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One year follow-ups of Chilean patients with COVID-19

Submission date
29/10/2020

Recruitment status
No longer recruiting

Registration date
02/11/2020

Overall study status
Completed

Last Edited
03/01/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.

In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.

Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.

This study aims to characterise the medium to long term effect that COVID-19 has on lung function, in the Chilean population.

Who can participate?
Adults over 18 years, who have tested positive for COVID-19 in the past 3 months.

What does the study involve?
Participants will attend two appointments (at the start of the study and again after 10 months) for a lung function test, chest scan, blood test, and to answer some questionnaires about their health.

What are the possible benefits and risks of participating?
None.

Where is the study run from?
1. Hospital Clinico Regional (Chile)
2. Complejo Asistencial (Chile)

When is the study starting and how long is it expected to run for?
September 2020 to July 2021

Who is funding the study?
1. Agencia Nacional de Investigacion y Desarrollo (ANID) (Chile)
2. Chilean Government

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
NCT04457505

Protocol serial number
COVID1005

Study information

Scientific Title
Analysis of the inflammatory response and its association with potential lung damage in recovered patients with severe, moderate, and asymptomatic COVID-19.

Acronym

LungCOVID

Study objectives
A significant percentage of patients (20%) infected with COVID-19 infection is expected to report symptoms and physiological consequences after one year of follow up. Our study hypotehis is that pulmonary damage is associated with the magnitude of the production of IL-6, TNF-α, IL-1, IL-8, IL-10 by neutrophils and monocytes activated via TLR (ssRNA) and B lymphocytes activated via BCR, we also plan to evaluate the mechanism of cellular acvtivation in response to SARS-COV2 virus in different subpopulations.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 22/10/2020, Comite Etico Cientifico Servicio de Salud Bio Bio (Ricardo Vicuna 147, Los Angeles, Chile; +56996895433; carlos.villarroel@ssbiobio.cl), ref: CEC:113
2. Approved 14/09/2020, Comite Etico Cientifico Servicio de Salud Concepcion (San Martin 1436, Concepcion, Chile; +56412722745; jrsaldias@ssconcepcion.cl), ref: CEC-SSC: 20-07-26

Study design
Multicenter observational study

Primary study design
Observational

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Risk factors and prognosis of pulmonary damage in after COVID-19 infection

Interventions
Patients with a medical record of SARS-COV2 infection (mild, moderate or severe COVID-19), will be evaluated at two predefined time-points (3 months and 10 months) after infection. We will include a medical consultation, sleep and respiratory symptoms evaluation; dyspnea will be measured using the modified medical research council (mMRC), and anthropometry (height, weight, neck, waist and hip circumference). A blood test exam using EDTA tube will be extracted for biochemical and hematological evaluation.

The cohort to be studied corresponds to men and women over 18 years of age who have been diagnosed with COVID-19 and 10 controls who do not have infectious or inflammatory diseases. COVID-19 patients will be divided into 3 groups: mild, moderate, and severe symptomatic, and will be recruited from different centers located in the Bio Bio Region, Chile (Hualqui, Complejo Asistencial Dr. Víctor Ríos Ruiz, Hospital Guillermo Grant Benavente, and the PreveGen). The sample collection will take place after signing informed consent. Two tubes with EDTA and two tubes without anticoagulant will be taken at month 2 and 10 after infection. The blood sample will be used for blood count, immunophenotype, and functional tests. The serum sample will measure antibodies and systemic inflammation parameters.

Serology: The measurement of anti-SARS-CoV-2 IgG and IgM antibodies will be performed using the 2019-nCoV IgG and 2019-nCoV IgG (MAGLUMI) chemiluminescent immunoassay kits

(MAGLUMI) with the MAGLUMI 600 kit (Snibe, sens: 98.5% esp: 98.7%) and the determination of specificity by luciferase immunoprecipitation system (LIPS) against recombinant SARS-CoV-2 proteins developed in the laboratory.
Cellular Immune Response and cytokine secretion: The separation of polymorphonuclear (PMN) and mononuclear cells (PBMCs) will be carried out by density gradient centrifugation with Polymorprep and Lymphoprep (Axis-Shield) at 2000rpm / 20min. 2x105 PMNs and PBMCs will be immunophenotyped with CD16 / CD14 / CD20 / CD56 / CD3 and CD147. 10x106 PBMCs will be used for the separation of CD14 + monocytes and B cells (Miltenyi). PMN and CD14 + will be activated with viral RNA, and netosis in PMN and MHC / CD86 overexpression in CD14 + will be evaluated. B lymphocytes will be activated with BCR antigens immobilized on latex beads, and extracted antigen, polarity index, and cell area calculation will be determined by confocal microscopy. Post-activation supernatant and serum samples will be used to measure IL-12, IL-6, TNF-a, IL-1, IL-8, IL-10 (BD), and chemokines (BioLegend).

Systemic Parameters: Serum samples will be depleted (Top12 Pierce Abundant Protein Depletion Spin Columns, ThermoFisher) and analyzed by nanoUHPLC (Bruker Daltonics) coupled to a timsTOF Pro mass spectrometer (Bruker Daltonics) using otof software with DDA. The data obtained will be analyzed using PEAKS Studio X +, Scaffold 4.2, MaxQuant software, using SARS CoV-2 and Human databases compiled from UNIPROT.

Respiratory function and clinical evolution: A clinical evaluation exploring COVID-19 symptoms, anthropometry, and Respiratory function will be performed through a high-resolution computed tomography of the total thorax, post bronchodilator spirometry, lung diffusing capacity for carbon monoxide (DLCO), and six minutes walking test, JAMAR dynamometer will be used for the evaluation of frailty
General health status surveys will be delivered with the BECK depression scale, HADS anxiety and mood scale, and quality of life using the Short form-12, and dyspnea using a modified medical research council questionnaire.

Changes in sleep after COVID-19 infection: We plan to evaluate the risk of sleep disorders using the following questionnaires: Pitburghs sleep severity index, Insomnia severity index (ISI), Epworth sleepiness scale (ESS), STOP-BANG questionnaire, the Spanish version of the sleep questionnaire Satisfaction, Alertness, Timing, Efficiency, and Duration (SATED). In addition, all participants will undergo a one-night home sleep apnea test (Apnea Link air, Australia), and seven- days of actigraphy (Condors instrument, Brasil).

Circadian rhythm will be measured using a 7- days actigraphy and Morningness-eveningness questionnaire (MEQ).

Intervention Type
Other

Primary outcome(s)
Pulmonary function measured at baseline and 10 months using:
1.1. Post bronchodilator spirometry
1.2. Lung diffusing capacity for carbon monoxide (DLCO)

Key secondary outcome(s))
Measured at baseline and 10 months (unless otherwise noted):
1. Immune response will be measured using flow cytometry, complement levels
2. Structural impairment will be measured using the Total severity score (TSS)

3. Sleep disorder breathing is measured using the respiratory disturbance index (RDI), and average point sleep questionnaires (STOP-BANG, ESS, SAQLI) at baseline.
4. Circadian rhythm will be measured using the circadian function index, M10, L5, cosinor, acrophase and mesor at baseline
5. Quality of life (Short form 12)
6. Depression (Beck depression inventory)
7. Anxiety and depression (Hospital anxiety and depression scale)

Completion date
30/07/2021

Eligibility

Key inclusion criteria
Laboratory-confirmed COVID-19 infection with either real-time PCR or Next Generation Sequencing (NGS)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Patients admitted to COVID-19-negative ICU

Date of first enrolment
22/10/2020

Date of final enrolment
30/06/2021

Locations

Countries of recruitment
Chile

Study participating centre
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Sponsor information

Organisation
University of Concepción

ROR
https://ror.org/0460jpj73

Funder(s)

Funder type
Government

Funder Name
Agencia Nacional de Investigacion y Desarrollo (ANID), Project COVID1005

Funder Name
Concurso VRID iniciacion, University of Concepcion

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		19/02/2021	19/03/2021	Yes	No
Results article		23/05/2022	24/05/2022	Yes	No
Results article		29/06/2021	05/10/2022	Yes	No
Results article		29/04/2022	05/10/2022	Yes	No
Results article		14/06/2022	05/10/2022	Yes	No
Results article		20/10/2023	03/01/2024	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes