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COVID-19 Pneumonia Phenotypes Detection with Electrical Impedance Tomography

https://doi.org/10.1515/cdbme-2022-1180

Abstract: It was reported that COVID-19 induced acute respiratory distress syndrome (ARDS) comes at least in two different phenotypes. Different responses and outcomes to typical positive end-expiration pressure (PEEP) trial are found in those different phenotypes. Lung recruitability during a PEEP trial can be used to identify different phenotypes to help improve the patient outcome. In this study, we analysed overdistention and collapse ratio with electrical impedance tomography (EIT) monitoring data on four severe COVID-19 pneumonia patients to identify their phenotypes. Results demonstrate the different patient responses to a PEEP trial, and showed the developing change in patient status over time. In one patient a possible phenotype transition was identified. We suggest that EIT may be a practical tool to identify phenotypes and to provide information about COVID-19 pneumonia progression.

Keywords: Electrical impedance tomography, COVID-19 pneumonia, phenotypes, collapse, overdistention

1 Introduction

Coronavirus disease 2019 (COVID-19) is caused by contagious severe acute respiratory syndrome coronavirus (SARS-CoV-2) and is currently an ongoing pandemic. COVID-19 is an evolving disease, and the relating pathophysiologic characteristics are developing over time [1]. A large proportion of intensive care unit (ICU) admitted severe respiratory failure cases of COVID-19 pneumonia fulfil the Berlin definition of acute respiratory distress syndrome (ARDS). Despite sharing the same etiology, different characteristics were found in the COVID-19 patients. A significant amount of the patients was reported with severe hypoxemia, but with peculiar coexistence of a near normal CT images, respiratory mechanics, and lung gas volume [1]. These patients were classified as L-type characterized by low elastance, low ventilation-to-perfusion (VA/Q) ratio, low lung weight and low recruitability. There exist H-type patients who have high elastance, high VA/Q ratio, high lung weight and high recruitability. The L-type patients' response to the positive end-expiratory pressure (PEEP) trial differs from H-type patients. Rather than follow up the treatment recommendations for ARDS patients, concerns arose that L-type COVID-19 pneumonia is different and should be treated as a distinct disease [1]. A common method to identify COVID-19 pneumonia phenotypes is through CT [2]. However, the COVID-19 pneumonia course has shown to develop quickly. The possible phenotype transitions from L-Type to H-Type were reported by different authors [1, 3]. Daily CT scans are not practical. It is suggested that physiological properties can be used as surrogates to identify L-type and H-type patients, for example respiratory system compliance and recruitability. Other available lung imaging techniques should also be considered to better assist clinicians in assessing the alterations in critically ill COVID-19 pneumonia patients [2] . Electrical impedance tomography (EIT) is a radiation-free functional imaging technique which has been clinically proven in terms of monitoring regional lung effects in mechanically ventilated patients with ARDS. EIT is capable of identifying overdistention and collapse during a PEEP trial [4], which plays an important role in detecting the different phenotypes of the COVID-19 pneumonia in addition to CT examinations. The purpose of this work is to validate a method to obtain additional information on the COVID-19 pneumonia phenotype diagnosis. Four severe COVID-19 patients were monitored by EIT during PEEP trials. Cumulative collapse and overdistention ratios were calculated and compared at each PEEP step.

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2 Methods

2.1 EIT related overdistention and collapse ratio

Compliance is a parameter to describe the elasticity of the respiratory system [4]. It is defined by the ratio between the change in respiratory system volume (ΔVol) and the driving

pressure ($P_{plateau}-$ PEEP) applied to the respiratory system. $P_{plateau}$ is the plateau pressure. Compliance is much smaller in ARDS patients compared with normal people, which is caused by reduced number of opened alveoli.
In EIT reconstructions, the volume change can be estimated by the related conductivity change in an EIT tidal image. It is reported that the volume change correlates well with the conductivity variation (ΔZ) derived from the EIT reconstructions, which makes the conductivity variation a reasonable surrogate for the volume change in compliance calculations [5].
During the mechanical ventilation, however, a global measurement of compliance may provide misleading results because opposite pathological phenomena in different lung regions can compensate each other. A regional lung monitoring facilitates the understanding of the heterogeneous behaviours of the lung tissue in terms of regional respiratory mechanics. EIT is capable of revealing regional lung response to a PEEP trial, or of assessing the lung recruitment potential in patients with ARDS in terms of pixel compliance (C_{pixel}) [4]. The C_{pixel} is calculated according to Eq. 1:

$$C_{pixel} = \frac{\Delta Z_{pixel}}{P_{plateau} - PEEP} \tag{1}$$

An EIT derived lung area is exampled in Figure 1a. For illustration, two pixels in different lung regions, pixel A and pixel B, were chosen. Instead of sharing the same compliance at the same PEEP setting, pixel A and pixel B are observed with different pixel compliances, as shown in Figure 1b.

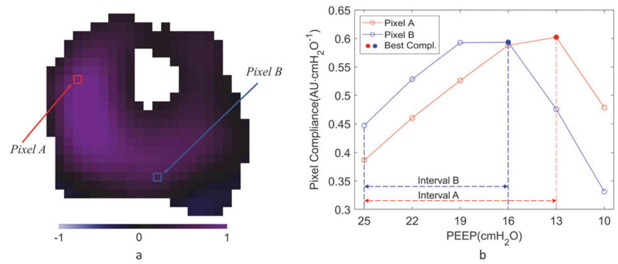

Fig. 1: (a) A lung area derived from an EIT image with 13 cmH_2O PEEP at the end of inspiration. Within the lung area, pixel A and B are at different locations; (b) Pixel compliances of pixel A and B during a decremental PEEP trial. The best pixel compliance is reached at different PEEP. Red circle: pixel A; blue circle: pixel B.

During a decremental PEEP trial, heterogeneous regional behaviours are observed. Some areas are found to show decreasing overdistention, while progressively some recruited areas might develop collapse. The reduction in overdistention is coupled to a rise in pixel compliance, while the collapse areas show a decrease in pixel compliance. It is assumed that the regional lung reaches the best compliance (C^*) when the corresponding pixel compliance is the largest. Different pixels can be observed with various behaviours in terms of compliance variation, e.g. in Figure 1b, where pixel A and B reach its best compliance at different PEEP levels. With the definition of the best pixel compliance (C^*_{pixel}), a pixel can be categorized as overdistended or collapsed. Our research used an algorithm to estimate the cumulative collapse and overdistention ratios to analyse the regional lung behaviours [4]:

1. using Equation 1 to calculate C_{pixel} at each PEEP step in a decremental PEEP trial;
2. for each pixel at each PEEP level, the pixel collapse ratio (CR_{pixel}) can be calculated as:

$$CR_{pixel} = \frac{C^*_{pixel} - C^{current}_{pixel}}{C^*_{pixel}} \tag{2}$$

   where the C^*_{pixel} is determined as the largest compliance of the corresponding pixel over the whole PEEP trial, $C^{current}_{pixel}$ is the corresponding pixel compliance at current PEEP level. The collapse ratio is set to 0 where the best compliance is not yet reached (e.g., interval A or B in Fig.1b). After reaching the best compliance, the collapse ratio is calculated by Equation 2. For example, in Figure 1b, pixel B reaches its best compliance at PEEP 16 cmH_2O, so the collapse ratios from PEEP 25 cmH_2O to 19 cmH_2O are set to 0, while the collapse ratios from 16 cmH_2O to 10 cmH_2O are calculated by Equation 2;
3. the cumulative collapse ratio (CR) at each PEEP step is calculated by weighted average of the pixel collapse ratio. The weight is the best pixel compliance:

$$CR = \frac{\sum(CR_{pixel} \times C^*_{pixel})}{\sum C^*_{pixel}} \tag{3}$$

   where the $\sum(CR_{pixel} \times C^*_{pixel})$ and $\sum C^*_{pixel}$ sum all the pixels within lung area;
4. cumulative overdistention ratio (OR) is calculated similarly, but the OR is set to 0 if the current PEEP level is less than the best compliance PEEP level.

2.2 Patient data

In our research, the analysis is conducted on retrospective datasets. The related study was approved by Human Investigation Review Board of the University of Szeged with approval number 67/2020-SZTE. The trial was registered on ClinicalTrials.gov under NCT04360837. Written informed consent was obtained from the patients or their legal representatives.
Our research evaluated four patients diagnosed with COVID-19 pneumonia, patient A, B, C, and D, respectively. CT was taken on each patient when admitted to hospital. All patients

were deeply sedated, intubated and ventilated. The ventilator was operated in pressure-controlled mode with a constant pressure increment of 15 cmH_2O above the PEEP setting during inspiration. A PEEP trial maneuver with an incremental and a decremental limb was conducted daily on all patients. During the incremental part, a 3 cmH_2O stepwise increase in PEEP from 10 cmH_2O to a maximum pressure of 25 cmH_2O are applied, which lead to an overall peak pressure of 40 cmH_2O. In the decremental limb, in steps of 3 cmH_2O the PEEP level was reduced from a maximum of 25 cmH_2O to a minimum of 10 cmH_2O. Each PEEP level was kept constant for two minutes with ongoing ventilation activity. For the included patients, each PEEP trial was monitored daily with bedside EIT device Dräger PulmoVista 500 (Dräger Medical, Lübeck, Germany). The device has 16 equidistantly distributed electrodes applied on chest circumference in the transverse plane between the 5th and 6th intercostal space. One reference electrode was placed at the abdomen. EIT monitoring data were obtained with adjacent injection current and adjacent voltage measurement. Time difference EIT images were reconstructed using the Newton-Raphson algorithm.

3 Results

Examples of the estimated collapse and overdistention areas from the first day of the investigated COVID-19 pneumonia patients are shown in Figure 2, respectively. The red areas indicate the corresponding lung area found to be overdistended, while the collapse areas are depicted in blue. From the exampled images at the first day, the cumulative overdistention areas for patient A and patient C are significantly larger than that of other patients. For patient B, the overdistention area is not that prominent at the first day, but cumulative collapse area is quite notable when PEEP was decreased. Collapse area is also very prominent for patient D in the decremental PEEP trial, while for patient A and patient C, the collapse area is small.
The cumulative overdistention ratio and the cumulative collapse ratio for each patient at different PEEP steps on each day are shown in Table 1. In Table 1, it was shown that the cumulative overdistention ratio decreased as PEEP decreased. Overdistention ratios for patient A and C are larger than that of patient B and D. Almost no overdistention is observed at the PEEP 13 cmH_2O for patient B and D, while patient A and C still have 10% of the overdistention ratio. All the patients show nearly no overdistention at PEEP 10 cmH_2O. Table 1 indicates that the cumulative collapse ratio increased in a decremental PEEP trial. In general, patient B is observed with larger collapse ratio than other patients. Except for patient A, other patients are observed to start with a collapse from PEEP 19 cmH_2O, but remain very small in this PEEP setting. The collapse in patient A starts at a lower PEEP of 16 cmH_2O. At PEEP level 10 cmH_2O, patient B and D show much larger collapsed areas than patient A and C. Patient B witnessed a steeper decreasing trend of the collapse ratio than other patients at PEEP 10 cmH_2O over the days.

4 Discussion

Four severe COVID-19 pneumonia patients were monitored with a bedside EIT device, and their data analysed to estimate the cumulative overdistention or collapse ratio during a decremental PEEP trial. The analysis implies that patient B is not as recruitable as the other three investigated patients. Patient B has higher respiratory system compliance, while patient A, C and D have lower respiratory system compliance. Together with CT images, patient B is L-type, while patient A, C and D fall under the definition of H-type patient. Patient B is observed with a possible transition from the L-type patient to the H-type patient as the cumulative collapse ratio at the lowest PEEP step decreased over time in addition to the respiratory system compliance deterioration. The transition was confirmed with the doctor who documented the data [6].

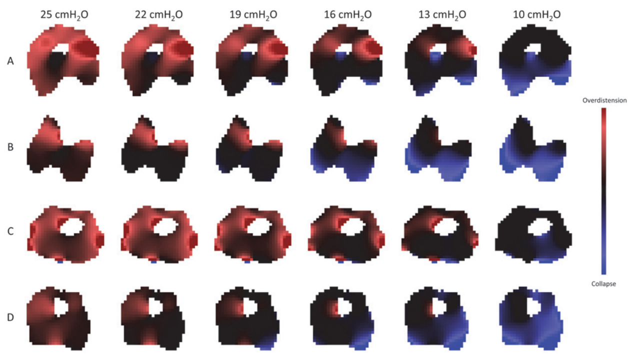

Fig. 2: Example images of the estimated pixel collapse and overdistention ratios at the first day of the EIT monitoring in different decremental PEEP steps. First row: patient A; second row: patient B; third row: patient C; fourth row: patient D.

In practice, PEEP effectiveness appears only in the intermediate COVID-19 phase, for example, H-type COVID-19 pneumonia patients [1]. It is confirmed as well that L-type patients respond better in terms of the reversed hypoxemia by an increase in FiO_2 when compared to the PEEP approach, and high flow nasal cannula for these patients can achieve a reduction in inspiratory effort [7, 8]. A careful monitoring of respiratory compliance and an accurate diagnosis of the COVID-19 pneumonia phenotype are crucial to guide the proper ven-

Tab. 1: Estimation of cumulative overdistention and collapse ratio* of each PEEP step on each day

Patient	Day	PEEP(cmH_2O)					
		25	22	19	16	13	10
A	1	0.50/0.00	0.39/0.00	0.28/0.00	0.18/0.02	0.09/0.08	0.00/0.25
	2	0.51/0.00	0.40/0.00	0.27/0.00	0.15/0.02	0.08/0.07	0.00/0.22
B	1	0.24/0.00	0.12/0.00	0.08/0.02	0.04/0.17	0.01/0.36	0.00/0.51
	2	0.31/0.00	0.16/0.00	0.09/0.02	0.05/0.12	0.01/0.27	0.00/0.46
	3	0.35/0.00	0.15/0.00	0.06/0.01	0.02/0.07	0.00/0.21	0.00/0.43
	4	0.35/0.00	0.20/0.00	0.09/0.03	0.03/0.09	0.01/0.25	0.00/0.47
	5	0.39/0.00	0.23/0.00	0.12/0.00	0.05/0.05	0.01/0.16	0.00/0.33
	6	0.42/0.00	0.24/0.00	0.10/0.01	0.02/0.04	0.00/0.14	0.00/0.34
	7	0.48/0.00	0.23/0.00	0.10/0.00	0.04/0.04	0.01/0.14	0.00/0.31
C	1	0.43/0.00	0.42/0.00	0.32/0.00	0.18/0.00	0.08/0.02	0.00/0.10
	2	0.51/0.00	0.40/0.02	0.29/0.02	0.18/0.03	0.08/0.08	0.00/0.12
	3	0.43/0.00	0.30/0.00	0.19/0.05	0.13/0.08	0.08/0.12	0.00/0.16
	4	0.43/0.00	0.33/0.00	0.25/0.02	0.16/0.07	0.09/0.17	0.00/0.26
D	1	0.26/0.00	0.14/0.00	0.07/0.02	0.02/0.09	0.01/0.24	0.00/0.45
	2	0.32/0.00	0.19/0.00	0.10/0.00	0.03/0.04	0.01/0.13	0.00/0.31
	3	0.39/0.00	0.27/0.00	0.14/0.02	0.05/0.05	0.00/0.17	0.00/0.33
	4	0.27/0.00	0.15/0.00	0.08/0.02	0.06/0.10	0.04/0.16	0.00/0.23
	5	0.40/0.00	0.15/0.00	0.03/0.00	0.02/0.10	0.01/0.23	0.00/0.36
	6	0.38/0.00	0.20/0.00	0.09/0.00	0.04/0.05	0.02/0.13	0.00/0.31
	7	0.33/0.00	0.19/0.00	0.13/0.02	0.06/0.04	0.02/0.13	0.00/0.20
	8	0.37/0.00	0.21/0.00	0.13/0.03	0.07/0.07	0.02/0.17	0.00/0.26
	9	0.23/0.00	0.11/0.00	0.03/0.01	0.01/0.08	0.00/0.20	0.00/0.35
	10	0.42/0.00	0.28/0.00	0.17/0.00	0.04/0.01	0.01/0.08	0.00/0.23
	11	0.35/0.00	0.19/0.00	0.11/0.01	0.07/0.04	0.02/0.19	0.00/0.31
	12	0.41/0.00	0.28/0.00	0.20/0.01	0.08/0.03	0.04/0.08	0.00/0.18

*Ratio is shown as Overdistention/Collapse.

tilation treatment that benefits the patient reaction and outcome. Our research suggests that EIT is capable of diagnosing COVID-19 pneumonia phenotype, and of monitoring respiratory mechanics during the COVID-19 progressive evolution. One of the limitations of this research is the estimation of a completely aerated lung status at the beginning of a decremental PEEP trial. With this estimation we calculated the relative ratios of the recruitable alveolar collapses. This is a limitation of time difference EIT that absolute amount of collapse cannot be obtained. Nonetheless, this protocol still can calculate a collapse ratio associated with the minimum possible collapse. The estimation of alveolar overdistention and collapse calculated from EIT data provides information including the whole lung status and regional lung behavior. In addition to the CT scans, EIT could be an assistive method that provides clinicians with progressive patient status.

5 Conclusion

The course of the COVID-19 pneumonia is still poorly understood and has shown to evolve over time. The evolving pathophysiological characteristics is related to the progressive variation of respiratory mechanics. Respiratory monitoring and time-sensitive adjustment to the treatment are necessary. Our research presents an EIT-based phenotype detection method in terms of alveolar overdistention and collapse, which is performed on four severe COVID-19 pneumonia patients. The result shows different reactions of the patients to a decremental PEEP trial, and may indicate a transition of a patient between different phenotypes. EIT may evolve into a useful and practical tool to aid with the classification of the different phenotypes of the COVID-19 patients in addition to the CT scans, and may provide additional information about the disease that facilitates decisions for an optimized treatment.

Author Statement

This research was partially supported by German Federal Ministry of Education and Research (MOVE 13FH628IX6) and H2020 MSCA Rise (#872488 DCPM). Authors state no conflict of interest. Informed consent has been obtained from all individuals included in this study. The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

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