STATISTICAL ANALYSIS PLAN

"Efficacy of Xylocaine-impregnated compress application in reducing per-procedural pain during ultrasound-guided trigger finger infiltration: a double-blind, randomized controlled study"

SAUTYLO

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Promoter: AP-HP

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1. Introduction

This statistical analysis plan is based on version 1 of protocol APHP210094/2021-002052-36 dated 5 July 2021. It defines the populations of analysis and the methods for evaluating the primary and secondary outcomes. The final version of the statistical analysis plan will be validated before the database is frozen.

2. Rationale of the study

Ultrasound-guided infiltrations of trigger fingers are a frequent and painful invasive procedure. However, there is no current recommendation for the management of intraprocedural pain, and in the majority of cases the infiltration is performed without prior skin anesthesia.
Xylocaine patches are controversially effective in the management of acute pain and in common practice they are not prescribed in advance, are poorly adapted to the topography of the finger, and thus are not applied. On the other hand, a recent study has shown the interest of administering lidocaine 2% by J-tip, a needle-free injection technique not available in France, before an infiltration of a trigger finger.

We hypothesize that a compress soaked in Xylocaine 20 mg/ml solution for injection, applied 15 minutes before the procedure, would reduce per-procedural pain.

3. Research objectives

3.1. Main objective

The main objective is to compare the effectiveness on per-procedural pain of an ultrasound-guided finger infiltration of a compress impregnated with Xylocaine 2% applied to the skin for 15 minutes before the procedure to that of a compress impregnated with physiological serum.

3.2. Secondary Objectives

The secondary objectives are, on the one hand, to evaluate adverse effects and, on the other hand, to evaluate the acceptability of pain during the procedure according to the patient and according to the operator.

4. Experimental design

4.1. Methodology

This is a single-center, randomized, double-blind, controlled study. Patients who meet the inclusion criteria and agree to participate in the study will be randomized to the experimental arm or the control arm at the time of the inclusion visit. The 1:1 randomization will be performed centrally.

4.2. Research Outline

Selection and inclusion are made at the same visit: the investigator, an experienced radiologist, confirms the clinical and ultrasound diagnosis of trigger fingers, confirms the inclusion and non-inclusion criteria, has the informed consent signed, includes and randomizes the patient.

On the same day as the inclusion visit: application of a compress 15 minutes before the infiltration, impregnated with xylocaine 20 mg/ml or physiological serum, before the ultrasound-guided infiltration is performed.
The evaluation of perprocedural pain immediately after the gesture, by numerical scale.

Table 1: Summary table of the chronology of the research

Actions	Selection, inclusion, randomization, and intervention
Information	X
Verification of inclusion and non-inclusion criteria	X
Consent	X
Medical examination	X
Randomization	X
Infiltration	X
IN PAIN	X
Adverse events	X
Acceptability of infiltration	X

5. Study population

5.1. Inclusion criteria

- Patients aged 18 years or older
- Trigger finger (clinical definition with painful difficulty or even protrusion when extending a finger) with indication for ultrasound-guided infiltration of cortisonic derivatives
- Preliminary medical examination
- Written consent
- Affiliation to a Social Security scheme

5.2. Non-inclusion criteria

- Neurological conditions affecting the hand, other than carpal tunnel syndrome
- Intra-articular infiltration of the hand or wrist ≤ 2 months
- Xylocaine allergy
- Contraindication to xylocaine or cortisonic derivatives
- Cognitive or behavioural impairments that make assessment impossible
- Persons referred to in Articles L 1121-5; 6 ; 8 ; 9 of the Public Health Code (protected adults, under guardianship or curatorship, etc.)
- Pregnancy and breastfeeding; Lack of contraception for women of childbearing age
- Participant unable to speak, read and write French

6. Evaluation criteria

6.1. Primary outcome

The primary outcome was the mean pain intensity during the procedure on a self-administered numerical scale (EN) (0: no pain; 100: maximum pain).

6.2. Secondary outcomes

Secondary outcomes are adverse events according to a self-administered open-ended question and the level of acceptability of pain during the procedure for the patient according to the patient himself and according to the operator on a self-administered NE (0, not at all acceptable and 100, completely acceptable).

7. Number of subjects needed

If we consider a difference in pain on the 15 mm numerical scale with a standard deviation of 20, an alpha risk of 5%, and a power of 80%, it is necessary to include 29 patients per arm. We therefore plan to include a total of 60 patients taking into account possible loss to follow-up.

8. Statistical analysis

The statistical analysis will be performed within the Necker Cochin URC/CIC blinded to the randomization arm, under the supervision of Dr. Hendy Abdoul, using R and/or SAS software version 9.4. No interim analysis is planned, the statistical analysis will be carried out at the end of the data collection, entry and consistency check.

All the tests carried out are bilateral, taking a first-α risk of 5% and a significance threshold p=0.05.

8.1. Definition of analysis populations

The main analysis will be performed on the intention-to-treat population, i.e. on all patients included in the study as they were randomized, regardless of the strategy actually received. All randomized patients will be analyzed in their randomization arm, according to a predefined statistical analysis plan.

Participants who are lost to follow-up will not be replaced. As all data are collected during the single study visit, it is expected that there will be little missing data on outcomes. In case of missing data on the primary outcome, a multiple imputation method will be performed.

8.2. Descriptive analysis

A descriptive analysis of the data will first be carried out. Quantitative variables will be described by their size, mean and standard deviation, median and interquartile range, and extended according to the distribution of the data. Qualitative variables will be described by their number, percentage and number of missing data.

8.2.1. Demographics

Age (in years), sex, level of education and professional status will be described in all patients.

Age	ID_AGE

Sex	ID_SEXE
Level of education	V_INC_NIV_ETUDE
Occupational status	V_INC_STATUT_PRO

8.2.2. Clinical data

Diabetes, dominant hand, intensity of symptoms in the last 48 hours, affected and infiltrated finger, affected pulley as well as weight, height and BMI will be described in all patients.
The intensity of the symptoms will be determined by the Quinnell scale (0: normal movement; 5: blocked finger).

Diabetes	V_INC_DIABETE
Dominant Hand	V_INC_MAIN_DOMIN
Finger affected and infiltrated today	V_INC_DOIGTS_INF
Right	V_INC_DOI_AFFECT_D
Left	V_INC_DOI_AFFECT_G
Pulley Affected	V_INC_POULIE
Weight	V_INC_POIDS
Waist	V_INC_TAILLE
BMI	V_INC_BMI
Intensity of symptoms	V_INC_INTENSITE_SYMP

8.3. Main analysis

The primary outcome is the level of pain, measured by an EN (0 – 100), which will be described in terms of mean, standard deviation, median, quartiles, and range.

Level of pain during infiltration	V_INTER_INTENS_MAX

This criterion will be compared between the experimental arm and the control arm. The comparison will be performed using the Student t-test or the nonparametric Wilcoxon-Mann-Whitney test if the variable does not follow a normal distribution (Shapiro-Wilk test).

A linear regression model can be performed to compare the level of pain in the two groups in order to take into account adjustment factors such as age, sex, diabetes, trigger finger classification and the average intensity of pain over the last 48 hours.

Level of pain during infiltration		V_INTER_INTENS_MAX
Adjustment factors:	Age	ID_AGE
	Sex	ID_SEXE
	Diabetes	V_INC_DIABETE
	Trigger finger classification	V_INC_DOI_AFFECT
	Average intensity of pain in the last 48 hours	V_INC_INTEN_MOYENNE

8.4. Secondary analyses

Secondary analyses will be performed on patients with data available for the analyzed endpoint.

8.4.1. Undesirable effects

The different variables related to adverse reactions associated with the Xylocaine patch will be described in terms of mean, standard deviation, median, quartiles and range for qualitative variables and in terms of population and percentage for quantitative variables.

Presence of ARs related to compress application	V_INTER_EI_COMPRESSE
Nature of the event	EI_NATURE
Duration of the IA	EI_DUREE/EI_DUREE_MIN
Intensity of ISIS	EI_INTENSITE
Severity of the AR according to the definition of PCBs	EI_GRAVITE

8.4.2. Acceptability of pain

The acceptability of pain during infiltration will be described in terms of mean, standard deviation, median, quartiles, and extent. It will be compared between the experimental arm and the control arm using the Student t-test or the nonparametric Wilcoxon-Mann-Whitney test if the variable does not follow a normal distribution (Shapiro-Wilk test).

Acceptability of pain during infiltration according to the patient	V_INTER_DOUL_INFILTR
Acceptability of pain during infiltration according to the operator	V_INTER_DOUL_ACCEP

A linear regression model can be performed to compare the acceptability of per-procedural pain according to the patient and then according to the operator in the two groups in order to take into account adjustment factors such as age, sex, diabetes, classification of trigger finger as well as the average intensity of pain over the last 48 hours.

Acceptability of pain during infiltration according to the patient		V_INTER_DOUL_INFILTR
Acceptability of pain during infiltration according to the operator		V_INTER_DOUL_ACCEP
Adjustment factors:	Age	ID_AGE
	Sex	ID_SEXE
	Diabetes	V_INC_DIABETE
	Trigger finger classification	V_INC_DOI_AFFECT