INTERMITTENT VERSUS CONTINUOUS SUCTION TECHNIQUE IN THE DIAGNOSIS OF PANCREATIC SOLID LESIONS. A PILOT STUDY

STUDY PROTOCOL 03/02/2019

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1. INTRODUCTION:

Solid lesions of the pancreas can be neoplastic or non neoplastic and it is important to accurately differentiate between them because of the poor prognosis related to pancreatic neoplasm. There are many types of solid pancreatic lesions: pancreatic adenocarcinoma, neuroendocrine tumor, lymphoma, solid pseudopapillary neoplasm and pancreatic metastasis.

There are several diagnostic methods for the study of pancreatic solid lesions. The different imaging test allow detection and characterization of those lesions, but most times an anatomopathological diagnosis is needed before stablishing the most appropriate treatment.

Endoscopic Ultrasound guided fine needle aspiration (EUS-FNA) is the diagnostic method of choice for the diagnosis of these lesions as it detects small lesions that sometimes cannot be found in radiological imaging test, evaluates vascular invasion and the presence of liver metastasis, and allows pancreatic puncture for a cytological diagnosis. EUS-FNA is the safest technique for pancreatic puncture and the least related to needle track seeding.

In order to gather as much material as possible different techniques have been proposed:

- Fanning technique and multiple pass technique: to guide the needle into different regions of the target lesions with or without removing the needle out of the lesion depending on wether the lesion is hard or soft.
- Use of stylet: there are no data clearly demonstrating that the use of suction increases the yield of EUS-FNA. Some authors do slow withdrawal of the stylet.
- Size of the needle: 19 gauge, 22 gauge, 25 gauge, depending on the localization, size and vascularization. There is increasing evidence that smaller needles offer at least similar results in diagnostic yield compared to larger needles and are also easier to manipulate.
- Use of suction: there is conflicting evidence in this point. Several studies have evaluated the use of high volume aspiration vs low volume aspiration, continous aspiration vs no aspiration and suction with empty syringe vs water-filled syringe but none is clearly better than other.

2. HIPOTESIS:

Intermittent suction improves the diagnostic yield of pancreatic lesions compared to standard (continuous) suction. Up to our knowledge this method has not been yet evaluated.

3. STUDY DESIGN:

Interventional study with diagnostic purpose, longitudinal, prospective, unicentric, blinded for participant and anatomopathologist, in patients with solid pancreatic lesions with indication of cytological sampling by Endoscopic Ultrasound refered to the Endoscopy Unit of Hospital Universitario de la Princesa from January 2019 to December 2019.

Following clinical practice, an endoscopic ultrasound fine-needle aspiration (EUS-FNA) with a 25 gauge needle will be performed to each participant. The patients will be divided into two arms with a 1:1 ratio:

a) Intermittent aspiration: Intervention arm. Endoscopic ultrasound will be done for the localization of the lesion and to localize the site of puncture. Prior to the puncture of the lesion the stylet is removed and a vacuum syringe is prepared with 10 cc of vacuum allowing the generation of continuous pressure inside and connected to the end of the needle. Once the lesion is punctured 15 movements in and out of the lesions will be made while the syringe is opened and closed on and off for a total of 3 times each pass. A total of 4 passes will be done in each lesion.
b) Continuous/standard aspiration: Same procedure but once the lesion is punctured 15 movements in and out of the lesions will be made while the syringe remains opened.

Randomization will be done with the generation of a computer-generated random list using Epidat 4.0. software (SERGAS®, Santiago de Compostela, Spain).

The endoscopic ultrasound will be done with an Olympus linear echoendoscope (GF-UTC 260 Olympus® Tokyo, Japan) under Propofol sedation by an Anesthesiologist.

Each pass will be sent to the pathologist separately to evaluate their individual characteristics and to determinate which one is diagnostic. A complete report will be done assessing:

a) Cellularity

b) Hematic contamination

c) Presence of cell block and possibility of doing immunohistochemistry

4. OUTCOME MEASSURES:

a. Primary outcome measure: Increase in diagnostic yield of pancreatic solid lesions

b. Secondary outcomes:

- Sample Celullarity: Number of malignant cluster of cells on each endoscopic pass
- Blood contamination: Percentaje of blood contamination of the slides
- Number of passes to reach a positive cytological diagnosis

5. ELEGIBILITY CRITERIA:

a) Inclusion Criteria:

- Pancreatic solid lesion
- Patients over 18 years old
- Suitable for endoscopy

b) Exclusion Criteria:

- Contraindication for endoscopy
- Active anticoagulant therapy
- Thrombocytopenia or coagulopathy in the absence of its correction prior to the procedure
- Absence of informed consent
- Pregnancy
- Not accessible lesion for endoscopic ultrasound puncture

6. STATISTICAL ANALYSIS PLAN:

Data will be expressed as means and standard deviation for quantitative variables or frequencies and percentages for the categorical ones. Variables with non-normal distributions will be represented as means and percentage ranges.

Randomization will be done with a computer-generated random list in a 1: 1 ratio. The chi-square test will be used to compare qualitative variables. Correlation kappa values will be offered between both methods. In order to evaluate the differences in diagnostic yield, the sensitivity after the completion of each pass will be calculated by correlating the continuous values of confusion with the final cytology with the Spearman test. The number of optimal passes depending on the method will be calculated by maximizing that the following passes would not modify the additional diagnostic yield more than 10% over the accumulated one. On the other hand, the cellularity and blood contamination graduated in its three levels will be contrasted between both methods with an analysis of McNemar. All the variables that could potentially modify the diagnostic yield of both methods will be compared with univariate and later multivariate analysis by means of logistic regression analysis with the STATA application (v13.0, StataCorp, College Station, Texas, USA). The protocol will be approved by the Ethical Committee of the Hospital Universitario de la Princesa before the start of the study.