Evaluation of the validity and reliability of muscle ultrasound in the detection of undernutrition

SAURON

Version n°5 of 22/09/2022

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Interventional research involving the human being with minimal risk and constraint

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PROTOCOL VERSION HISTORY

Version	Date	Reason for the change
1	08/03/2022	Modification following a request for a supplement for submission to the PPC
2	22/03/2022	Modification following the suspensive opinion of the CPP
3	10/05/2022	Modification following the suspensive opinion of the CPP
4	07/07/2022	Modification following the suspensive opinion of the CPP
5	22/09/2022	Modification following the suspensive opinion of the CPP

RESEARCH SUMMARY

Manager	Forcilles Hospital-Cognacq-Jay Foundation
Person who directs and supervises the research	Aymeric LE NEINDRE
Title	Evaluation of the validity and reliability of muscle ultrasound in the detection of undernutrition
Acronym	SAURON
Protocol version	n°5 of 22/09/2022
Rationale / context	In France, the prevalence of undernutrition in hospitalized patients varies from 30 to 50%. Undernutrition is strongly associated with a decrease in the patient's functional abilities and an increase in morbidity and mortality and healthcare expenses. In 2019, the Global Leadership Initiative on Malnutrition (GLIM) published an international consensus report on diagnostic criteria for undernutrition (1). The diagnostic criteria are numerous, and include etiological criteria such as reduced food intake; an inflammatory setting; symptoms such as anorexia, fatigue; phenotypic criteria such as weight loss, body mass index (BMI), fat to lean mass ratio, fluid retention, and muscle function. Muscle mass is described as a major diagnostic criterion, since it is on the one hand a direct indicator of protein catabolism related to undernutrition, but also a reflection of functional impairment in the patient, as it is directly associated with functional capacities, autonomy and prognosis. Ultrasound is a reproducible method of muscle assessment. It allows the evaluation of muscle thickness or cross-sectional area of a muscle, the reduction of which, a marker of atrophy, is strongly correlated to its loss of strength and to reference measurements. In addition, ultrasound can be used to assess muscle quality, particularly by evaluating the echogenicity of the muscle. The echogenicity increases when the muscle is altered, linked to the presence of fatty infiltrate and fibrous tissue. The use of ultrasound in the evaluation of the patient's nutritional status, as a tool for assessing muscle function, is developing in the ICU and is associated with an increase in the patient's comorbidities. Studies remain limited to a few patient populations, do not report clear cut-off values to define muscle pathological status, and require more precise definition of ultrasound measurement protocols. We hypothesize that muscle ultrasound is reliable and valid in the evaluation of muscle function during the screening of undernutrition in a population of patients hospitalized in diabetology-obesity, pneumology, oncology and gastro-nutrition, under 70 years old.
Main Objective	To evaluate the reliability and validity of muscle ultrasound in the context of screening for undernutrition in hospitalized patients
Secondary objectives	- Evaluate the correlation of muscle ultrasound with standard measures of muscle function; - Compare the diagnostic ability of muscle function assessment tools on undernutrition; - Evaluate the association of muscle ultrasound measurements with patient morbidity and mortality: • Length of hospitalization; • Mortality rate; • Autonomy at discharge.

Research Diagram	Prospective, monocentric, interventional cohort study with minimal risks and constraints falling within the scope of article L.1121-1 of the Public Health Code.
Inclusion criteria	- Admitted in short stay and follow-up care and rehabilitation of diabetes-obesity, pneumology, oncology and gastro-nutrition; - Age between 18 and 70 years at inclusion; - Affiliation with a social security system or beneficiary of such a system ; - Oral, free, informed and express consent of the patient or his/her family member.
Non-inclusion criteria	- Impossibility of performing bioelectrical impedancemetry ; - Patient refusal to participate in the study; - Pregnancy (a pregnancy test should be performed if in doubt); - Breastfeeding woman; - Person subject to a safeguard of justice measure ; - Patient under guardianship or curatorship; - Patient in care limitation; - Sampling in the ineligible study group.
Primary endpoint	The primary endpoint is the diagnostic accuracy (sensitivity, specificity) of muscle ultrasound in undernutrition in patients hospitalized in short-stay and follow-up care and rehabilitation of diabetes-obesity, pneumology, oncology and gastro-nutrition.
Secondary endpoints	Secondary endpoints will be: - Correlation measurements of muscle ultrasound with: • Bioelectrical impedancemetry; • Handgrip; • Walking speed. - Comparison of the diagnostic accuracy in undernutrition of muscle ultrasound with those of : • Bioelectrical impedancemetry; • Handgrip; • Walking speed. - Measure of association of muscle ultrasound measures with patient morbidity and mortality: • Length of hospitalization (days); • Mortality: proportion and date of occurrence of death among patients included during hospitalization; Autonomy at discharge: Activities Daily Living (ADL) score
Comparison group	Patients hospitalized in short stay and follow-up care and rehabilitation of diabetes-obesity, pneumology, oncology and gastro-nutrition.
Number of subjects needed	118
Expected number of centers	1
Duration of the research	21 months
Statistical analysis of the data	Inter and intra-examiner reliability will be assessed by calculating the intra-class correlation coefficients. Validity will be assessed by calculating the areas under the ROC curve (Receiver Operating Characteristics) and the calculation of sensitivities, specificities, positive and negative predictive values. The gold standard test for diagnosing impaired muscle function is bioelectrical impedance. Descriptive statistics will use the usual statistical tests after verification of the distribution of the variables (Chi2 or Fisher's test, t-test, anova or their non-parametric equivalents Wilcoxon and Kruskal-Wallis tests). The variables will be compared by the appropriate tests according to the type of variables (quantitative or qualitative) and their distribution.

Expected benefits	The results of this study will make it possible to verify whether ultrasound is a reliable and valid tool in the evaluation of peripheral muscle function in the context of screening for undernutrition. On the other hand, they will allow us to propose threshold values for the alteration of muscle function and to provide information on the ultrasound characteristics of the muscle in the undernourished patient and their association with the prognosis of the patient. The different tools could lead to a different estimation of the reduction of muscle mass and therefore a different prevalence of undernutrition. The results of our study will help to evaluate this and to guide professionals in the choice of tools to evaluate muscle function.
Source of funding	Forcilles Hospital-Cognacq-Jay Foundation
Independent Supervisory Committee planned	No

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1 Rationale for the research

1.1 Epidemiology and morbidity of undernutrition

Undernutrition, whether related to disease, poverty, hunger, war or natural disasters, affects more than one billion people worldwide (1). In France, an empirical estimate suggests a prevalence of undernutrition among hospitalized patients of about 2 million (2) or 30 to 50% (3). It should be noted that undernutrition is very common in and out of hospital. It is widely accepted that undernutrition can be caused by a deficit in nutrient intake or malabsorption. However, it is now known that the inflammatory state present during illness is associated with undernutrition (1). The inflammatory state promotes anorexia and decreased intake but also increases basal metabolic rate and muscle catabolism. Undernutrition is marked by a decrease in all markers of muscle mass (1). It is thus strongly associated with a decrease in the patient's functional capacities and an increase in morbidity and mortality and in health care costs (1,4-6).

1.2 International consensus on the definition of undernutrition

In 2019, the Global Leadership Initiative on Malnutrition (GLIM) published an international consensus report on diagnostic criteria for undernutrition (1). The diagnostic criteria are numerous, and include etiological criteria such as reduced food intake; an inflammatory context; symptoms such as anorexia, fatigue; phenotypic criteria such as weight loss, body mass index (BMI), fat to lean mass ratio, fluid retention, and muscle function. GLIM has chosen to select the most relevant criteria among the etiological and phenotypic criteria:

- Etiological criteria: reduced food intake and inflammatory state of the patient;
- Phenotypic criteria: weight loss, BMI, and reduced muscle mass. The presence of at least one etiological criterion and one phenotypic criterion is mandatory to make the diagnosis of undernutrition (Table 1).

Table 1: Diagnostic criteria for undernutrition

Phenotypic criteria			Etiological criteria	
Weight loss (%)	**Low BMI (kg/m)²**	**Reduction in muscle mass**	**Reduction of food intake or absorption**	**Inflammato ry situation**
> 5% in the last 6 months or > 10% beyond 6 months	< 20	Reduction evaluated by a validated measurement technique*.	≤ 50% of food intake > 1 week or any reduction > 2 weeks, or any gastrointestinal pathologies or symptoms impacting assimilation or absorption	Acute pathologies or certain chronic or malignant pathologies
≥ 5% in 1 month or ≥ 10% in 6 months or loss ≥ 10% from usual weight prior to start of the disease	< 18,5	Quantified Reduction* * (QR)	Same as	Same as

* Suggested methods of measuring muscle mass: Dual X-ray Absorptiometry (DEXA); bioelectrical impedancemetry; CT or MRI. In the absence of these tools, anthropometric measurements such as arm or leg circumference can be used. Grip strength measurement is considered a complementary measure. The threshold values are those of Cruz et al (7).

** Methods of measuring muscle mass proposed by the HAS:

Muscle mass is described as a major diagnostic criterion, since it is on the one hand a direct indicator of protein catabolism related to undernutrition, but also a reflection of functional impairment in the patient, as it is directly associated with functional capacities, autonomy and prognosis (1). Different measurement tools are suggested, such as bioelectrical impedancemetry, ultrasound or magnetic resonance imaging, leaving the choice of tool to the clinicians, depending on experience and local resources. Handgrip measurement is considered a complementary measure.

GLIM recommends an assessment of the risk of undernutrition, using validated questionnaires such as the NRS (Nutritional Risk Screening) or the MNA-SF (Mini Nutritional Assessment-Short Form). The degree of severity of undernutrition is only assessed on the basis of phenotypic criteria.

The severity of undernutrition can then be determined (Table 2).

Table 2: Classification of the severity of undernutrition

Moderate undernutrition	Severe undernutrition
• BMI < 20 kg/m2 • Weight loss of 5-10% in the last 6 months or 10-20% beyond 6 months • Mild to moderate reduction in muscle mass	• BMI < 18.5 kg/m2 • Weight loss of >10% in the last 6 months or >20% beyond 6 months • Severe reduction in muscle mass
• 17 < BMI < 18.5 kg/m2 • Weight loss ≥ 5% in 1 month or ≥ 10% in 6 months or loss ≥ 10% from usual weight before onset of illness • Measurement of albumin by immunoelectrometry or immunoturbidimetry > 30 g/L and < 35 g/L.	• BMI < 17 kg/m2 • Weight loss ≥ 10% in 1 month or ≥ 15% in 6 months or loss ≥ 15% from usual weight before onset of disease • Measurement of albumin levels by immuno-electrometry or immunoturbidimetry < 30 g/L

1.3 Roles of professionals in screening for undernutrition

In general, and more particularly in the Forcilles hospital, dieticians play a major role in detecting undernutrition (8,9). They ensure a prospective watch on the patient's admission to the hospital, with the collection of indicators related to BMI and weight loss, in collaboration with the nurses and care assistants. They also carry out a dietary consultation to clarify the above criteria, to evaluate the reduction of intake and absorption, in collaboration with the physician, and the realization of body composition measurements, such as bio-electrical impedancemetry. The evolution of the definition of undernutrition, with an important place in the muscular and functional evaluation of the patient, implies new actors: the physiotherapist and the Adapted Physical Activity Teacher (APAT). Indeed, they have expertise in the evaluation of the patient's muscular function and functional capacities. As part of their diagnostic assessment, the physiotherapist is used to evaluating muscle function by dynamometry (10), as well as the patient's functional capacities by field tests or the use of scores. The EAPA also participates in the performance of field tests.

The collaboration between dieticians, physiotherapists, EAPAs, nurses, care assistants and doctors thus makes it possible to meet the need to screen for undernutrition according to this new definition.

1.4 Assessment of muscle function

Physical therapists and EAPAs use different tools to assess different aspects of muscle function, such as strength or walking speed in more functional tests.

Isometric grip strength is strongly correlated with lower extremity muscle strength, and is a pejorative marker of mobility in weakness (7). It has been

observed a linear relationship between grip strength and patient disability as measured by the Katz independence scale (11). In addition, grip strength has been shown to be a good predictor of the patient's clinical condition (12). The measurement of grip strength, using a dedicated dynamometer, also has the advantage of being simple and reproducible (13) and has reference values adjusted for sex and BMI (14).

Gait speed is another indicator used to assess muscle function. It is associated with lower limb strength and is a predictor of disability and mobility limitation (7). Usual walking speed is most often measured over a distance of 4 or 6 m and has reference values adjusted for sex and height (12).

Dietitians also participate in the evaluation of muscle function by measuring body composition in terms of lean and fat mass. They perform bioelectrical impedancemetry, which allows estimation of body fat and lean mass volumes by measuring the resistance of biological tissues to a low-intensity, high-frequency sinusoidal electric current through electrodes (7). This measurement method is simple to use, inexpensive, reproducible and feasible in bedridden patients (7). It also correlates very well with MRI and reference values are obtained in various adult populations (15,16).

1.5 Muscle ultrasound and undernutrition

Ultrasound is a reproducible method of muscle assessment (17-19). It allows the assessment of muscle thickness or cross-sectional area of a muscle, the reduction of which is a marker of atrophy and is strongly correlated with its loss of strength and reference measurements (17). In addition, ultrasound can be used to assess muscle quality, particularly by evaluating the echogenicity of the muscle. Echogenicity increases with muscle damage, related to the presence of fatty infiltrate and fibrous tissue (17-19). Complementary measurements such as pennation angle, fascicular length or fibrillations allow to complete the description of the muscle state (19).

Muscle ultrasonography is becoming increasingly used among the tools for assessing muscle function, especially in sarcopenia found in many pathological situations (18-20). Its use in the evaluation of the patient's nutritional status, as a tool for assessing muscle function, is developing in the ICU and is associated with an increase in the patient's comorbidities (21,22). Studies remain limited to a few patient populations, do not report clear cut-off values to define muscle pathological status, and require more precise definition of ultrasound measurement protocols (17,21).

1.6 Research hypothesis

We hypothesize that muscle ultrasound is reliable and valid in the evaluation of muscle function during the screening of undernutrition in a population of hospitalized patients in diabetology-obesity, pneumology, oncology and gastro-nutrition, under 70 years of age.

2 Originality of the research

Ultrasound is a relatively simple and inexpensive tool compared to other methods of measuring body composition (DEXA or MRI) and provides additional information on muscle quantity and quality compared to the usual tools for measuring muscle function (Handgrip, functional tests). To our knowledge, no study has evaluated muscle ultrasound in the context of screening for undernutrition in a large patient population. On the one hand, this study will make it possible to evaluate the reliability and validity of ultrasound in the assessment of muscle deterioration during undernutrition and to propose threshold values of muscle function deterioration. On the other hand, it will provide information on the ultrasound characteristics of the muscle in the undernourished patient and their association with the prognosis of the patient.

3 Objective

3.1 Main objective

The main objective of this study is to evaluate the reliability and validity of muscle ultrasound in the context of screening for undernutrition in patients hospitalized in short-stay and follow-up care and rehabilitation of diabetology-obesity, pneumology, oncology and gastro-nutrition.

3.2 Secondary objectives

The secondary objectives will be, in patients hospitalized in short stay and follow-up care and rehabilitation of diabetes-obesity, pneumology, oncology and gastro-nutrition:

- Evaluate the correlation of muscle ultrasound with standard measures of muscle function;
- To compare the diagnostic capacity of muscle function assessment tools on undernutrition;

- Evaluate the association of muscle ultrasound measurements with patient morbidity and mortality:
    - Length of hospitalization;
    - Mortality rate;
    - Autonomy at discharge.

4 Judging criteria

4.1 Primary endpoint

The primary endpoint is the reduction in muscle mass measured by ultrasound thickness of the rectus femoris. The reduction in muscle mass measured by ultrasound will be used to estimate the diagnostic accuracy (sensitivity, specificity) of muscle ultrasound using bioelectrical impedancemetry as the reference examination.

4.2 Secondary endpoint

Secondary endpoints will be:

- Correlation measurements of muscle ultrasound with:
    - Bioelectrical impedancemetry;
    - Handgrip;
    - Walking speed.
- Comparison of the diagnostic accuracy in undernutrition of muscle ultrasound with those of :
    - Bioelectrical impedancemetry;
    - Handgrip;
    - Walking speed.
- Measure of association of muscle ultrasound measurements with patient morbi-mortality:
    - Length of hospitalization (days);
    - Mortality: proportion and date of occurrence of death among patients included during hospitalization;
    - Autonomy at discharge: Activities Daily Living (ADL) score, **Appendix 1).**

5 Eligibility Criteria

5.1 Inclusion criteria

Patients with the following criteria will be included:

- Admitted in short stay and follow-up care and rehabilitation of diabetology-obesity, pneumology, oncology and gastro-nutrition;
- Age between 18 and 70 years at inclusion;
- Affiliation with a social security system or beneficiary of such a system ;
- Oral, free, informed and express consent of the patient or his/her family member.

5.2 Non-inclusion criteria

Patients with the following criteria will not be included:

- Impossible to perform the ultrasound;
- Impossibility of performing bioelectrical impedancemetry ;
- Incapacity to consent;
- Patient refusal to participate in the study;
- Pregnancy (a pregnancy test should be performed if in doubt);
- Breastfeeding woman;
- Person subject to a safeguard of justice measure ;
- Patient under guardianship or curatorship;
- Patient in care limitation;
- Sampling in the ineligible study group.

5.3 Recruitment procedures

Patients will be recruited prospectively and consecutively within the short stay and follow-up care and rehabilitation services of diabetology-obesity, pneumology, oncology and gastro-nutrition of the Forcilles Hospital. The dietician of the unit identifies the patients upon admission to the service.

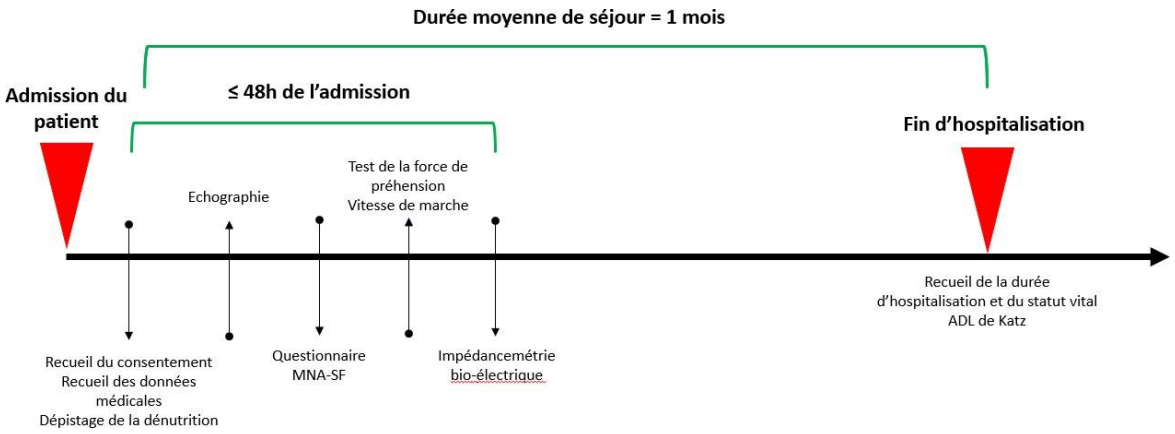
In 2020, according to PMSI data, 1128 patients under 70 years of age were hospitalized in our short-stay and follow-up care and rehabilitation services for diabetes-obesity, pneumology, oncology and gastro-nutrition. The monthly recruitment target is 6 patients, with a potential of 94 patients per month.

6 Research design

6.1 Type of study

This is a prospective, monocentric, interventional cohort study with minimal risks and constraints falling within the scope of Article L.1121-1 of the Public Health Code.
The research will be conducted in accordance with the protocol.

6.2 Research Diagram



6.3 Provisional research schedule

The duration of the recruitment will be 20 months with a follow-up of the patients during their entire hospitalization in the care unit, i.e. approximately 30 days (average length of stay), i.e. a total duration of the study estimated at 21 months.

- Submission to PPC: July 2022
- Start of inclusions: November 2022
- Duration of the inclusion period: 20 months
- Duration of participation for each patient: 30 days
- End of inclusions: July 2024
- Total duration of the research: 21 months
- Communication in congress: congress of medical societies of oncology, surgery, pneumology, nutrition and gastroenterology
- Publication: October 2024

6.4 Location of the study

The study will take place at the Forcilles Hospital, in the short stay and follow-up care and rehabilitation departments of diabetology-obesity, pneumology, oncology and gastro-nutrition.

7 Description of the usual care

7.1 Usual course of treatment

Patients admitted to short-stay and follow-up care and rehabilitation for diabetes-obesity, pneumology, oncology and gastro-nutrition benefit from medical, nursing and rehabilitation examinations and care. All of this care will not be modified within the framework of this protocol. Physiotherapists and dieticians provide their diagnostic assessment and rehabilitation on medical prescription. The EAPAs participate in the functional evaluation of the patient and carry out physical activities adapted to the patient, also on medical prescription.

As part of the screening for undernutrition in our establishment, the dieticians ensure a prospective and systematic collection of the patient's weight and its evolution over the last few months, of his BMI and an evaluation of the food intake, within 48 hours of the patient's admission to the service. The estimation of the patient's intake is done in collaboration with the nursing assistant.

The nurse's aide carried out a systematic measurement of grip strength when the patient was admitted to the ward (**Appendix 2**). A plan to train the nursing assistants to carry out this measurement has been set up by the physiotherapists.

The physical therapist or EAPA performs the measurement of the patient's walking speed routinely upon admission to one of these services (**Appendix 3**).

7.2 Standard evaluation procedures

7.2.1 Nutritional assessment

At the patient's admission, a dietetic evaluation is performed by the dietician following the recommendations issued by the French Association of Dieticians-Nutritionists (AFDN) and the HAS. The dietitian collects all the data needed to detect malnutrition, such as weight, height, BMI, albumin level, and grip strength and walking speed (performed by the caregiver and the physiotherapist or the EAPA). The dietician also looks for possible obstacles to feeding such as dental condition, swallowing problems or digestive discomfort.

The doctor looks for different pathologies impacting digestive absorption such as shortened or shortened stool syndromes, gastrectomies, pancreatic insufficiency etc. He also looks for factors of aggression such as cancers, chronic progressive diseases, infections etc.
All these data allow us to estimate the theoretical nutritional needs of the patient and to adapt the nutritional management. A follow-up of the ingestations is carried out by the dietician in collaboration with the nurses' aides.

7.2.2 Anthropometric measurements

When the patient is admitted, the ward's nurses and orderlies measure the patient's weight and height. When the patient can maintain the erect position, a conventional scale and a measuring rod are used for the measurements. If the patient cannot maintain this position, a weighing chair and a laser meter are used.
In order to evaluate the weight loss before hospitalization, the previous weight is sought in a hospitalization report or another recent medical document. A contact with the attending physician is also made in order to obtain information concerning the patient's weight follow-up. When this information is not available, the previous weight given by the patient is collected.

7.2.3 Biological measurements

On admission, a biological sample is usually taken from patients at risk of undernutrition in order to measure pre-albumin, albumin and C-reactive protein (CRP). These elements make it possible to determine the severity of undernutrition when it is present, according to the diagnostic criteria of the HAS.

7.2.4 Measurements of muscle function

Measurement of grip strength ("Handgrip")

The gripping force is evaluated with the Jamar® hydraulic force gauge by the caregiver.
The patient is in a sitting position, on a chair with a backrest, with his feet on the floor. The device is placed in the patient's hand. The patient is instructed to squeeze the dynamometer as hard as possible.
The measurement is made on the dominant side of the patient. The homolateral shoulder is in adduction (elbow to body), without extension or flexion and in neutral rotation. The elbow is flexed to 90° and in neutral prono-supination. The wrist is in neutral position. Three trials will be performed, and

the best value (in Kg) of the different tests is retained (see measurement procedure in **Appendix 2).**

Measurement of the walking speed ("Gait speed")

Walking speed (m/s) is measured on a 4-meter course, in a corridor, by the EAPA or the physiotherapist. The course is marked out on the ground. The course is marked out with markings on the ground and there are also 1-metre run-up and run-down zones. The patient is instructed to walk the course at a normal speed and not to complete the distance as quickly as possible. The course is completed 3 times and the best time (in seconds) is recorded (see procedure in **Appendix 3**).

7.3 Definition of undernutrition

Undernutrition is defined according to the GLIM diagnostic method:

Phenotypic criteria			Etiological criteria	
Weight loss (%)	**Low BMI (kg/m)^2**	**Reduction in muscle mass**	**Reduction of food intake or absorption**	**Inflammatory situation**
> 5% in the last 6 months or > 10% beyond 6 months	< 20	Reduction evaluated by a validated measurement technique*.	≤ 50% of food intake > 1 week or any reduction > 2 weeks, or any gastrointestinal pathologies or symptoms impacting assimilation or absorption	Acute pathologies or certain chronic or malignant pathologies

The diagnosis of undernutrition is positive if an etiological and a phenotypic criterion are present. This assessment will be preceded by a MNA-SF (**Appendix 4**). The methods for measuring the reduction in muscle mass are described in section "**7.2.4. Measurement of muscle function**".

Among patients with undernutrition, severe undernutrition is defined as:

Moderate undernutrition	Severe undernutrition
• BMI < 20 kg/m2 • Weight loss of 5-10% in the last 6 months or 10-20% after 6 months • Mild to moderate reduction in muscle mass	• BMI < 18.5 kg/m2 • Weight loss of >10% in the last 6 months or >20% beyond 6 months • Severe reduction in muscle mass

The prevalence of undernutrition was defined as the proportion of patients with moderate and/or severe undernutrition among the patients included in the study.

8 Evaluation procedure added by the research

8.1 Mini-Nutritional Assessment Short Version (MNA-SF) score

The MNA-SF is a validated nutritional risk screening tool that can be applied by health professionals (see **Appendix 4**). It was developed by Rubenstein (23), based on the MNA.
Completed in less than five minutes, it can identify a decrease in food intake, an acute pathology or stress and a decrease in BMI. It also includes two questions related to the frailty of the elderly, mobility and neuropsychological problems (dementia, depression).
The MNA-SF classifies individuals as "undernourished" with a score between 0 and 7 points, "at risk for undernutrition" with a score between 8 and 11 points, and "satisfactory nutritional status" with a score between 12 and 14 points. Patients considered "undernourished" and "at risk of undernutrition" should receive a nutritional status assessment.

8.2 Bioelectrical impedancemetry

Bioelectrical impedancemetry is performed in the patient's room using the Z-Metrix impedance meter from Bioparhom. The test is performed when the patient is admitted to the ward.
The patient is positioned in dorsal decubitus, inclined at 30 degrees. The patient must rest for at least 15 minutes before the measurement. Four electrodes will be placed:

- On the flat of the back of the hand;
- At the wrist, at the level of the head of the ulna, in the intertendinous hollow;
- At the ankle, above the external malleolus;
- Above the previous electrode, spaced about 4 fingerbreadths apart.

This non-invasive test quantifies muscle, lean and fat mass as well as bone and water mass. The values are expressed in kilograms and as a percentage of body weight (see measurement procedure in **Appendix 5**).
The following clues will be collected:

- Muscle mass index (in kg/m^2);
- The non-fat mass index (in kg/m^2).

The operator performing the bioelectrical impedancemetry will be blind to the results of other examinations performed on the patient.
The threshold used will be 7 Kg/m2 for men and 5.7 Kg/m2 for women, as recommended (Cederholm T et al. Clin Nutr 2019)

8.3 Muscle ultrasound

8.3.1 Operator training

Ultrasound measurements are performed by one of the investigating physiotherapists, who is not involved in the management of the patient. The physiotherapist is authorized to perform ultrasound subject to training (Avis du Conseil National de l'Ordre des Masseurs-Kinésithérapeutes (2015)). The training of the operator corresponds to the following:

- 3 days of theoretical and practical training;
- Over 100 ultrasounds supervised by an experienced practitioner.

Similarly, all the physiotherapists performing the ultrasound scans are already involved in other research projects using lung, diaphragm and peripheral muscle ultrasound: https://clinicaltrials.gov/ct2/show/NCT02474797, https://clinicaltrials.gov/ct2/show/NCT02881814, https://clinicaltrials.gov/ct2/show/NCT04373811 and https://clinicaltrials.gov/ct2/show/NCT04800783.

8.3.2 Realization of the measurement

A linear probe will be used for measurements of thickness, echogenicity and cross-sectional area of the rectus femoris and vastus intermedius, according to the procedure described in **Appendix 6**. The patient is placed in the supine position (as strict as possible), with the lower limbs in extension and in a neutral position of rotation. The probe is placed on the anterior aspect of the thigh, 2/3 of the distance between the anterior superior iliac spine and the upper edge of the patella, in line with the femur.

In order to evaluate inter and intra-examiner reproducibility, the tests will be performed by two different operators and twice by the same operator, i.e. 3 identical examinations in total. In the transverse plane, the distance between the upper and lower fascia of the muscle body will be measured, directly on a frozen image. The thickness of the rectus femoris and the vastus intermedius will be measured on the right side at rest, without patient participation. The average of 3 measurements per muscle is retained to improve the reliability of the measurement.

The cross-sectional area (CSA) will also be measured. Also in the transverse plane, the cross-sectional area of the rectus femoris and the vastus intermedius will be measured using the "caliper" function to trace the limits of the muscle and measure its surface. On the same frozen image, echogenicity will be measured using the Image J software® using the entire muscle surface.

The pennation angle of the rectus femoris will also be measured in a longitudinal plane. The

operator performing the ultrasound will be blinded to the results of the other examinations performed on the patient.

9 Conduct of the research

9.1 Pre-inclusion visit

9.1.1 Verification of inclusion and non-inclusion criteria

When a patient is admitted to short stay and follow-up and rehabilitation care for diabetes-obesity, pneumology, oncology and gastro-nutrition, one of the investigators checks the presence of the inclusion criteria and the absence of the non-inclusion criteria in the institution's computerized medical record.

9.1.2 Sampling of the population

A potential of 94 patients per month eligible for this study are admitted in short stay and follow-up care and rehabilitation of diabetes-obesity, pneumology, oncology and gastro-nutrition. We anticipate a maximum inclusion of 6 patients per month for logistical reasons.
In order to obtain a representative sample of this patient population in the study, we will sample the patient population upon admission, if he/she meets the eligibility criteria and before the patient is informed and consented. The patient will be randomly assigned to either the eligible or ineligible group. Patients in the ineligible group will not be included in the study, but the number of these patients will be collected.
Patients will be sampled via a centralized random drawing system available via the internet, according to a pre-established list. This list will be programmed in advance by the study statistician. The sampling will be stratified on the care service, and unbalanced using random blocks in order to obtain a number of eligible patients of 10 per month (in order to take into account possible refusals of participation). Only the hospital's research coordinator will know the sampling list.

9.1.3 Patient information and consent

When all the criteria allow the inclusion of the patient, the investigator informs the patient of the purpose of the study during a visit to the room. The investigator provides the patient with all the information described in the information note (**Appendix 7**) and, if necessary, obtains the patient's free, informed and express oral consent. This consent will be recorded in the patient's computerized medical record.
The state of consciousness of certain patients (confusion, cognitive disorders) at the time of their admission will not allow them to receive information related to the research and the collection of consent and

the information will be given to the person close to the patient who has been declared a trusted person (**Appendix 8**). At any time, if the patient's neurological or cognitive state allows it, the patient will be informed of this research and his or her express oral consent will be requested for the possible continuation of the research (**Appendix 9**).
In the event of a new ban on visits to hospital wards due to the health crisis, information and oral consent from the trusted support person will be given by telephone or video conference.

9.2 Inclusion visit

The inclusion visit will take place within 48 hours of the patient's or family member's consent to participate in the study. The following data will be collected:

- Age, weight, height, BMI, gender (male/female);
- Hospitalization Service;
- Reason for hospitalization;
- Background;
- Reduced food intake or absorption;
- Inflammatory situation;
- Biological markers (albumin, pre-albumin, CRP) if applicable;
- Nutritional data (weight evolution over the last months, theoretical needs, ingestas) ;
- Mini-Nutritional Assessment Short-Form (MNA-SF);
- Autonomy Score (Katz ADL);
- Ultrasound measurements;
- Bioelectrical impedancemetry data;
- Grip force (Handgrip);
- Walking speed.

9.3 Follow-up visit

A follow-up visit will be conducted daily to collect the patient's vital status and to verify if a discharge or transfer is planned. In the event of discharge or transfer, the following data will be collected:

- Length of hospitalization (in days);
- Vital status (death yes/no) ;
- Autonomy score (Katz ADL).

9.4 End of research visit

The end-of-research visit will take place at the patient's discharge or death. The following data will be collected:

- Length of hospitalization (in days);
- Vital status (death yes/no) ;
- Autonomy score (Katz ADL)

9.5 Summary table

	Pre-inclusion	**Inclusion visit**	**End of research visit**
Patient information and consent	✓		
Performing a pregnancy test in case of doubt	✓		
Collection of basic data (age, weight, sex, BMI, medical history)		✓	
Collection of the service and the reason for hospitalization		✓	
Associated pathologies		✓	
Biological markers		✓	
Nutritional data		✓	
MNA-SF		✓	
Ultrasound		✓	
Bio-electrical impedancemetry		✓	
Handgrip, Walking speed		✓	
Katz ADL		✓	✓
Vital status			✓
Length of hospitalization			✓

10 Statistical aspects

10.1 Calculation of the number of subjects needed

Reproducibility of ultrasound

With an expected intraclass correlation coefficient of at least ρ_1 = 0.8, a minimum value ρ_0 = 0.70 considered acceptable, a number of observations k= *2*, a risk α= *0.05*, and a power of 80%, it is necessary to include 118 patients for the study of intra- and inter-examiner reproducibility of ultrasound (24).

Ultrasound Validity:

With an expected sensitivity and specificity of at least 90% and 85%, respectively, an estimated prevalence of muscle impairment of 45% to 60% in our hospitalized patients, for a risk α= *0.05* and a maximum width of the confidence interval of 10%, it is necessary to include between 87 and 109 patients (25).

Therefore, it will be necessary to include 118 patients to meet the primary objective of evaluating the validity and reliability of peripheral muscle ultrasound.

10.2 General aspects

Descriptive statistics will be based on means (+/- standard deviation) or medians [interquartile range] depending on the distribution of quantitative variables. Qualitative variables will be described in terms of numbers and percentages. Univariate comparisons will use the usual statistical tests after verification of the distribution of the variables (Chi2 or Fisher's test, t-test, anova or their non-parametric equivalents Wilcoxon and Kruskal-Wallis tests). Paired sample tests will be used if necessary.

Tests will be performed at the 5% significance level. The 95% confidence intervals will be provided for each estimate.

The calculations will be done using SPSS v21 IBM and R software (version 3.6.1, http://www.R- project.org).

10.3 Morbidity and mortality criteria

10.3.1 Length of hospitalization

The length of stay is defined as the number of days of presence in the inclusion service, from the patient's admission to the final discharge. Temporary transfers to another hospital department for an examination or an intervention are not considered discharges.
A special statistical treatment (**described in section 11.4**) will be carried out on the length of hospital stay, given the impact of death on the length of stay.

10.3.2 Mortality

Number of deaths out of the total number of patients included. A specific statistical treatment (**described in section 11.4**) will be performed on the mortality rate.

10.3.3 Katz Activities Daily Living (ADL) Score

The Katz ADL score (**Appendix 1**) is completed within 48 hours prior to (scheduled) hospital discharge by the patient's caregiver or nurse. The total score is out of 6. A score of less than 3 indicates major dependence, a score of 0 indicates total dependence.
The Katz ADL score will be treated as a discrete numerical variable.

10.4 Analysis of the main objective

Inter- and intra-examiner reliability will be assessed by calculating intra-class correlation coefficients.
Validity will be assessed by calculating the areas under the ROC curve (Receiver Operating Characteristics) and calculating sensitivities, specificities, positive and negative predictive values.
The reference test for the diagnosis of impaired muscle function is bioelectrical impedance. The cut-off values used for the diagnosis of impaired muscle function are those recommended by GLIM (1): Appendicular Skeletal Muscle Index (ASMI) < 7 kg/M2 in men and < 5.7 kg/m2 in women.

10.5 Secondary objectives

10.5.1 Correlation of muscle ultrasound with standard measures of muscle function

Measures of association between quantitative variables will be performed using Pearson's or Spearman's correlation coefficients depending on the distribution of the data. Measures of association between qualitative variables will be performed using the Chi-square or Fisher test depending on the distribution of the data.
The agreement between quantitative variables will be evaluated using the Bland-Altman method and that between qualitative variables using the Kappa coefficient.

10.5.2 Compare the diagnostic capacity of muscle function assessment tools on undernutrition

The diagnostic capabilities of the different tools for measuring muscle function (Handgrip, gait speed, bioelectrical impedance and muscle ultrasound) will be compared by ROC curves.

10.5.3 Evaluate the association of muscle ultrasound measurements with patient morbidity and mortality

Morbidity and mortality will be compared between the groups with and without ultrasound-determined muscle function impairment, comparing length of hospital stay, mortality, and independence at discharge.

Length of hospitalization

There is a relationship between the incidence of mortality and all of the length of stay variables. Length of stay will therefore be analyzed using a competitive risk method, which takes into account the fact that patients who die are no longer eligible for length of stay analysis (26).
The estimator also provides the probability of in-hospital death, so the probability of hospital discharge versus death at any time after study inclusion can be assessed simultaneously.

Mortality rate

The estimation of mortality rates will be performed by the Kaplan and Meier method. Comparison of the 2 curves will be performed by a Logrank test. The mortality rates in the 2 groups will be estimated via the survival curves.

ADL

The ADL score will be compared between the 2 groups using the discrete numerical variable comparison tests described in the general aspects.

11 Expected results in terms of scientific and professional advances

The results of this study will make it possible to verify whether ultrasound is a reliable and valid tool in the evaluation of peripheral muscle function in the context of screening for undernutrition. On the other hand, they will allow us to propose threshold values for the alteration of muscle function and to provide information on the ultrasound characteristics of the muscle in the undernourished patient and their association with the prognosis of the patient. The different tools could lead to a different estimation of the reduction of muscle mass and therefore a different prevalence of undernutrition. The results of our study will help to evaluate this and to guide professionals in the choice of tools to assess muscle function.

12 Expected benefits and risks for patients

12.1 Minimal risks and constraints added by the research

All medical and paramedical examinations and management are usually performed except for the MNA-SF questionnaire, muscle ultrasound and bioelectrical impedancemetry, which will be performed systematically in the patients included. The MNA-SF questionnaire is very quick (less than 5 minutes) and therefore causes very little inconvenience to the patient apart from an additional visit by a caregiver. Bioelectrical impedancemetry is a tool for assessing body composition using electrodes applied to the skin surface. The examination lasts an average of 15 minutes and is non-invasive and painless. The minimal constraint is related to the placement of the electrode and the duration of the examination. The ultrasound is also non-invasive and painless. The 3 ultrasounds performed will last about 30m. The minimal constraint is related to the installation of the ultrasound probe and the duration of the examination.

12.2 Expected benefits for the patient

Ultrasound is a relatively simple and inexpensive tool compared to other methods of measuring body composition (DEXA or MRI) and provides additional information on muscle quantity and quality compared to the usual tools for measuring muscle function (Handgrip, functional tests). The results of this study will make it possible to propose to the patient a reliable and valid evaluation tool, more easily available and less restrictive in the evaluation of the muscular quality during undernutrition. This could lead to a wider and more precise evaluation of this muscular impairment in order to propose more adapted therapeutic solutions (exercise training, weight training, nutrition).

13 Feasibility

Taking into account the inclusion and non-inclusion criteria, possible refusals of patients to participate in the research, potential exclusions and recruitment experience, we estimate a minimum recruitment capacity of 50% of patients admitted to short-stay and follow-up and rehabilitation care for diabetes-obesity, pneumology, oncology and gastro-nutrition, i.e. 47 patients per month, with a monthly recruitment target of 6 patients over 20 months.

In addition, screening for undernutrition is usually performed on all patients admitted to these services within our establishment. Dietitians, nurses and physicians are trained and accustomed to perform this screening. Bio-electrical impedancemetry by dieticians and muscle ultrasound by physiotherapists are already performed on some patients. The addition of these examinations in the framework of research is therefore feasible.

In addition, the teams have experience in clinical research, as they are already involved in other research projects as sponsors and investigating centers. The medical and rehabilitation teams are involved in other ongoing research projects (https://clinicaltrials.gov/ct2/show/NCT02881814, https://clinicaltrials.gov/ct2/show/NCT02474797 and https://clinicaltrials.gov/ct2/show/NCT04373811).

14 Ethical and regulatory aspects

The Forcilles-Fondation Cognacq-Jay hospital promoter and the person(s) directing and supervising the research undertake that this research will be carried out in compliance with law n°2004-806 of August 9, 2004 relating to public health policy and the regulatory provisions in force (articles L.1121-1, L.1121-2 and L.1121-3 of the Public Health Code. The data recorded during this research will be subject to computerized processing in compliance with Law No. 78-17 of January 6, 1978 on information technology, files and freedoms, as amended by Law No. 2018-493 of June 20, 2018 (Decree No. 2018-687 of August 1, 2018) and Order No. 2018-1125 of December 12, 2018. The research will be conducted in accordance with this protocol.

14.1 Role of the promoter

The research commission of the Forcilles-Fondation Cognacq-Jay hospital, promoter of this research, submits the file to the opinion of the concerned Committee for the Protection of Persons (CPP) (CPP Ile de France 2) whose opinion will be notified in the information note intended for the persons concerned.
The natural or legal person who initiates this research, ensures its management and verifies that its financing is provided for, is called the sponsor.

14.2 Submission to PPC

This research will be submitted to a Committee for the Protection of Persons, which will be drawn by lot in the framework of the "Jardé Law" (Article L.1121-4 of the Public Health Code, Decree No. 2016-1537 of November 16, 2016, which went into effect on November 18, 2016). The opinion of the above-mentioned committee is notified in the information note intended for the persons concerned. A copy of this opinion and a summary of the research will be sent to the ANSM.

14.3 Data protection

This research is subject to the law n°78-17 of January 6, 1978 relating to data processing, files and freedoms modified by the law n° 2018-493 of June 20, 2018 (decree n° 2018-687 of August 1, 2018). Information on the rights of persons participating in this research (right of access and rectification, right to object to the transmission of data covered by professional secrecy likely to be used in the context of this research) is included in the information note intended for the patient.

A reference methodology specific to the processing of personal data operated within the framework of biomedical research defined by Law 2004-806 of August 9, 2004 as falling within the scope of Articles L.1121-1 et seq. of the Public Health Code was updated by the CNIL in May 2018 (Deliberation No. 2018-153 of May 3, 2018) following the publication of European Regulation No. 2016/679 (General Data Protection Regulation). This methodology allows a simplified declaration procedure when the nature of the data collected in the research is compatible with the list provided by the CNIL in its reference document. This study is part of the MR001 reference methodology to which the Forcilles-Fondation Cognacq-Jay hospital has committed to comply.

14.4 Insurance

The Sponsor takes out insurance covering its own civil liability and that of any participant involved in the research, regardless of the nature of the relationship between the participants and the Sponsor (article L.1121-10 of the Public Health Code). The sponsor also ensures the compensation of the harmful consequences of the research for the person who takes part in it and for his or her beneficiaries, unless it can prove that the damage is not attributable to its fault or to that of any other party involved, without being able to invoke the act of a third party or the voluntary withdrawal of the person who had initially agreed to take part in the research. When the sponsor is not liable, the victims may be compensated under the conditions set out in article L.1142-3.

The Forcilles-Fondation Cognacq-Jay hospital has taken out insurance under contract n°163607 guaranteeing its civil liability as well as that of any intervening party with the company SHAM for the entire duration of the research, in accordance with article L.1121-10 of the Public Health Code.

14.5 Substantial change to the protocol

The investigator or coordinator informs the research commission of the Forcilles-Fondation Cogacq-Jay hospital of any proposed modification of the protocol. Any substantial modification will be submitted by the sponsor of this research to the CPP for its opinion.

14.6 Disclosure and Express Consent

In accordance with article L.1122-1 of the Public Health Code, the information given to the persons who are to be involved in the research is the subject of a written document submitted beforehand to the personal protection committee. The ethical opinion of the CPP Nord Ouest IV has been requested.

The investigator of the center proposes to the patient, or to a relative if the patient is unable to participate, to take part in the study. The investigator informs the patient orally about the study and gives him/her the information note. If the patient gives free, informed and express oral consent to participate in the protocol, the information given orally and in writing, as well as the collection of oral consent, will be recorded in the patient's medical record.

In the case where a relative of the patient has given consent, as soon as possible, the patient will be informed of this research and asked for oral consent for the possible continuation of the research.

Patients are free to participate or withdraw from the study at any time in accordance with Article 21 of the GDPR. Data collected until the patient withdraws consent will be used unless specifically requested by the patient. The withdrawal of consent by the patient and the agreement to use or not the previously collected data will be traced in the patient's medical record.

When the research is completed, the individual may be informed of the overall results of the research in the manner specified in the disclosure document.

14.7 Anticipated deadline for publication of results in an international journal

The deadline for the publication of the results is 30 months.

14.8 Data management

All information required by the protocol must be provided in the e-CRF and an explanation given by the investigator for any missing data. Data should be entered into the e-CRF as they are obtained, whether they are clinical or paraclinical data.

For each subject, an identification code (corresponding to the center number-inclusion number-Initial Last Name-Initial First Name) will be assigned. The data collected will be confidential and coded (only the identification code will appear). The concordance table linking the assigned identification code and the participant's name will be kept by the sponsor in a file with limited computer access rights.

The e-CRFs will be created on DATACAPT (https://www.datacapt.com) and accessible only to those involved in the research (investigators, CRAs, CTEs and data managers), with limited access rights for each according to the level of access required.

At the end of the inclusion and data collection period, all data collected on the e-CRF will be exported in a password-protected Excel® file. Data processing and statistical analysis will be performed at the Forcilles-Fondation Cognacq-Jay hospital.

The sponsor is responsible for the data and no use or transmission to a third party can be made without its prior agreement.

The specific documents of a type 2 interventional research ("Loi Jardé", decree n° 2016-1537 of November 16, 2016, which went into effect on November 18, 2016) with minimal risks and constraints will be archived by all parties for 15 years after the end of the research.

This indexed archiving includes:

- successive versions of the protocol (identified by version number and date);
- correspondence;
- Inclusion list or register;
- the data collection document ;
- research-specific appendices;
- the final report of the research.

The database used for the statistical analysis must also be archived by the person responsible for the analysis (paper or computer).

14.9 Human and financial resources

The Forcilles-Fondation Cognacq-Jay hospital is equipped with human, material and technical resources to carry out this research project.

14.10 Data properties

The Forcilles-Fondation Cognacq-Jay hospital is responsible for the data and no use or

transmission to a third party may be made without its prior agreement.

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16 Annexes

16.1 Appendix 1: Katz ADL (Activities in Daily Living) Scale (27)

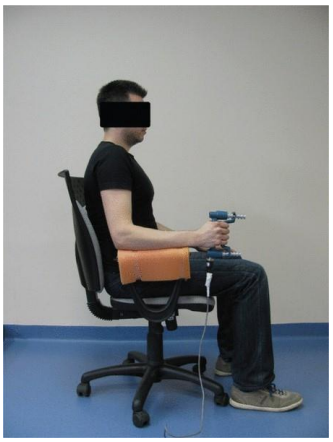
Items	Valeurs	Résultat
Hygiène corporelle		
Autonomie	1	
Aide partielle	0,5	
Dépendant	0	
Habillage		
Autonomie pour le choix des vêtements et l'habillage	1	
Autonomie pour le choix des vêtements et l'habillage, mais a besoin d'aide pour se chausser	0,5	
Dépendant	0	
Aller aux toilettes		
Autonomie pour aller aux toilettes, se déshabiller et se rhabiller ensuite	1	
Doit être accompagné ou a besoin d'aide pour se déshabiller ou se rhabiller	0,5	
Ne peut aller aux toilettes seul	0	
Locomotion		
Autonomie	1	
A besoin d'aide	0,5	
Grabataire	0	
Continence		
Continent	1	
Incontinence occasionnelle	0,5	
Incontinent	0	
Repas		
Mange seul	1	

16.2 Appendix 2: Handgrip Usage Protocol

The patient will be in a sitting position, on a chair with a backrest, feet on the ground.
The shoulder will be in adduction (elbow to body), without extension or flexion, and in neutral rotation. The elbow will be placed at 90° of flexion and in neutral prono-supination. The wrist should also be in neutral position. The practitioner will slightly hold the elbow and the base of the JAMAR dynamometer® in order to avoid positioning changes. The grip force measurement will include 3 measurements on each limb, alternating with a rest (1 minute: time to note the score of the measurement and to quietly settle the person in the position for the next measurement).

The dominant hand will be chosen by the participant by answering the following question: "Are you right or left handed?

The instructions are: "Lean back against the backrest. Take the handle in your hand, keep your elbow close to your body and your forearm straight in front of you" and progressively tighten the handle over 2 to 3 seconds to reach a maximum tightening that must also be maintained for 2 to 3 seconds, without moving the other joints (wrist, elbow and shoulder).
Encouragement will be given to the person during the clamping seconds to motivate the patient as much as possible: "Go ahead and clamp, clamp... hard, HARD! TIGHT! ...and you release".
It will be noted if a pain appears and limits the grip.



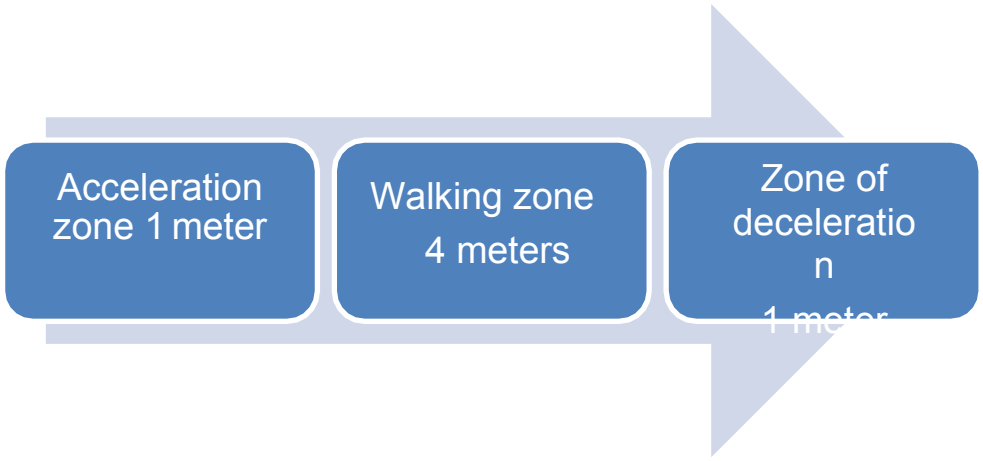
16.3 Appendix 3: Gait speed test protocol

The walking speed (m/s) is measured on a 4-meter course, in a corridor. The course is marked out with ground markings. The course is marked out on the ground. 1-meter run-up and run-down zones are also marked out. The patient is instructed to walk the course at a normal speed and not to complete the distance as quickly as possible. The course is completed 3 times and the best time (in seconds) is retained.

The examiner runs the course at a usual speed and at a maximum speed without running so that the usual speed instruction is well integrated by the patient.

The examiner starts the stopwatch when the first foot crosses the end of the run-up line and stops it as soon as the first foot crosses the 4m line. (see figure below).

The walking speed is determined by dividing the distance by the time taken to walk that distance, giving a result in m/s.



16.4 Appendix 4: Mini-Nutritional Assessment Short-Form (MNA-SF) Score (23)

A. Does the patient have a loss of appetite?

Has he/she eaten less in the last 3 months due to lack of appetite, digestive problems, chewing or swallowing difficulties?

0 : severe anorexia ;
1 1: moderate
anorexia; 2: no
anorexia

B. Recent weight loss (< 3 months)

0: loss > 3 kg; 1:
don't know ;
2: weight loss between 1 and 3
kg; 3: no weight loss

C. Motor skills

0 From bed to chair;
1 1: autonomous inside;
2: leaves the home

D. Acute illness or psychological stress in the last 3 months?

0: yes;
2: no

E. Neuropsychological problems

0 dementia or severe depression;
1 1: dementia or moderate
depression; 2: no psychological
problems

F. Body mass index (BMI) = weight/(height)² in kg/m².

0: BMI < 19;

1: 19 < IMC < 21 ;

2: 21 < IMC < 23 ;

3 : BMI > 23

Screening score (maximum subtotal = 14 points)

Between 0 and 7 points: malnourished

Between 8 and 11 points: at risk of malnutrition

Between 12 and 14 points: satisfactory nutritional status

16.5 Appendix 5: Bioelectrical Impedance Measurement Protocol

The placement of the electrodes is important for obtaining optimal results. For a hemi-body measurement, four electrodes are placed as shown in figures 1 and 2.

Figure 1: Installation of electrodes 1 and 2 corresponding to cables 1 and 2.

Be careful, never place the electrode on a bone. The first electrode is placed on the flat of the back of the hand. It is easier to place it if the point of your patient is tight. The second electrode is placed on the wrist at the level of the head of the ulna, in the intertendinous hollow. Figure 1 shows how to place these two electrodes

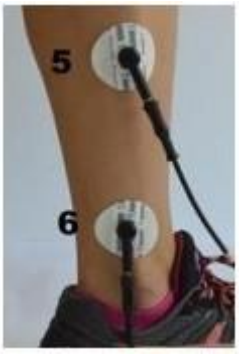


Figure 2: Installation of electrodes 3 and 4 corresponding to cables 3 and 4.

The third electrode is placed on the ankle above the external malleolus. Finally, to place the last electrode, simply take your hand, put it over the malleolar electrode, count 4 finger crosses and place the fourth electrode. Figure 2 shows how to place these two electrodes.

It is recommended that the patient has removed any jewelry (watch, bracelet) as well as any objects that may be in his pockets. If your connection, the positioning of the device or the quality of the subject's skin cause measurement errors, pop-ups will alert you and advise you to check your connection. Be careful, the patient's or user's body must not be in contact with the box or connectors 1 to 4 during the measurement. This can induce short circuits or parallel currents and thus falsify the measurement. The device must not be positioned on the patient. No contact should be made

between the hand and the subject's thigh, or between the thighs. If the thighs of your undressed subject are touching and it cannot be done otherwise, you can put a cloth in contact with the thighs.

Example of results (Figure 3):

The 3 clues will highlight:

- Body fat, reflects the patient's nutritional status: Normal if between the gauges, underweight or lean below, overweight between the high and low markers +5%, obesity above the upper bound +5% ;
- Bone content, will reflect bone fragility if the value is below the bottom of the gauge;
- Muscle mass: will reflect the amount of muscle in the body, allows to evaluate the impact of physical activity, protein intake, and to detect undernutrition.

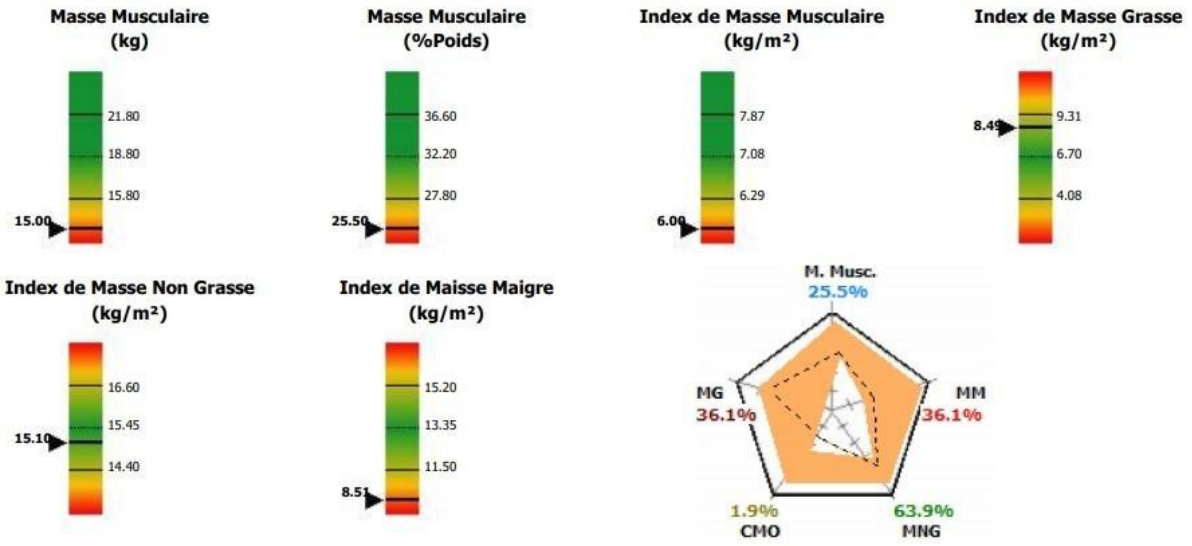


Figure 3: Indices measured with the bio-electrical impedance meter (example of a clinical case)

16.6 Appendix 6: Protocol for performing muscle ultrasound

A linear probe will be used for the measurements. A set of predefined settings of the gain and depth parameters will be used for all measurements.

Patient positioning

The patient is installed in dorsal decubitus (as strict as possible), with the lower limbs in extension and neutral position of rotation.

Placement of the probe

The probe is placed in contact with the skin via an ultrasound gel. The pressure exerted with the probe is perpendicular to the plane of the bed, in line with the femur and must be as low as possible to obtain a representative image of the muscle. Excessive pressure will cause deformation of the subcutaneous tissues and therefore of the muscle. There are two ways of orienting the probe: in the transverse or sagittal plane.

Measurements on the quadriceps

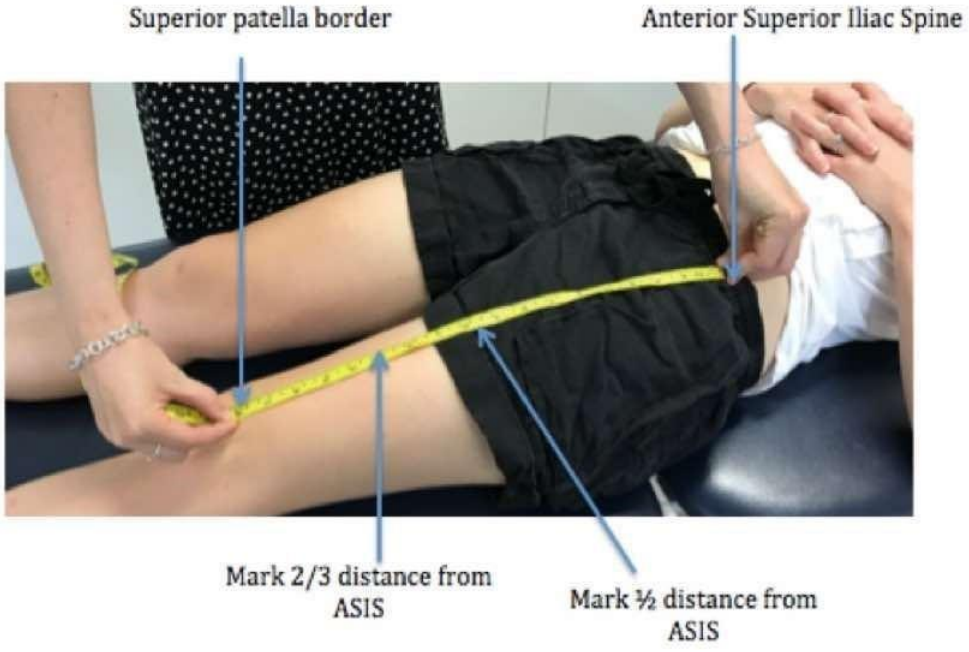


Figure 1

The probe is placed on the anterior aspect of the thigh, 2/3 of the way from the anterior superior iliac spine to the upper edge of the patella, plumb with the femur (**Figure 1**) (39). The muscle chiefs studied were the rectus femoris and the vastus intermedius.

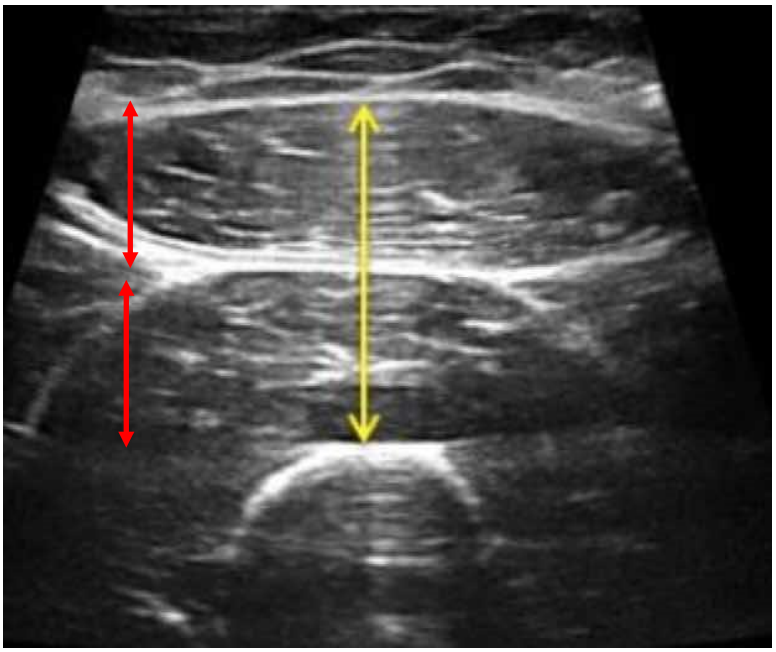


Figure 2

Muscle thickness

In the transverse plane, measurement of the distance between the upper and lower fascias of the muscle body (Figure 2). It is measured directly on a frozen image. The thickness of the rectus femoris (DF) and the vastus intermedius (VI) will be measured on the right. The average of 3 measurements will be taken.

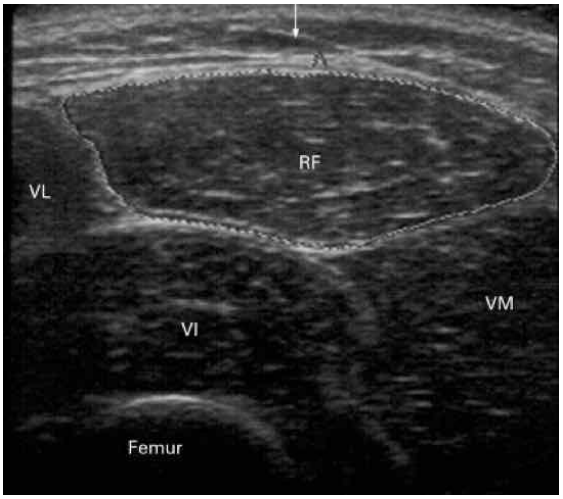


Figure 3

Cross-Sectional Area (CSA):

Still in the transverse plane, measure the cross-sectional area of the rectus femoris using the caliper to delineate the boundaries of the rectus femoris (Figure 3).

Pennation angle

Place the probe along the axis of the rectus femoris muscle. The angulation of the muscle fibers in relation to the underlying fascia becomes visible (pennation of the fibers (Figure 4)). Record the image. The angle between a muscle fiber and the underlying fascia will be measured only on the rectus femoris, on the Image J software.

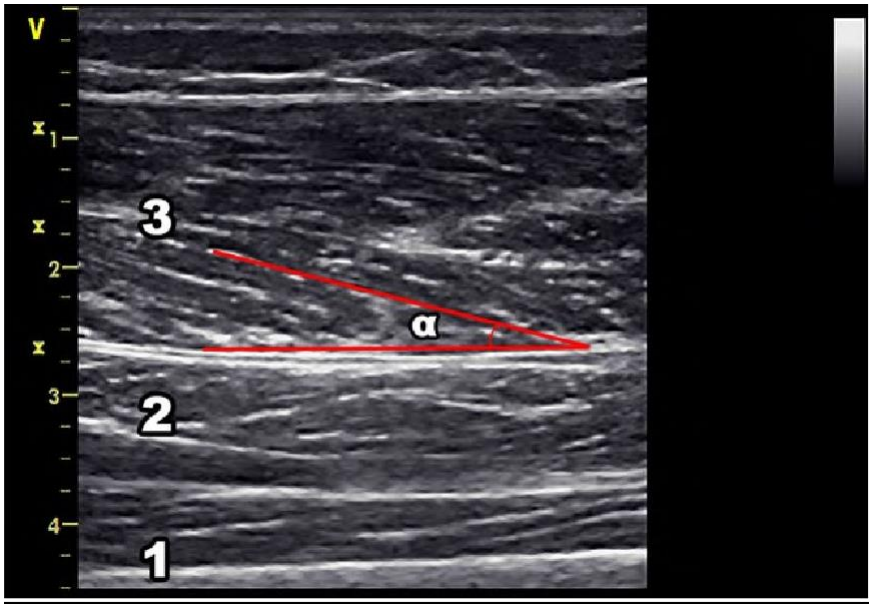


Figure 4

Echogenicity

Save the image used to measure the thickness and the sectional area. In the Image J software, delineate the entire muscle sectional area and analyze the variations in gray levels. The software provides a histogram with an overall gray level value ranging from 0 to 255 - 0 corresponding to black and 255 to white (28).

16.7 Appendix 7: Patient Information Note

SAURON

"Evaluation of the validity and reliability of muscle ultrasound in the detection of undernutrition"

RCB ID : 2022-A00581-42

PRINCIPAL INVESTIGATOR
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RESEARCH PROMOTER
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In France, the prevalence of undernutrition in hospitalized patients varies from 30 to 50%. Undernutrition is strongly associated with a decrease in the patient's functional capacities and an increase in morbidity and mortality and in health care costs. Muscle mass is described as a major diagnostic criterion, since it is on the one hand a direct indicator of protein catabolism related to undernutrition, but also a reflection of functional impairment in the patient, as it is directly associated with functional capacities, autonomy and prognosis. Ultrasound is a reproducible method for muscle assessment. However, studies remain limited to a few patient populations, and do not report clear threshold values to define the pathological status of the muscle.

We hypothesize that muscle ultrasound is reliable and valid in the evaluation of muscle function during the screening of undernutrition in a population of hospitalized patients in diabetology-obesity, pneumology, oncology and gastro-nutrition, under 70 years of age.

Madam, Sir,

Dr. ....., investigator of the study, practicing in the short stay/SSR service of diabetology-obesity/pneumology/oncology/gastro-nutrition of the Forcilles-Fondation Cognacq-Jay hospital, invites you to participate in this research.

Your decision to participate is entirely free and voluntary.

Please read the information below carefully, ask any questions you may have, and take as much time as you wish to reflect on your decision to participate in this research.

You are hospitalized in a short-stay/SSR diabetes-obesity/pneumology/oncology/gastro-nutrition department as part of the treatment of your pathology or a check-up. Your state of health requires screening for possible malnutrition in order to adapt your medical and paramedical care.

WHAT IS THE PURPOSE OF THIS RESEARCH?

The objective of this research is to evaluate the reliability and validity of muscle ultrasound in the context of screening for undernutrition. On the other hand, we wish to evaluate the correlation of muscle ultrasound with the usual measures of muscle function and to compare their diagnostic accuracy.

HOW DOES THIS RESEARCH WORK?

As part of your hospitalization in the department, we propose to study your muscle function, your body composition and your risk of undernutrition. To this end, we will perform an ultrasound of your thigh muscle, a bio-electrical impedancemetry and a self questionnaire to screen for undernutrition.

The ultrasound examination is painless, non-invasive and risk-free. It will be performed 3 times by the physiotherapist within 48 hours of your admission to the department, using the ultrasound machine, an ultrasound probe and gel water. The first 2 ultrasound examinations will be performed by the same physiotherapist, the 3rd^{ème} will be performed by another physiotherapist. The 3 ultrasound examinations take about 30 minutes.

Bioelectrical impedance measurement is also a painless, non-invasive and risk-free examination. It is performed by the dietician by placing 4 electrodes: one on the hand, one on the wrist, one on the ankle and one on the leg. Connected to a computer, they will allow us to measure your lean mass and your fat mass. The impedance measurement will be performed once, within 48 hours of your admission to the department and will last about 15 minutes.

In addition, we will ask you a few questions as part of the Mini-Nutritional Assessment questionnaire, which will take less than 5 minutes.

YOUR CONSTRAINTS IN THIS RESEARCH?

The constraints of this research consist of 3 ultrasound scans, 1 bio-electrical impedance measurement and 1 questionnaire, for a maximum total duration of 50 minutes.

POSSIBLE ADVERSE EFFECTS

Since your participation in this protocol does not involve any treatment other than that which is currently recommended or any other modification of the conventional management adapted to your health condition, no adverse effects are expected.

- **No additional treatment will be administered**
- **No additional blood tests will be required**.

Impedance measurement and ultrasound will be performed transcutaneously, i.e. by placing electrodes or a probe on your skin. These examinations are therefore non-invasive and completely painless.

Your participation in this research will not incur any additional costs compared to those you would have had in the usual follow-up of your disease.

WHAT ARE THE EXPECTED BENEFITS OF THIS RESEARCH?

Ultrasound is a relatively simple and inexpensive tool compared to other methods of measuring body composition (DEXA or MRI) and provides additional information on muscle quantity and quality compared to the usual tools for measuring muscle function (Handgrip, functional tests). The results of this study will make it possible to propose to the patient a reliable and valid evaluation tool, more easily available and less restrictive in the evaluation of the muscular quality during undernutrition. This could lead to a wider and more precise evaluation of this muscular impairment in order to propose more adapted therapeutic solutions (exercise training, weight training, nutrition).

WHAT ARE THE REQUIREMENTS TO PARTICIPATE IN THIS STUDY?

In order to participate in this research, you must be affiliated with or benefit from a social security plan. However, your participation in this research will not generate any additional costs for you compared to those incurred in the usual care.

NUMBER OF PATIENTS EXPECTED AND DURATION OF RESEARCH?

This research will last 21 months with a 20-month recruitment period in order to include 118 patients.

WHAT DATA IS COLLECTED FOR RESEARCH?

The medical data collected during this study will be processed in a computerized, coded and confidential manner. The main data collected will be anthropometric data (age, weight, height, etc.), related to medical history, nutritional status, biological check-ups, and the results of check-ups by rehabilitation professionals (physiotherapists, dieticians, EAPA). No information bearing your name will be provided to anyone except the physician in charge of the study and authorized personnel. All data collected will be confidential and coded, in accordance with the modified law of January 6, 1978 called "Loi Informatique et Libertés", and in accordance with the General Regulation on Data Protection (RGPD), and then analyzed within the clinical research office of the Forcilles-Fondation Cognacq-Jay hospital, promoter of the research. The identification list (correspondence between your code for the study and your identity) will be kept strictly confidential.

In accordance with current regulations, the data will be kept until the final research report is produced and then archived for 15 years.

The person responsible for processing the data is the promoter, Hôpital Forcilles-Fondation Cognacq-Jay, route de Servon 77150 Férolles-Attilly.

LEGAL BASIS FOR DATA PROCESSING

The processing of data is based on the legitimate interests of the controller, Article 6 paragraph 1 point f, read in conjunction with the necessity of the processing for scientific research purposes, Article 9 paragraph 2 point j, of the European Regulation No. 2016/679 (GDPR).

WHAT ARE YOUR RIGHTS?

Your participation in this research is **completely free and voluntary**. You have the right not to participate in this research.

You cannot be included in an interventional research protocol with minimal risks and constraints without having been informed beforehand. The sponsor must provide you with all the necessary explanations concerning this research, which must comply with the provisions of Article 13 of European Regulation No. 2016/679 (General Data Protection Regulation, RGPD). In accordance with article L.1122-1 of the Public Health Code, the entire research file has been submitted to the Northwest IV Committee for the Protection of Individuals, which issued a favorable opinion on xx/xx/xxxx.

The Forcilles-Fondation Cognacq-Jay hospital has taken out insurance under contract no. 163607 guaranteeing its civil liability and that of all those involved with the company SHAM.

You can stop your participation in the research at any time without justification. This will not affect the quality of the care and treatment provided to you or your relationship with your

doctor. The data collected until the withdrawal of
your consent will be used unless you expressly request it. Indeed, according to Article 17 of the GDPR, you have the right to request the deletion of your data already collected. The sponsor may object to the request for deletion of data if this would compromise the research, provided that it has informed you in advance and is able to justify this. Your withdrawal of consent and agreement to use or not use your previously collected data will be tracked in your medical record.

In accordance with the provisions of Articles 15 and 16 of Regulation (EU) 2016/679 of 27 April 2016 (General Data Protection Regulation), you have a right of access, rectification, deletion of these or a limitation of processing. You can find out more about your rights by visiting the CNIL website page https://www.cnil.fr/fr/reglement-europeen-protection-donnees/chapitre3. In accordance with the provisions of Article 21 of the RGPD, you also have the right to object to the transmission of data likely to be used in this research and to be processed. Your request must be addressed to the Data Protection Officer of the Cognacq-Jay Foundation, either by e-mail to dpo@cognacq-jay.fr or by post to the following address: Hôpital Forcilles-Fondation Cognacq-Jay, Délégué à la Protection des Données, route de Servon 77150 Férolles-Attilly. You also have the right to lodge a complaint with the Commission Nationale de l'Informatique et des Libertés - CNIL (French personal data control authority, website: www.cnil.fr).
In application of the provisions of article L. 1111-7 of the Public Health Code, you may also access all of your medical data directly or through a doctor of your choice.
Your medical file will remain confidential and can only be consulted under the responsibility of the doctor in charge of your treatment, as well as by the health authorities and by persons duly mandated by the Forcilles-Fondation Cognacq-Jay hospital for research and subject to professional secrecy.
If, after having read all this information and discussed all aspects with the doctor in charge of the research, you have had sufficient time to think about your decision and you decide to participate in this research, the research information and your oral consent will be notified and dated in your medical record.

Your participation in this study requires that we inform your treating physician, unless you object.

The agreement to participate in this research is free and voluntary.

You may refuse or withdraw your consent at any time without explanation or prejudice.

ANY QUESTIONS?

The Dr. _____ (tel _____) is at your disposal for any additional information you may require before and during the research.

Dr. _____ The investigator of the study, Dr. D., certifies that he has obtained the patient's oral consent and has recorded it in his medical record. Date of consent collection: ____ / ____ / ____ Investigator's signature:

16.8 Appendix 8: Information Note to the Family Member

SAURON

"Evaluation of the validity and reliability of muscle ultrasound in the detection of undernutrition"

RCB ID : 2022-A00581-42

PRINCIPAL INVESTIGATOR
Dr Aymeric LE NEINDRE, physiotherapist, doctor of science
Forcilles Hospital
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Email : aleneindre@cognacq-jay.fr

RESEARCH PROMOTER
Clinical Research Unit Hôpital
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Phone : 01.60.64.60.93
Fax : 01.60.02.15.09
alopes@cognacq-jay.fr

In France, the prevalence of undernutrition in hospitalized patients varies from 30 to 50%. Undernutrition is strongly associated with a decrease in the patient's functional capacities and an increase in morbidity and mortality and in health care costs. Muscle mass is described as a major diagnostic criterion, since it is on the one hand a direct indicator of protein catabolism related to undernutrition, but also a reflection of functional impairment in the patient, as it is directly associated with functional capacities, autonomy and prognosis. Ultrasound is a reproducible method for muscle assessment. However, studies remain limited to a few patient populations, and do not report clear threshold values to define the pathological status of the muscle.

We hypothesize that muscle ultrasound is reliable and valid in the evaluation of muscle function during the screening of undernutrition in a population of hospitalized patients in diabetology-obesity, pneumology, oncology and gastro-nutrition, under 70 years of age.

Madam, Sir,

Because of his condition which makes him unable to receive and understand the information that will be given to him, we are transmitting to you the information and the proposal of participation of Mr., Ms., Mr. (delete as appropriate) (last name, first name) in the study presented below, under the responsibility of
of Dr. ..... , the study investigator.

Your opinion, as for this participation, is entirely free and voluntary.

Please read the information below carefully, ask any questions you may have, and take as much time as you wish to reflect on whether or not your loved one should participate in this research.

ATTENTION

You can only give your consent :

- you and the patient you are caring for are not legally prohibited from giving such consent;

- if the patient you are caring for is covered by social security;

- if you consider that your decision would likely be that of the patient you are caring for;

- if you feel fully informed;

- if you were able to ask the doctor in charge of the study all the questions you wanted to ask about the research and the way it was going to be carried out, and if you consider that you were given satisfactory answers (if, during the study, you have new questions, you can ask them to the doctor in charge of the study, in particular if they concern the interest of the study, the ratio of benefits and risks or the usefulness of collecting certain data from your loved one) ;

- if you feel free to give your consent to such participation;

- if you accept that the patient you are caring for may not agree with you and when they get better and are consulted again, do not give consent to continue their participation.

Even if you give your consent today, you may withdraw it at any time and study-related procedures will be stopped as quickly as possible so that no harm will come to the patient. The relationship and quality of current or future care that the patient will receive will not be changed in any way should this occur. The information collected previously to this stop will be used unless you do not want it to be used. You will need to inform the patient's physician who will suggest appropriate medical follow-up.

Your loved one is hospitalized in a short-stay/SSR diabetes-obesity/pneumology/oncology/gastro-nutrition department as part of the treatment of his/her

pathology or for a check-up. His or her state of health requires screening for possible malnutrition in order to adapt medical and paramedical care.

WHAT IS THE PURPOSE OF THIS RESEARCH?

The objective of this research is to evaluate the reliability and validity of muscle ultrasound in the context of screening for undernutrition. On the other hand, we wish to evaluate the correlation of muscle ultrasound with the usual measures of muscle function and to compare their diagnostic accuracy.

HOW DOES THIS RESEARCH WORK?

As part of your loved one's hospitalization in the department, we propose to study his/her muscle function, body composition and risk of undernutrition. To this end, we will perform an ultrasound of the thigh muscle, a bio-electrical impedance measurement and a self-questionnaire to detect undernutrition.

The ultrasound examination is painless, non-invasive and risk-free. It will be performed 3 times by the physiotherapist within 48 hours of your admission to the department, using the ultrasound machine, an ultrasound probe and gel water. The first 2 ultrasound examinations will be performed by the same physiotherapist, the 3rd^{ème} will be performed by another physiotherapist. The 3 ultrasound examinations take about 30 minutes.

Bioelectrical impedance measurement is also a painless, non-invasive and risk-free examination. It is performed by the dietician by placing 4 electrodes: one on the hand, one on the wrist, one on the ankle and one on the leg. Connected to a computer, they will allow us to measure our lean body mass and our fat mass. The impedance measurement will be performed once, within 48 hours of your loved one's admission to the department and will last about 15 minutes.

In addition, we will ask her a few questions in the "Mini- Nutritional Assessment" questionnaire, which will take less than 5 minutes.

THE CONSTRAINTS IN THIS RESEARCH?

The constraints of this research for your loved one consist of 3 ultrasounds, 1 bio-electrical impedance measurement and 1 questionnaire, for a maximum total duration of 50 minutes.

POSSIBLE ADVERSE EFFECTS

Since your loved one's participation in this protocol does not involve any treatment beyond what is currently recommended or any other modifications to the conventional management adapted to his or her health condition, no adverse effects are expected.

- **No additional treatment will be administered**
- **No additional blood tests will be required**.

Impedance measurement and ultrasound will be performed transcutaneously, i.e. by placing electrodes or a probe on your skin. These examinations are therefore non-invasive and completely painless.

Your loved one's participation in this research will not result in any additional costs compared to those that would have been incurred in the usual follow-up of his or her illness.

WHAT ARE THE EXPECTED BENEFITS OF THIS RESEARCH?

Ultrasound is a relatively simple and inexpensive tool compared to other methods of measuring body composition (DEXA or MRI) and provides additional information on muscle quantity and quality compared to the usual tools for measuring muscle function (Handgrip, functional tests). The results of this study will make it possible to propose to the patient a reliable and valid evaluation tool, more easily available and less restrictive in the evaluation of the muscular quality during undernutrition. This could lead to a wider and more precise evaluation of this muscular impairment in order to propose more adapted therapeutic solutions (exercise training, weight training, nutrition).

WHAT ARE THE REQUIREMENTS TO PARTICIPATE IN THIS STUDY?

In order to participate in this research, your loved one must be affiliated with or benefit from a social security plan. However, participation in this research will not result in any additional costs for your loved one compared to those incurred in the usual care.

NUMBER OF PATIENTS EXPECTED AND DURATION OF RESEARCH?

This research will last 21 months with a 20-month recruitment period in order to include 118 patients.

WHAT DATA IS COLLECTED FOR RESEARCH?

The medical data collected during this study will be processed in a computerized, coded and confidential manner. The main data collected will be anthropometric data (age, weight, height, etc.), related to medical history, nutritional status, biological check-ups, and the results of check-ups by rehabilitation professionals (physiotherapists, dieticians, EAPA). No information bearing your family member's name will be provided to anyone except the physician in charge of the study and

authorized personnel. All data collected will be kept confidential, in accordance with the modified law of January 6, 1978 called "Loi Informatique et Libertés", and in accordance with the General Data Protection Regulation (RGPD), and coded and analyzed within the clinical research office of the Forcilles-Fondation Cognacq-Jay hospital, promoter of the research. The identification list (correspondence between the code of your relative for the study and his identity) will be kept strictly confidential.

In accordance with current regulations, the data will be kept until the final research report is produced and then archived for 15 years.

The person responsible for processing the data is the promoter, Hôpital Forcilles-Fondation Cognacq-Jay, route de Servon 77150 Férolles-Attilly.

LEGAL BASIS FOR DATA PROCESSING

The processing of data is based on the legitimate interests of the controller, Article 6 paragraph 1 point f, read in conjunction with the necessity of the processing for scientific research purposes, Article 9 paragraph 2 point j, of the European Regulation No. 2016/679 (GDPR).

WHAT ARE YOUR RIGHTS?

Your loved one's participation in this research is **entirely free and voluntary**. The sponsor of your loved one must provide you with all the necessary explanations concerning this research, which must comply with the provisions of Article 13 of European Regulation No. 2016/679 (General Data Protection Regulation, RGPD). In accordance with article L.1122-1 of the Public Health Code, the entire research file has been submitted to the North West IV Committee for the Protection of Individuals, which issued a favorable opinion on xx/xx/xxxx.

The Forcilles-Fondation Cognacq-Jay hospital has taken out insurance under contract no. 163607 guaranteeing its civil liability and that of all those involved with the company SHAM.

You may stop your loved one's participation in research at any time without justification. This will not affect the quality of the care and treatment provided to your loved one or his/her relationship with his/her doctor. The data collected until the withdrawal of consent will be used unless you expressly request it. Indeed, in accordance with Article 17 of the RGPD, your loved one has the right to request the deletion of data about him or her already collected. The sponsor may object to the request for deletion of data if this would compromise the research, provided that it has informed you in advance and is able to justify this. Withdrawal of consent and agreement to use or not use previously collected data will be tracked in your loved one's medical record.

In accordance with the provisions of Articles 15 and 16 of Regulation (EU) 2016/679 of 27 April 2016 (General Data Protection Regulation), your loved one has the right to
of access, rectification, deletion or limitation of processing. You can find out more about his or her rights by visiting the CNIL website page https://www.cnil.fr/fr/reglement-europeen-protection-donnees/chapitre3. In accordance with the provisions of Article 21 of the RGPD, your loved one also has the right to object to the transmission of data likely to be used in the context of this research and to be processed. His/her request must be addressed to the Data Protection Officer of the Cognacq-Jay Foundation, either by e-mail to dpo@cognacq-jay.fr, or by post to the address: Hôpital Forcilles-Fondation Cognacq-Jay, Délégué à la Protection des Données, route de Servon 77150 Férolles-Attilly. The user also has the right to file a complaint with the Commission Nationale de l'Informatique et des Libertés - CNIL (French authority for the control of personal data, website: www.cnil.fr).
In application of the provisions of article L. 1111-7 of the Public Health Code, your loved one may also access all medical data concerning him or her, either directly or through a physician of his or her choice.
Your loved one's medical file will remain confidential and can only be consulted under the responsibility of the doctor in charge of your treatment, as well as by the health authorities and by persons duly mandated by the Forcilles-Fondation Cognacq-Jay hospital for research and subject to professional secrecy.
If, after reading all this information and discussing all aspects with the doctor in charge of the research, you have had sufficient time to think about your decision and you agree to your loved one's participation in this research, the research information and your oral consent will be recorded and dated in your loved one's medical record.

Your participation in this study requires that we inform your treating physician, unless you object.

THE AGREEMENT TO PARTICIPATE IN THIS RESEARCH IS FREE AND VOLUNTARY.

YOU MAY REFUSE OR WITHDRAW YOUR CONSENT AT ANY TIME WITHOUT EXPLANATION OR PREJUDICE.

The Dr. _____ (tel _____) is at your disposal for any additional information you may require before and during the research.

Dr. _____ The study investigator certifies that he/she has obtained oral consent from the patient's family member and has recorded it in the patient's medical record. Date of consent collection: ____/____/____ Investigator's signature:

16.9 Appendix 9: Patient Information Note for Continuing Research

SAURON

"Evaluation of the validity and reliability of muscle ultrasound in the detection of undernutrition"

RCB ID : 2022-A00581-42

PRINCIPAL INVESTIGATOR
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alopes@cognacq-jay.fr

In France, the prevalence of undernutrition in hospitalized patients varies from 30 to 50%. Undernutrition is strongly associated with a decrease in the patient's functional capacities and an increase in morbidity and mortality and in health care costs. Muscle mass is described as a major diagnostic criterion, since it is on the one hand a direct indicator of protein catabolism related to undernutrition, but also a reflection of functional impairment in the patient, as it is directly associated with functional capacities, autonomy and prognosis. Ultrasound is a reproducible method for muscle assessment. However, studies remain limited to a few patient populations, and do not report clear threshold values to define the pathological status of the muscle.

We hypothesize that muscle ultrasound is reliable and valid in the evaluation of muscle function during the screening of undernutrition in a population of hospitalized patients in diabetology-obesity, pneumology, oncology and gastro-nutrition, under 70 years of age.

Madam, Sir,

Due to your state of consciousness, we were unable to ask for your prior consent and you were included on ...../... ...../ in a research entitled SAURON.

In accordance with the law (article L.1122-1-3 of the Public Health Code), the trusted person you have designated or your parent/relative has been asked to agree to your participation in this research.

Now that you are capable of understanding and expressing your wishes, we ask for your consent to continue your participation in this research.

The doctor told you that you were free to accept or refuse further participation in this research.

YOUR DECISION TO PARTICIPATE IS ENTIRELY FREE AND VOLUNTARY.

Please read the information below carefully, ask any questions you may have, and take as much time as you wish to reflect on your decision to participate in this research.

You are hospitalized in a short-stay/SSR diabetes-obesity/pneumology/oncology/gastro-nutrition department as part of the treatment of your pathology or a check-up. Your state of health requires screening for possible malnutrition in order to adapt your medical and paramedical care.

WHAT IS THE PURPOSE OF THIS RESEARCH?

The objective of this research is to evaluate the reliability and validity of muscle ultrasound in the context of screening for undernutrition. On the other hand, we wish to evaluate the correlation of muscle ultrasound with the usual measures of muscle function and to compare their diagnostic accuracy.

HOW DOES THIS RESEARCH WORK?

As part of your hospitalization in the department, we propose to study your muscle function, your body composition and your risk of undernutrition. To this end, we will perform an ultrasound of your thigh muscle, a bio-electrical impedancemetry and a self questionnaire to screen for undernutrition.

The ultrasound examination is painless, non-invasive and risk-free. It will be performed 3 times by the physiotherapist within 48 hours of your admission to the department, using the ultrasound machine, an ultrasound probe and gel water. The first 2 ultrasound examinations will be performed by the same physiotherapist, the 3rd^{ème} will be performed by another physiotherapist. The 3 ultrasound examinations take about 30 minutes.

Bioelectrical impedancemetry is also a painless, non-invasive examination and does not

presents no risk. It is performed by the dietician by placing 4 electrodes: one on the hand, one on the wrist, one on the ankle and one on the leg. Connected to a computer, they will allow us to measure your lean mass and your fat mass. The impedance measurement will be performed once, within 48 hours of your admission to the department and will last about 15 minutes.

In addition, we will ask you a few questions as part of the Mini-Nutritional Assessment questionnaire, which will take less than 5 minutes.

YOUR CONSTRAINTS IN THIS RESEARCH?

The constraints of this research consist of 3 ultrasound scans, 1 bio-electrical impedance measurement and 1 questionnaire, for a maximum total duration of 50 minutes.

POSSIBLE ADVERSE EFFECTS

Since your participation in this protocol does not involve any treatment other than what is currently recommended or any other modification of the conventional management adapted to your health condition, no adverse effects are expected.

- **No additional treatment will be administered**
- **No additional blood tests will be required**.

Impedance measurement and ultrasound will be performed transcutaneously, i.e. by placing electrodes or a probe on your skin. These examinations are therefore non-invasive and completely painless.

Your participation in this research will not incur any additional costs compared to those you would have had in the usual follow-up of your disease.

WHAT ARE THE EXPECTED BENEFITS OF THIS RESEARCH?

Ultrasound is a relatively simple and inexpensive tool compared to other methods of measuring body composition (DEXA or MRI) and provides additional information on muscle quantity and quality compared to the usual tools for measuring muscle function (Handgrip, functional tests). The results of this study will make it possible to propose to the patient a reliable and valid evaluation tool, more easily available and less restrictive in the evaluation of the muscular quality during undernutrition. This could lead to a wider and more precise evaluation of this muscular impairment in order to propose more adapted therapeutic solutions (exercise training, weight training, nutrition).

WHAT ARE THE REQUIREMENTS TO PARTICIPATE IN THIS STUDY?

In order to participate in this research, you must be affiliated with or benefit from a social security plan. However, your participation in this research will not generate any additional costs

for you compared to those incurred in the usual care.

NUMBER OF PATIENTS EXPECTED AND DURATION OF RESEARCH?

This research will last 21 months with a 20-month recruitment period in order to include 118 patients.

WHAT DATA IS COLLECTED FOR RESEARCH?

The medical data collected during this study will be processed in a computerized, coded and confidential manner. The main data collected will be anthropometric data (age, weight, height, etc.), related to medical history, nutritional status, biological check-ups, and the results of check-ups by rehabilitation professionals (physiotherapists, dieticians, EAPA). No information bearing your name will be provided to anyone except the physician in charge of the study and authorized personnel. All data collected will be confidential, in accordance with the modified law of January 6, 1978 called "Loi Informatique et Libertés", and in accordance with the General Data Protection Regulation (RGPD), and will be coded and analyzed within the clinical research office of the Forcilles-Fondation Cognacq-Jay hospital, promoter of the research. The identification list (correspondence between your code for the study and your identity) will be kept strictly confidential.

In accordance with current regulations, the data will be kept until the final research report is produced and then archived for 15 years.

The person responsible for processing the data is the promoter, Hôpital Forcilles-Fondation Cognacq-Jay, route de Servon 77150 Férolles-Attilly.

LEGAL BASIS FOR DATA PROCESSING

The processing of data is based on the legitimate interests of the controller, Article 6 paragraph 1 point f, read in conjunction with the necessity of the processing for scientific research purposes, Article 9 paragraph 2 point j, of the European Regulation No. 2016/679 (GDPR).

WHAT ARE YOUR RIGHTS?

Your participation in this research is **completely free and voluntary**. You have the right not to participate in this research.

You cannot be included in an interventional research protocol with minimal risks and constraints without having been informed beforehand. The sponsor must provide you with all the necessary explanations concerning this research, which must comply with the provisions of Article 13 of European Regulation No. 2016/679 (General Data Protection Regulation, RGPD). In accordance with article L.1122-1 of the Public Health Code, the entire research file has been submitted to the North West IV Committee for the Protection of Individuals, which issued a favorable opinion on xx/xx/xxxx.

The Forcilles-Fondation Cognacq-Jay hospital has taken out insurance under contract no. 163607 guaranteeing its civil liability and that of all those involved with the company SHAM.
You can stop your participation in the research at any time without justification. This will not affect the quality of the care and treatment provided to you or your relationship with your doctor. The data collected until you withdraw your consent will be used unless you expressly request it. Indeed, in accordance with Article 17 of the GDPR, you have the right to request the deletion of your data already collected. The sponsor may object to the request for deletion of data if this would compromise the research, provided that it has informed you in advance and is able to justify this. The withdrawal of your consent and the agreement to use or not use your previously collected data will be tracked in your medical record.

In accordance with the provisions of Articles 15 and 16 of Regulation (EU) 2016/679 of 27 April 2016 (General Data Protection Regulation), you have a right of access, rectification, deletion of these or a limitation of processing. You can find out more about your rights by visiting the CNIL website page https://www.cnil.fr/fr/reglement-europeen-protection-donnees/chapitre3. In accordance with the provisions of Article 21 of the RGPD, you also have the right to object to the transmission of data likely to be used in this research and to be processed. Your request must be addressed to the Data Protection Officer of the Cognacq-Jay Foundation, either by e-mail to dpo@cognacq-jay.fr or by post to the following address: Hôpital Forcilles-Fondation Cognacq-Jay, Délégué à la Protection des Données, route de Servon 77150 Férolles-Attilly. You also have the right to lodge a complaint with the Commission Nationale de l'Informatique et des Libertés - CNIL (French personal data control authority, website: www.cnil.fr).
In application of the provisions of article L. 1111-7 of the Public Health Code, you can also access all of your medical data directly or through a doctor of your choice.
Your medical file will remain confidential and can only be consulted under the responsibility of the doctor in charge of your treatment, as well as by the health authorities and by persons duly mandated by the Forcilles-Fondation Cognacq-Jay hospital for research and subject to professional secrecy.
If, after having read all this information and discussed all aspects with the doctor in charge of the research, you have had sufficient time to think about your decision and you decide to participate in this research, the research information and your oral consent will be notified and dated in your medical record.

Your participation in this study requires that we inform your treating physician, unless you object.

THE AGREEMENT TO PARTICIPATE IN THIS RESEARCH IS FREE AND VOLUNTARY.

YOU MAY REFUSE OR WITHDRAW YOUR CONSENT AT ANY TIME WITHOUT EXPLANATION OR PREJUDICE.

ANY QUESTIONS?

The Dr. _____ (tel _____) is at your disposal for any additional information you may require before and during the research.

Dr. _____ The investigator of the study, Dr. D., certifies that he has obtained the patient's oral consent and has recorded it in his medical record. Date of consent collection: ____ / ____ / ____ Investigator's signature:

17 List of investigators

LIST OF INVESTIGATORS			
FIRST NAME, LAST NAME	**ROLE**	**FUNCTION**	**CONTACT INFORMATION**
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