The Impact Of Tissue Micro-RNA Profile From EUS-FNA In Pancreatic Adenocarcinoma Identifiers: NCT04765410

Unique Protocol ID: PDACmiRNA

14.04.2026

Study protocol

A prospective, observational, multicenter study was conducted including 57 patients with solid pancreatic tumor (diagnosed by imaging methods) from March 2019 to September 2021. Patient follow-up was conducted over 2 years and 6 months, consisting of periodic telephone visits at 1 month, 3 months, 6 months, 1 year, 2 years, and 2½ years (until the end of the study), respectively, collecting the following data: history and ECOG score. Of the 57 patients enrolled in the study: 45 were confirmed with PDAC at histopathology examination, 5 patients were diagnosed with chronic pancreatitis (this being the comparative group in the second study); 1 patient was diagnosed with primary pancreatic lymphoma, 6 patients were not confirmed with PDAC at histopathology analysis. Of the 45 patients confirmed with PDAC, 2 patients were excluded as the biopsy sample was not sufficient to perform miRNA processing. This left 43 patients, from which 2 patients were excluded as ouliers, hence 41 patients formed the study group. This was done using SPSS statistical processing software, a program for the detection of values significantly different from the mean of the study group (outlier detection). Exclusion from the study group was based on PCA Analysis (Principal Component Analysis) which classifies patients according to total miRNA expression. The primary hypothesis is the correlation of tissue miRNA expression (echoendoscopically sampled from PDAC patients) with patients' clinical, biological and imaging characteristics, tumour aggressiveness, response to specific treatment and prognostic factors.

Statistical Analysis Plan

Statistical analysis was performed using Statistical Package for the Social Sciences SPSS software (version 28.0, SPSS Inc., Chicago, IL) and Microsoft Office Professional Plus 2016 Excel. SPSS and Excel were used for graphical representations. Using the Shapiro-Wilk test (<0.05) we observed that the distribution of the data in the second study was not normal, therefore non-parametric tests were used. For the analysis of categorical variables, we used the Chi-Square test, as in some cases the number of patients per category was relatively small. The Pearson/Spearman correlation coefficient was used to estimate correlations between continuous variables. Independent t-tests or Mann-Whitney test were used for analysis of continuous data, expressed as mean ± standard deviation or mean standard error. The Kruskal-Wallis test was used to compare groups and to compare different parameters within

the study group if there were at least 3 categories. Statistical significance was given by p-values <0.05 and fold regulation is significant if below -2 or above 2.

Results

Poor survival was associated with older age, high ECOG status, presence of metastases and large tumor size, associations that were shown to be statistically significant ($p<0.05$). Pair-wise analysis demonstrated reduced expression of 25 miRNAs in the study group. We can observe that the lowest values of miRNAs in the study group (the most powerful from the study) were: miR-148a, miR-99a, miR-125b, miR-132, miR-195 (ordered in descending order corresponding to fold regulation).

Malnutrition remains an poor prognostic factor in PDAC. In our study we detected statistically significant differences between miR-143, miR-29b, miR-34b and miR-99a levels among undernourished patients. There was a statistically significant trendline between low miR-100 values and increased tumor size ($p=0.060$ on Kruskall-Wallis analysis). Vascular invasion is a negative prognostic marker, and when analyzing miRNA profile we observed statistically significant differences between miR-10a levels among patients with vascular invasion and without vascular invasion ($p=0.028$). Thus patients with vascular invasion have lower miR-10a levels.

Patient Name:

INFORMED CONSENT TO PARTICIPATE IN A CLINICAL STUDY

TITLE: The Impact of Endoscopic Ultrasound in Pancreatic Tumors – The MicroRNA Profile in Pancreatic Adenocarcinoma and Its Effect on Survival, Prognosis, and Treatment Response

INVESTIGATORS: Dr. Mircea Diculescu, Dr. Mihai Ciocîrlan, Dr. Cătălina Vlăduț, Dr. Mădălina Ilie, Dr. Oana Plotogea, Dr. Mariana Jinga, Dr. Vasile Balaban, Dr. Raluca Simona Costache, Dr. Maria Dobre

What is the pancreas?
The pancreas is an endocrine and exocrine gland associated with the digestive tract, located in the abdomen, just behind the stomach and duodenum.

What is a pancreatic tumor and what needs to be done?
A pancreatic tumor can be "benign" (for example, due to an inflammation of the pancreas called "chronic pancreatitis") or, unfortunately, "malignant," meaning "pancreatic cancer." Once the type of tumor is determined, appropriate treatment will be recommended. There are several types of pancreatic cancers, each requiring different treatments. Since the nature of this tumor is currently unknown, an endoscopic biopsy has been recommended.

How will the procedure be performed?
Under anesthesia, a special endoscope (a flexible tube with a camera at the end) will be introduced through the mouth into the esophagus, then into the stomach and duodenum. This special endoscope also has a small ultrasound device at its tip, which allows visualization of the tumor located behind the stomach or duodenum. Using the ultrasound, the tumor will be accurately located, and a very fine needle will be inserted into the tumor to aspirate cells. The tumor will be punctured several times to collect as many cells as possible, which will then be examined under a microscope to establish a correct diagnosis.

What is the purpose of this clinical study?
Pancreatic cancer remains a significant challenge in the medical field, being the fourth leading cause of cancer-related deaths worldwide. It is estimated that it will soon surpass breast cancer, becoming the third leading cause of cancer deaths. The ability to diagnose through endoscopic ultrasound and obtain a histopathological sample during the procedure brings us closer to understanding this disease. Furthermore, analyzing these samples and identifying gene expression offers valuable insights, with important future implications for targeted cancer therapy. The aim of this study is to create a data registry including pancreatic cancer patients to contribute to high-quality large-scale clinical studies. The goal is to identify early diagnostic markers for pancreatic cancer in the future. This will be achieved by collecting blood samples and tissue samples obtained via endoscopic fine-needle aspiration.

Who can participate in this clinical study?

Participants must be at least 18 years old and have an imaging-based diagnosis of a pancreatic tumor. The study will include a total of 48 patients from various tertiary centers.

What procedures will be performed for research purposes?
All participants will complete a questionnaire about their health status. This questionnaire can be in electronic or paper format and will be transferred to a database via the internet to protect confidentiality. Completing the questionnaire will take about 10 minutes.

A blood sample will be collected upon hospital admission (before the endoscopic ultrasound procedure), with one extra vial taken for circulating microRNA analysis. The blood will be centrifuged immediately after collection, and the serum or plasma will be frozen.

From the endoscopic biopsy, a tissue fragment will be analyzed for microRNA expression. It will be preserved immediately after collection in RNA-stabilizing solutions to prevent RNA degradation.

All biological samples will be stored at -80°C until processing and kept in the Molecular Pathology Laboratory at the "Victor Babeș" National Institute of Pathology for 5 years. After this period, the samples will be destroyed.

PROCEDURES FOR PATIENTS PARTICIPATING IN THE RESEARCH STUDY
During hospitalization, you will complete a written questionnaire, and your data will be entered into a database. An extra vial of blood will be collected for microRNA analysis, and a tumor tissue sample will be taken via endoscopic ultrasound for tissue microRNA analysis. We will contact you by phone at 1 month, 3 months, 6 months, and 1 year to monitor your health status and disease progression.

Your research data may be viewed by other investigators not associated with the study, but your name and personal identifiers will be removed to ensure anonymity. Sharing research data helps address complex issues like pancreatic pathology and may be necessary for future studies.

Patients participating in the study will have:

1 extra vial of blood collected (during routine blood tests at hospital admission)

1 tissue fragment preserved in RNA-stabilizing solution (collected during endoscopic ultrasound and fine-needle aspiration)

What are the possible risks, side effects, and discomforts of this study?
Participation in this study does not carry additional risks beyond those of the standard procedures for pancreatic cancer patients undergoing endoscopic ultrasound and fine-needle aspiration. The risks are minimal and similar to those described in the standard consent form, including acute pancreatitis, bleeding, perforation, infection, and anesthesia-related risks. There

is also a slight chance that the biopsy may not retrieve any cells, preventing an accurate diagnosis.

Personal data privacy is strictly protected, and a detailed confidentiality protocol is in place to prevent data breaches. No personal information obtained during the study will be made public.

What are the possible benefits of participating in this study?
You will not personally benefit from participating in this research. However, the detection of microRNA expression in pancreatic tumors may help future studies and the development of new treatments that could benefit other patients.

Will I be informed about new risks discovered during the study?
You have the right to be informed about the overall results of the study and any new findings that might affect your decision to continue participation. General information will be provided upon request.

Will I incur any costs for procedures performed during the study?
No costs related to the study procedures will be charged to you or your insurance provider, as these are part of routine medical care. The hospital will be billed as usual for any routine procedures.

Will I be paid for participating in this study?
You will not receive any compensation for participating in this research study. Your participation may contribute to future discoveries, but no financial benefits are anticipated from potential inventions.

Who will know about my participation in this study?
All personal information regarding your involvement will remain confidential and known only to the principal investigator and their collaborators.

Is my participation in this research study voluntary?
Your participation is entirely voluntary. You are not obligated to participate and can withdraw at any time without any consequences. Upon written request, your documents will be destroyed immediately. You will continue to receive the same quality of medical care regardless of your decision.

Your doctor may be part of the research team and will be interested in both your well-being and the quality of the study. You can seek a second medical opinion at any time from a doctor not involved in the study. Participation in the study is not mandatory.

INFORMED CONSENT - FIRM ACCEPTANCE FORM Patient identification number:

The undersigned Mrs./Ms./Mr. (please strike out unnecessary options) (name, surname)..... freely and voluntarily agrees to participate in the biomedical study entitled: Pancreatic Steatosis – an Independent Risk Factor for Pancreatic Tumors, with the principal investigator Dr. (name, surname) .....

I declare that:

- The doctor who informed me and answered all my questions specified that my participation is voluntary and that I can exercise my right to withdraw from the study at any time.
- I understand that I can ask questions about any aspect of the study during its course, and the investigators listed on the first page of this informed consent will answer them. Any questions regarding my rights as a participant in the research study will be addressed by the coordinating physician.
- I authorize genetic studies to be performed on the tissues collected during the fine-needle aspiration as part of the endoscopic ultrasound, as well as on other biological materials (blood).
- I have benefited from a medical consultation before participating in this study, and the results were communicated to me.
- I understand that I can withdraw my consent to participate in this study at any time, for any reason, without any liability, provided I inform the doctor responsible for my participation. Terminating my participation will not affect my relationship with the doctor.
- I am aware that I have the right to request, through my doctor, access to the overall study results when they become available.
- I have not received any remuneration, of any kind, direct or indirect, in exchange for my acceptance or consent to participate in the study.

By signing this informed consent, I agree to participate in this study. I will receive a copy of the informed consent.

....

Participant's Name Date

.....

Participant's Signature

Adults (over 18 years) with impaired cognitive functions who cannot provide informed consent ..... (patient's name). The above-mentioned patient cannot provide informed consent for participation in the research study.

.....	.....
Representative's Name	Relationship to the Patient
.....	.....
Legal Representative's Signature	Date