# ROX INDEX IN PATIENTS WITH COVID-19 WHO USED HIGH FLOW THERAPY AND ELMO

*ÍNDICE ROX EM PACIENTES COM COVID-19 QUE USARAM TERAPIA DE ALTO FLUXO E ELMO*

*ÍNDICE ROX EN PACIENTES CON COVID-19 QUE USARON TERAPIA DE FLUJO ALTO Y ELMO*

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## ABSTRACT

To evaluate the ROX index in monitoring patients with respiratory failure by COVID-19. Cross-sectional study carried out at the Hospital São José, in Ceará. Patients with COVID-19, hospitalized from January to July, who used high flow oxygen therapy (HFT) combined with ELMO were included. Data were collected by review of medical records. Statistical analyses were performed with Excel Microsoft 365 software. Forty patients were included in this research. Most were male (67.5%). The mean of age was 51.9 years; 65% of patients were successful with TAF/ELMO therapy. ROX index was a predictor of success or failure at the 24th and 48th hours. There was a strong correlation between the ROX index and the final PaO2/FiO2. Low ROX index values were associated with a higher risk of intubation.
**Descriptors:** *COVID-19; noninvasive ventilation;Respiratory Insufficiency.*

## RESUMO

Avaliar o índice ROX na monitorização de pacientes com insuficiência respiratória por COVID-19. Estudo transversal realizado no Hospital de Doenças Infecciosas São José, no Ceará. Foram incluídos indivíduos com COVID-19, internados no período de janeiro a julho, que utilizaram terapia de alto fluxo de oxigênio (TAF) combinado com ELMO. A coleta de dados ocorreu através da revisão de prontuários. Os dados foram analisados através do software Excel Microsoft 365. No período do estudo, 40 pacientes foram incluídos nesta pesquisa. A maioria era do sexo masculino (67,5%). A média de idade foi de 51,9 anos; 65% dos pacientes obtiveram sucesso com a terapia TAF/ELMO. Índice ROX foi preditor de sucesso ou falha na 24ª e 48ª hora. Houve uma forte correlação entre o índice ROX e a PaO2/FiO2 final. Baixos valores do índice ROX foram associados a um maior risco de intubação.
**Descritores:** *COVID-19; ventilação não invasiva; Insuficiência respiratória.*

## RESUMEN

Evaluar el índice ROX en el seguimiento de los pacientes con insuficiencia respiratoria por COVID-19. Estudio transversal realizado en el Hospital de las Enfermedades Infecciosas São José, en Ceará. Se incluyeron individuos con COVID-19, hospitalizados de enero hasta julio, que utilizaron oxigenoterapia de alto flujo (HFT) combinada con ELMO. La recolección de los datos se llevó a cabo mediante la revisión de los registros médicos. Los datos se analizaron mediante el software Excel Microsoft 365. Durante el período del estudio, se incluyeron 40 pacientes en esta investigación. La mayoría eran hombres (67,5%). La edad media fue de 51,9 años; El 65% de los pacientes tuvieron éxito con la terapia TAF / ELMO. La media del índice ROX fue mayor a las 24 y 48 horas. Hubo una fuerte correlación entre el índice ROX y la PaO2 / FiO2 final. Los valores bajos del índice ROX se asociaron con un mayor riesgo de intubación.
**Descriptores:** *COVID-19; Ventilación no invasiva; Insuficiencia respiratoria.*

## INTRODUCTION

The disease caused by the new coronavirus (COVID-19) has spread rapidly all over the world, being considered a pandemic by the World Health Organization in March 20201. The severe form of COVID-19 occurs in about 20% of patients, being characterized by a picture of acute hypoxemic respiratory failure (ARI), requiring the use of oxygen therapy and admission to the intensive care unit (ICU). This led to a collapse of healthcare systems during the two epidemic waves in 2020 and 2021 [2].

The high mortality rate related to the use of invasive mechanical ventilation and the numerous complications related to this strategy, such as ventilator-induced lung injury (VILI), have resulted in an increasing demand for non-invasive therapies to treat IRpA [3-6]. In the second epidemic wave, High Flux Oxygen Therapy (HFT) and helmet (ELMO) with continuous positive airway pressure (CPAP) were widely used in patients with moderate hypoxemia, even outside the ICU, mainly due to the scarcity of beds for critically ill patients [5,7-10]. The TAF system, combined with the use of the ELMO helmet, can improve gas exchange, thus reducing the patient's respiratory effort 10-11. The benefits of these systems are reflected in the improvement of arterial oxygen pressure ($PaO_2$) and the ratio of $PaO_2$ to the inspired fraction of oxygen ($FiO_2$), as well as peripheral oxygen saturation ($SpO_2$) and respiratory rate (f) [11].

Therapies with non-invasive ventilatory support, when well tolerated and monitored through blood gas parameters, can lead to a reduction in orotracheal intubation rates, which, in the face of a pandemic of this magnitude, are important for the health system, as it leads to a reduction in mortality and length of stay[12]. However, one of the main dilemmas in the management of IRpA in COVID-19 is not delaying the intubation of patients who are not responding adequately to non-invasive ventilation (NIV) [13].

The ROX index [($SpO_2/FiO_2$)/respiratory rate] has been proposed as an easy-to-apply tool to predict the outcome in patients with respiratory failure caused by COVID-19, especially in hospitalized patients who are using the high-flow system. oxygen. When this index is < 4.88 in the first 04-24 hours, patients are identified as being at high risk of failure in the high-flow oxygen system [14].

Fast and simple tools that are predictive of the success or failure of TAF/ELMO combination therapy are needed to support clinical decisions of multiprofessional teams. Thus, considering that the ELMO helmet is a system that works with high oxygen flow and continuous CPAP, we believe that the ROX index can be a good tool in the evaluation of TAF/ELMO combination therapy. Therefore, the aim of this study was to evaluate the use of the ROX index in monitoring patients with ARF secondary to COVID-19, who used TAF/ELMO therapy.

## METHODS

This is an observational and cross-sectional study, carried out at the Hospital for Infectious Diseases São José (HSJ), a tertiary hospital of the Unified Health System (SUS), a reference for infectious diseases in Northeastern Brazil. The study is part of the project approved by the Research Ethics Committee of Hospital São José under opinion nº 4.366.829 (CAAE 35017820.1.0000.5044) and followed all the ethical precepts applied to the research, according to resolution nº 466/12 of the National Council All individuals with COVID-19 who were hospitalized from January to July in the semi-intensive unit for patients with COVID-19 and who used combined non-invasive ventilatory support (TAF/ELMO) were included.

Data collection was carried out through the review of medical records and non-invasive respiratory monitoring forms from the Physiotherapy service of that hospital. Sociodemographic, clinical, laboratory and ventilatory parameters related to TAF/ELMO were collected. The variables described were age, gender, comorbidities, days of symptoms, respiratory rate and oxygen support used on admission, length of hospital stay, time of combined therapy use, therapy parameters (Flow L/min, $FiO_2$, PEEP) , $PaO_2$, $PaO_2/FIO_2$ ratio. The ROX index [($SpO_2/FiO_2$) /f] during the use of the ELMO was described in the times of 02 hours, 04 hours, 24 hours and 48 hours after admission. Patients whose data in medical records were incomplete were excluded. The TAF system used in the semi-intensive unit was the Optiflow®, Fisher Paykel MR850 humidifier, and the ELMO 1.0 10 helmet. We considered therapy failure when there was a need for orotracheal intubation.

Data were analyzed using Excel Microsoft 365 software. Continuous data were expressed as mean and standard deviation (SD) and categorical variables as frequencies. Student's T test was used to assess the mean ROX index values between success/failure and start/end of combined therapy groups. Pearson's correlation test between the ROX index and the $PaO_2/FiO_2$ ratio was used to assess the improvement in hypoxemia. We considered as statistically significant the p value $\leq 0.05$.

## RESULTS

From January to June 2021, a total of 49 patients used TAF/ELMO in the semi-intensive unit of the HSJ. Eleven patients were excluded. Five were admitted in the process of failure of the combined therapy, coming from other inpatient units, and four patients had incomplete information in their medical records. In total, 40 patients were included in this research. Most were male (n=27; 67.5%). Mean age was 51.9 years (± 15.9), and mean time of symptoms on admission was 9.1 days (± 2.6). The most used oxygen support on admission was the reservoir mask (Table 1). As for the outcomes of the use of TAF/ELMO therapy, we observed that 65% were successful and 35% of the patients evolved to invasive mechanical ventilation (IMV). Death occurred in five patients (12.5%), all on IMV.

**Table 1** – Clinical and epidemiological characteristics of patients with COVID-19, who used TAF/ELMO, HSJ, in the period January-June 2021.

| Characteristics | Nº (%) or Average (± DP) |
| --- | --- |
| **Genre** | |
| Male | 27 (67,5) |
| Female | 13 (32,5) |
| **Comorbidities*** | |
| Systemic Arterial Hypertension | 18 (45,0) |
| Obesity | 11 (27,5) |
| Diabetes Mellitus | 05 (12,5) |
| HIV Infection | 03 (7,5) |
| Neoplasm | 03 (7,5) |
| Anxiety Disorder | 03 (7,5) |
| **Ventilatory support (Admission)** | |
| Reservoir Mask | 26 (65,0) |
| Nasal Oxygen Catheter | 14 (35,0) |
| **Symptoms Time (days)** | 9,1 ± 2,6 |
| **Respiratory Rate (rpm)** | 23,7 ± 2,9 |
| **TAF/ELMO Therapy Time (days)** | 5,7 ± 3,3 |
| **Hospitalization time (days)** | 20,9 ± 15,4 |

*29 patients had at least one or more comorbidities and 11 patients had no comorbidities.

**Fonte –** Own authorship. Survey Data (2021).

When evaluating the positive end-expiratory pressure (PEEP) value while using TAF/ELMO therapy, we observed a fixed value of 10 cmH2O in all patients. The other ventilatory parameters are described in table 2.

**Figure 1 –** Correlation between the ROX index and the PaO2/FiO2 ratio at the beginning (1A) and at the end (1B) of TAF/ELMO therapy in patients with COVID-19, HSJ, January-June/2021..
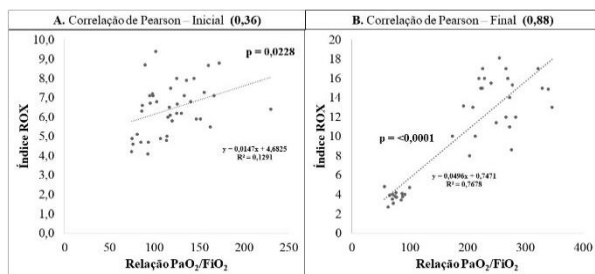


**Fonte –** Own authorship. Survey Data (2021).

**Table 2** – Ventilatory parameters at the beginning and end of TAF/ELMO therapy, HSJ, in the period January-June 2021.

| Variables | Start of therapy | End of therapy | p - valor |
| --- | --- | --- | --- |
| **PaO$_2$ (mmHg)** | 68,6 ± 11,8 | 82,7 ± 19,8 | 0,000 |
| **Fluxo (L/min)** | 40,8 ± 4,1 | 37,4 ± 7,6 | 0,015 |
| **FiO$_2$** | 0,7 ± 0,2 | 0,5 ± 0,2 | <0,0001 |
| **PaO$_2$/FiO$_2$ Ratio** | 106,4 ± 45,4 | 198,5 ± 98,3 | <0,0001 |

$p < 0.05$ - Student's t test
PaO2 - Arterial Partial Pressure of Oxygen / FiO2 - Inspired Oxygen Fraction

**Fonte –** Own authorship. Survey Data (2021).

The variation of the ROX index in the first 48 hours occurred as follows: start of therapy (4.1 - 9.4), 02 hours (4.6 - 9.0), 04 hours (4.5 - 9.0), 24 hours (4.4 - 10.3) and 48 hours of therapy (2.7 - 18.1). We observed that in the first 24 hours, no patient had a value ≤ 3.85. After 48 hours of therapy, we observed that seven patients (17.5%) had a value below 3.85. When we evaluated the index value ≥ 4.88, we observed that at the beginning of therapy 34 patients (85%) had an index above 4.88; in 02 hours, 36 (90%), 04 and 24 hours, 38 (95%) in both; and 26 (65%) within 48 hours. Patients with a ROX index between 3.85 and 4.88 were also evaluated. We observed that six patients (15%) had these values at admission; after 02 hours of therapy, four patients (10%); between 04 and 24 hours, two patients (5%) in both periods; and seven patients (17.5%) after 48 hours.

The mean ROX index from onset to 48 hours of application, comparing patients and success vs. failure during TAF/ELMO therapy is described in table 3.

**Table 3** – Média do índice ROX em sucesso vs. falha da terapia TAF/ELMO, HSJ, no período de janeiro-junho de 2021.

| Variables | Sucess | Failure | p - value |
| --- | --- | --- | --- |
| **Initial ROX** | 6,5 ± 1,42 | 6,3 ± 1,21 | 0,744 |
| **ROX 02 hours** | 6,4 ± 1,11 | 6,2 ± 0,93 | 0,636 |
| **ROX 04 hours** | 6,6 ± 1,17 | 6,1 ± 0,81 | 0,119 |
| **ROX 24 hours** | 7,2 ± 1,71 | 6,1 ± 0,92 | 0,041 |
| **ROX 48 hours** | 13,8 ± 2,76 | 3,8 ± 0,56 | <0,0001 |

$p < 0.05$ - Teste T de Student

**Fonte –** Own authorship. Survey Data (2021).

In Figure 1, we assess the correlation between the ROX index and the initial (1A) and Final (1B) PaO2/FiO2 ratio

## DISCUSSION

In this study, we observed that the ROX index is a simple tool that can be used in patients with pneumonia caused by COVID-19 who use FAT/ELMO, proving to be a good predictor of the need for intubation

in patients who evolved to therapy failure. As a consequence, high ROX index values were associated with an improvement in hypoxemia, identified through the improvement in the PaO2/FiO2 ratio.

The COVID-19 pandemic instigated an acceleration in the process of technological development and innovation for the promotion of public health, as was the case with the manufacture of the Elmo[15]. This assisted breathing helmet, of Ceará origin, was developed in a short period by through a public-private partnership, to provide positive pressure without the need for intubation, to optimize the management of acute respiratory failure by COVID-19[10]. According to the National Policy on Health Technology Management[16], to guarantee the principle of integrality, the health system must use and incorporate technologies that are efficient and safe, whose benefits are greater than their risks.

In this context, it is important that there are indicators that can guide SUS managers in the evaluation process so that appropriate technologies are incorporated in health systems and services 16. Therefore, our proposal is that, as the ROX index, it proved to be an index with good discriminative validity, differentiating between those who succeeded or failed in the ELMO/TAF combination therapy, this index could be used in future studies as an indicator to assess the effectiveness of non-invasive support through the high-flow system in patients with insufficiency hypoxemic respiratory.

Studies published for the first time on the ROX index in patients with severe pneumonia in the ICU and who used TAF reported that a value greater than 4.88 was associated with the success of the therapy. And values below 3.85 represented a high risk of failure, and the need for orotracheal intubation should be reflected[13,17]. The ROX index was validated in 2019 in 191 patients from France and Spain, and was used as a tool to predict the success or failure of FAT therapy. Patients who had values ≥ 4.88 after two hours of TAF were less likely to need IMV. Throughout the study period, the values most associated with failures occurred at times 12 and 24 hours after the beginning of TAF[18-19]. Another study carried out in ICU patients who used TAF observed higher ROX index values in patients who were successful with the therapy, when compared to those who evolved with failure (12.7 vs 10.2; p = 0.002)[20]. Similar to In previous studies, we observed in our research that, among patients who progressed to IMV, the mean ROX index values were comparatively lower in those individuals who progressed to TAF/ELMO therapy failure, especially within 48 hours.

A recent study using the ROX index for monitoring TAF oxygen therapy in patients with COVID-19 demonstrated that values below 4.88 were predictors of IMV, with a sensitivity of 81% and a specificity of 38%. Another study found that patients with comorbidities had lower ROX index values on the 1st day of hospitalization[14,17].
ROX index values between 3.85 and 4.88 are still doubtful for decision making, being considered as a "grey zone". The best course of action should be based on increasing the frequency of measuring the index to guide the conduct at the bedside[17]. In our study, four patients had the index in the "grey zone" when evaluated in the 24th hour and there was no intubation . However, seven patients had the ROX index in the "grey zone" at the 48th hour, all of which progressed to IMV. Authors suggest that if a patient is in the "grey zone" within 12 hours, ROX can be evaluated again after an hour or two. If the score increases, the patient should be considered more likely to succeed; if there is a decrease in value, intubation is more likely to occur; and if the score remains unchanged, a reassessment can be performed after one hour 19.

In a study carried out with patients who used TAF for the treatment of hypoxemic respiratory failure secondary to COVID-19, the parameters of the ROX index and the PaO2/FiO2 ratio gradually increased in the group that was successful, after six hours of therapy. In the group that evolved to failure, these parameters gradually decreased (p < 0.0001) 21. Our findings showed that the correlation of the ROX index with the PaO2/FiO2 was stronger in the 48th hour, demonstrating that the ROX index can be a Applicable tool for TAF/ELMO combination therapy, predictor of improvement in hypoxemia with these NIV strategies.

This study had some limitations that need to be discussed. First, it is an observational and retrospective study. Furthermore, the eligible sample was small and therefore the results cannot be generalized. Prospective and controlled studies should be performed to validate this tool as a predictor of success or failure with the use of TAF/ELMO therapy

## FINAL CONSIDERATIONS

The ROX index, after starting non-invasive support, was a significant predictor of success or failure during treatment with TAF/ELMO. The routine use and monitoring of the index has proven to be potentially useful to guide the decision to intubate patients with COVID-19, especially those with acute respiratory failure, even for treatment outside the ICU. Low ROX

index values were associated with a higher risk of failure. Therefore, this index appears to be a promising tool for early identification of failure of non-invasive support with TAF/ELMO. However, as this is an observational and retrospective study with a small sample, other studies are needed to validate these findings.

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