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Computed tomography-guided percutaneous biopsy of pancreatic masses

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Introduction Pancreatic cancer is the seventh leading cause of cancer death worldwide [1]. Because of its aggressive nature, it accounts for almost as many deaths as cases. The diagnosis of pancreatic tumors is usually made using imaging studies such as ultrasound (US), computed tomography (CT), or magnetic resonance. According to National Comprehensive Cancer Network (NCCN) guidelines, patients with resectable pancreatic cancer should be treated with surgery without a prior biopsy with the exception of patients with high-risk features that are recommended to be treated with neoadjuvant therapy. However, pathologic diagnosis is required in patients with non-resectable tumors that are to be treated with neoadjuvant therapy [2]. Pancreatic cancer is resectable at diagnosis in only 20% of cases [3], so a large group of patients requires a biopsy.

The pancreatic adenocarcinoma NCCN guidelines [2] recommend endoscopic ultrasound (EUS)-guided biopsy as a method of choice when neoadjuvant therapy is considered. Fine needle aspiration (FNA) is no longer recommended since core biopsy gives a higher

diagnostic yield [4]. This is especially important when genetic testing is required. CT-guided biopsy can be performed when EUS-guided biopsy is not feasible. However, there are very few studies on CT-guided core needle biopsy of pancreatic masses.

The primary aim of this study is to present the diagnostic yield and safety of CT-guided biopsy of pancreatic mass. The secondary objective is to evaluate CT-guided biopsy efficacy as a salvage procedure after failed EUS–guided biopsy, ultrasound-guided FNA, surgical biopsy, or endoscopic retrograde cholangiopancreatography (ERCP)-guided biopsy.

Patients and methods The Bioethical Committee waived the need for its formal consent due to the retrospective nature of this study. The research was conducted following the Declaration of Helsinki. The retrospective analysis was done on a prospectively maintained database, including percutaneous CT-guided core biopsies of pancreatic masses in 102 consecutive patients. Each patient had contrast-enhanced CT or magnetic resonance imaging (MRI) done (including native, arterial, and venous phases), which revealed a pancreatic mass.

CT-guided biopsy was done in patients in whom EUS-guided biopsy was not feasible or failed. Regarding the coagulation profile, the limits that allowed us to perform the procedure were: INR <1.5 and platelet count >50 000/ml.

One of three interventional radiologists with at least 5 years of experience in CT-guided procedures performed the biopsies. The procedures were done at the interventional CT suite (320-row Aquilion One, Toshiba, Japan). An unenhanced CT scan was done at the beginning of the procedure and compared with previous contrast-enhanced CT or MRI to plan the optimal needle path. If the risk of arterial injury was high, contrast-enhanced CT was also done during the procedure. Ultrasound was available at each procedure and performed just before taking a sample to ensure the needle was away from critical structures such as arteries.

An 18G biopsy gun (Max-Core, BD, USA) with a 22 mm penetration depth was used to perform the procedures. The coaxial technique was applied in all biopsies (17G TruGuide coaxial needle, BD, USA). Apart from typical sharp-tip stylet these needles come with additional blunt-tip stylet. Whenever the coaxial needle was near blood vessel the blunt-tip stylet was inserted to avoid puncture of the artery or vein and decrease the risk of bleeding. The fat traversing route was preferred [5], but when it was not available transhepatic or transgastric approach was selected. All procedures were done under local anesthesia.

After needle removal, an unenhanced CT of the upper abdomen was performed to identify possible complications. The complications were noted immediately after the procedure and then within 30 day period according to the Clavien-Dindo classification [6].

Technical success was defined as obtaining at least one tissue sample. Positive, diagnostic, biopsy was defined as a presence of at least one sample that allowed to make histopathological diagnosis according to pathological report. Sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated. The gold standard used for calculation of these metrics was a combined data from histopathological report, further diagnostic studies, performed surgeries as well as clinical information about the course of the disease.

The following data were collected: location and size (longest diameter) of the tumor, number of samples taken, pathological diagnosis, and patient radiation dose in terms of DLP.

All the data analyses were performed using statistical libraries available for Python and R (R Foundation for Statistical Computing, www.r-project.org).

Results The analysis included percutaneous CT-guided core biopsies in 102 consecutive patients (55 women and 47 men) with the mean (SD) age of 65 (9) years. The

masses were located in the pancreatic head (48), body (40), or tail (14). The median size of the lesion was 39 mm (first quartile (Q1): 30 mm; third quartile (Q3): 49.75 mm).

One to five (mean 2) tissue samples were taken. The following needle access routes were used: anterior (65), posterior (9), transgastric (15), transhepatic (11), and lateral (2).

Technical success was achieved in 100% of cases. The overall diagnostic accuracy, sensitivity, specificity, PPV, and NPV were 90.2%, 89.6%, 100%, 100%, and 37.5%, respectively. In 33 patients, CT-guided core biopsy of the pancreatic mass was done after other biopsies failed. Twenty-eight (84.8%) of such salvage CT-guided core biopsies were successful (Table 1).

Radiation dose in terms of DLP had a median of 654 mGy*cm (Q1: 433.75 mGy*cm; Q3: 874.50 mGy*cm). Contrast-enhanced CT during the procedure was done in 16 patients.

The following pathological findings were reported: adenocarcinoma (79), lymphoma (1), ductal carcinoma (1), neuroendocrine tumor (2), chronic lymphoblastic leukemia (1), renal cell carcinoma metastasis (1), serous cystadenoma (1), inflammation (6) Samples counted in this study as non-diagnostic (10) were reported because of insufficient tissue, presence of necrosis, or normal pancreatic tissue.

No major complications were noted. None of the patients required readmission or prolonged hospitalization. One patient experienced postprocedural abdominal pain that resolved after being given paracetamol and morphine within 2 hours; no further analgesic treatment was necessary (Clavien-Dindo grade I). Very small hematomas (<2 cm in diameter) were seen on post-procedural CT scans however none of them was clinically overt and they were classified as type 1 according to Bleeding Academic Research Consortium classification [7].

Discussion Percutaneous CT-guided core biopsy is an established method of obtaining cancer tissue for pathologic diagnosis in many organs. However, it is less frequently used in

pancreatic mass diagnosis than EUS-guided biopsy or aspiration, and there are very few publications on this subject.

This study aimed to report the effectiveness and safety of CT-guided core needle biopsy of pancreatic masses. Technical success of 100% and clinical success of 90.2% are similar to previous studies on that subject. In the study by Strobl et al[8], 89.8% of CT-guided biopsies delivered tissue that allowed to make a definitive pathological diagnosis. Similar results (86%) were reported by Li et al[9]. In some studies, the results were even better, with clinical success reaching 98.1% [10] and 100% [11].

The literature on EUS-guided biopsy of pancreatic masses reports similar results in terms of effectiveness. The meta-analysis by Yang et al[12] revealed pooled sensitivity of 84% (range 43–100%). The most extensive study on EUS-guided fine needle biopsy involved 852 patients [13]. The authors of this study revealed an overall accuracy of 85.6% % and a sensitivity of 83.3%. In the study by Chen et al. [14], adequate histological yield was obtained in 87.5 % of the EUS- fine needle biopsy (FNB) samples.

For 33 patients, CT-guided percutaneous core needle biopsy was a salvage procedure after failed biopsies performed with other means (EUS-guided biopsy, ultrasound-guided fine needle biopsy, ERCP, or surgery). The success rate of the salvage CT-guided biopsies was 84.8%. It indicates that CT-guided core needle biopsy can often get reliable tissue samples even if other methods fail.

NCCN guidelines do not recommend an ultrasound-guided pancreatic biopsy. This is probably because of the advantages of CT over ultrasound guidance. CT guidance provides better visualization of the pancreas, adjacent organs, and the needle, which is crucial for the procedure's safety. The air in the stomach or intestine impairs visibility on ultrasound images, while it does not reduce the quality of images acquired with CT. Some studies on ultrasound-

guided pancreatic biopsy [15,16] show promising results in accuracy. However, they report a slightly higher major complication rate (2%) that should be considered.

No major complications were noted—no patients required readmission or prolonged hospitalization. One patient experienced post-procedural pain that required morphine and subsided within several hours. Very small hematomas (<2 cm) were seen in 2 patients but without clinical significance. No other complications were seen. Regarding serious adverse events, the results are similar to other publications on CT-guided pancreatic biopsy [10,11,17], which also reported no major complications. The results of our study compare favorably to studies on EUS-FNB - Thomsen et al[13] reported a 5.4% complication rate with 2.3% of acute pancreatitis. In the study by Lin et al[18], the reported adverse events rate of EUS–guided biopsy was 5.8%, with 4.2% of patients presenting with bleeding. The transgastric and transhepatic approach was not related to increased complication risk, similar to the article by Hsu et al[17].

These excellent safety results are associated with high-resolution CT images, which allowed precise visualization of the pancreas as well as the entire needle path. The possibility to perform contrast-enhanced CT is advantageous when multiple vessels are near the tumor, and the risk of bleeding is high. Lack of bleeding episodes are most likely associated with the use of blunt-tip stylets that move the blood vessels away from the needle rather than puncture them.

In the context of precision medicine it is worth noting that specimens obtained in CT-guided core needle biopsies (18G) typically result in more tissue than EUS biopsies (22G) thus increasing chances of obtaining adequate specimens not only for histopathologic diagnosis but also Next Generation Sequencing (NGS). Somatic profiling can identify potentially actionable genetic alterations. However, utility and impact on overall survival of targeted therapies in case of pancreatic adenocarcinoma is still to be fully elucidated. Recent studies showed that

up to 28% of advanced pancreatic cancer patients might have potentially targetable variants [19]. One of the most common mutations found in pancreatic cancers are KRAS alterations which are present in about 90% of cases. However targeting them still remains a challenge. In KRAS wild-type patients there is plenty of alternative driver aberrations. [20] In pancreatic cancer patients somatic testing should include various genetic alterations, in example fusions (ALK, NRG1, NTRK, ROS1, FGFR2 and RET), microsatellite instability, mismatch repair deficiency as well as mutations in BRAF, BRCA1/2, KRAS and PALB2 genes [2].

The study has several limitations that should be mentioned. It is a single-center study, and the analysis was retrospective. Also, no comparisons with other methods were performed. Prospective, comparative studies should be probably the next step in the research on this subject.

The results of this study show high effectiveness and excellent safety profile of CT-guided core needle biopsy of pancreatic lesions.

GR conceived the concept of the study. GR and JF contributed to the design of the research. All authors were involved in data collection and data analysis. All authors edited and approved the final version of the manuscript.

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Table 1 Results of computed tomography-guided core biopsies performed after failed biopsies performed under different guidance

Previous failed biopsy	Number of patients	Number of successful salvage CT-guided core biopsies
EUS-guided	14	11 (78.6%)
ERCP	5	5 (100%)
Ultrasound-guided FNA	11	9 (81.8%)
Surgery	3	3 (100%)
Total	33	28 (84.8%)

Abbreviations: CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; FNA, fine needle aspiration

Short title: Computed tomography-guided percutaneous biopsy of pancreatic masses