNO in supine CXR is difficult because it is not readily obvious and there are no specific signs to identify it. Our **first study** thus evaluated simple parameters measured or derived from bedside CXR (gold standard follow-up method after CD insertion) that could raise suspicion of CD malposition after insertion for PNO drainage through the safe triangle in non-trauma mechanically ventilated critically ill patients. Greater foreshortening of the CD and a steep angle of inclination of the CD above the horizontal at chest entry should raise suspicion of CD migration and mandate further investigation by LUS to rule out a residual PNO occult on CXR. In this study, we assumed that a migrating CD inserted from the safe triangle would turn upward and laterally and later dorsally and that this trajectory would result in the CD pointing steeply upward after entering the pleural cavity and later foreshortening on CXR.

It is important to consider the implications of detecting CD malposition, especially in the context of non-trauma patients with respiratory failure on aggressive IPPV. While some suggested that hemodynamically stable mechanically ventilated patients should be only observed (C. G. Ball et al., 2010; Kirkpatrick et al., 2013), other studies were inconclusive (Ouellet et al., 2009). In contrast to occult PNOs in trauma that do not always require chest drainage (C. G. Ball et al., 2010; Kirkpatrick et al., 2013; Ouellet et al., 2009) the rates of PNO progression may be higher in non-trauma patients and those with respiratory failure on aggressive IPPV as they may therefore potentially enlarge due to positive respiratory pressure (Brook et al., 2009).

The potential consequences of a secondary occult or small residual ventral PNO in patients on IPPV may limit lung recruitment, and as thus cause increased requirements for mechanical ventilation, and hindered weaning, and may potentially enlarge and progress into a life-threatening tension PNO (Baldt et al., 1995; Ball et al., 2003; Enderson et al., 1993; Karnik & Khan, 2001; Lim et al., 2005). This highlights the importance of accurately identifying CD malposition in these patients.

To our best knowledge, this is the first study to systematically evaluate the malposition of a CD for PNO drainage from parameters assessed on CXR.

In the **second study**, we went further to utilize LUS to locate the CD post-drainage, since LUS provides a non-invasive and bedside method that can potentially rule out the presence of a residual PNO post-drainage and potentially eliminating the need for a thoracic CT scan and reducing the risk associated with patient transport.

This study shows that a CD may be located on LUS under the anterior chest wall in 86% of patients post-drainage and represents an important sign of successful pleural drainage with full lung expansion, an aspect that has not been described so far (**Figure 4.1**) to the best of our knowledge. Failure to locate the CD carries a significant risk of a residual PNO occult on CXR, which must be excluded on LUS (Volpicelli et al., 2012). The presence of a CD in between the pleural layers on LUS represents an additional important sign excluding a residual PNO, particularly in the apical lung regions with limited lung sliding and lung pulse (Lichtenstein & Menu, 1995). With its limitations caused by interfering ribs, the findings may help to exclude a PNO particularly in lung hyperinflation like in COPD, bullous emphysema, post thoracic surgery, and in patients with consolidated lungs on ECMO and a lung-protective mechanical ventilation. Furthermore, a parallel course of the CD to a rib was found in 10% of patients without any other LUS signs of a PNO.

This finding coupled with the findings of the 1st study may further optimise patient care, seeing as the degree of CD foreshortening on CXR estimated with the help of a CDI implies a high risk of an occult ventral pneumothorax. Another clinical finding that warrants the exclusion of an occult/residual PNO by LUS is a continuous air leak from the inserted CD. In contrast to the conclusions of the 1st study, the risk of a residual/occult pneumothorax is likely not significant with a steep angle of inclination of the CD found on CXR.

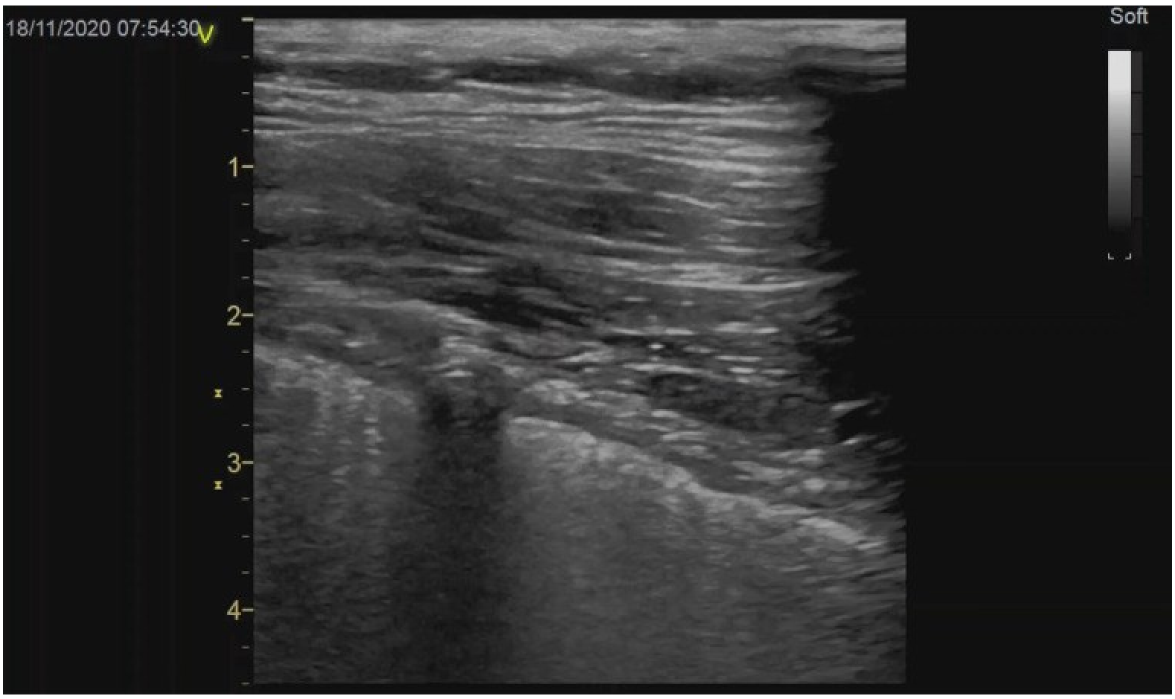

Figure 4.1 - Chest ultrasound of the anterior chest wall in a patient with COVID-19 ARDS after drainage of a PNO due to barotrauma. The linear transducer depicts a CD in the transverse plane in between the enhancing visceral and parietal pleura.

In part two (**Study 3**), LUS has proven to be a valuable tool in the assessment of PE and PEv in patients with severe ARDS treated with ECMO. As our research highlights, there are certain factors that can impact the accuracy of the assessment of PEv in these patients. The method of multiplying the maximum transverse pleural separation at the base of the lung in millimetres by 20 has been formulated and independently verified in mechanically ventilated patients (Balik et al., 2006; Peris et al., 2010). This method assumes an aerated lung floating in pleural fluid but may not be accurate in extensively consolidated and less buoyant lungs which greatly displace the PE, particularly in severe ARDS treated with ECMO. This inaccuracy opens the door to large prediction errors and an underestimation of the PEv in patients with extensive lung consolidations which may therefore be detrimental to patient care.

In the concluding part of our work (**Study 4**), we sought to shed light on the impact of radiographic imaging methods on the ICU outcomes of critically ill patients with severe ARDS. The findings revealed intriguing insights into the potential benefits of routine bedside CXR imaging in aggressively ventilated patients with severe cardiorespiratory failure, particularly those undergoing ECMO treatment. In this arena, our study showed potential benefit of routine bedside CXRs in aggressively ventilated patients with severe cardiorespiratory failure. Considering the ventilator settings (**Table 3.3.1 - 1**) and the barotrauma rates of up to 33%, this approach seems to be fully justified. Importantly, 2/3 of the patients were obese, and 1/5 were morbidly obese (Balik et al., 2022), increasing the side effects and risks of mechanical ventilation. Obesity causes functional changes in the respiratory system, leading to decreased end-expiratory lung volume, increased incidence of airway closure, and atelectasis formation, as well as modifications in lung and chest wall mechanics. These changes account for the high incidence of gas exchange impairment, alterations in respiratory mechanics, and hemodynamic compromise (Ball & Pelosi, 2019; De Jong et al., 2020). From a pathophysiological perspective, it is also worth noting that adiposity is linked to the production of various inflammatory mediators and hormones (e.g. leptin) (Silva et al., 2012).

Albeit retrospective, this study shows that, besides some primary indications, the need for CT scanning did not correlate with better survival outcomes in the ICU, suggesting that the frequency of radiographic imaging was not a determining factor in the ICU outcome of aggressively ventilated patients. It should be noted that patients who needed fewer CT scans tended to experience a more favourable disease course, indicating a potential link between the frequency of radiographic imaging and disease-related complications.

A combination of ultrasound, echocardiography, and CXR appeared to be sufficient for up to 3/4 of patients with severe ARDS, avoiding the need for a CT scan. The CT scanning approach can have negative implications due to the transfer of ICU patients to the radiology suite, which is not always safe in severe illnesses with the risk of instability associated with transport (Beckmann et al., 2004; Foley et al., 2002; Revel et al., 2020; Richmond et al., 2018). There is also an increased transport-associated workload for the ICU staff, which can be a sensitive issue at times of shortage. Epidemiology issues and the transmission of contagious diseases, e.g., COVID-19, are important factors with implications for an out-of-ICU environment where disinfection and cleaning are required in the CT suite, which can interrupt routine work.

Moreover, whilst delving into the financial implications of CT imaging on the reimbursement of care, coupled with the logistical challenges and safety concerns associated, we found that the rates of CT in our cohort around 27%, therefore, the estimated savings on 292 patients with severe ARDS were up to EUR 100.000 if a CT had been ordered in 100% of cases over the period of two years. This underscores the multifaceted impact of imaging methods on the healthcare system as a whole.

Limitations and challenges of the studies

Lung ultrasound is a valuable diagnostic tool for various respiratory conditions, but it does have some limitations. One of the main limitations is that it can be less sensitive in detecting small or distant lesions compared to other imaging techniques such as CT scans. Additionally, the interpretation of lung ultrasound images can be subjective and may vary between clinicians interpreting the images. Furthermore, the quality of the images may be affected by patient factors such as obesity, chest dressings, chest deformations, and subcutaneous emphysema, as well. Finally, lung ultrasound may not be suitable for all patients, particularly those with severe respiratory distress.

In **part one**, due to the retrospective nature of the study one, the study was limited by the small number of patients with malpositioned CDs, which therefore raises important considerations for further research. Future studies may benefit from a prospective design with a larger patient population to investigate and validate the utility of CD foreshortening and the angle of inclination of the CD. Furthermore, exploring the potential impact of different radiographic techniques on the measured parameters could provide valuable information on the reliability and reproducibility of these findings in clinical practice. The limitations posed by interobserver variability in the study warrant further exploration in the form of a multivariate analysis combining significant findings such as CD position on LUS, CDI, and air leak, which could lead to a more precise interpretation.

In **part two** (study 3), potential sources of error included variability of mean airway pressures regardless of a PEEP close to 10cmH_2O in all patients on ECMO, and interobserver variability, which sheds light on the potential challenges in accurately assessing pleural fluid volume and lung consolidations using LUS.

In **part three** (study 4), the retrospective nature of the analysis and the lack of data on potential further imaging methods undertaken post-discharge from the ICU may have impacted the assessment of hospital outcomes. Furthermore, seeing as the CT table has a weight limitation, availability of this method for some extremely obese patients may have been limited.

Benefit of our work

Addressing the aforementioned shortcomings and research gaps, the whole purpose of this dissertation work was to comprehensively explore the relationship between radiographic imaging methods (CT/CXR) in critically ill patients in the era of growing use of LUS which provides valuable insight into the potential benefits and considerations associated with different imaging modalities. The findings underscore the need for a nuanced approach to imaging in the intensive care setting, considering not only patient safety, but also clinical efficacy, financial, logistical, and patient-centred factors to provide tailored, high-quality patient care.

LUS can be used in resource limited settings, especially in third world countries where a there is a lack of trained radiologists and infrastructure limitations pertaining to CT scan availability. This means that clinicians who are well trained can offer and provide accurate care and make clinical decisions that will better benefit the patient.

In the context of Czech Republic, where LUS is largely being done by pulmonologists and critical care clinicians, there should be a push for radiologists to integrate into the training of LUS in the form of courses and lectures, so they can be better versed with the aspects of LUS and participate in the image gently movement (paediatric imaging) and the ALARA principle.

Future trends

One future trend in LUS is the increasing use of artificial intelligence (AI), deep learning (DL), and machine learning algorithms (MLA) which can be used to analyse LUS images automatically and to aid the non-expert clinician in interpreting the images. This can help to improve the accuracy and speed of diagnosis, as well as to identify early signs of lung disease (Khan et al., 2023; Kuroda et al., 2023; Nhat et al., 2023; Russell et al., 2021; Wang et al., 2022). Furthermore, in the advent of infectious diseases, such as the recent COVID-19, where there is use of AI-robotics and tele-examination to remotely examine patients in order to curb cross contamination in these instances (Akbari et al., 2021; Al-Zogbi et al., 2021; Wang et al., 2021, 2022).

Another interesting emerging avenue pertaining to LUS is the use of contrast enhanced lung ultrasound (CEUS). So far, studies have looked at peripheral consolidations where they sought to differentiate neoplastic from non-neoplastic peripheral consolidations (Sartori et al., 2013). Trenker et al. (Trenker et al., 2017) sought to objectivise findings of peripheral pleural consolidations in patients with no signs on PE on CT but are clinically suspected of a PE and concluded that these consolidations likely represented embolic consolidations. Other studies (Tee et al., 2020; Yusuf et al., 2022) in this field have recently looked at subpleural consolidations seen in COVID-19 patients and have characterized them as microinfarcts as they were found to be avascular.

5 Conclusion

LUS has cemented itself in the area of critical care as the workhorse of critical care imaging where different lung pathologies can be examined.
Our work investigated CD positioning on CXR and LUS and we showed that it can be related to residual pneumothoraces which are potentially harmful in mechanically ventilated patients. We also challenged the established method of quantifying PEv on LUS in patients with heavily consolidated lungs on ECMO and we found out that there is an underestimation of PEv in this subset of patients. Lastly, a combination of LUS, echocardiography, and CXR appeared to be sufficient in up to 3/4 of patients with severe ARDS, avoiding the need for serial CT scanning as it did not correlate with better survival outcomes in the ICU.

As more clinicians receive training in lung ultrasound, and ultrasound technology continues to advance (CEUS, AI), widespread integration of LUS into clinical practice is expected, especially in third world countries where resources are limited. Overall, lung ultrasound holds great promise as a cost-effective and efficient diagnostic modality for respiratory diseases not only in the critically ill, but also in patients with various pulmonary pathologies.
Furthermore, we also advocate for LUS to be incorporated into the training of radiologists so that they participate in the image gently movement (paediatric imaging) and the ALARA principle.

6 References

Akbari, M., Carriere, J., Meyer, T., Sloboda, R., Husain, S., Usmani, N., & Tavakoli, M. (2021). Robotic Ultrasound Scanning With Real-Time Image-Based Force Adjustment: Quick Response for Enabling Physical Distancing During the COVID-19 Pandemic. *Frontiers in Robotics and AI*, *8*, 645424. https://doi.org/10.3389/FROBT.2021.645424/BIBTEX

Al-Zogbi, L., Singh, V., Teixeira, B., Ahuja, A., Bagherzadeh, P. S., Kapoor, A., Saeidi, H., Fleiter, T., & Krieger, A. (2021). Autonomous Robotic Point-of-Care Ultrasound Imaging for Monitoring of COVID-19–Induced Pulmonary Diseases. *Frontiers in Robotics and AI*, *8*, 645756. https://doi.org/10.3389/FROBT.2021.645756/BIBTEX

Baldt, M. M., Bankier, A. A., Germann, P. S., Pöschl, G. P., Skrbensky, G. T., & Herold, C. J. (1995). Complications after emergency tube thoracostomy: assessment with CT. *Radiology*, *195*(2), 539–543. https://doi.org/10.1148/RADIOLOGY.195.2.7724780

Balik, M., Maly, M., Huptych, M., Mokotedi, M. C., & Lambert, L. (2023). Prognostic Impact of Serial Imaging in Severe Acute Respiratory Distress Syndrome on the Extracorporeal Membrane Oxygenation. *Journal of Clinical Medicine 2023, Vol. 12, Page 6367*, *12*(19), 6367. https://doi.org/10.3390/JCM12196367

Balik, M., Plasil, P., Waldauf, P., Pazout, J., Fric, M., Otahal, M., & Pachl, J. (2006). Ultrasound estimation of volume of pleural fluid in mechanically ventilated patients. *Intensive Care Medicine*, *32*(2), 318–321. https://doi.org/10.1007/s00134-005-0024-2

Balik, M., Svobodova, E., Porizka, M., Maly, M., Brestovansky, P., Volny, L., Brozek, T., Bartosova, T., Jurisinova, I., Mevaldova, Z., Misovic, O., Novotny, A., Horejsek, J., Otahal, M., Flaksa, M., Stach, Z., Rulisek, J., Trachta, P., Kolman, J., … Blaha, J. (2022). The impact of obesity on the outcome of severe SARS-CoV-2 ARDS in a high volume ECMO centre: ECMO and corticosteroids support the obesity paradox. *Journal of Critical Care*, *72*, 154162. https://doi.org/10.1016/J.JCRC.2022.154162

Ball, C. G., Dente, C. J., Kirkpatrick, A. W., Shah, A. D., Rajani, R. R., Wyrzykowski, A. D., Vercruysse, G. A., Rozycki, G. S., Nicholas, J. M., Salomone, J. P., & Feliciano, D. V. (2010). Occult pneumothoraces in patients with penetrating trauma: Does mechanism matter? *Canadian Journal of Surgery*, *53*(4), 251. https://doi.org/10.1016/j.yccm.2010.11.046

Ball, C. G., Hameed, S. M., Evans, D., Kortbeek, J. B., & Kirkpatrick, A. W. (2003). Occult pneumothorax in the mechanically ventilated trauma patient. In *Canadian Journal of Surgery* (Vol. 46, Issue 5, pp. 373–379). Canadian Medical Association. /pmc/articles/PMC3211710/?report=abstract

Ball, L., & Pelosi, P. (2019). How i ventilate an obese patient. *Critical Care*, *23*(1), 1–3. https://doi.org/10.1186/S13054-019-2466-X/FIGURES/1

Beckmann, U., Gillies, D. M., Berenholtz, S. M., Wu, A. W., & Pronovost, P. (2004). Incidents relating to the intra-hospital transfer of critically ill patients. An analysis of the reports submitted to the Australian Incident Monitoring Study in Intensive Care. *Intensive Care Medicine*, *30*(8), 1579–1585. https://doi.org/10.1007/S00134-004-2177-9

Bouhemad, B., Zhang, M., Lu, Q., & Rouby, J. J. (2007). Clinical review: Bedside lung ultrasound in critical care practice. In *Critical Care* (Vol. 11, Issue 1, p. 205). https://doi.org/10.1186/cc5668

Brook, O. R., Beck-Razi, N., Abadi, S., Filatov, J., Ilivitzki, A., Litmanovich, D., & Gaitini, D. (2009). Sonographic detection of pneumothorax by radiology residents as part of extended focused assessment with sonography for trauma. *Journal of Ultrasound in Medicine : Official Journal of the American Institute of Ultrasound in Medicine*, *28*(6), 749–755. https://doi.org/10.7863/JUM.2009.28.6.749

De Jong, A., Wrigge, H., Hedenstierna, G., Gattinoni, L., Chiumello, D., Frat, J. P., Ball, L., Schetz, M., Pickkers, P., & Jaber, S. (2020). How to ventilate obese patients in the ICU. *Intensive Care Medicine*, *46*(12), 2423. https://doi.org/10.1007/S00134-020-06286-X

Enderson, B. L., Abdalla, R., Frame, S. B., Casey, M. T., Gould, H., & Maull, K. (1993). Tube thoracostomy for occult pneumothorax: a prospective randomized study of its use. *The Journal of Trauma*, *35*(5), 726–729; discussion 729. https://doi.org/10.1097/00005373-199311000-00013

Engdahl, O., Toft, T., & Boe, J. (1993). Chest Radiograph—A Poor Method for Determining the Size of a Pneumothorax. *Chest*, *103*(1), 26–29. https://doi.org/10.1378/CHEST.103.1.26

Ferguson, N. D., Fan, E., Camporota, L., Antonelli, M., Anzueto, A., Beale, R., Brochard, L., Brower, R., Esteban, A., Gattinoni, L., Rhodes, A., Slutsky, A. S., Vincent, J. L., Rubenfeld, G. D., Taylor Thompson, B., & Marco Ranieri, V. (2012). The Berlin definition of ARDS: An expanded rationale, justification, and supplementary material. *Intensive Care Medicine*, *38*(10), 1573–1582. https://doi.org/10.1007/S00134-012-2682-1/TABLES/4

Foley, D. S., Pranikoff, T., Younger, J. G., Swaniker, F., Hemmila, M. R., Remenapp, R. A., Copenhaver, W., Landis, D., Hirschl, R. B., & Bartlett, R. H. (2002). A review of 100 patients transported on extracorporeal life support. *ASAIO Journal (American Society for Artificial Internal Organs : 1992)*, *48*(6), 612–619. https://doi.org/10.1097/00002480-200211000-00007

Havelock, T., Teoh, R., Laws, D., & Gleeson, F. (2010). Pleural procedures and thoracic ultrasound: British Thoracic Society pleural disease guideline 2010. *Thorax*, *65*(SUPPL. 2). https://doi.org/10.1136/thx.2010.137026

Karnik AM, & Khan FA. (2001). *Pneumothorax and barotrauma* (Parillo JE & Dellinger RP., Eds.; 2nd ed). Mosby.

Khan, U., Afrakhteh, S., Mento, F., Fatima, N., De Rosa, L., Custode, L. L., Azam, Z., Torri, E., Soldati, G., Tursi, F., Macioce, V. N., Smargiassi, A., Inchingolo, R., Perrone, T., Iacca, G., & Demi, L. (2023). Benchmark methodological approach for the application of artificial intelligence to lung ultrasound data from COVID-19 patients: From frame to prognostic-level. *Ultrasonics*, *132*, 106994. https://doi.org/10.1016/J.ULTRAS.2023.106994

Kirkpatrick, A. W., Rizoli, S., Ouellet, J. F., Roberts, D. J., Sirois, M., Ball, C. G., Xiao, Z. J., Tiruta, C., Meade, M., Trottier, V., Zhu, G., Chagnon, F., & Tien, H. (2013). Occult pneumothoraces in critical care: A prospective multicenter randomized controlled trial of pleural drainage for mechanically ventilated trauma patients with occult pneumothoraces.

Journal of Trauma and Acute Care Surgery, *74*(3), 747–755. https://doi.org/10.1097/TA.0B013E3182827158

Kuroda, Y., Kaneko, T., Yoshikawa, H., Uchiyama, S., Nagata, Y., Matsushita, Y., Hiki, M., Minamino, T., Takahashi, K., Daida, H., & Kagiyama, N. (2023). Artificial intelligence-based point-of-care lung ultrasound for screening COVID-19 pneumoniae: Comparison with CT scans. *PLOS ONE*, *18*(3), e0281127. https://doi.org/10.1371/JOURNAL.PONE.0281127

Lichtenstein, D. A., & Menu, Y. (1995). A Bedside Ultrasound Sign Ruling Out Pneumothorax in the Critically III: Lung Sliding. *Chest*, *108*(5), 1345–1348. https://doi.org/10.1378/CHEST.108.5.1345

Lim, K. E., Tai, S. C., Chan, C. Y., Hsu, Y. Y., Hsu, W. C., Lin, B. C., & Lee, K. T. (2005). Diagnosis of malpositioned chest tubes after emergency tube thoracostomy: Is computed tomography more accurate than chest radiograph? *Clinical Imaging*, *29*(6), 401–405. https://doi.org/10.1016/J.CLINIMAG.2005.06.032

Mokotedi, M. C., Lambert, L., Simakova, L., Lips, M., Zakharchenko, M., Rulisek, J., & Balik, M. (2018). X-ray indices of chest drain malposition after insertion for drainage of pneumothorax in mechanically ventilated critically ill patients. *Journal of Thoracic Disease*, *10*(10), 5695–5701. https://doi.org/10.21037/jtd.2018.09.64

Mokotedi, M. C., Malý, M., & Balík, M. (2023). Imaging of COVID-19 in critical care with a focus on chest ultrasound. *Anesteziologie a Intenzivni Medicina*, *34*(2), 61–68. https://doi.org/10.36290/AIM.2023.022

Nhat, P. T. H., Van Hao, N., Tho, P. V., Kerdegari, H., Pisani, L., Thu, L. N. M., Phuong, L. T., Duong, H. T. H., Thuy, D. B., McBride, A., Xochicale, M., Schultz, M. J., Razavi, R., King, A. P., Thwaites, L., Van Vinh Chau, N., Yacoub, S., Thao, D. P., Kien, D. T., … Gomez, A. (2023). Clinical benefit of AI-assisted lung ultrasound in a resource-limited intensive care unit. *Critical Care*, *27*(1), 1–8. https://doi.org/10.1186/S13054-023-04548-W/FIGURES/4

Ouellet, J. F., Trottier, V., Kmet, L., Rizoli, S., Laupland, K., Ball, C. G., Sirois, M., & Kirkpatrick, A. W. (2009). The OPTICC trial: a multi-institutional study of occult pneumothoraces in critical care. *The American Journal of Surgery*, *197*(5), 581–586. https://doi.org/10.1016/J.AMJSURG.2008.12.007

Peris, A., Tutino, L., Zagli, G., Batacchi, S., Cianchi, G., Spina, R., Bonizzoli, M., Migliaccio, L., Perretta, L., Bartolini, M., Ban, K., & Balik, M. (2010). The Use of Point-of-Care Bedside Lung Ultrasound Significantly Reduces the Number of Radiographs and Computed Tomography Scans in Critically Ill Patients. *Anesthesia & Analgesia*, *111*(3), 687–692. https://doi.org/10.1213/ANE.0b013e3181e7cc42

Revel, M. P., Parkar, A. P., Prosch, H., Silva, M., Sverzellati, N., Gleeson, F., & Brady, A. (2020). COVID-19 patients and the radiology department – advice from the European Society of Radiology (ESR) and the European Society of Thoracic Imaging (ESTI). *European Radiology*, *30*(9), 4903–4909. https://doi.org/10.1007/S00330-020-06865-Y/FIGURES/5

Richmond, K. M., Warburton, K. G., Finney, S. J., Shah, S., & Reddi, B. A. J. (2018). Routine CT scanning of patients retrieved to a tertiary centre on veno-venous extracorporeal membrane oxygenation: a retrospective risk benefit analysis. *Perfusion*, *33*(6), 438–444. https://doi.org/10.1177/0267659118763266

Russell, F. M., Ehrman, R. R., Barton, A., Sarmiento, E., Ottenhoff, J. E., & Nti, B. K. (2021). B-line quantification: comparing learners novice to lung ultrasound assisted by machine artificial intelligence technology to expert review. *Ultrasound Journal*, *13*(1), 1–7. https://doi.org/10.1186/S13089-021-00234-6/TABLES/5

Sartori, S., Postorivo, S., Vece, F. Di, Ermili, F., Tassinari, D., & Tombesi, P. (2013). Contrast-enhanced ultrasonography in peripheral lung consolidations: What's its actual role? *World Journal of Radiology*, *5*(10), 372. https://doi.org/10.4329/WJR.V5.I10.372

Silva, P. L., Pelosi, P., & Rocco, P. R. M. (2012). *Mechanical ventilation in obese patients*.

Tee, A., Wong, A., Yusuf, G. T., Rao, D., & Sidhu, P. S. (2020). Contrast-enhanced ultrasound (CEUS) of the lung reveals multiple areas of microthrombi in a COVID-19 patient. *Intensive Care Medicine*, *46*(8), 1660–1662. https://doi.org/10.1007/S00134-020-06085-4/FIGURES/1

Trenker, C., Apitzsch, J. C., Pastor, S., Bartelt, S., Neesse, A., & Goerg, C. (2017). Detection of peripheral embolic consolidations using contrast-enhanced ultrasonography in patients with no evidence of pulmonary embolism on computed tomography: A pilot study. *Journal of Clinical Ultrasound*, *45*(9), 575–579. https://doi.org/10.1002/JCU.22511

Via, G., Storti, E., Gulati, G., Neri, L., Mojoli, F., & Braschi, A. (2012). *Lung ultrasound in the ICU: from diagnostic instrument to respiratory monitoring tool*.

Volpicelli, G., Elbarbary, M., Blaivas, M., Lichtenstein, D. A., Mathis, G., Kirkpatrick, A. W., Melniker, L., Gargani, L., Noble, V. E., Via, G., Dean, A., Tsung, J. W., Soldati, G., Copetti, R., Bouhemad, B., Reissig, A., Agricola, E., Rouby, J. J., Arbelot, C., … Petrovic, T. (2012). International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Medicine*, *38*(4), 577–591. https://doi.org/10.1007/s00134-012-2513-4

Wang, J., Peng, C., Zhao, Y., Ye, R., Hong, J., Huang, H., & Chen, L. (2021). Application of a Robotic Tele-Echography System for COVID-19 Pneumonia. *Journal of Ultrasound in Medicine*, *40*(2), 385–390. https://doi.org/10.1002/JUM.15406

Wang, J. ;, Yang, X. ;, Zhou, B. ;, Sohn, J. J. ;, Zhou, J. ;, Jacob, J. T. ;, Higgins, K. A. ;, Bradley, J. D. ;, Liu, T., Wang, J., Yang, X., Zhou, B., Sohn, J. J., Zhou, J., Jacob, J. T., Higgins, K. A., Bradley, J. D., & Liu, T. (2022). Review of Machine Learning in Lung Ultrasound in COVID-19 Pandemic. *Journal of Imaging 2022, Vol. 8, Page 65*, *8*(3), 65. https://doi.org/10.3390/JIMAGING8030065

Yusuf, G. T., Wong, A., Rao, D., Tee, A., Fang, C., & Sidhu, P. S. (2022). The use of contrast-enhanced ultrasound in COVID-19 lung imaging. *Journal of Ultrasound*, *25*(2), 319–323. https://doi.org/10.1007/S40477-020-00517-Z/FIGURES/3

A Appendix

A.1 Publication overview

Mokotedi, M. C., & Balik, M. (2017). Is the mechanism of re-expansion pulmonary oedema in a heart-lung interaction? *BMJ Case Reports*, *2017*. https://doi.org/10.1136/bcr-2017-219340 **IF 0.9**

Mokotedi, M. C., Lambert, L., Simakova, L., Lips, M., Zakharchenko, M., Rulisek, J., & Balik, M. (2018). X-ray indices of chest drain malposition after insertion for drainage of pneumothorax in mechanically ventilated critically ill patients. *Journal of Thoracic Disease*, *10*(10), 5695–5701. https://doi.org/10.21037/jtd.2018.09.64 **IF 2.5**

Balik, M., Mokotedi, M. C., Maly, M., Otahal, M., Stach, Z., Svobodova, E., Flaksa, M., Rulisek, J., Brozek, T., & Porizka, M. (2022). Pulmonary consolidation alters the ultrasound estimate of pleural fluid volume when considering chest drainage in patients on ECMO. *Critical care (London, England)*, *26*(1), 144. https://doi.org/10.1186/s13054-022-04018-9 **IF 15.1**

Maly, M., Mokotedi, M. C., Svobodova, E., Flaksa, M., Otahal, M., Stach, Z., Rulisek, J., Brozek, T., Porizka, M., & Balik, M. (2022). Interpleural location of chest drain on ultrasound excludes pneumothorax and associates with a low degree of chest drain foreshortening on the antero-posterior chest X-ray. *The ultrasound journal*, *14*(1), 45. https://doi.org/10.1186/s13089-022-00296-0 **IF 3.4**

Balik, M., Maly, M., Huptych, M., Mokotedi, M. C., & Lambert, L. (2023). Prognostic Impact of Serial Imaging in Severe Acute Respiratory Distress Syndrome on the Extracorporeal Membrane Oxygenation. *Journal of clinical medicine*, *12*(19), 6367. https://doi.org/10.3390/jcm12196367 **IF 3.9**

Mokotedi, M.C., Malý, M., & Balík, M. (2023). Zobrazovací metody u těžkých forem covid-19 se zaměřením na hrudní ultrasonografii. *Anesteziologie a intenzivní medicína*, *34*(2), 61-68 **IF 0.1**