The use of forced oscillation technique for monitoring of lung mechanics during covid-19 pneumonia

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Abstract

Forced oscillation technique (FOT) is non-invasive method, that does not require the patient's participation and allows to evaluate lung and airways mechanics. The question addressed by the study is whether Computerized Tomography (CT) and FOT data correlate between and whether FOT allows to follow up the course of covid-19 pneumonia during the acute intrahospital and recovery period.

Material, patients and methods

In the study were involved 30 intrahospital treated spontaneously breathing, oxygen dependent patients with moderate severity SARS-CoV-2 induced pneumonia. (CT) scans were quantitatively assessed by CT-scoring method. During the hospital stay and 3 months after the discharge lung function was measured by FOT method.

Results

During acute period resistance values R5 and R5-20 were elevated above the upper limit of normal (ULN) in 28% and 50% of all patients respectively. Reactance indices X5, AX and Fres exceeded ULN in 55%, 68% and 66% of cases. Significant correlations were observed between PaO2/FiO2, the time spent in the hospital and R5, X5, AX and Fres expressed as % of predicted. Significant correlations between FOT indices and CT-score was not found. After 3 months 18 patients were compared. R5-20 from 316;−171/+583 decreased to 122;−56/+266 % pred. P=0,0075. AX from 448;−275/+731 decreased to 213;−131/+347 % pred,p=0,0112 and Fres from 171;−143/+200 to 130;−110/+150 %pred, p=0,0081.

Study has shown that FOT method reliably reflects the pathological changes in lung mechanics and allows to monitor the course of covid-19 disease, but it cannot substitute for CT.

Introduction

Monitoring of lung affections induced by SARS Cov-19 virus is important because of gradual involvement into pathological process new structures, starting with proximal airways, then involving distal airways, alveoli, blood vessels, followed by endotheliolitis and thrombosis of lung vessels [1],[2]

Forced oscillation technique (FOT) is based on application of multifrequent airwaves into patients airways during spontaneous breathing and simultaneous recording of changes that occur in airflow and pressure in the breathing line. Method doesn't ask for any patients cooperation. The oscillations are superimposed on tidal breathing pattern and examination lasts no longer than one minute. [3, 4]. It allows the method to be used even in patients with severe oxygen deficiency. The main advantage of FOT technique is that recordings are performed during tidal breathing, avoiding deep inspirations and forced expirations which are used in spirometry recordings, because these manoeuvres could change functional status of lungs by opening more airspaces, or in opposit, inducing bronchoconstriction. Besides it, in diseased lungs such manoeuvres can induce patients self inflicted lung injury (p-SILI) This point is
especially important to take into account in persons with covid-19 pneumonia [5]. Another advantage is that FOT technique may be applied both for humans and experimental animals[6].

FOT was evented in 1956 [7] and lot of studies have performed since that time to understand deeper the lung tissue response to airwave induced energy and to find the most suitable applications of the method.

Total impedance to induced air waves consists of resistive, elastic and inertance components. Resistive component reflects the airflow resistance and could characterise the condition of airways, but elastic component, named reactance, should characterise the compliance of the respiratory system.

Studies on airways artificial models [8] and on small animals [9] allowed to get deeper understanding of the association between FOT indices and particular parameters of lung mechanics.

At the first glance it was expected that resistance component measured by FOT will correlate to obstructive pattern, but reactance (elastic component) – with restrictive one, however more detailed studies revealed that, paradoxically, airways obstruction more strongly influenced reactance than the resistance parameters [10] [11]. At the same time it remains true that restrictive diseases like pulmonary fibrosis and other chronic interstitial lung diseases manifest in oscillometric recordings as changes in reactance [12] [13] [14].

Reactance is the sum of elastic and inertance components of total impedance. This index has a negative value compared to resistance and develop out of phase because it express the potential energy accumulated during the inflation of airways and lungs by oscillatory wave. The inertance component acts in phase, reducing the impact given by elastic recoil. As the inertance grows with increasing of oscillation frequencies the major impact of elastic component in X_{rs} is seen at lowest oscillatory frequencies, practically at 5 Hz [3].

Lung autopsy data in covid-19 victims reveal a diffuse alveolar damage, patchy consolidation zones, presence of thrombi in large and small blood vessels [15]. Radiologists describe the signs of organizing pneumonia [16] [17]. All these changes are expected to increase the lung elastic recoil which should manifest as an increase of respiratory system reactance (X_{rs}) in oscillometric measurements.

Taken these facts together the FOT seems to be a promising method for evaluation of severity of lung damage in SARS-CoV-2 induced lung damage in both the acute and recovery periods of the disease.

At the start of our study we could not find in literature any study carried out on SARS-CoV-2 affected patients in acute phase using FOT technique.. Recently a paper of Tamminen et al from Tampere university, Finland was published [18]. Colleagues observed Covid-19 infected patients in acute phase of disease using Trmoflo C-100 instrument, the same as we do. However, the observed were outpatients with mild course of disease without signs of lung injury.

Our aim was to test IOS technique on more severely affected patients with signs of pneumonia confirmed on CT scans during their hospital stay
Material And Methods

Study subjects

For participation in the study were invited 60 SARS-CoV-2 positive patients treated at P. Stradins University Hospital, Riga, Latvia between February and May 2021. All patients had signs of pneumonia, confirmed by CT scans. All who gave written consent for participation in the study underwent lung examination with airwave oscillometry system (AOS). Majority of patients besides of covid-19 infection had different comorbidities. Most severe patients requiring artificial ventilation and those with comorbidities that could influence lung function, like persistent asthma, COPD, or third- and fourth-class heart failure, were not included in the study.

Finally recruited were 30 covid-19 pneumonia affected patients. Among them were patients with II-type diabetes mellius and overweight. Patients were further classified based on the degree of hypoxemia as mild (200 mm Hg ≤ PaO₂/FI O₂ ≤ 300 mm Hg), moderate (100 mm Hg ≤ PaO₂/FI O₂ ≤ 200 mm Hg), and severe (PaO₂/FI O₂ ≤ 100 mm Hg) according to Berlin Definition of ARDS severity [19].

As patients were supplied with additional oxygen using different devices, the index FiO₂ in some cases had to be recalculated from the gas flow rate. In cases when arterial blood samples were not available PaO₂ was calculated from SpO₂ [20].

This study was approved by the Ethics Committee of P. Stradins University hospital. All subjects gave written informed consent.

Study design

During the stay in the hospital each other day, if the patients status allowed FOT measurements were performed. Another parameters characterising the patient status, like breathing frequency (BF), SpO₂, or PaO₂, SaO₂, oxygen delivery rate were recorded as well.

Three months after the discharge from the hospital the patients were invited to repeat FOT measurements.

Methods

Forced oscillation technique (FOT)

Lung examination was carried out using the airwave oscillometry system (AOS). Tremoflo-100 Thorasys, Montreal, Canada. Measurements were performed according to “Technical standards for respiratory oscillometry” accepted by ERS official document in 2020 [4]. As in the majority of cases patients were connected to additional oxygen supply system by facemask or nasal cannula, during the examination time, which did not exceed one minute, patients were disconnected from the gas supply system. Measurements were taken in a sitting position using mouthpiece, containing bacterial/viral filter, and
nose clip avoiding the gas leak. Assistant or the patient himself supported his mouth floor by thumbs and cheeks by remaining fingers to avoid the airwave shunting. Three valid recording trials were performed. Between trials patient had short rest periods and, if necessary, received an oxygen support.

CT scans

. CT scans usually were carried out in the day of admittance to hospital. In more severe cases repeated CT scans were performed during the hospital stay. The severity of lungs affection was quantitatively assessed by CT scoring [19]. Briefly, each of the five lung lobes was assessed for degree of involvement and classified as none (0%), minimal (1–25%), mild (26–50%), moderate (51–75%), or severe (76–100%). No involvement corresponded to a lobe score of 0, minimal involvement to a lobe score of 1, mild involvement to a lobe score of 2, moderate involvement to a lobe score of 3, and severe involvement to a lobe score of 4. An overall lung “total severity score” was reached by summing the five lobe scores (range of possible scores, 0–20).[16] .

Analysis

Following FOT parameters were checked: - respiratory resistance at 5 Hz (R5), frequency dependence of resistance (R5 –R20), resonance frequency (Fres), reactance at 5Hz (X5) and reactance area (AX). Indices were presented both in absolute values and as percent of predicted. according to reference values by Oostween et al 2013 [21].

Microsoft 365 Excel and TIBCO Software® were used for statistical data processing

Before performing the analysis, the conformity of the data to the normal distribution was checked. The distribution was evaluated by Chi-square test and after Kolmogorov-Smirnov test.

1. Two methods were used for statistical analysis:

   2. one-way regression analysis, if the dependent and independent factors were continuous.

2) one-way repeated measures analysis of variance (repeated ANOVA)

In the case of regression analysis, the results were obtained as the regression equation with the corresponding curve and correlation coefficient (r), coefficient of determination (r²) and significance (p value). If regression analysis was performed and neither the dependent nor the independent factor were transformed then

the curve was described by the linear regression equation as in

formula: \( y = b_0 + b_1 x \)
In the case of analysis of variance, the results were expressed as the arithmetic mean ± 95% confidence interval. The difference between the groups was considered significant if p < 0.05.

If the distribution did not correspond to normal, logarithmic or square root transformation was used.

**Results**

Data presented in Table 2. suggest that in two thirds of patients the reactance indicators AX and X5 were out of normal range. Less than one third of patients had elevated total airways resistance R5. However, the value R5-20, characterizing small airways resistance was out of normal limits in 47% of our patients. Figure 1. demonstrates the association between oscillometry variables versus days before the discharge from the hospital. Dots on the figure reflect individual values of resistance and reactance recorded during the hospital period in all included individuals regardless the severity of their disease. The reference point at this graph is the day of discharge from the hospital, when patients were no longer oxygen dependent. Figure 1. Correlation between FOT indices versus days before the discharge Regression analysis reveals significant association between the time spent in the hospital and reactance values X5, AX and Fres. Significant association was also found with total airway resistance indicator R5. As the day of discharge approached, oscillometry variables diminished, however, did not reach the reference levels. Figure 2. reflects the association between patients oxygen dependence and the oscillometry parameters. Oxygen dependence presented as PaO2 /FiO2 associated significantly with elevated reactance parameters X5, AX, Fres, and airways resistance R5 as well. Figure 2. Correlation of FOT indices with PaO2 /FiO2 Deeper insight into association between FOT parameters and other indicators of disease severity during the hospital period gives table 3. Oscillometry variables here are presented as percentages of individual predicted normals. Lowest p values characterising high association with oxygenation index (PaO2/FiO2) was characteristic for all FOT parameters, except of R5-20, but high association with time spent in hospital was characteristic for reactance parameters only – X5, AX and Fres. At the same time association of FOT indices with CT score was not observed. Three months after the discharge from the hospital for repeated control arrived only 18 patients. Table 4. compares the mean changes of oscillometry parameters in the same patients after the period of recovery using repeated ANOVA method. Frequency dependence of resistance (R5-20), which was significantly elevated during the hospital period of this group reaching 317% of predicted value, after 3 months had returned to the level close to normal range. At the same time total resistance (R5), which during the hospital period was only slightly above the predicted values; did not change significantly. All the reactance values (X5, Fres, AX) during the hospital period were significantly above the predicted individual levels. Three months later significant improvement was observed in AX and Fres, whether expressed in absolute values or as percentage of predicted. AS well table shows the values of Z-score and the percentage of patients whose oscillometric parameters were above the upper limit of normal (ULN) during the hospital period and after 3 months. The p-value confirms significant reduction of cases with abnormal X5, AX and R(5-20) indices after 3 months recovery. However, in more than 20% of cases these variables remained elevated, indicating on small airways obstruction in these persons.
Discussion

The study has shown that airwave oscillometry realised with portable device can be sucessfully applied for monitoring the lung function in oxygen dependent patients with covid-19 pneumonia. Applied method in patients with moderate course of disease reveals significant deviations from normal lung mechanics. Majority of cases may be qualified as hetrogenious obstructive pattern with small airways involvement. Observed changes in lung mechanics did not change significantly during the period spent in the hospital, but returned to normal level three months later in majority of patients.

Elevated oscillometric parameters correlated with indicators of disease severity, such as PaO2/FiO2 and duration of period spent in the hospital, however, did not correlate with CT score. This point contradicted to our start hypothesis and asks for deeper analysis.

First, the method we chose for evaluation of CT image analysis was handy, as it allowed to get numerical data that fit good for statistical analysis. However, the method was not able to distinguish the character of attenuations and,as well. the detailed localization of lesions. Besides it, pathologic processes staying behind oscillometric and radiologic findings may be different

SARS-CoV-2 infection starts with affection of upper airways, rich of ACE2 receptors, necessary for virion endocytosis. Virions spread gradually down the airways tree reaching alveoli. Alveoli contain lot of SARS-CoV-2 binding sites that allows virions to disrupt the alveolar capillary network, the terminal pulmonary arterioles and induce inflammatory process. Lung biopsy dicovered endothelialitis and microvascular thrombosis.[1] [2] Radiologic examinations at initial stage of disease find mild ground-glass attenuations in lungs periphery that are considered as manifestations of microvascular injury [17, 22]. Lung mechanics during this stage is characterized by high lung compliance and predominance of ventilation over perfusion[23]. Spread of radiologic attenuation and signs of consolidation reflect the progressing of inflammatory process, alveolar recruitment and parenchymal consolidation [22].

Lung mechanics at this phase is characterized by decrease of lung compliance and increase of pressure swings in oesophageal recordings [24]. Described changes in oscillometric recordings manifest as elevated reactance parameters like X5, AX and Fres, observed in our study. reflecting increased lung elastance. At the same time elevated reactance parameters went in parallel with increase of resistance values, especially R5-20, indicating to small airways obstruction.

When part of airways become occluded, certain volume of alveoli collapse that leads to overinflation of remaining alveolar compartment and correspondingly increase of lung elastance. So, small airways obstruction may give an impact into the loss of lung compliance. However, the influence on lung density will be opposite. Overinflation of lungs will reduce the lung density and increase the permeability for x-rays

. The association between airways resistance and reactance of the respiratory system was demonstrated in dog lung model experiments carried out by Lutchen and Gillis in 1997[25] and Kaczka et al in 1985
Moderate elevation in R5 combined with gross elevation of R5-20 and the reactance indices X5, AX and Fres observed in our patients is typical for heterogenous small airways occlusion stated in model experiments.

Patients' follow-up during recovery period after covid-19 disease have discovered signs of air trapping indicative of small airways disease.

Quantitative CT analysis of regional ground-glass opacities was performed using inspiratory and expiratory image-matching to measure regional air trapping. Air trapping correlated with the residual volume–to–total lung capacity ratio [27]. Authors found that in survivors of COVID-19, small airways disease was observed even 6 months after acute period and occurred independently of initial infection severity [27]. Similar studies conducted at different time intervals after the acute period of covid-19 confirm the damage to small airways [28, 29]. Some authors consider that the method of inspiratory and expiratory CT image-matching to measure regional air trapping is more precise way to reveal small airways disease than lung function testing methods [30].

Air entrapment can be based on various pathological processes in the small airways starting with wall collapse during the expiratory phase that occur due to loss of elastic support from lung parenchyma, increase of bronchial muscle tone and inflammatory oedema.

Our data show that signs of small airways affection are much more common during the acute period of covid-19 disease compared to time after 3 months. As well the causes inducing the airways damage in acute period and after the recovery should be different. Typical patologic process in acute period of covid-19 pneumonia is immunothrombosis affecting pulmonary microcirculation. To explain frequent pulmonary infarctions in covid-19 cases McGonagle and colleagues [31] proposed a three-component theory of lung parenchymal oxygenation, in which the bronchial artery played the main role. Two other oxygen sources were pulmonary artery and alveolar air. As oxygen diffusion from alveoli is affected, but pulmonary artery blood contains the venous blood, bronchial artery becomes the main oxygen source. If thrombosis occludes this route of oxygen supply, lung infarction develops [31].

Severe changes in bronchial artery network described Ackermann and colleagues [32] by studying the autopsy material of covid-19 pneumonia victims using hierarchical phase-contrast tomography. Authors demonstrated excessive neovascularization with formation bronchiopulmonary shunt vessels, remodeling of peribronchial vessels and vasa vasorum [32].

Remodeling of bronchial circulation system may significantly affect the blood supply to bronchi resulting in their narrowing or even total closure. Such changes may be irreversible and lead to remodeling of peripheral lungs.

This theory is well supported by our observations during acute illness and those of other researchers studying the recovery period. When the hospital stay came to an end, normal oxygenation status recovered quickly, however oscillometer parameters indicating on small airways obstruction were far from
normal. Only after three months recovery significant improvement was reached in majority, but not all the patients.

**Conclusions**

Study has shown that FOT method reliably reflects the pathological changes in lung mechanics and allows to monitor the course of covid-19 disease, but it cannot substitute for CT. Besides it, the method made it possible to discover that the small airways play an important role in the pathogenesis of lung damage in covid-19 pneumonia, especially in acute phase of the disease. Recovery was slow and after 3 months mild lung function impairment remained.

**Declarations**

**Ethical approval**

This study was approved by the Ethics Committee of Pauls Stradins University hospital.

All subjects gave **written consent to participate** in the study.

**Consent to publish** was not applicable because all personal data of studied subjects were kept confidential and were not included in this paper.

**Competing interests**

Authors have no competing interests that might be perceived to influence the results and/or discussion reported in this paper.

**Authors contributions:**

I, Taivans supervised this research programme, wrote the main manuscript text. L.Grima made recordings on the patients during their hospital stay,

L. Zvaigne performed and evaluated CT recordings on patients.

N. Jurka and V. Gordjushina made statistical calculations and prepared figures and tables,

G. Strazda made measurements on patients 3 months after the discharge.

All authors reviewed the manuscript.

**Funding**

No funding was received for this study

**Availability of data and materials**

All data and materials lied on the basis of this study are available from the corresponding author by request.
References


**Tables**

Table 1. Patients characteristics
### Table 2. Mean values, Z-score and upper limits of normal for FOT indices recorded during intrahospital stay in 30 COVID-19 pneumonia patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>M-95</th>
<th>M+95</th>
<th>Z-score</th>
<th>Z-95</th>
<th>Z+95</th>
<th>n&gt;ULN</th>
<th>%&gt;ULN</th>
</tr>
</thead>
<tbody>
<tr>
<td>R5</td>
<td>4.27</td>
<td>3.67</td>
<td>4.87</td>
<td>0.69</td>
<td>0.22</td>
<td>1.16</td>
<td>8/30</td>
<td>27</td>
</tr>
<tr>
<td>R5-20</td>
<td>0.95</td>
<td>0.68</td>
<td>1.26</td>
<td>1.72</td>
<td>1.00</td>
<td>2.44</td>
<td>14/30</td>
<td>47</td>
</tr>
<tr>
<td>X5</td>
<td>-2.50</td>
<td>-3.09</td>
<td>-1.91</td>
<td>-2.53</td>
<td>-3.58</td>
<td>-1.49</td>
<td>16/30</td>
<td>53</td>
</tr>
<tr>
<td>AX</td>
<td>15.78</td>
<td>11.62</td>
<td>21.42</td>
<td>2.15</td>
<td>1.72</td>
<td>2.57</td>
<td>19/30</td>
<td>63</td>
</tr>
<tr>
<td>Rf</td>
<td>22.24</td>
<td>19.93</td>
<td>24.82</td>
<td>2.10</td>
<td>1.68</td>
<td>2.52</td>
<td>19/30</td>
<td>63</td>
</tr>
</tbody>
</table>

ULN – upper limit of normal, n>ULN – number of patients exceeding ULN value, %>ULN – percent of patients exceeding ULN value.

Table 3. p-values of correlation between FOT indices and parameters characterizing COVID-19 pneumonia severity.
<table>
<thead>
<tr>
<th>Independent variable on X axis</th>
<th>Dependent variable on Y axis</th>
<th>R</th>
<th>$r^2$ (determination coefficient)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO2/FiO2</td>
<td>R5% pred</td>
<td>0.349</td>
<td>0.121</td>
<td>0.0031</td>
</tr>
<tr>
<td>PaO2/FiO2</td>
<td>R5-20% pred</td>
<td>-0.173</td>
<td>0.030</td>
<td>0.158</td>
</tr>
<tr>
<td>PaO2/FiO2</td>
<td>X5% pred</td>
<td>0.332</td>
<td>0.110</td>
<td>0.0051</td>
</tr>
<tr>
<td>PaO2/FiO2</td>
<td>AX% pred</td>
<td>0.454</td>
<td>0.206</td>
<td>0.0001</td>
</tr>
<tr>
<td>PaO2/FiO2</td>
<td>RF% pred</td>
<td>0.434</td>
<td>0.189</td>
<td>0.0002</td>
</tr>
<tr>
<td>Day before discharge</td>
<td>R5% pred</td>
<td>0.223</td>
<td>0.050</td>
<td>0.0695</td>
</tr>
<tr>
<td>Day before discharge</td>
<td>R5-20% pred</td>
<td>0.117</td>
<td>0.014</td>
<td>0.348</td>
</tr>
<tr>
<td>Day before discharge</td>
<td>RF% pred</td>
<td>0.276</td>
<td>0.076</td>
<td>0.0237</td>
</tr>
<tr>
<td>Day before discharge</td>
<td>X5% pred</td>
<td>0.409</td>
<td>0.167</td>
<td>0.0006</td>
</tr>
<tr>
<td>Day before discharge</td>
<td>AX% pred</td>
<td>0.459</td>
<td>0.211</td>
<td>0.0001</td>
</tr>
<tr>
<td>CT (score)</td>
<td>R5% pred</td>
<td>0.128</td>
<td>0.016</td>
<td>0.445</td>
</tr>
<tr>
<td>CT (score)</td>
<td>R5-20% pred</td>
<td>0.050</td>
<td>0.003</td>
<td>0.771</td>
</tr>
<tr>
<td>CT (score)</td>
<td>X5% pred</td>
<td>0.233</td>
<td>0.054</td>
<td>0.159</td>
</tr>
<tr>
<td>CT (score)</td>
<td>AX% pred</td>
<td>0.242</td>
<td>0.059</td>
<td>0.149</td>
</tr>
<tr>
<td>CT (score)</td>
<td>RF% pred</td>
<td>0.198</td>
<td>0.039</td>
<td>0.233</td>
</tr>
</tbody>
</table>

**Bold numbers indicate reliability > 95%**

Table 4. Patients data during the hospital stay and 3 months after the discharge
<table>
<thead>
<tr>
<th>Value</th>
<th>During the hospital stay</th>
<th>3 month after the discharge</th>
<th>Repeated measure ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOT</strong></td>
<td>Mean</td>
<td>M-95%</td>
<td>M+95%</td>
</tr>
<tr>
<td>R5</td>
<td>4.34</td>
<td>3.62</td>
<td>5.07</td>
</tr>
<tr>
<td>R5%</td>
<td>128.2</td>
<td>100.60</td>
<td>155.72</td>
</tr>
<tr>
<td>R5-20</td>
<td>1.01</td>
<td>0.66</td>
<td>1.43</td>
</tr>
<tr>
<td>R5-20%</td>
<td>316.7</td>
<td>171.9</td>
<td>583.6</td>
</tr>
<tr>
<td>X5</td>
<td>-2.53</td>
<td>-3.30</td>
<td>-1.75</td>
</tr>
<tr>
<td>X5%</td>
<td>202.4</td>
<td>116.1</td>
<td>288.6</td>
</tr>
<tr>
<td>Fres</td>
<td>22.31</td>
<td>19.01</td>
<td>26.18</td>
</tr>
<tr>
<td>Fres%</td>
<td>171.9</td>
<td>143.8</td>
<td>200.0</td>
</tr>
<tr>
<td>AX</td>
<td>17.4</td>
<td>11.1</td>
<td>27.5</td>
</tr>
<tr>
<td>AX%</td>
<td>448.8</td>
<td>275.5</td>
<td>731.2</td>
</tr>
<tr>
<td><strong>Z-mean</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R5</td>
<td>0.876</td>
<td>0.152</td>
<td>1.600</td>
</tr>
<tr>
<td>R5-20</td>
<td>2.113</td>
<td>1.025</td>
<td>3.202</td>
</tr>
<tr>
<td>X5</td>
<td>-3.25</td>
<td>-4.974</td>
<td>-1.522</td>
</tr>
<tr>
<td>AX</td>
<td>2.254</td>
<td>1.581</td>
<td>2.927</td>
</tr>
<tr>
<td>Fres</td>
<td>1.955</td>
<td>1.286</td>
<td>2.624</td>
</tr>
<tr>
<td><strong>%&gt;ULN</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>R5</td>
<td>29.4</td>
<td>12.8</td>
<td>54.2</td>
</tr>
<tr>
<td>R5-20</td>
<td>64.7</td>
<td>40.4</td>
<td>83.2</td>
</tr>
<tr>
<td>X5</td>
<td>64.7</td>
<td>40.4</td>
<td>83.2</td>
</tr>
<tr>
<td>AX</td>
<td>64.7</td>
<td>40.4</td>
<td>83.2</td>
</tr>
<tr>
<td>Fres</td>
<td>52.9</td>
<td>30.2</td>
<td>74.5</td>
</tr>
</tbody>
</table>

FOT – oscillometry variables; Z-mean- mean Z-score values; % >ULN – Percent of patients exceeding upper limit of normal; bold fonts indicate p – value below 0.05.
Figures

1. Correlation between FOT indices versus days before the discharge
Figure 2

Correlation of FOT indices with PaO2/FiO2