Study Protocol And Statistical Analysis

Ambispective cohort study with survival analysis was conducted in a high-complexity clinic in Medellín, Colombia.

The study included patients over 18 years of age, hospitalized with Covid-19 pneumonia confirmed by positive Real-Time Reverse Transcription Polymerase Chain Reaction for SARS-CoV2 (RT-PCR SARS-Cov2) by Berlin protocol. The patients should also have radiological confirmation of Pneumonia. After obtaining informed consent, patients were treated according to the institutional protocol (from June 11 to September 14, 2020) with dexamethasone if the patient required supplemental oxygen. Since September 15, 2020, the management protocol was changed from dexamethasone to methylprednisolone 250 to 500 mg daily for three days, followed by prednisone 50 mg orally every day for 14 days (the doce was based on management reports in SARS-CoV and the experience of these specialties in the management of fulminant Pneumonia and organized Pneumonia in the institution). All patients received ivermectin one drop/kg for three days to prevent Loeffler syndrome due to corticosteroids. The patients were not randomly selected.

As exclusion criteria, contraindications associated with corticosteroids were considered, dissent for medical management, death in the first 24 hours, patient in palliative care or with a life expectancy of less than six months. If the patient required admission to the ICU and did not receive at least two doses of the corticosteroid, was withdrawn from the cohort to follow (In the ICU protocol, only dexamethasone 6 mg is given intravenously). If the patient receives at least two doses of methylprednisolone but did not continue with prednisone, they were not included, but their outcome continued to be monitored. Patients who also received less than two days of dexamethasone treatment were withdrawn from study follow-up. Colchicine was administered by clinic protocol since July 1; this variable was included in the patients evaluated.

Upon admission, laboratory tests were performed, such as hemogram, kidney, liver function tests, arterial blood gases, lactate dehydrogenase, D-dimer, serum ferritin, and C-reactive protein. Low molecular weight heparins were prescribed to all patients to prevent thromboembolism during their hospital stay.

Pneumonia was classified as mild if it did not require supplemental oxygen, and severe was defined by the presence of hypoxemia or the need for supplemental oxygen, septic shock syndrome, or multisystem compromise. Acute Respiratory Distress Syndrome (ARDS) was defined by the presence of bilateral pulmonary infiltrates not explained by an etiology other than Covid-19 and PaFi less than 300. The arterial blood gases results during each patient hospitalization were evaluated to determine the evolution of ARDS. Cytokine Release Syndrome (CRS) was defined as ventilatory impairment plus two of the following: C-reactive protein (CRP) greater than 10 mg / dl (reference value = 0-1mg / dl), Serum ferritin greater than 1000 ng / ml (reference value = 30-400 ng / ml), D-dimer greater than 900 ng / ml (Reference value = less than 500 ng / ml). Recovery time was determined as the time until hospital discharge when each of the following criteria were met: decrease in laboratory severity markers, improvement in symptoms,

and decrease in oxygen requirement until nasal cannula or supplementary oxygen removal.

Standardization was carried out in the observation of the researcher, thus guaranteeing adequate techniques in collecting information. With these data, a database was built in Microsoft Excel, and before the analysis, it was subjected to quality control.

Once all the variables had been collected, the quantitative variables were expressed in terms of their sample median (together with their respective 95% bootstrap confidence intervals) and were compared using a two-sided Mann & Whitney hypothesis test. Qualitative variables were expressed in absolute values, along with their respective percentage values (%). Comparing the MTP vs. DXM treatment performance was carried out through the response variable 'Recovery Time', measured in days, which expresses the recovery time until discharge if at least two doses of the respective treatment have been received. This analysis was carried out through a survival analysis model with Cox regression, and it was proved that the risks were proportional, from two stages: in the first, a robust Cox regression was carried out to identify the predictor variables that explain the hazard ratio (HR), avoiding a possible interference of outlier observations in the partial likelihood estimation. In the second stage, with the significant variables ('Treatment' and 'Colchicine'), a new model was estimated for the point estimates and their 95% confidence intervals. These statistical analyzes were performed in the R statistical software through the *coxrobust* package to perform the robust Cox regression and *survival* package for traditional Cox regression.