Fondation Cognacq-Jay
HÔPITAL FORCILLES

Construction and assessment of a new ultrasound score for the swallowing disorders diagnosis in at-risk patients

DARC-VADOC

Diagnostic AccuRaCy eValuation of **AeroDigestive** ultrasOund sCore

Version n°2 of 18/12/2020

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Interventional research involving humans with minimal risk and minimal burden (Type 2 HIPR)

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PROTOCOL VERSION HISTORY

Version	Date	Reason for the amendment
N°2	**18/12/2020**	**Responses to the IRB**

SUMMARY OF THE RESEARCH

Manager	Forcilles Hospital-Cognacq-Jay Foundation
Person who directs and monitors the research	BOURRY Natacha
Title	Construction and assessment of a new ultrasound score for the swallowing disorders diagnosis in at-risk patients attending a day hospital
Acronym	DARC-VADOC
Protocol version	n°2 of 18/12/2020
Rationale / context	The management of swallowing disorders requires a good understanding of the mechanisms or structures causing the disorder. Clinical assessment lacks precision and diagnostic reliability. Imaging examinations, although more accurate, are still based on the subjective analysis of the examiner, lack standardisation and require human and technical resources that are often inaccessible to the clinician. In this context, ultrasound, which can be performed at the patient's bedside, is non-invasive, non-irradiating and allows the qualitative and quantitative evaluation of the different structures involved in swallowing, opens up new evaluation perspectives.
Main Objective	To construct an ultrasound score to diagnose swallowing disorders in at-risk patients attending a day hospital.
Secondary objectives	- To evaluate the validity and reliability of a new ultrasound score for the diagnosis of swallowing disorders. - To assess the reliability and validity of hyoid bone ascension in the diagnosis of swallowing disorders; - To evaluate the reliability and validity of the digastric muscle thickening fraction in the diagnosis of swallowing disorders; - To evaluate the reliability and validity of the genohyoid thickening fraction in the diagnosis of swallowing disorders; - To assess the reliability and validity of the amount and duration of lingual movement in the diagnosis of swallowing disorders.
Research scheme	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	- Patients admitted to the day hospital ; - Patients with a medical indication for videofluoroscopy; - Medical prescription for physiotherapy assessment; - Ultrasound operator available; - Patient at least 18 years old at the time of inclusion; - Affiliation with a social security scheme or beneficiary of such a scheme ; - Oral, free, informed and express consent of the patient.
Non-inclusion criteria	- Patient with total laryngectomy ; - Patient's refusal to participate in the study ; - Known pregnancy ; - Person subject to a legal protection measure ; - Cognitive impairment incompatible with understanding instructions; - Patient under guardianship or curatorship ;

	- Patient in care limitation.
Primary endpoint	Selection of the variables composing the score based on their diagnostic accuracy and their contribution to the predictive model.
Secondary evaluation criteria	- To evaluate the reproducibility and diagnostic accuracy of the ultrasound score in the diagnosis of swallowing disorders; - To evaluate the reproducibility and diagnostic accuracy of hyoid bone ascension in the diagnosis of swallowing disorders; - To evaluate the reproducibility and diagnostic accuracy of the digastric muscle thickening fraction in the diagnosis of swallowing disorders; - To evaluate the reproducibility and diagnostic accuracy of the genohyoid thickening fraction in the diagnosis of swallowing disorders; - To evaluate the reproducibility and diagnostic accuracy of the amount and duration of lingual movement in the diagnosis of swallowing disorders.
Comparison groups	Videofluoroscopy will be used as a reference examination.
Number of subjects needed	100
Expected number of centres	1
Duration of the research	25 months
Statistical analysis of data	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). The ultrasound variables will be compared between the 2 groups by the appropriate tests according to the type of variables (quantitative or qualitative) and their distribution. The selection of variables in the prediction model will be performed by multivariate logistic regression based on the AIC. The study of inter and intra-examiner reproducibility will be evaluated with the Kappa coefficient. The threshold of the ultrasound score defining the presence of swallowing disorders will be determined using ROC (Receiver Operating Characteristic) curve analysis. Sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios and the diagnostic ODD-Ratio will be estimated.
Expected benefits	We expect excellent reliability and validity of ultrasound in the diagnosis of swallowing disorders, which would make it possible to propose an alternative examination to videofluroroscopy that would be more easily performed on an outpatient basis, non-invasive and non-irradiating.
Source of funding	Forcilles Hospital-Cognacq-Jay Foundation
Independent Supervisory Committee planned	No

LIST OF ABBREVIATIONS

DOSS	Dysphagia Outcome and Severity Scale
HDJ	Day Hospital
FEES	Swallowing fibroscopy
NOT	Penetration-Aspiration Scale
ROC	Receiver Operating Characteristics
SC	Clinical score
SRH	Follow-up and rehabilitation care
VFSS	Videofluoroscopy

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1 Rationale for the research

1.1 Swallowing disorders

Swallowing is the mechanism that allows food to be grasped, prepared in the oral cavity and then propelled from the oropharynx to the stomach while protecting the airways. This is a complex semi-reflexive sensory-motor mechanism involving many functions and anatomical structures. It involves more than fifty muscles, six cranial pairs and cortical structures, including the fronto-parietal operculum, the primary sensorimotor cortex and the anterior insula association. (1)

Impairment of any of these functions or structures of swallowing, whether neurological, muscular or mechanical, resulting in partial or total inability to transport the bolus of food to the lower digestive tract is called dysphagia or swallowing disorder.

In some clinical contexts, the particularly high prevalence of these disorders motivates the quasi-systematic screening of patients. This is the case, for example, in intensive care, ENT oncology and post-stroke. (2)(3)

The presence of swallowing disorders can lead to undernutrition, dehydration or the development of inhalation pneumonitis. (4)(5) These complications related to swallowing disorders are associated with an increase in patient morbidity and mortality, mainly in terms of increased length of stay, hospital costs, readmission rates and mortality. (6)(7)(8)

The complexity of the swallowing mechanism, as well as the lack of specificity of the symptoms often encountered, requires a multidisciplinary assessment (9). The lack of precision of clinical tests will require the use of additional imaging or endoscopy. (6)(10)

1.1. Background to the onset of swallowing disorders

Swallowing disorders, although under-diagnosed (8)The prevalence of swallowing disorders, although under-diagnosed, can be as high as 30% in hospitalised patients. (11) This prevalence is particularly high in certain clinical situations such as neurological disorders or diseases like Parkinson's disease (80%) (12)neuromuscular diseases (80%) (13) or post-stroke (81%) (14). In head and neck cancers, especially after surgery, the prevalence can be as high as 61%; (15). In intensive care, they may be the consequence of intubation, tracheotomies and prolonged mechanical ventilation, (16)(17)(7) or even the reason for admission to the intensive care unit. (18)(5)

1.2 Day hospital for swallowing disorders

Dysphagia is a historically important disorder at Forcilles because of its prevalence in the population admitted to hospital. Various health professionals are organised around the multidisciplinary management of these disorders in the different departments of the hospital.
The need to bring together this expertise, in order to meet the growing demand from independent professionals and other surrounding health establishments, in particular the geriatric, acute medicine and ENT cancer departments, led to the creation of a swallowing day hospital (HDJ).
Most patients admitted to HDJ have sarcopenia, ENT cancers and/or have had long periods of mechanical ventilation and may still have a tracheostomy.
The HDJ therefore welcomes patients with the risk factors described above for swallowing disorders. The examinations that will be carried out are prescribed by the doctor responsible for the medical care of the patient.
The following equipment is available in the HDJ: an endoscopy column and the medical equipment necessary to monitor the patient's vital parameters; a radiology room with the necessary equipment for videofluoroscopy and two consultation rooms. Thus, within this HDJ, a doctor is involved, responsible for the unit, who ensures the medical evaluation of the patient, the carrying out of medical examinations when they are indicated and the submission of the end of hospitalisation report; a radiologist doctor who ensures the carrying out of imaging examinations; physiotherapists and speech therapists in charge of the clinical assessment of the patient and dieticians who carry out a consultation in order to detect and manage any undernutrition, and also to adapt the patient's diet to the food textures recommended by the speech therapists following their assessment.

1.3 Diagnostic strategy for swallowing disorders

1.3.1 Clinical assessment

Clinical assessment of swallowing includes analytical evaluation of the structures involved and the use of composite tests or feeding trials. The clinician may also use self-report questionnaires to assess the patient's feelings to guide exploration. (19)
As part of the analytical assessment, the speech and language therapist, after reading the medical record and interviewing the patient, assesses structures such as the lips, cheeks and tongue, and explores the cranial nerves and reflexes involved in swallowing. (20)(21)
He will also assess the pharyngeal phase during palpation of the larynx and cervical auscultation during swallowing. (22)

For feeding trials, many standardised tests are described in the literature. They are based on a swallow test and the clinician's identification of signs such as coughing, oxygen desaturation or voice changes, which may indicate inhalation. (20) These tests differ in the amount of test food administered, the variability of its texture, and their methodology.

Many studies have assessed the validity of these tests and the clinical examination for swallowing disorders. The majority of these studies have focused on screening in a post-stroke patient population, thereby validating some of these tests in this patient population. (23)(24) Several reviews of the literature have been carried out in recent years and all agree on the heterogeneity of the studies, the large number of existing assessment methods and the lack of a standardised test with sufficient predictive value in different populations such as neurological and neuromuscular diseases, cancers of the ENT sphere, in elderly subjects or in intensive care patients (8)(10)(13)(25).

Furthermore, these assessments remain based on the feeding trial and do not allow for the diagnosis of deficiencies in the structures and functions involved in swallowing and therefore to orientate the therapeutic strategy.

1.3.2 Radiology and fibroscopy

The literature agrees that videofluoroscopy (VFSS) and swallowing fibroscopy are the gold standards for swallowing assessment. (26)(27) Different quantities and textures, which will evolve progressively according to the outcome of the first feeding trials, will be used to assess the patient's swallowing abilities.

Real-time visualization of swallowing will allow the clinician to objectify inhalation as a sign of a swallowing disorder (28) and to estimate its severity by means of scores such as the "Dysphagia outcome and severity scale" (DOSS) or the "Penetration-Aspiration Scale" (PAS). (29)(30)(31) (**Appendices 1 and 2**).

For VFSS, the liquids/foods administered to the patient are mixed with barium in order to follow the course of the food bolus. This allows the assessment of all three phases of swallowing and a better assessment of the oral phase compared to nasofibroscopy of swallowing (FEES). However, it does not allow the analysis of the anatomy of structures and requires the patient to be transported to an equipped room and exposed to radiation.

The FEES, thanks to its location at the tip of the epiglottis during the examination, has the advantage of allowing the evaluation of tissues, possible local trauma or the presence of secretions. In addition, it allows the evaluation of the sensitivity of the larynx. However, this examination is often uncomfortable for the patient and requires the frequent use of a local anaesthetic which alters sensitivity. (6) Physiological movements during swallowing make it

difficult to see the vocal cords. The examiner will have to lower the fiberscope afterwards to look for signs of inhalation. Furthermore, there is a lack of a standardised protocol. (32)

1.3.3 Ultrasound evaluation

It allows the qualitative and quantitative assessment of the structures involved in the three phases of swallowing: the strength of the tongue, the kinetics of the lingual propulsion, the thickness of the supra- and infra-hyoid muscles at rest and during swallowing, the ascent of the hyoid bone and the larynx, and the mobility and diameter of the upper esophageal sphincter.

The application of ultrasound in swallowing assessment has been described for many years. (33) It is an easy to use, reproducible, bedside tool that is non-invasive and non-irradiating.

Ultrasound assesses the kinetics of the tongue for abnormal movements and the contractility and thickness of the oropharyngeal muscles to diagnose possible dysfunction. (34)(35)

Ultrasound will allow quantitative and qualitative analysis of lingual kinetics during swallowing, in particular looking for abnormal movement patterns. (36)(37)

It is also possible to quantify the movement in search of a propulsion defect. (38)(39) It also allows qualitative and quantitative assessment of the geniohyoid, mylohyoid and digastric muscles.

The thickness of these muscles at rest and during swallowing and their echogenicity can be quantified.(40)(41) The measurement of the thickness of these muscles is reproducible and its accuracy in assessing the digastric muscles has been compared with MRI, showing a very good correlation. (42)(45)

During this second phase of swallowing, it will also be possible to measure the duration and distance of hyoid bone elevation, reflecting laryngeal elevation. (43)(44)(45) A decrease in hyoid bone elevation associated with a decrease in lingual contraction capacity as seen on ultrasound can explain dysphagia. (46)

Finally, ultrasound can be used to assess the displacement and diameter of opening and closing of the upper oesophageal sphincter (USO), allowing the detection of dysphagia related to USO damage. (47)

This ultrasound evaluation will complement the clinical evaluation of reflexes, cranial pairs or the patient's posture or vigilance, with a quantitative analysis of the structures mentioned above, for which the clinical examination lacks precision and reliability and needs to be supplemented by complementary examinations. (48)(49)

This quantitative, reproducible, non-invasive, non-radiating, bedside ultrasound analysis represents a promising tool for clinical practice to monitor patient progress. (50)

Numerous studies have investigated the use of ultrasound as a diagnostic tool for swallowing disorders in different patient populations. (43)(51)(52) However, these studies are limited by their small size, often include healthy subjects, do not usually define a threshold value necessary for diagnosis and do not combine the evaluation of the different structures involved in swallowing.

1.4 Research hypothesis

We hypothesise that an ultrasound score is reliable and valid in the assessment of swallowing disorders in at-risk patients admitted to the swallowing day hospital.

2 Objective

2.1 Main objective

The main objective of this study is to construct an ultrasound score to diagnose swallowing disorders in at-risk patients attending a day hospital.

2.2 Secondary objectives

In at-risk patients admitted to a day hospital Swallowing :

- To evaluate the validity and reliability of a new ultrasound score for the diagnosis of swallowing disorders.
- To assess the reliability and validity of hyoid bone ascension in the diagnosis of swallowing disorders;
- To evaluate the reliability and validity of the digastric muscle thickening fraction in the diagnosis of swallowing disorders;
- To evaluate the reliability and validity of the genohyoid thickening fraction in the diagnosis of swallowing disorders;
- To assess the reliability and validity of the amount and duration of lingual movement in the diagnosis of swallowing disorders.

3 Outcome

3.1 Primary outcome

The main outcome is the selection of the variables composing the score based on their diagnostic accuracy and their contribution to the predictive model.

3.2 Secondary outcomes

The secondary outcomes will be :

- To evaluate the diagnostic accuracy and reproducibility of the ultrasound score in the diagnosis of swallowing disorders
- To evaluate the reproducibility and diagnostic accuracy of hyoid bone ascension in the diagnosis of swallowing disorders
- To evaluate the reproducibility and diagnostic accuracy of the digastric muscle thickening fraction in the diagnosis of swallowing disorders
- To evaluate the reproducibility and diagnostic accuracy of the genohyoid thickening fraction in the diagnosis of swallowing disorders
- To evaluate the reproducibility and diagnostic accuracy of the amount and duration of lingual movement in the diagnosis of swallowing disorders

4 Eligibility criteria

4.1 Inclusion criteria

Patients with the following criteria will be included:

- Patients admitted to the day hospital ;
- Patients with a medical indication for videofluoroscopy ;
- Medical prescription for physiotherapy assessment ;
- Ultrasound operator available;
- Patient at least 18 years old at the time of inclusion;
- Affiliation with a social security scheme or beneficiary of such a scheme ;
- Oral, free, informed and express consent of the patient.

4.2 Non-inclusion criteria

Patients with the following criteria will not be included:

- Patient with total laryngectomy ;
- Patient's refusal to participate in the study ;
- Known pregnancy ;
- Person subject to a legal protection measure ;
- Cognitive impairment incompatible with understanding instructions;
- Patient under guardianship or curatorship ;
- Patient in care limitation.

4.3 Recruitment procedures

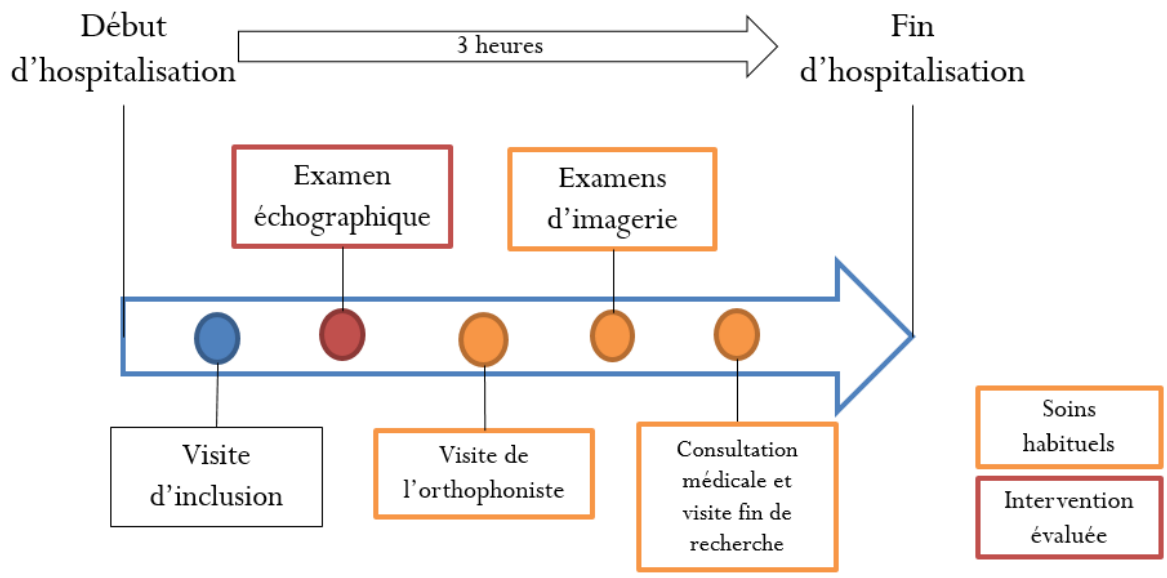
Patients will be recruited prospectively and consecutively in the HDJ Déglutition of the Forcilles Hospital, the only inclusion centre. The doctor in charge of the unit identifies the patients during the initial consultation.
The number of annual admissions is 108 patients. The monthly recruitment target is 4 patients.

5 Research design

5.1 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.

5.2 Research scheme



5.3 Provisional research timetable

The recruitment period will be 25 months with a half-day follow-up of patients, for a total estimated study duration of 25 months.

- Submission to IRB: November 2020
- Start of inclusions: January 2021
- Duration of the inclusion period: 25 months
- Duration of each patient's participation: half a day
- End of inclusions: February 2023
- Total duration of the research: 25 months
- Communication in congresses: Société de Rénimation de Langue Française ; Congrès de Pneumologie de Langue Française ; Journées Francophones en Kinésithérapie ; Association de Rééducation Oro-Maxillofaciale ; SEPAR ;
- Publication: July 2023

5.4 Location of the study

The study will take place at the Forcilles Hospital, in the HDJ dedicated to the evaluation of swallowing disorders.

6 Description of the usual care in HDJ deglutition

6.1 Description of the usual course of the HDJ

A total of three patients can be admitted each week in this HDJ, one patient per half-day in each of the three half-days dedicated to it. This HDJ lasts approximately three hours and starts with the reception of the patient by the nurse and continues with :

- Clinical examination and swallowing test (physiotherapist and speech therapist) ;
- Nasofibroscopy (ENT doctor) ;
- Videofluoroscopy (radiologist) ;
- Dietetic consultation (dietician) ;
- Medical consultation (delivery of the hospital report).

After all investigations have been carried out and before the dietetic consultation, a consultation meeting is held between the doctor, the speech therapist and the dietician of the unit. This meeting allows the therapeutic strategy and any necessary adaptations to be defined.

After the meeting, the dietician receives the patient in consultation and informs him/her of the recommendations necessary to maintain or recover a satisfactory nutritional status, while following the adaptations of the mode of feeding possibly decided in the consultation meeting.

Finally, the patient is received by the doctor in charge of the unit who gives him the hospitalization report.

All examinations and consultations are carried out within the usual framework of the HDJ Déglutition and are systematically prescribed by the doctor in charge.

6.2 Standard assessment procedures

6.2.1 Clinical examination of swallowing

The speech and language therapist studies the patient's medical file and takes note of the reason for hospitalisation (and possibly of the swallowing disorder assessments and treatments carried out previously). The SLT then carries out a clinical assessment of the patient.

This assessment consists of two parts: the clinical examination and the swallowing test.

This examination consists mainly of observation and palpation of the different structures at rest and during active movements (praxis) and counter-resistance requested by the speech therapist. This allows the evaluation of :

- The tone and mobility of the lips, tongue, cheeks, soft palate and temporomandibular joints;
- Reflex and airway protection mechanisms;

- Cranial pairs involved in swallowing and the oro-maxillofacial sphere;
- Posture and motor control of the head, cervical spine and upper limbs.

Following these investigations, swallowing trials with different textures are routinely performed.(28) The speech and language therapist will look for signs of swallowing disorders such as coughing or voice changes.

6.2.2 Videofluoroscopy

This examination takes place in the radiology department of the Forcilles Hospital. It is the last examination performed by the patient. The electro-radiology manipulator (MER) carries out the examination on the prescription and under the supervision of the radiologist, as defined by the legal framework for this examination. The speech therapist is present to collect information useful for the assessment and the possible proposal of rehabilitation. Swallowing tests with different textures and quantities are carried out. The details of the order of the swallowing tests, the textures and quantities used are described in **Annex 3**.

7 Evaluation procedure added by the research

A swallowing ultrasound will be added as part of the research.

7.1 Operator training in ultrasound

The ultrasound examination will be performed by a physiotherapist, blind to the totality of the examinations performed on the patient. The details of the ultrasound examination carried out within the framework of the protocol can be found in **appendix 4**.

The operator training is as follows:

- 3 days of theoretical and practical training;
- More than 100 ultrasounds supervised by a radiologist;
- Two years of independent practice.

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 and https://clinicaltrials.gov/ct2/show/NCT04373811

7.2 Practical details of the ultrasound examination

The examination, the details of which can be found in **Appendix 4,** is carried out using a Sonoscape Expert 2 ultrasound scanner (Digital Color Doppler Ultrasound System; Sonoscape medical corp. China) equipped with a linear probe (7-10 MHZ) and a convex probe (3-5 MHZ). Both probes will be used for each of the swallowing trials.
In order to assess inter- and intra-examiner reliability, the tests will be performed by two different operators and twice by the same operator, i.e. 3 identical examinations in total, in the first 20 patients included.
The duration of an examination will not exceed 15 minutes, i.e. a total duration of the ultrasound examination of 45 minutes for the first 20 patients (15 minutes for examination, 3 examinations).
The patient is in a sitting position and performs salivary swallowing attempts on request of the operator.

The convex probe will be placed under the chin, in the sagittal plane and between the edges of the hyoid bone and the mandible. The acoustic shadows of these bones will allow us to localise the structures and centre the image. (53)(54)

The following elements will be assessed:

- The position of the hyoid bone at rest and during swallowing;
- The thickness of the geniohyoid at rest and during swallowing;
- The contractility of the tongue ;
- The duration of contraction of the geniohyoid ;
- The number of swallowing attempts.

The linear probe will also be placed submentally, along a transverse axis, in order to qualitatively and quantitatively evaluate the suprahyoid muscles (55)
Qualitative analysis will be performed using the Heckmatt Score. (56) Quantitative analysis will be performed by measuring the thickness of the muscles at rest and during contraction. These two measurements will be used to calculate its thickening fraction. The thickness of the muscle is calculated by quantifying the distance between the upper and lower fascia of the muscle.

7.3 Semiology in aerodigestive tract ultrasound

The different dysfunctions of the structures or functions involved in swallowing can be defined on ultrasound by the following signs

(1) Lingual dysfunction (53)(57)(54):
   a. Abnormal movement pattern ;
   b. Several attempts identified;
   c. Decreased range of motion ;
   d. Decrease in thickness.

(2) Suprahyoid muscle dysfunction (58)(59) :
   a. Decrease in signal strength ;
   b. Fat invasion and poorly defined muscle boundaries;
   c. Decrease in thickness or surface area compared to contralateral ;
   d. Decreased mobility and thickening fraction compared to contralateral.

(3) Genohyoid dysfunction (55)(60) :
   a. Decreased thickening fraction.

(4) Laryngeal ascension defect (60)(58) :
   a. Ascension <1.5cm. measured indirectly by assessment of hyoid bone ascension.

8 Conduct of the research

8.1 Pre-inclusion visit

8.1.1 Checking inclusion and non-inclusion criteria

When a patient is admitted to the HDJ, the doctor in charge of the unit checks the presence of the inclusion criteria and the absence of the non-inclusion criteria in the medical file sent to him by the doctor referring the patient and in the patient's computerised file, if applicable.

8.1.2 Patient information and consent

When all the criteria allow the inclusion of the patient, the investigating physician informs the patient of the purpose of the study during a consultation. He/she provides the patient with all the information described in the information note (**appendix 5**) and, if necessary, obtains the patient's free, informed and express oral consent. This consent will be recorded in the patient's computerised medical record.

8.2 Inclusion visit

The inclusion visit takes place when the patient agrees to participate in the study. The following data will be collected:

(1) Basic data :
   a. Age, gender, height, weight ;
   b. Medical history :
      i. Oral language disorders ;
      ii. Stay in intensive care: indicate if the patient required mechanical ventilation, tracheotomy, nasogastric tube;
      iii. Neurological alterations/diseases: previous stroke; Parkinson's; ALS; dementia;
      iv. Cervical, ENT or oesophageal surgery, (attach surgical report) ;
      v. Orthodontic treatment.

(2) Information on nutritional status ;

(3) Presence or absence of a tracheostomy at the time of the examination;

(4) Presence or absence of a nasogastric tube at the time of the examination ;

(5) Data on care :

a. Professional who requested hospitalization ;
b. Diagnostic hypothesis of the referring clinician ;
c. Information on the management of swallowing disorders ;
d. Dietary adaptations.

8.3 Visit of the ultrasound operator

The ultrasound examination is the first examination performed in order to maintain the operator's ultrasound blindness. It will take place in the consultation room provided in the HDJ.

8.4 Visit from the speech therapist

This visit takes place following the ultrasound examination. Before the visit and the clinical examination, the speech and language therapist will read the patient's medical file. The SLT then carries out the clinical examination in the usual way.

8.5 Performing imaging tests

Imaging examinations will take place after the ultrasound examination and the SLT visit. They will be carried out in accordance with the procedure described in **Appendix 3**. After the imaging tests have been carried out and depending on the results, the speech and language therapist will adapt the advice on food textures to the patient.
Following this examination and taking into account the results of the various investigations carried out during the day, the speech and language therapist will summarise the assessment and choose the dietary adaptations. The degree of severity corresponding to the DOSS scale, details of which are given in **Appendix 1**, will be noted in the observation booklet.

8.6 End of research visit

This visit takes place during the end-of-day consultation. It is carried out by the doctor in charge of the unit, who gives the patient the hospitalization report and ensures the transcription of the information in the research observation book.

8.7 Summary table

	Pre-inclusion	Inclusion	Visit of the ultrasound operator	Visit from the speech therapist	Performing imaging tests
Information for the patient or relative	✓				
Collection of basic data (age, sex, BMI, medical history)		✓			
Collection of the reason for hospitalisation in HDJ		✓			
Collection of information on medical and rehabilitation care		✓			
Clinical examination				✓	
Ultrasound examination			✓		
VFSS					✓
DOSS and PASS information					✓

9 Statistical aspects

9.1 Calculating the size of the study

The calculation of the number of subjects required is based on the number of explanatory variables to be included in the multiple logistic regression model to construct the ultrasound score. The "1 variable per 10 events" rule is applied. (61)

A total of 5 variables will be collected and analysed as described above (see 9.5), with an estimated prevalence of swallowing disorders of 50%.

There are therefore potentially 5 variables to be included in the predictive model, i.e. a required number of 100 patients.

9.2 General aspects

Descriptive statistics will be based on means (+/- standard deviation) or medians [minimum-maximum] 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).

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

Measures of association between quantitative variables will be made 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.

Calculations will be made using IBM SPSS v21 and R software (version 3.6.1, www.R-project.org).

9.3 Potential variables of the ultrasound score

Structures assessed		Results	Weighting
Language			
	Abnormal movement	Yes/No	
	> 1 attempt identified	Yes/No	
	Range of motion	< threshold > threshold (only to be defined)	
	Thickness	< threshold > threshold (threshold to be defined)	
Suprahyoid muscles			
	Signal strength (Heckmatt score)	1-4	
	Poorly defined fat involution and muscle boundaries	Yes/No	
	Decreased surface area compared to contralateral	Surface < threshold (threshold to be defined)	
	Thickening fraction compared to contralateral	< threshold > threshold (only to be defined)	
Geniohyoid			
	Decreased thickening fraction	< threshold > threshold (only to be defined)	
Laryngeal ascension			
	Ascension measured indirectly by assessment of hyoid bone ascension	< threshold > threshold (only to be defined)	

9.4 Determination of classes and thresholds of quantitative variables

The hypothesis of a linear relationship between the logit of the diagnosis of swallowing disorders objectified by VFSS and the quantitative variable will be tested. If it is verified, the variable will be dichotomised. The threshold used will be determined using ROC (Receiver

Operating Characteristic) curve analysis, which will allow the threshold for which sensitivity and specificity are maximum to be retained. (62)
The variables for which the hypothesis is not verified will be split into classes. (63)

9.5 Selection of variables to be included in the score

Patients will be classified into 2 groups according to the diagnosis obtained with VFSS: positive group (presence of swallowing disorders) and negative group (absence of swallowing disorders). The ultrasound variables will be compared between the 2 groups by appropriate tests according to the type of variables (quantitative or qualitative) and their distribution. The results of these comparisons will be used to select the ultrasound variables showing a difference between the 2 groups ($p < 0.20$) for inclusion in the multivariate logistic regression. (62)(63)

9.6 Weighting of variables

The previously selected ultrasound variables will be included in the model predicting the presence of swallowing disorders. Multiple logistic regression with variable selection using the Akaike information criterion (AIC) method will be used. The presence of multicollinearity between variables will also be investigated and the variable eliminated if necessary.
Variables that do not improve the predictive model will thus be removed from the score.
The scores for each variable resulting from the multivariate logistic regression will be used to weight each variable in the ultrasound score. (62)(63)

9.7 Score validation

9.7.1 Reliability

With the correlation coefficient $\rho = 0.80$, a minimum value of the desired correlation coefficient $\rho_0 = 0.50$, a number of observations $k = 2$, $\alpha = 0.05$ and $\beta = 0.20$, the critical value for α from the normal distribution is 1.645 and the critical value for β from the normal distribution is 0.842. It is necessary to include 20 patients.
The study of inter and intra-examiner reproducibility will be evaluated with the Kappa coefficient. (64)

9.7.2 Validity

The threshold of the ultrasound score defining the presence of swallowing disorders will be determined using Receiver Operating Characteristic (ROC) curve analysis.

Sensitivities, specificities, positive and negative predictive values and the diagnostic Odd ratio will be calculated to determine the diagnostic accuracy of the score.

10 Expected results in terms of scientific and professional advances

This study will allow the construction and evaluation of the reliability and validity of a new ultrasound score in the diagnosis of swallowing disorders. To our knowledge, no study has evaluated the performance of an ultrasound score in the diagnosis of swallowing disorders.
The analysis of the different structures involved in swallowing will also provide knowledge on the impairment of the functions and structures involved in swallowing. This may allow to better orientate the therapeutic strategy, both medical and rehabilitation.
Moreover, as the ultrasound examination is non-invasive, non-irradiating, can be performed in a simple consultation room and requires minimal cooperation from the patient, it could be an alternative to videofluroroscopy, currently the reference examination.
Swallowing ultrasound could thus also be a tool for monitoring the effectiveness of the treatments implemented, since it can be performed frequently without adverse effects.
The results of this study will only be applicable to a population of patients consulting a day hospital for suspected swallowing disorders, mostly related to ENT surgery or a prolonged stay in an intensive care unit. Further multicentre work and in other population categories to improve external validity.

11 Expected benefits and risks for patients

11.1 Minimal risks and constraints added by the research

The risks and constraints for the patient will only be the extra time spent by the patient on the ultrasound. Ultrasound is a non-invasive, non-irradiating and totally painless tool.

11.2 Expected benefits for the patient

Ultrasound allows a quantitative and qualitative evaluation of the structures involved in swallowing disorders. It is a non-invasive, non-irradiating diagnostic tool that can be performed in a consultation. To our knowledge, there is no ultrasound score for the diagnosis of swallowing disorders. Videofluoroscopy is an irradiating examination, requiring the displacement of the patient and mobilizing a specialized multidisciplinary team. We expect excellent reliability and validity of ultrasound in the diagnosis of swallowing disorders, which

would make it possible to propose an alternative examination to videofluoroscopy that would be more easily performed on an outpatient basis, non-invasive and non-irradiating.

12 Feasibility

The Forcilles Hospital has a technical platform dedicated to the HDJ deglutition with a capacity of three patients per week, at a rate of one patient per day for three days. Given the difficulty of the surrounding health structures to have the human and technical resources to carry out the examinations proposed in this HDJ deglutition, many patients are referred to the Forcilles Hospital. The data relating to admissions over the last two years allow us to envisage 90 patients over a 10-month period.

The medical and physiotherapy team has experience in clinical research, as they are already 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).

Taking into account the inclusion and non-inclusion criteria, possible refusals of patients to participate in the research, potential exclusions and the recruitment experience, we estimate a minimum recruitment capacity of 50% of patients with risk factors for swallowing disorders admitted to HDJ for evaluation of these disorders, i.e. 100 patients in 25 months

13 Ethical and regulatory aspects

The Forcilles-Fondation Cognacq-Jay hospital promoter and the person(s) directing and supervising the research undertake to ensure that this research is carried out in accordance with law n°2004-806 of 9 August 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 computerised processing in compliance with law n°78-17 of 6 January 1978 relating to information technology, files and freedoms, amended by law n° 2018-493 of 20 June 2018 (decree n° 2018-687 of 1° August 2018) and order n° 2018-1125 of 12 December 2018.

The research will be conducted in accordance with this protocol.

13.1 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 relevant Comité de Protection des Personnes

(CPP) (CPP Ouest III) whose opinion will be notified in the information note intended for the persons concerned.
The natural or legal person who initiates the research, manages it and ensures that it is financed is called the sponsor.

13.2 Submission to the PPC

This research will be submitted to a Committee for the Protection of Individuals, which will be drawn by lot within the framework of the "Jardé law" (article L.1121-4 of the Public Health Code, decree no. 2016-1537 of 16 November 2016, which came into force on 18 November 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.

13.3 Data protection

This research is subject to law n°78-17 of 6 January 1978 relating to information technology, files and freedoms as amended by law n° 2018-493 of 20 June 2018 (decree n° 2018-687 of 1 August 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 carried out in the context of biomedical research defined by Law 2004-806 of 9 August 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 3 May 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.

13.4 Insurance

The Sponsor takes out insurance covering its own civil liability and that of any person involved in the performance of the research for the entire duration of the research, regardless of the nature of the links between the participants and the Sponsor (Article L.1121-10 of the Public

Health Code). The sponsor is also responsible for the compensation of the harmful consequences of the research for the person who undergoes it and for that of his or her dependents, unless it can be proved that the damage is not attributable to its fault or to that of any other party involved, without the possibility of invoking the act of a third party or the voluntary withdrawal of the person who initially agreed to undergo the research. Where 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 no. 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.

13.5 Substantial amendment 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.

13.6 Information note and express consent

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

The investigator at the centre offers the patient, or a relative if the patient is incapacitated, to participate in the study. The investigator informs the patient orally of the terms of 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 event that a relative of the patient has given consent, as soon as possible, the patient will be informed of the 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 the patient expressly requests otherwise. The withdrawal of consent by the patient and the agreement to use or not the data previously collected will be traced in the patient's medical file.

When the research is completed, the person who is to be the subject of the research may be informed of the overall results of the research in a manner to be specified in the information document.

13.7 Expected deadline for publication of results in an international journal

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

13.8 Data management

For each subject, an identification code (corresponding to the centre number-inclusion number-Initial Surname-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 principal investigator in a file with computer restricted access rights. The data will be entered into a password protected Excel® file held by the principal investigator. Data processing and statistical analysis will be carried out at the Forcilles-Fondation Cognacq-Jay hospital.
The promoter is the owner of the data and no use or transmission to a third party can be made without his prior agreement.
The specific documents of a type 2 interventional research ("Loi Jardé", decree n° 2016-1537 of 16 November 2016, which came into force on 18 November 2016) with minimal risks and constraints will be archived by all parties for a period of 15 years after the end of the research.
This indexed archive includes :

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

13.9 Human and financial resources

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

13.10 Data properties

The Forcilles-Fondation Cognacq-Jay Hospital is the owner of the data and no use or transmission to a third party may be made without its prior agreement.

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15 ANNEXES

15.1 Appendix 1: Dysphagia Outcome and Severity Scale

Completely oral feeding: normal diet

- Level 7: Normal in all situations
- Level 6: Functional swallowing; with functional limitations/independent with modifications

Modified scheme and/or adaptations

- Level 5: Mild dysphagia; mild monitoring, may require restriction of one type of texture
- Level 4: Mild to moderate dysphagia: intermittent monitoring, one or two restricted textures
- Level 3: Moderate dysphagia: full assistance, supervision, two or more restricted textures

Need for additional artificial nutrition

- Level 2: Moderate to severe dysphagia: significant assistance or need for strategies with partial oral feeding (tolerates at least one texture with use of strategies)
- Level 1: Severe dysphagia: no oral feeding: unable to tolerate oral intake

15.2 Appendix 2: Penetration-aspiration scale

Category	Score	Description
No penetration or suction	1	The material does not fit into the VA
Penetration	2	The material enters the VA, remains above the vocal cords and is ejected from the VA
	3	The material enters the VA, remains above the vocal cords and is not ejected from the VA
	4	Material contacts the vocal cords and is ejected from the VA
	5	Material contacts the vocal cords and is not ejected from the VA
Suction	6	Material enters the VA, passes through the vocal cords and is ejected into the larynx or out of the VA
	7	The material enters the VA, passes through the vocal cords, and is not ejected from the trachea despite patient effort
	8	The material enters the VA, passes through the vocal cords and no ejection effort is made by the patient

15.3 Appendix 3: Procedure for performing Videofluoroscopy

- **Conduct of the examination :**

The examination must be carried out in the presence of the radiologist and the doctor and speech therapist responsible for the HDJ care.

All professionals will ensure that they have the necessary equipment to monitor the patient's vital parameters. If alterations in vital parameters, patient discomfort or any other reason for stopping the examination, the doctor will fill in the adverse event sheet.

If the examination could not be finalised, the patient will be excluded from the protocol. The exclusion of the patient for non-interpretable examination will be noted in the research observation booklet.

Swallowing trials will be conducted in the quantities and textures described above. The food will be mixed with barium to allow for vision.

For each trial, we will ask the patient to take the food/liquid and swallow it after the professional has indicated.

Tests 1-4 will be performed in lateral projection. Test 5 will be performed in anteroposterior projection.

- **Patient position:**

- Lateral projection (trials 1-4) :

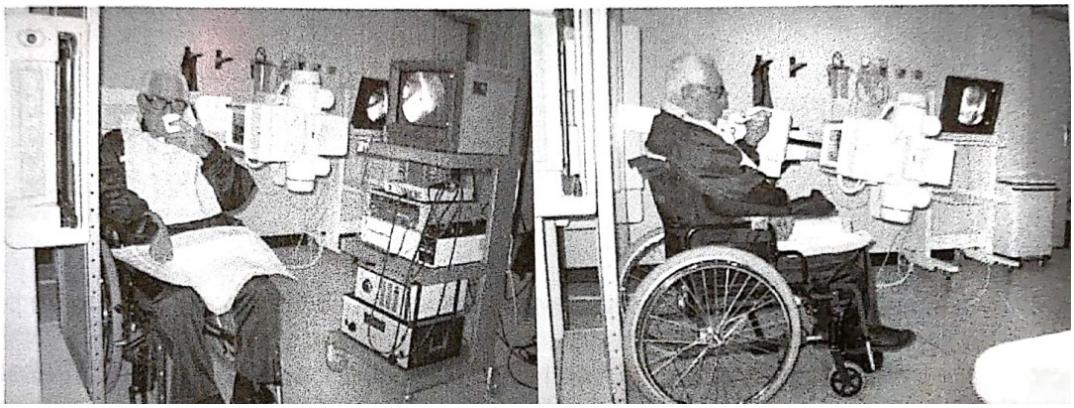
The patient is seated and the image is oriented to find a vertical alignment of the C2-C4 vertebrae. The anterior-inferior border of C4 and the body of the hyoid bone will be used as a reference for the evaluation of laryngeal movement. (74)(75).

- Anteroposterior projection (try 5) :

Again the patient will be seated, perpendicular to the rays, in a comfortable position.

Swallowing tests of fine liquid in a glass will be performed to observe unilateral abnormalities (asymmetry, paralysis or paresis).

Figure1. Example of projections and patient set-up. Taken from : "La réhabilitation de la déglutition chez l'adulte" Woissar-Bassols V.



- **<u>Sequence of testing</u> :**

Chronology of the tests	Product and quantity	Signs of disorder (yes/no)	Specify the structure(s)/function(s) in deficit	Pathophysiological mechanism	PAS score
1	5ml of the fine liquid				
2	5ml of the thick liquid				
3	Drink 30ml from a glass				
4	Chew and swallow 1 teaspoon of solid food				
5	Drinks 30ml of the thin liquid from a glass				

Record, for each food trial :

- The onset of swallowing disorder signs
- The structure(s) suspected of causing the disorder. If the cause of the disorder has not been identified, the SLT will indicate "NI".
- The pathophysiological mechanism identified, according to the table above
- The score corresponding to the PAS scale

Reminder of the physiopathological mechanisms that can be demonstrated:

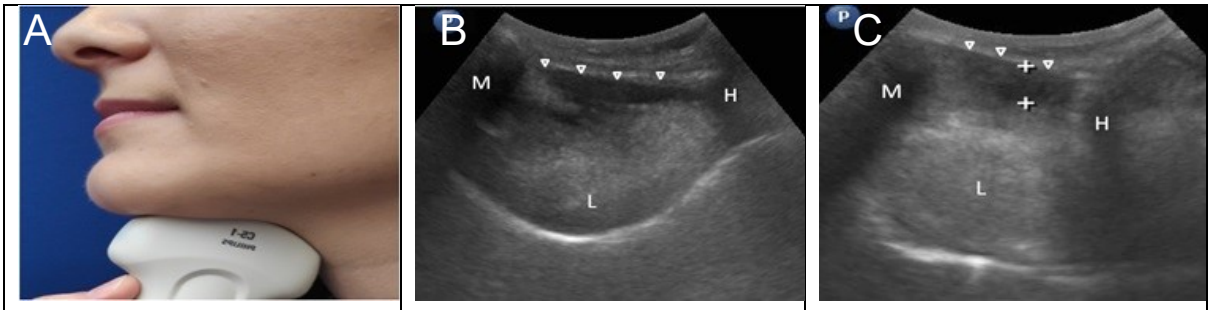
N°	Pathophysiological mechanism	N°	Pathophysiological mechanism
1	Anterior closure defect of the oral cavity	**7**	Failure to initiate pharyngeal time
2	Posterior closure defect of the oral cavity	**8**	Lingual propulsion defect
3	Velopharyngeal closure defect	**9**	Pharyngeal propulsion defect
4	Failure to initiate oral time	**10**	Failure of the tongue base to recede
5	Defects in the control of the food bowl	**11**	Laryngeal ascension defect
6	Failure to transport orally	**12**	Failure to open the SSO

Reminder of the foods that can be used for each texture: *Palmer et al. Dysphagia (1993)*

Category	Examples
Fine liquid	Fruit juice, soda, water
Thick liquid	Gazpacho milshake
Ultra thick liquid	Yoghurt, pudding
Mouldable solid (type A)	Mashed potatoes, soft cookies
Special solid (type B)	Hamburguer
Multitexture (type C)	Spaghetti with meat, beef steak

15.4 Appendix 4: Details of the ultrasound measurements

1. Calculation of geniohyoid thickening

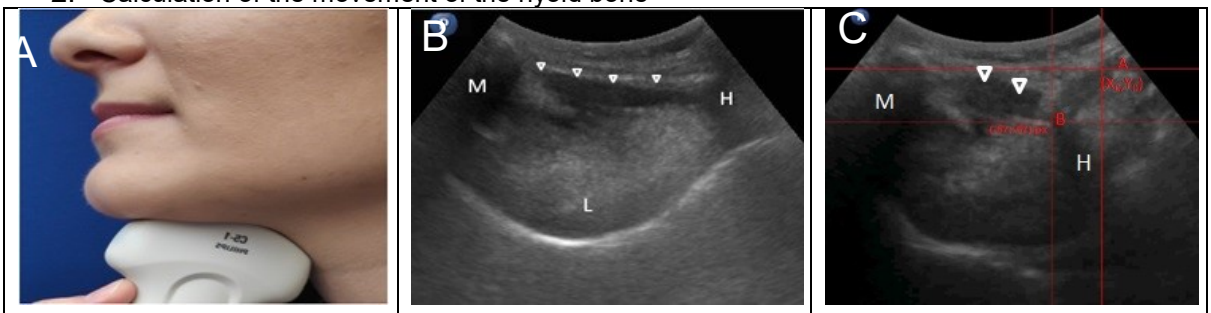


A: *Position of the probe*

B: *Anatomical landmarks: shadow cone produced by the mandible (M); shadow cone produced by the hyoid bone (H); tongue body (L); Geniohyoid (white arrows)*

C: Increase in thickness of the Geniohyoid, represented by the two symbols (+)

2. Calculation of the movement of the hyoid bone

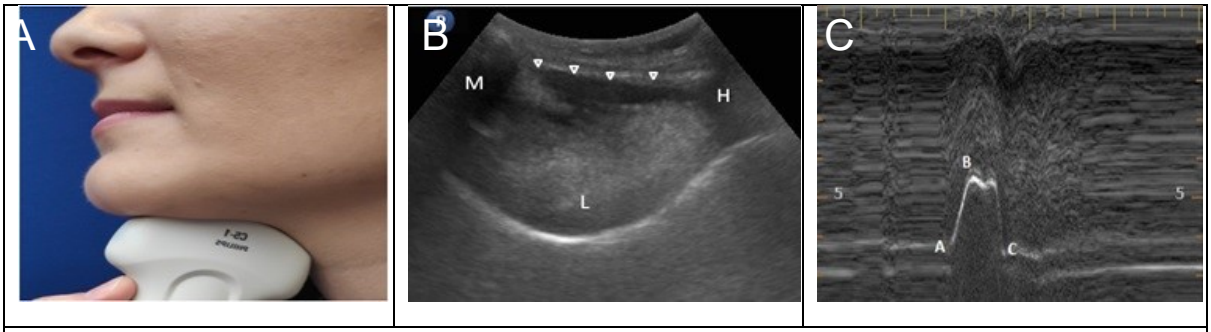


A: *Position of the probe*

B: *Anatomical landmarks: shadow cone produced by the mandible (M); shadow cone produced by the hyoid bone (H); tongue body (L); Geniohyoid (white arrows)*

C: *Calculation of the displacement of the hyoid bone by the difference between the rest position -A(X_0 ;Y_0)- and the end position B(X_1 ;Y_1)*

3. Calculation of lingual propulsion during propulsion

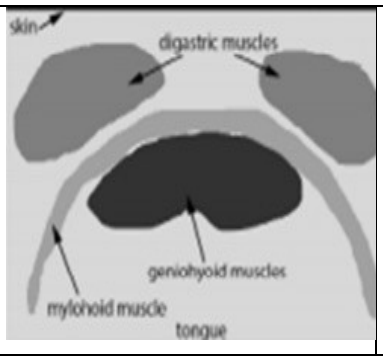


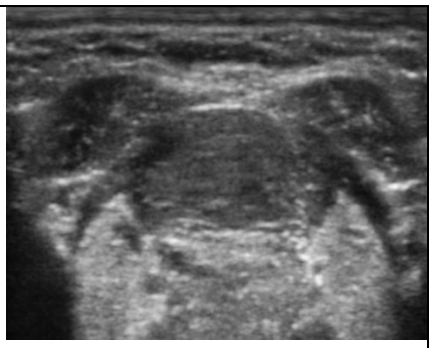
A: *Position of the probe*

B: *Anatomical landmarks: shadow cone produced by the mandible (M); shadow cone produced by the hyoid bone (H); tongue body (L); Geniohyoid (white arrows)*

C: In TM mode. Calculation of the movement at half the distance between the mandible and the hyoid. The amount of movement of the tongue is represented by the distance A-B. The duration of the movement is represented by the distance A-C.

4. Measurement of the thickness of the suprahyoid muscles





A: *Position of the probe*

B: *Frontal section of the supra-hyoidal musculature*

C: Ultrasound image of image B. The thickness of the digastric muscles is calculated by the distance between the upper and lower fascia

15.5 Annex 5. Information note given to the patient

DARC VADOC

"Construction and assessment of a new ultrasound score of swallowing disorders diagnosis in patients with risk factors attending a day hospital

RCB ID: 2020-A02942-37

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Dear Sir or Madam,

Dr. ....., investigator of the study, working in the Deglutition Day Hospital 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 admitted to the Swallowing Day Hospital because you have risk factors associated with swallowing disorders and you require a thorough evaluation of these disorders. The aim of this hospitalisation is to carry out a complete swallowing assessment.

What is the purpose of this research?

The aim of this research is to construct a new ultrasound score for the diagnosis of swallowing disorders, to measure its reliability and reproducibility, and to propose it as an alternative to videofluoroscopy.

How does this research work?

As part of the usual swallowing assessment examinations that you will undergo in the Swallowing Day Hospital, we propose to study the structures and functions involved in swallowing (tongue, hyoid bone and neck muscles) using an ultrasound scan.
The ultrasound examination is painless, non-invasive and risk-free. It is carried out by the physiotherapist, using the ultrasound machine, an ultrasound probe and gelled water, over a period of 15 minutes. In order to evaluate the reproducibility of the ultrasound measurements, a 2ème physiotherapist will perform the ultrasound according to the same procedure, also for a duration of 15 minutes. Finally, the 1er physiotherapist will repeat the ultrasound, again according to the same procedure, for a duration of 15 minutes. The addition of the ultrasound to your examinations will add up to a total of 45 minutes. This will allow us to assess whether the measurements made by the same operator at 2 different times or by 2 different operators are similar.

Your constraints in this research?

The constraints of this research consist in having 3 ultrasound scans of the neck, over a maximum of 45 minutes.

Possible adverse effects

As your participation in this protocol does not involve any administration of treatment other than that which is currently recommended or any other modification of the conventional management in the Swallowing Day Hospital, no adverse effects are expected.

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

The ultrasound will be performed transcervically, i.e. by placing the probe on your neck. The examination is therefore non-invasive, completely painless and does not involve exposure to X-rays.
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?

We expect excellent reliability and validity of ultrasound in the diagnosis of swallowing disorders, which would make it possible to propose an alternative examination to videofluroroscopy that would be more easily performed on an outpatient basis, non-invasive and non-irradiating.

What are the conditions for participating in this study?

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

Number of patients planned and duration of research?

This research will last 25 months with a 25 month recruitment period to include 100 patients.

What data is collected for the research?

The medical data collected during this study will be processed in a computerised, coded and confidential manner. No information bearing your name will be provided to anyone except the doctor in charge of the study and authorized personnel. All the data collected will be confidential and coded and then analysed by the Clinical Research Commission 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 the regulations in force, the data will be kept until the final research report is produced and then archived for 15 years.

The data controller is the promoter, Hôpital Forcilles-Fondation Cognacq-Jay, route de Servon 77150 Férolles-Attilly.

What are your rights?

Your participation in this research is **entirely 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. Your doctor 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, GDPR). In accordance with article L.1122-1 of the Public Health Code, the entire research file has been submitted to the CPP XXX, which issued a favourable 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 participating 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 withdrawal of your consent and the agreement to use or not your previously collected data will be traced in your medical file.

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, erasure or restriction of processing. You can find out more about your rights by visiting the CNIL website 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 the context of 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 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 reflect on 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 file.

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?

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

15.6 List of investigators

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