SARS-Cov-2 / Covid-19 related-study at CHUV: Synopsis and practical aspects

Sponsor / Sponsor-Investigator	N.A
Study Title:	Impact of Nutritional Status on COVID-19 infection Outcomes
Short Title / Study ID:	INCOVO study
Protocol Version and Date:	Version 1.0 / 20.04.2020
Study category and Rationale	Retrospective multicenter observational cohort study of prospectively collected data
Clinical Phase:	Not applicable
Background and Rationale:	At present, risk factors for severe pneumonia due to SARS Coronavirus disease 2019 (COVID-19) are still under investigation. Although malnutrition is a recognized risk factor for compromised outcomes in patients with pulmonary infections, there are currently no data about the nutritional status of COVID-19 infected patients and associated outcomes. Therefore, the goal of this study is to determine the relationship between nutritional status as a potential predictor of severe forms of COVID-19 infection/pneumonia and associated outcomes
Objective(s):	To evaluate associations between nutritional status and outcomes in patients with COVID-19 infections, specifically: • The severity of COVID-19 infection • The admission rate to the Intensive Care Unit (ICU) • The rate of intubation • The rate of COVID-19 related deaths • The length of overall hospitalization • The length of ICU stay • The type of associated complications

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Outcome(s):	**Primary outcome:** The relationship between nutritional status at admission and clinical outcomes of COVID-19 infection: severe respiratory distress syndrome, mechanical ventilation, admission to ICU, death **Secondary outcomes**: • Relationship between nutritional status and: • Length of hospitalization • Length of ICU stay • Length of mechanical ventilation • Rate of nosocomial infections **Other outcomes of interest:** The relationship between nutritional status and disease outcomes will be evaluated in specific subgroups including but not limited to: • Sex • Age • Comorbidities (chronic kidney disease, hypertension, diabetes mellitus, liver disease, chronic pulmonary disorders, immunosuppressive disorders, tobacco use)

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Study design:	**The INCOVO study is a retrospective cohort study of prospectively collected data.** All the data are collected prospectively in the investigation centers. Based on institutional guidelines, a nutritional screening is performed in all the patients admitted for COVID19 infection. Moreover, the nutritional status and the listed parameters of the hospitalized patients with COVID-19 infections are followed longitudinally during the hospitalization until discharge or death. **Request for a waiver of the Informed Consent Process based on article 34 LRH:** Patients admitted at the CHUV for COVID-19 infections are expected to have a heterogenous clinical presentation with a broad spectrum of severity. Some of them will be directly admitted to the ICU with no capacity of giving informed consent, some will be rapidly discharged home before giving their informed consent, and others can provide informed consent. Using exclusively data of patients who have provided informed consent could therefore bias the study and its results. For these reasons, a waiver of the informed consent process appears to be the best option to address this dilemma. **Refusal of participation:** The project investigators certify that no personal data related to health status or any biological material is used in case of written refusal, or documented oral refusal by the patient.
Inclusion / Exclusion criteria:	All adult patients admitted to the for COVID-19 infections. **Inclusion criteria**: Male and female patients who meet the following criteria will be included in the study • Age > 18 year • Confirmed COVID-19 infection by real time reverse transcriptase polymerase chain reaction (RT-PCR). **Subjects who do not meet these criteria are excluded from the study.**

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Measurements and procedures:	**Clinical parameters collected at admission, day 8, and at discharge:** • Age, Sex • Medical history: hypertension, diabetes mellitus, immunosuppressive disorders, other comorbidities • Long term therapeutics, in particular anti-hypertensive drugs, anti-diabetic treatments, immunosuppressive drugs • Short-term therapy for symptom relief administered prior to admission (including, among others, NSAID, acetaminophen, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) • Height (cm), weight (kg), BMI (kg/m²) • Blood pressure, heart rate and rhythm, temperature • Nutritional Risk Score (Kondrup et al. 2002) • Nutritional support received before admission and during hospitalization • Albumin, prealbumin (transthyretin), creatinine, CRP, complete blood count, liver function tests • Peripheral oxygen saturation (SpO_2); PaO2/FiO2 ratio.
Study Product / Intervention:	Not applicable
Control Intervention (if applicable):	Not applicable
Number of Participants with Rationale:	Given the retrospective design of the study we did not define a definite number of participants.
Study Duration:	Time frame: from March 1st 2020 until publication of data
Study Schedule:	N.A

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Statistical Considerations:	**Sampling:** The convenience sampling method will be used because random sampling will not be feasible under the epidemic situation of the COVID-19 outbreak. **Sample size estimation**: The sample size will not be estimated based on the statistical power. We will collect as many cases as possible. **Analysis principles:** • All tests will be two-sided, the nominal level of type I error will be 5% and the confidence level for all confidence intervals will be 95%. There will be no imputing of missing values. The number of observations used in a given analysis will be reported. • Subgroup analyses will be carried out irrespective of whether there is a significant treatment effect on the primary outcome. • Analyses will be conducted with validated statistical tools. The trial flow chart of inclusion will be displayed in a diagram. The report will include the number of patients who met the inclusion criteria and the number of non-included patients. • Patients characteristics and baseline comparisons: Description and statistical inference of the patients' characteristics; nutritional parameters and laboratory findings will be presented by the disease severity and the composite endpoint. Discrete variables will be summarized by frequencies and percentages. Percentages will be calculated according to the number of patients for whom data is available. Continuous variables will be summarized by median +/- standard deviation. Statistical inference of continuous variables will be performed using a t-test or Wilcoxon rank-sum tests as appropriate. The Pearson's Chi-square test or Fisher exact test will be used, as appropriate, for categorical data. Baseline measures for all patients will be tabulated. • For the primary outcome and other outcomes, multivariable analyses will be performed. The candidate risk factors include comorbidities, treatments, age, sex, nutritional parameters and laboratory findings, and the development of complications. Other candidate risk factors that are of biological interest or clinically important, or statistically significant, could be included in the multivariable models. The sub-distribution hazard ratios with 95% confidence interval will be reported. • Subgroup analysis: Subgroup analyses will be carried out for the primary and secondary outcomes.

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Biobanking / use of existing biobank	This study does not include a biobanking process or the use of existing biobank.
Available resources (staff, budget)	This project will be a subject of a national grant application.

Schedule of Study-visits, additional data/sample collection and other non-routine assessments

Collected data	Admission	1 week	Discharge
Age	X		
Sex	X		
Medical history/ comorbidities	X		
Prior drug therapy	X		
Height (cm)	X		
Weight (kg)	X	X	X
BMI (kg/m²)	X	X	X
Nutritional risk score	X	X	X
Nutritional support received	X	X	X
Albumin	X	X	X
Prealbumin	X	X	X
Creatinine/ eGFR	X	X	X
CRP	X	X	X
Complete blood count	X	X	X
Liver function	X	X	X
Oxygen saturation	X	X	X
Outcomes			X

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