

Results. The PCA model was able to distinguish the three classes of patients' samples (positive for COVID-19, negative controls, positive controls) with an overall accumulated variance of 94.27 percent. The PLS-DA model presented the best performance (accuracy, sensitivity, and specificity of 93%, 98% and 88%, respectively). Increased levels of the biomarkers uridine (linked to glucose homeostasis, lipid, and amino acid metabolisms), 4-hydroxyphenylacetyl carnitine (metabolite from the tyrosine metabolism; probably associated with anorexia) and ribothymidine (resulting from oral and fecal microbiota alterations) were significantly associated with COVID-19.

Conclusions. Three different and updated ML-based algorithms were developed to predict COVID-19 diagnosis; PLS-DA led to the most accurate results. High levels of some metabolites were found as potentially predictors of the disease. These biomarkers should be further evaluated as potential therapeutic targets in well-designed clinical trials. These ML-based models can help the early diagnosis of COVID-19 and guide the development of tailored interventions.

PD34 Neuron-specific Biomarkers Associated With Neurological Manifestations In COVID-19: An Evidence Mapping Systematic Review

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Introduction. We aimed to map and synthesize the available evidence on neuron-specific biomarkers related to COVID-19.

Methods. A systematic review and qualitative evidence mapping synthesis was performed (PROSPERO-CRD42021266995). Searches were conducted in PubMed and Scopus, and complemented by manual search (July 2021). We included observational studies of any design assessing neurological biomarkers in adult patients (>18 years; with or without neurological comorbidities) diagnosed with COVID-19. Methodological quality of nonrandomized studies (case-control, cohorts) was assessed using the Newcastle-Ottawa Scale.

Results. Overall, 14 studies (n=485 patients) conducted in Sweden (n=4 articles, 28.5%), Germany (n=3; 21.4%), USA (n=3; 21.4%), Canada, France, Italy and Norway (n=1 study each) were included. The most reported neurological symptoms (n=13 studies, 92.8%) were headache, confusion, general weakness, loss of smell/taste, cognitive impairments and behavioral changes. Prevalent neurological conditions included encephalopathies, neuropathies, myopathies, and delirium; most critical cases presented cerebrovascular events (n=4 studies, 28.5%). Hypertension, diabetes, obesity, dyslipidemia, and chronic lung disease were the most reported comorbidities. Eight different neuron-specific biomarkers were found in primary studies: neurofilament-light chain – NfL (n=10 studies; 71.4%), glial fibrillary acidic-protein – GFAP (n=5; 35.7%), tau protein (n=5; 35.7%), neurofilament-heavy chain – NfH, S100B

protein, ubiquitin C-terminal hydrolase L1 – UCH-L1, neuron-specific enolase and beta protein-amyloid – A β (n=1 study each). These biomarkers were found both in cerebrospinal fluid and blood/plasma samples even without an evident cytokine storm. In patients with COVID-19, NfL and GFAP can act as sensitive indicators of neuroaxonal and astrocytic damages, respectively. Increased levels of NfL were significantly associated with severe COVID-19, unconsciousness and longer stay in the intensive care unit (p<0.05). Studies had an overall poor to moderate methodological quality.

Conclusions. We identified eight neuron-specific biomarkers that should be further studied as prognostic factors of COVID-19. These findings can also guide the development of targeted therapies against SARS-CoV-2. Additional well-designed clinical trials are needed to strengthen this evidence and help understand the mechanisms of neurological symptoms and sequelae after COVID-19 infection.

PD35 Mortality And Risk Factors Associated With Dialysis Patients With COVID-19 In A Brazilian Supplementary Health Service

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Introduction. Patients with chronic kidney disease (CKD) and COVID-19 are at high risk of adverse outcomes due to the presence of comorbidities. However, it is still unclear whether dialysis therapy is associated with a worse prognosis in patients infected with SARS-CoV-2. The objectives were to assess mortality and risk factors associated with a worse prognosis of these patients (e.g., age, sex, comorbidities, Intensive Care Admission [ICU] admission, and need for invasive mechanical ventilation [IMV]).

Methods. An observational, descriptive, retrospective study was conducted in the private healthcare maintenance organization (Unimed-BH) of Belo Horizonte and 33 surrounding cities in Brazil. We used data collected from the organization's database. We included adult inpatients with CKD on previous dialysis therapy who tested positive for COVID-19, from February 2020 to June 2021. **Results.** During the period, 16182 patients were admitted to Unimed-BH with a diagnosis of COVID-19. Of these, 333 (2%) had dialysis CKD. Male patients were 180 (54%), age ranged from 22.85 to 95.75 years and the mean was 60.91 years. Of the 333 patients, 109 (32.7%) were admitted to the ICU, and 56 (16.8%) required IMV. Among the 14 comorbidities analysed, the mean number of comorbidities was 6, with 93 (27.9%) dyslipidaemia, 74 (22%) diabetic, 270 (81%) hypertensive, 25 (7.5%) asthmatic, 42 (12.6%) with

chronic pulmonary disease (CPD) and 122 (36.6%) with congestive heart failure (CHF). There were 66 (19.8%) deaths, 29 (43.9%) were male, the mean age was 60.8 years, and 23 patients (34.8%) were elderly (>60 years). Among the patients who died, 55 (83.3%) were in the ICU and 46 (69.7%) on IMV. The mean number of comorbidities was 9.27 being 16 (24.2%) dyslipidaemia, 44 (66.6%) diabetic, 60 (90.9%) hypertensive, 5 (7%) asthmatic, 10 (15%) with CPD and 32 (48.5%) with CHF.

Conclusions. Dialysis patients appear more susceptible to unfavourable outcomes than the general population. Our findings are similar to those reported in the world literature which is still scarce. It is important to conduct more studies on this population.

PD36 Outcomes Of Centenaries Hospitalized Due To COVID-19 In A Private Healthcare System

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Introduction. Life expectancy is increasing worldwide. However, during the COVID-19 pandemic, people 100 years or more (centenaries) were challenged by a potentially fatal disease. We evaluated the outcome of centenaries hospitalized due to COVID-19 in a private healthcare system of Belo Horizonte/Brazil (Unimed-BH).

Methods. Administrative data were collected from the hospital database. Patients were included if they had a severe adult respiratory syndrome due to coronavirus type 2 (SARS-CoV-2) ribonucleic acid identified by quantitative real-time reverse transcriptase polymerase chain reaction (RT-qPCR) or by the International Code of Disease-10th review (ICD-10) hospitalization codes U07.1, B34.2, or B97.2.

Results. From March 1 2020 to October 31 2021, 316.4 ± 12.9 centenaries/month were registered. Eighteen hospitalizations due to COVID-19 were identified. Median age was 101.8 years (interquartile range [IQR]:100.7,103.0). Most patients were female (83%). There was a median of 6.0 morbidities per patient (IQR:5.3,7.8), range 2-12 morbidities, among 71 possible morbidities. The most described morbidities were systemic arterial hypertension (94%), dementia (61%), and congestive heart failure (61%). Median length of hospitalization was 6.5 days (IQR:3.3,8.0). No patient was dialyzed. Seven (39%) patients died during hospitalization, of whom 3 (17%)

were admitted to the Intensive Care Unit and 2 (11%) were oxygenated by invasive mechanical ventilation. No other patients were admitted to the Intensive Care Unit or invasively mechanically ventilated.

Conclusions. Although the hospitalization rate was low, the mortality rate during hospitalization was high among centenaries. Further research is required to evaluate the actual risks of centenaries to be infected by SARS-CoV-2 and the subsequent outcomes.

PD37 High-Dose Vitamin D For The Treatment Of COVID-19

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Introduction. The aim of this EUnetHTA (European Network for Health Technology Assessment) Rolling Collaborative Review on high dose vitamin D for the treatment of COVID-19 was to inform health policy at an early stage in the life cycle of therapies and to monitor ongoing studies in the format of a Living Document.

Methods. The systematic literature search was conducted in Medline, Pubmed, medRxiv, bioRxiv, arXivso, Cochrane COVID-19 Study Register, ClinicalTrials.gov, ISRCTN Registry, EU Clinical Trials Register. The first search was done in January 2021, and the last in November 2021. English and German randomized controlled studies (RCTs) investigating treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected individuals with high dose vitamin D₂, D₃ or their metabolites were included if examining mortality, length of hospital stay, viral burden, clinical progression, hospitalization rates, intensive care unit (ICU) admission, mechanical ventilation, quality of life or adverse events. Two reviewers independently screened search results and assessed risk of bias and certainty of evidence. One reviewer extracted study data, checked by another.

Results. Of the nine RCTs published to date, two investigate calcifediol, one calcitriol and six vitamin D₃. All used different dosing regimens. Disease severity and proportion of vitamin D deficiency varied between studies. Calcifediol treated patients in one study required significantly less ICU admissions than untreated patients. Vitamin D₃ in another study led to significantly more SARS-CoV-2 PCR-negative patients before day 21 than placebo. There were no other significant differences between groups. Twenty-five RCTs are ongoing, five of them with over 1,000 patients.

Conclusions. The current evidence is heterogenous regarding form and dosage of vitamin D, baseline disease severity and baseline vitamin D deficiency. There is currently no standardized/recommended level of what constitutes a (beneficial) "high dose". Most results did not show significant differences between vitamin D treated groups and no vitamin D / placebo groups. Many of the studies are very small and certainty of evidence is predominantly low or very low.