SARCO-COVID STUDY: MEASUREMENT OF MASS LOSS SKELETAL MUSCULAR IN THE HOSPITALIZED PATIENT WITH COVID-19 DIAGNOSIS

PROTOCOL:

Version 2.0

Last updated on the 12th of February of 2021 and approved by the Research Review Board on the 16th of February of 2021

	NAME	AREA
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COINVESTIGATED OR	MARCOS FRAGIEL SAAVEDRA	INTERNAL MEDICINE

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1. SUMMARY OF THE STUDY

1. Type of request:

Observational validation study of prognostic test based on clinical parameters, analytical and ultrasound.

2. Identification of promoter:

Working Group on Ultrasound of the Spanish Society of Internal Medicine (GT Eco-SEMI).

3. Study title:

"SARCO-COVID: Measurement of the loss of skeletal muscle mass in the patient hospitalized with a diagnosis of COVID-19 ".

4. Protocol Code:

MIR / HEEIZ_2021_03

5. Principal investigator. Address of your workplace:

Dr. Yale Tung Chen and Dr. Marcos Fragiel Saavedra.

University Hospital of Emergencies Nurse Isabel Zendal.

AV. Manuel Fraga Iribarne, 2, 28055 Madrid

6. Centers in which the study is planned:

It is a study that will be carried out at the Nurse Isabel Emergency Hospital Zendal (Madrid).

7. Design:

Observational validation study of prognostic test based on clinical parameters,

analytical and ultrasound.

8. Clinical Research Ethics Committee that evaluates the study:

Following the guidelines of the center, the study will be evaluated by the Ethics Committee of Clinical Research of the San Carlos Clinical Hospital.

9. Rationale

The COVID-19 pandemic is having a devastating global impact, and adults Older people who suffer from it have a higher risk of death from the disease. Nevertheless, survivors of the disease are at greater risk of suffering from diseases such as sarcopenia, more common in younger adults and with greater severity of disease.

Sarcopenia (from the Greek terms " *sarx"* (meat) and " *penia"* (poor quality)) today it is considered one of the most relevant syndromes, and the substrate of many of the health problems of the elderly and hospitalized patients, increasing by itself morbidity and mortality, and of course reducing activity and functional recovery. Of fact is deeply related to frailty, functional decline, falls, osteoporosis and different metabolic disorders (hydrocarbon intolerance) and homeostasis (thermoregulation) of the elderly. Sarcopenia is present in the 5-13% of people between 60 and 70 years old and in 11- 50% of the population over 80 years.

The diagnosis of sarcopenia has advanced in recent years by establishing itself in different consensuses homogeneous criteria that necessarily combine two elements: general loss of strength accompanied by loss of muscle mass skeletal. Today there are three consensuses for the diagnosis of sarcopenia: the international (IWGS), European (EWGSOP), and the most recent of a cohort American (FNIH). In all of them, the measurement of skeletal muscle mass constitutes one of the two diagnostic criteria.

The main methods to measure this muscle loss that are established are the imaging techniques (computerized tomography (CT), magnetic resonance imaging (MRI),

Dual energy X-ray absorptiometry (DEXA) and ultrasound.

The most common ultrasound measurements used for this purpose are thickness muscle (cm) at the point of the ultrasound path of maximum muscle thickness, the area of cross section (area calculated by the basic software at the point of maximum muscle thickness), and the angle of pennation (angle formed between the muscular fascia deep and muscle fibers). The first two measurements can be made in several long muscles, while the pennation angle is usually performed mainly in the

medial gastrocnemius muscle (internal twin). They are easy to obtain, bloodless and reproducible.

Research efforts at this point in the pandemic should focus on in the longer-term consequences of the disease, sequelae such as sarcopenia in patients who have suffered COVID-19. At the same time, doctors must be every time more aware of the condition and its measurement integrated into clinical practice. The knowledge that studies such as the one proposed will provide will allow the development of specific interventions.

The risk of sarcopenia should be considered when conducting an evaluation of the risk / benefit of the established treatment (for example, dexamethasone), and assess a multidisciplinary treatment that includes dietary contributions.

10. Main objectives

1. Main hypothesis:

- Patients admitted for COVID-19 present a progressive loss of mass muscle, both due to the inflammatory state, decreased intake, bedridden due to hospitalization and derivative of treatment (eg corticosteroid therapy).

2. Main objective:

- Quantify the loss of muscle mass in hospitalized patients in areas of Medicine Inmate diagnosed with COVID-19.

3. Secondary objectives:

- Analyze the clinical characteristics and prevalence of sarcopenia in patients included in the study.
- Analyze the thickness and cross-sectional area of the muscles in all patients rectus femoris, vastus medialis, vastus lateralis, medial calf and the angle of pennation of the medial twin.
- Analyze the correlation between ultrasound parameters and analytical parameters (nutritional, inflammatory).
- Determine the relationship between muscle loss and treatment received

(dexamethasone, methylprednisolone, prednisone).

- Determine the relationship between muscle loss and days of hospitalization or severity of illness.

11. Study population and total number of patients

Patients over 18 years of age who are admitted to the hospital and whose primary diagnosis and reason for staying is COVID-19 pneumonia. The The prevalence of sarcopenia in hospitalized patients is 15-20%. Assuming a alpha risk of 0.05 and beta risk of 0.2 in a one-sided contrast, 64 subjects are required to detect a difference equal to or greater than 20% loss of muscle mass. It has been an estimated loss to follow-up rate of 0%.

12. Schedule and expected date of completion

The study will begin in **February 2021** , with an **estimated duration of 3 months** (1 month for application, 1 month for data collection, 1 month for results analysis and preparation of articles and / or communications).

2. GENERAL INFORMATION

to. Project identification.

Protocol code: MIR / HEEIZ_2021_03

Promoter: Working Group on Ultrasound of the Spanish Society of Internal Medicine (GT Eco-SEMI).

Qualification:

"SARCO-COVID: Measurement of the loss of skeletal muscle mass in the patient hospitalized with a diagnosis of COVID-19 ".

b. Principal researchers. Work center address:

Dr. Yale Tung Chen and Dr. Marcos Fragiel Saavedra.

University Hospital of Emergencies Nurse Isabel Zendal.

AV. Manuel Fraga Iribarne, 2, 28055 Madrid

c. Research Center.

Hospital de Emergencias Nurse Isabel Zendal.

d. Ethical Committee for Clinical Research.

Following the guidelines of the center, the study will be evaluated by the Ethics Committee of

Clinical Research of the Hospital Clínica San Carlos, whose composition is already known accredited by the Ministry of Health. The study will be evaluated by the CEIC of each hospital where the study will be performed.

and. Expected duration of the project.

The study will begin in **February 2021** , with an **estimated** duration **of 3 months** (1 month for application, 1 month for data collection, 1 month for results analysis and preparation of articles and / or communications). The estimated timetable for the development of the study:

Presentation to CEIC: February 2021.

Data collection: March 2021.

Analysis of results: April 2021

Preparation of articles, communications: April 2021.

F. Reason for the project.

The COVID-19 pandemic is having a devastating global impact, and adults Older people who suffer from it have a higher risk of death from the disease. Nevertheless, survivors of the disease are at greater risk of suffering from diseases such as sarcopenia, more common in younger adults and with greater severity of disease.

Sarcopenia (from the Greek terms " *sarx"* (meat) and " *penia"* (poor quality)) today it is considered one of the most relevant syndromes, and the substrate of many of the health problems of the elderly and hospitalized patients, increasing by itself morbidity and mortality, and of course reducing activity and functional recovery. Of fact is deeply related to frailty, functional decline, falls, osteoporosis and different metabolic disorders (hydrocarbon intolerance) and homeostasis (thermoregulation) of the elderly. Sarcopenia is present in the 5-13% of people between 60 and 70 years old and in 11- 50% of the population over 80 years.

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The main methods to measure this muscle loss that are established are the imaging techniques (computerized tomography (CT), magnetic resonance imaging (MRI), Dual energy X-ray absorptiometry (DEXA) and ultrasound.

The most common ultrasound measurements used for this purpose are thickness muscle (cm) at the point of the ultrasound path of maximum muscle thickness, the area of

cross section (area calculated by the basic software at the point of maximum muscle thickness), and the angle of pennation (angle formed between the muscular fascia deep and muscle fibers). The first two measurements can be made in several long muscles, while the pennation angle is usually performed mainly in the medial gastrocnemius muscle (internal twin). They are easy to obtain, bloodless and reproducible.

Research efforts at this point in the pandemic should focus on in the longer-term consequences of the disease, sequelae such as sarcopenia in patients who have suffered COVID-19. At the same time, doctors must be every time more aware of the condition and its measurement integrated into clinical practice. The knowledge that studies such as the one proposed will provide will allow the development of specific interventions.

The risk of sarcopenia should be considered when conducting an evaluation of the risk / benefit of the established treatment (for example, dexamethasone), and assess a multidisciplinary treatment that includes dietary contributions.

g. Objectives of the study.

1. Main hypothesis:

• Patients admitted for COVID-19 present a progressive loss of mass muscle, both due to the inflammatory state, decreased intake, bedridden due to hospitalization and derivative of treatment (eg corticosteroid therapy).

2. Main objective:

• Quantify the loss of muscle mass in hospitalized patients in areas of Medicine Inmate diagnosed with COVID-19.

3. Secondary objectives:

• Analyze the clinical characteristics and prevalence of sarcopenia in patients included in the study.

• Analyze the thickness and cross-sectional area of the muscles in all patients rectus femoris, vastus medialis, vastus lateralis, medial calf and the angle of pennation of the medial twin.

- Analyze the correlation between ultrasound parameters and analytical parameters (nutritional, inflammatory).
- Determine the relationship between muscle loss and treatment received (dexamethasone, methylprednisolone, prednisone).

3. TYPE OF STUDIO AND DESIGN

to. Clinical study phase

Observational validation study of prognostic test based on clinical parameters, analytical and ultrasound.

b. Definition of study population

Patients over 18 years of age who are admitted to the hospital and whose primary diagnosis and reason for staying is COVID-19 pneumonia. For a 95% confidence interval, with a precision level of 3%, an estimated loss in

about 3% of muscle mass in COVID-19 patients for an admission less than 10 days, we hope to recruit 124 patients. A loss to follow-up rate has been estimated 0%.

Subjects will be followed up during hospitalization and one month after the time of recruitment. The 30-day follow-up will be done by reviewing the history clinic, and a telephone contact would be made.

After signing the Informed Consent, the parameters included in the Data Collection Notebook, included in Annex I.

All examinations will be labeled by a unique code, the history number clinic and archived in digital format.

c. Inclusion and exclusion criteria.

Patients who meet the following criteria will be included:

- Over 18 years old, men or women.
- Main diagnosis is pneumonia due to COVID-19

- Subjects who, after having received the information on the design, the purposes of the project, the possible risks that may arise from it and that in any moment they can deny their collaboration, verbally grant their consent to participate in the study.

The exclusion criteria to participate in the study are:

- Refusal of the patient to participate in the study.
- Present a malignant neoplasm in active phase except Ca spino- or basal cell in local stage
- Clinical situation of agony.
- Amputation of limb (s).

d. Origin of the data:

The data will be collected prospectively.

and. Schedule and expected date of completion:

The study will begin in **February 2021** , with an estimated duration **of 3 months** (1 month for application, 1 month for data collection, 1 month for results analysis and preparation of articles and / or communications).

and. Sample size:

Patients over 18 years of age who are admitted to the hospital and whose primary diagnosis and reason for staying is COVID-19 pneumonia. For a 95% confidence interval, with a precision level of 3%, an estimated loss in about 3% of muscle mass in COVID-19 patients for an admission less than 10 days, we hope to recruit 124 patients. A loss to follow-up rate has been estimated 0%.
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clinic, and a telephone contact will be made.

Four. V ARIABLES IN EVALUATION

Data to collect:

* PRIMARY VARIABLE:

to. Variables related to ultrasound:

To collect these variables, the GE VENUE will be used, the linear probe will be used (5.5–7.5 MHz) (General Electrics Healthcare, Madrid, Spain).

All patients will undergo a muscle ultrasound upon admission to the center and prior to upon discharge, using the usual muscle sweep technique. The ultrasound will be performed on the rectus femoris, vastus medialis, vastus lateralis and medial calf muscles. They will be measured:

- Muscle thickness in its cross section (in mm), in the plane of maximum thickness

in longitudinal sweep

- Cross-sectional area (in cm^2) in the plane of maximum area in the scan longitudinal

- Angle of penation (in degrees) of the medial twin, using the base of the angle the deep muscle fascia and as an angle the maximum inclination of the you muscle mass.

This exam will be carried out by 5 experienced physicians according to the criteria of the ACEP (American College of Emergency Physicians) and who carry out more than 10 studies ultrasounds per week and at least 3 years of experience in the performance and interpretation of ultrasound examinations. A reliability study will not be conducted given the limitation in the time and current healthcare pressure.

In addition, to avoid the possible bias that inter-operator variability would suppose in these circumstances, the research team was provided with a training program and designed internal training consisting of:

- Theoretical course on basic, systematic musculoskeletal ultrasound, medication, etc.

- Practical seminars in which an ultrasound machine and healthy models will be used to your measurement.
- Supervised practical training with real hospital patients until assessing an adequate measurement of at least 5 patients.
- The team of 5 doctors adequately trained in this technique were specific to this trial to avoid protocol deviations and any other form of interoperator variability.

* SECONDARY VARIABLES:

to. Demographic variables:

- Age. Sex.

b. Clinical variables:

- Symptoms and time of evolution.

- Usual treatments.

- Previous illnesses.

- Barthel scale prior to admission and discharge.

c. Variables related to physical examination:

- Blood pressure (systolic, diastolic), heart rate (HR), respiratory rate (FR), oxygen saturation (SO2), Temperature (Tº).

d. Analytical and image variables:

- Upon arrival: blood count (Hb and leukocytes - Neutrophils and Lymphocytes), biochemistry (creatinine, urea, CRP, AST, ALT, IL-6) and arterial blood gas (pO2, pCO2, lactate, pH). In the pertinent indications, it will be collected if available: Procalcitonin, CK, LDH, NT-ProBNP, D-Dimer, Troponin I.

- Control analysis: Hemoglobin, leukocytes, lymphocytes, Albumin, prealbumin, Total proteins, Calcemia, Phosphataemia, Ferritin, Vitamin D, Folic Acid, Vitamin B12, Creatinine, Cholesterol, Triglycerides.

- Chest X-ray and / or chest CT.

and. Nutritional Variables:

- o **Current weight and height** : if it cannot be measured, self-reported.
- o **Recent weight loss**
- o Measurement of **muscle strength** , using **dynamometry** (average of 3 measurements)

in dominant arm.

- o **Circumference of the calf.**
- o Body composition using **impedance** measurement (BIA) that estimates the **mass muscular skeletal muscle.**
- o Pass the **SARC-F questionnaires** , as a universal screening method: 5 questions in less than 1 minute.
- o Establish criteria for malnutrition (**MUST questionnaire**) and **frailty** (criteria Friend).

Minnesota Brief Physical Activity Questionnaire

F. Treatment-related variables:

- Treatment according to clinical practice: drug, duration and dose.

g. Variables related to evolution:

- Degree of functional recovery at 30 days (Barthel scale) and quality questionnaire life (EuroQol-5D). Adverse events or complications during the next 30 days of admission. Any event will be considered **complications after 30 days** unexpected event requiring treatment or medical attention, within 30 days of the episode (whether hospitalized or not), generally clinical worsening, readmission or mortality.

5. METHODOLOGY

to. Selection of study cases

Patients over 18 years of age who are admitted to the Hospital and whose primary diagnosis is COVID-19 pneumonia.

For this, patients who meet the criteria of inclusion. After granting verbal consent, the parameters included in the Data Collection Notebook, included in Annex I.

All examinations will be tagged with a unique code and history number
Hospital clinic, and archived in digital format.

b. Information collection:

Once the patient has been recruited, the objectives and procedures of the study will be explained,
He will provide the information sheet and you will be asked for your informed consent.

Then, according to the usual clinical practice, an evaluation will be carried out
clinic that includes anamnesis, physical examination and extraction of laboratory tests, as well as other
complementary tests that are considered appropriate for the patient's situation. A) Yes
Also, at the time of the first assessment, a muscle ultrasound of the
lower limbs, repeating it prior to discharge. All the variables collected will be collected
in section 4 of this protocol.

The duration of the follow-up will be 30 days, the presence of complications in
this time, by reviewing the medical history, as well as functional recovery
(Barthel scale), and will be contacted by telephone, to pass a quality questionnaire of
life (EuroQol-5D).

Any unexpected event that requires treatment or
medical care, including mortality. Any undesirable effects will be collected
observed, during hospitalization, and during follow-up for the next 30 days.

* *The patient's CRF will include:*

Demographic variables, physical examination, laboratory findings, related to the
diagnosis, treatment, as well as clinical evolution (see Annex I).

* *Usual intervention:*

According to the usual management of COVID-19 infection, individualizing its use
at the discretion of the responsible physician.

It must be taken into account that **the use of ultrasound will be carried out according to the current international recommendations (detailed below), and that strict measures will be followed to avoid contagion, it does not imply under any circumstances delay in the administration of treatment.**

MECHANISMS TO AVOID CONTAGION

Unlike the description of the ultrasound findings, the protocol of disinfection in the exploration is intended to be maximum, since we would not be providing any benefit if we were in this way helping to spread the virus.

The contagion probability has been evaluated and compared with the X-ray of chest (crowded waiting rooms, patients transferred by relatives who can infect, difficulty to move), or even in front of a stethoscope or pulse oximeter. The ultrasound probe does not have a contact surface greater than the stethoscope, and the disinfection measures to be taken with the probe will be in any case those marked by the Ministry.

For the patient: mask and gloves, exclusive room isolated from the rest for address suspected COVID. At the entrance of the hospital, a person awaits patients who come on suspicion, they are provided with a mask and gloves. Then they enter the consultation. (Within the usual protocol designed by the center)

For personnel: FFP2 mask, PPE, gloves; following the recommendations given from Primary / Preventive Care.

For the ultrasound system (including probe cable): wash first with enzymatic detergent and then with alcohol 96%; before and after; for all ultrasound except the probe.

For the probe: virucidal 99% alcohol-free (Clinell®).

In addition, an ultrasound can optionally be performed covering the probe

with a condom, which will be discarded after assessing each patient. The quality of the image does not deteriorate and is one more protective measure for the probe, completely minimizing the risk of contagion; although it is an expense extra.

The probe support area on the ultrasound machine will be cleaned with detergent enzymatic and alcohol 96%. It will also be covered with a glove, which dispose of after each patient in such a way as to avoid as much as possible contact between the probe handle and the ultrasound machine.

After each day, the ultrasound machine will also be washed with bleach diluted with water (1:50), following the recommendations of the Ministry of Health.

PROCEDURE FOR CLEANING THE MATERIAL ECOGRAPHY

The ultrasound machine will be at all times in the consultation reserved for attention to suspected COVID.

Before carrying out: hand washing with soap and water. Will wash first with enzymatic detergent (optional) and then with alcohol 96% all the surface of the ultrasound system including cable and ultrasound support area, except for the probe. The tube will be cleaned with Clinell®.

During the procedure: the examination will be done with the “dirty” hand in contact with the patient avoiding touching the rest of the ultrasound machine to the extent the possible. The other hand (“clean”) will be left to handle the ultrasound machine (amplitude, gain, zoom, ...).

After completion: it will be washed again with 96% alcohol. Washing hands.

Wait at least until the ultrasound machine has dried after the disinfection procedure before restarting the process.

c. Practical considerations:

INCLUSION PHASE:

All patients admitted to HEEIZ hospital will be selected. I know will verify that they meet the inclusion criteria and none of the exclusion criteria, and they will be informed of the objectives and procedures of the study, giving them the information sheet and requesting their verbal informed consent.CRF

COMPLIANCE:

The diagnostic and therapeutic management of the patient will be carried out according to clinical practice usual, filling in the CRF all demographic variables, physical examination, diagnostic, ultrasound and follow-up variables that appear in section 4 of this protocol.

FOLLOW-UP OF PATIENTS:

Patients will be followed up to day 30 after inclusion in this study (well, after hospital discharge or until the day of death if it occurs before day 30), in order to evaluate the main variables. The follow-up will be done by reviewing the electronic medical record, and will be contacted by phone.

ANALYSIS OF RESULTS:

Once the follow-up of the last patient has been completed, the statistical analysis of the results and the final study report will be prepared.

FINANCING:

This is an unfunded study sponsored by researchers. The promoter (Group of GTEco-SEMI ultrasound) will provide the necessary material (information, notebook, methodology and logistics) to carry out the study.

d. Schedule:

The total duration of the project is estimated at **03 months** .

	FEBRUARY	MARCH	APRIL	APRIL
Authorization request by the CEIC and classification by AEMPS	•			
Identification of patients		•		
Data Collect		•		
Study database		•		
Statistic analysis			•	
Elaboration of the report final				•

Table 1. Study development

and. Statistic analysis

The variables will be expressed by total numbers and percentages for the variables categorical, and central values with measures of dispersion (mean and standard deviation / median and interquartile range if not normal distribution) for quantitative variables.

For the comparisons, the following statistical tests will be carried out: Chi ^{2} and obtaining of the odds ratio with 95% confidence intervals (for the comparison of variables qualitative); Student's t (and Spearman test) (to obtain the difference of means / ranges); and Pearson's R (to determine the correlation between the variables quantitative). The data will be analyzed using SPSS statistical analysis software. 20.0.

Data in absentia will not be charged and will be left as lost.

6. A SPECTS ETHICAL

to. General and particular rules for researchers.

Researchers will strictly adhere to the provisions of this protocol and the good clinical practice, fully completing the data collection sheets.

Following the guidelines of the center, the study will be evaluated by the Ethics Committee of the Research with drugs from the San Carlos Clinical University Hospital. The current revision of the Helsinki declaration is the accepted basis for ethics in human research, and must be scrupulously followed and respected by all persons involved in said research.

b. Informed consent.

All patients will be informed, before starting the study, of the objectives, procedures and discomforts and risks of the study according to a specific information sheet. Blade Informed consent information appears in the annex to this protocol.

c. Benefit-risk assessment for research subjects:

As it is a study that does not modify healthcare practice, it does not imply any added risk for patients. Ultrasound is a harmless technique, it requires the application of a gel water-soluble conductor, and can cause minor discomfort such as pain from the pressure exerted, redness or a small bruise.

d. Security and confidentiality devices.

The information disseminated and obtained by the implementation of this study is considered confidential and should be treated as such at all times.

Only the investigators will know the data (patient initials and history number) that can identify patients. Initials and patient record number will be separated of the rest of the notebook, and will not be entered in the study database. The patient will be identified by a numerical code in order to respect the confidentiality of the Personal data of patients, as established by Organic Law 3/2018, of December 5, of Protection of Personal Data and guarantee of digital rights. The collection and management of samples will follow the indications established in Law 14/2007, of July 3, on research biomedical.

In order to guarantee the confidentiality of the study data, they will only have access to the

The researcher and his team of collaborators, the Ethics Committee for Clinical Research, the relevant health authorities and the promoter's representatives.

The researcher agrees to collect, record and report the data in a reliable way and correct, responding to its updating and quality before the appropriate audits.

Patients will be identified by a number, both in the e-CRF and in the database. I know will guarantee the total confidentiality of the data, in particular the identity of the participants.

The data of the researchers and the study will be entered and processed in a proprietary file of PROMOTOR that will be responsible for the file before the Spanish Agency for Data Protection (AEPD). It will be ensured that they will be treated in accordance with the provisions of the Protection Law of Personal Data, exclusively for the development and good end of the study.

When personal data belonging to the Researcher and / or patients is archived or processed, The Promoter will take the appropriate measures to protect and prevent access to this data, for part of unauthorized third parties.

Any data required by the protocol may be subject to audits by the promoter, independent organizations and / or competent authorities, but the confidentiality of the data it will always be an indispensable condition.

and. Interference with the doctor's prescription habits.

In no case will the study interfere with the care tasks, nor will it modify the doctor's prescription habits.

F. Pertinence of exploration by IP

The IP is certified for the performance of Clinical Ultrasound by WINFOCUS and SEMES, SEMI, in addition to having the Certification in Echocardioscopy by SEMI-SEC, which justifies its aptitude to carry out this research project.

7. BIBLIOGRAPHY

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ANNEX I:

DATA COLLECTION NOTEBOOK

CRF SARCO-COVID: Measurement of Skeletal Muscle Loss

in hospitalized patients diagnosed with COVID-19

PATIENT ID
AGE AND SEX
Comorbidity

CARDIOP MY AUNT?

PERSONAL PREVIOUS ETV OR FAMILY?

HTA / DM ?

IRC?

Obesity?

NEUMOPA AUNT?

IMMUNOSUPPRESSION?

Others?

Usual treatment

Main symptoms and time of evolution

DYSPNOEA OTHERWISE

FEVER OTHERWISE

ASTENIA / MIALGIAS OTHERWISE

DIARRHEA / NAUSEA OTHERWISE

COUGH OTHERWISE

PAIN THORACIC OTHERWISE

WEIGHT LOSS> 5% IN 3 MONTHS OTHERWISE

TA
SO2
T°

FC
FR
Weight (kg)

Size (cm)	**Weight loss>**
Circumference waist	**Circumference calf**
Dynamometry B. dominant (mean of 3)	

Bioimpedanceometry

TBW: total body toilet	**MM: muscular mass**
FFM: fat free mass	**FM: fat masS**
BCM: body cell mass	

Hb	**Leucos (Nt, L)**
Creatinine	**Urea**
AST	**ALT**
LDH	**Lactate**
pO2	**pCO2**
pH	**CK**
D-dimer	**procalcitonin**
PCR	**Troponin I**
Nt Pro-BNP	**IL-6 / Ferritin**

Albumin	**Prealbumin**
Total proteins	**Calcemia**
Phosphataemia	**Vitamin D**
Folic acid	**B12 vitamin**
Cholesterol	**Triglycerides**

FEMORAL STRAIGHT D ENTRY		**INTERNAL VAST D AL ENTRY**		**EXTERNAL VAST D AL ENTRY**	
Thickness maximum (mm)	**Sectional area (cm2)**	**Thickness maximum (mm)**	**Sectional area (cm2)**	**Thickness maximum (mm)**	**Sectional area (cm2)**

FEMORAL STRAIGHT I TO HIGH		**INTERNAL VAST I TO HIGH**		**EXTERNAL VAST I TO HIGH**	
Thickness maximum (mm)	**Sectional area (cm2)**	**Thickness maximum (mm)**	**Thickness maximum (mm)**	**Sectional area (cm2)**	**Thickness maximum (mm)**

INTERNAL TWIN D AT INCOME			**INTERNAL TWIN I ON ADMISSION**		
Thickness maximum (mm)	**Sectional area (cm2)**	**Angle of Penalty (in degrees)**	**Thickness maximum (mm)**	**Sectional area (cm2)**	**Angle of Penalty (in degrees)**

INTERNAL TWIN D ALTA		**INTERNAL TWIN I ALTA**			
Thickness maximum (mm)	**Sectional area (cm2)**	**Thickness maximum (mm)**	**Thickness maximum (mm)**	**Sectional area (cm2)**	**Thickness maximum (mm)**

ATB	**Anti-IL 6**	**Corticosteroids (days and max dose)**	**Corticosteroid bolus (dose and days)**	**Anticoagulant**
O2 (modality)	**NIMV**	**VM**	**You go amines.**	**ECMO**

BARTHEL PREVIOUS ON ENTRY (date)	**WORST BARTHEL DURING ADMISSION (date)**	**BARTHEL AL HIGH (date)**	**BARTHEL AL MONTH OF RECLUT. (date)**

SARC-F	**MUST**	**FRAGILITY**	**MINNESOTA**

Loss Follow-up Mortality **Adverse Event (description)**

MINNESOTA REDUCED

FRIED AND WALSTSON CRITERIA

DYNAMOMETRY

MIR / HEEIZ_2021_03 protocol *Version 2.0. February 2021*

ANNEX II:

COMMITMENT OF CONFIDENTIALITY OF THE INVESTIGATORS TO THE CEIC

COMMITMENT OF THE INVESTIGATORS AND CONFIDENTIALITY

Dr. Yale Tung Chen and Dr. Marcos Fragiel Saavedra.

Principal investigator. Principal Co-Investigator

University Hospital of Emergencies Nurse Isabel Zendal.

AV. Manuel Fraga Iribarne, 2, 28055 Madrid

It states:

- Who know and agree to participate as principal investigators in the study titled: " SARCO-COVID: Measurement of Skeletal Muscle Loss in the hospitalized patient diagnosed with COVID-19 "
- That they undertake that each subject is treated and controlled following the established in the protocol approved by the Research Ethics Committee.
- That it will respect the ethical requirements and standards applicable to this type of study
- That they undertake to maintain strict confidentiality of the data of personal character from the source.
- That the results obtained from the study may be disclosed in Congresses, scientific meetings and publications, always safeguarding the confidentiality of personal data.

In Madrid to **27** of **January** 2021

Dr. Yale Tung Chen ***Dr. Marcos Fragiel Saavedra***

Principal investigator Principal Co-Investigator

ANNEX III: INFORMATION SHEET AND INFORMED CONSENT

INFORMATION SHEET AND INFORMED CONSENT

Study Title: SARCO-COVID: Measurement of Muscle Loss skeletal structure in hospitalized patients diagnosed with COVID-19

PROMOTER: Working Group on Ultrasound of the Spanish Society of Medicine Internal

PRINCIPAL RESEARCHERS: Dr. Yale Tung Chen and Marcos Fragiel Saavedra

CENTER: Hospital de Emergencias Nurse Isabel Zendal.

INTRODUCTION

We are writing to you to inform you about a research study in the that you are invited to participate. The study has been approved by the Ethics Committee of Clinical Research of the Hospital de Emergencias Nurse Isabel Zendal.

Our intention is only that you receive the correct information and enough for you to evaluate and judge whether or not you want to participate in this study. For Please read this information sheet carefully and we will clarify any doubts you may have. may arise after explanation. In addition, you can consult with the people who consider appropriate.

BACKGROUND AND OBJECTIVES

On March 11, the World Health Organization (WHO) declared the state of "global pandemic" caused by coronavirus 2, when Asia was already infected and in Europe the situation began to unleash.

The spread of COVID-19 began around 11 months ago and today you could say that it already covers the entire planet. At the beginning of 2020, the different

Health alerts warned of a highly contagious disease that caused very disparate pictures, aggravated by previous comorbidities and becoming life-threatening in situations of immunodeficiency and serious pathologies pre-existing.

Patients suffering from this disease are at risk, both for the disease, as by the treatment that is prescribed, they have an increased risk of suffering loss of muscle mass, although we still do not know quantitatively the impact that has this process.

Clinical ultrasound is an imaging test performed by the doctor responsible for your care, which provides us with information about the state of your muscles and your muscle mass. As for risks, this is a safe use-based test ultrasound that have not shown harmful effects in humans.

VOLUNTARY PARTICIPATION

You should know that your participation in this study is voluntary and that you can decide not participate or change your decision and withdraw consent at any time without that this entails negative consequences for you in your future care relationship.

GENERAL DESCRIPTION OF THE STUDY

124 patients with coronavirus pneumonia will participate in the study (COVID-19), of both sexes and of legal age, who enter this center.

If you decide to participate, in addition to treatment, imaging tests or blood samples that are drawn in routine clinical practice for diagnostic and therapeutic treatments, a muscle ultrasound will be performed.

The study consists of performing muscle ultrasounds to patients in the internal medicine service. The development of the test will last 5 minutes approximately and we will need access to the clinical data of the study participants to complete the outcome assessment.

A muscle ultrasound of the lower limbs will be performed upon admission and prior to discharge, by the investigating physicians, including an assessment muscle of the lower extremities. Within a month of your admission, it could be contacted by telephone by the research team to make some brief questions about your condition.

In addition, a nutritional assessment will be performed by a team of endocrinologists of the center, with 3 questionnaires to know their level of physical activity, frailty and malnutrition. It will be done as part of this assessment: weight, height,

measurement of muscle strength, measurement of calf circumference and a measurement of body composition by impedance measurement (estimates the muscular body composition by means of a pair of electrodes which are connected to a machine that processes information)

It will not delay or modify in any case the treatment to be received.

All the procedures that will be performed will be the usual ones for the diagnosis and treatment of your COVID-19 infection.

BENEFITS AND RISKS DERIVED FROM YOUR PARTICIPATION IN THE STUDY

You will not have any health benefits from participating in this study.

Ultrasound is a harmless technique, it requires the application of a gel water-soluble conductor, and may cause minor discomfort such as pressure pain exerted, redness or a small bruise.

If you have questions or need clarification about these terms or expressions do not hesitate to consult with the members of the research team.

PUBLICATION OF RESULTS

The results of the study will be made public, according to one of the channels accepted by the scientific community, maintaining in any case the confidentiality and right of the participants.

CONFIDENTIALITY

The treatment, communication and transfer of personal data of
All participating subjects will comply with the provisions of Regulation (EU) 2016/679 of the European Parliament and of the Council of April 27, 2016 Protection Data (RGPD).

Both the Center and the Promoter are responsible respectively for the processing of your data and undertake to comply with the protection regulations of data in force. The Research Ethics Committees, the representatives of the Health Authority in inspection matters and the personnel authorized by the Promoter, They can only access to verify personal data, procedures of the clinical study and compliance with the rules of good clinical practice (always maintaining the confidentiality of the information).

In accordance with the provisions of the aforementioned legislation, you can exercise the

rights of access, rectifica on, opposition and deletion of your data, for which you should talk to your study doctor. In addition to the rights you already know (access, modification, opposition and cancellation of data) can now also limit the treatment of data that are incorrect, request a copy or transfer to a third (portability) the data that you have provided for the study. To exercise your rights, contact the study principal investigator Dr. Yale Tung Chen or the Delegate of Data Protection of the Jose Manuel Laperal González center [tel. 91426998 / e-mail: protecciondedatos.sanidad@madrid.org]

We remind you that the data cannot be deleted even if you stop participating in the trial to ensure the validity of the research and comply with legal duties and drug authorization requirements. You also have the right to address the Data Protection Agency if you are not satisfied.

Both the center and the Promoter are responsible respectively for the processing of your data and undertake to comply with the protection regulations of data in force. The data collected for the study will be identified by means of a code, so that information that can identify you is not included, and only your

study doctor / collaborators may relate said data to you and your clinic history. Therefore, your identity will not be revealed to anyone except to health authorities, when required or in cases of medical emergency. The Research Ethics Committees, representatives of the Health Authority in inspection matter and the personnel authorized by the Promoter, may only access to verify personal data, clinical study procedures and the compliance with the rules of good clinical practice (always maintaining the confidentiality of information).

The Researcher and the Promoter are obliged to keep the data collected for the study at least up to 25 years after completion. Subsequently, his Personal information will only be kept by the center for the care of your health and by the sponsor for other scientific research purposes if you had granted your consent to do so, and if permitted by law and applicable ethical requirements.

If we transfer your encrypted data outside the EU to the entities of our group, service providers or scientific researchers who collaborate with us, the participant's data will be protected with safeguards such as contracts or other mechanisms by the data protection authorities.

QUESTIONS AND INFORMATION

In case of doubts about the study or your rights, you can contact Dr. Yale Tung Chen or any of the doctors on the research team at the Telephone number of the doctor responsible for the HEEIZ (651.630.523), available 24 hours a day.

Volunteer signature:

Name:
Date:

For the research team:

Name:
Date: