Percutaneous Ultrasound-guided Core Needle Biopsy of Solid Pancreatic Masses: Results in 250 Patients

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ABSTRACT: *Background.* To determine the diagnostic accuracy and complications of percutaneous sonographic (US)-guided core needle-needle biopsy in the diagnosis of solid pancreatic masses.

Methods. Cases of US-guided percutaneous core needle biopsy of solid pancreatic masses performed in our department between July 2009 and June 2015 were analyzed retrospectively. The demographic data, lesions' size and location, pathology results, accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and complications of the biopsies were determined.

Results. A total of 250 patients (150 males, 100 females; age range, 16–88 years; mean age, 64.3 $\pm$ 12.1 years) were included in the study. The overall diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of all 250 biopsies were 94.8%, 94.3%, 97.2%, 99.5%, and 75%, respectively, and changed to 98.4%, 99%, 94.7%, 99%, and 94.7%, respectively, after the biopsy was repeated in 12 patients. Four (1.6%) major complications, including a pseudoaneurysm of the gastroduodenal artery, and three cases of acute pancreatitis, and one (0.4%) minor complication (a vaso-vagal syncope), were observed. There was no biopsy-related death.

Conclusions. US-guided percutaneous core needle biopsy is a safe and highly effective method with acceptable complication rates in the diagnosis of solid pancreatic masses. *J Clin Ultrasound* **44**:470–473, 2016; Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/jcu.22362

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INTRODUCTION

Pancreatic cancer is one of the most common causes of cancer-related death in the world.[1,2] Only 15% of patients have a resectable tumor, and the tumors in the remaining 85% of patients are nonresectable because of distant metastasis or local invasion at the time of diagnosis. A pancreatic biopsy is not recommended in patients with resectable pancreatic tumors before surgery except when neoadjuvant therapy is being considered. However, biopsy is required for a definitive diagnosis for chemoradiotherapy in patients with unresectable tumors or in patients with resectable tumors who are medically unsuitable for surgery, and also in conditions that require different treatment protocols such as primary lymphoma, mesenchymal tumors, metastasis to the pancreas, and focal pancreatitis mimicking neoplastic disease.[3–6] In this article, we present our clinical experience with percutaneous sonographic (US)-guided core needle biopsy for solid pancreatic masses.

METHODS

US-guided percutaneous core needle biopsies performed in our department between July 2009 and June 2015 in a total of 250 consecutive patients for diagnosis of suspiciously malignant solid pancreatic masses with or without necrotic/cystic component were analyzed retrospectively. This retrospective study was approved by our institutional research ethics board. Indications for biopsy were based on clinical examination, elevated cancer embryonic antigen, US, CT, and MRI findings. Anticoagulation or aspirin therapy

was stopped 1 week before the biopsy. Informed consent was obtained from all patients.

Patients were placed in the supine position, and anterior access was used for biopsy procedures in all patients. When a direct access to the lesion was impossible, transhepatic or transenteric routes were used. US examination was performed using a Nemio or Xario US scanner and a 1–6-MHz convex-array transducer (Toshiba Medical Systems, Tokyo, Japan), and assessment of the pancreatic lesion's characteristics such as size, location, and relation to the blood vessels was conducted. Thereafter, under standard sterile conditions, local anesthesia was administered by infiltrating 15–20 ml of 1% lidocaine to the peripancreatic space, subcutaneous tissue, and skin using a 20-gauge Chiba needle. With the US probe in the transverse view, using a free-hand technique, a biopsy was taken from the pancreatic mass using an 18-gauge semi-automatic Tru-cut biopsy needle with an adjustable sample notch (10 mm–20 mm) (Geotek Medical, Ankara, Turkey) (Figure 1). Between one and three biopsies were taken depending on the adequacy of the cores obtained and the patient's tolerance. The cores were sent to the pathology department for histopathological assessment. All patients were monitored for at least 4 hours following the procedure for acute complications. The final diagnosis was determined by surgical results, clinical course, and follow-up imaging. Procedure-related complications were identified by reviewing clinical notes, follow-up imaging, and laboratory findings.

A biopsy result was considered a true positive when the pathology result was positive for malignancy. A biopsy result was considered a true negative when the pathology result was negative for malignancy without further evidence of malignancy by imaging and clinical follow-up or a repeat biopsy. A biopsy result was considered a false negative when the pathologic or clinical results proved positive for malignancy. A biopsy result was considered a false positive when subsequent evidence resulted in an alternative diagnosis. Diagnosis of fibroadipose or fibromuscular tissue, normal parenchyma, and insufficient or inadequate material were categorized as nondiagnostic results.

The demographic data, size, and localization of the mass, pathology results of the biopsy, and complications were recorded for each patient. Minor and major complications were defined according to the guidelines for percutaneous needle biopsy of the Society of Interventional Radiology.[7] Diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were calculated. Statistical analysis was conducted using the SPSS software version 14.0 for Windows (SPSS Inc., Chicago, IL).

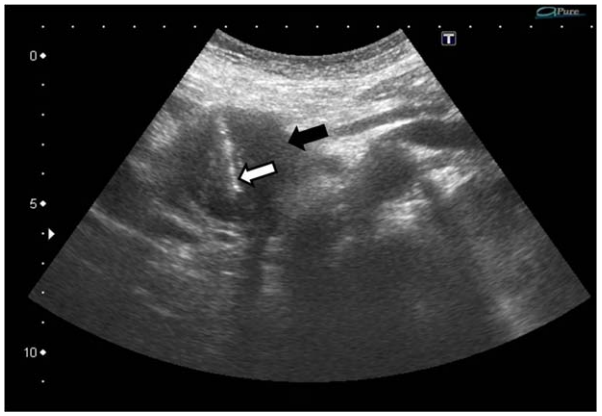

FIGURE 1. Transverse sonogram shows a 4-cm hypoechoic mass (black arrow) in the head of the pancreas. Post-firing sonogram shows the echogenic needle in the mass (white arrow). Pathology confirmed an adenocarcinoma.

RESULTS

A total of 250 patients (150 males, 100 females; age range, 16–88 years; mean age, 64 ± 12 years) were included in the study. The mean mass size was 3.9 ± 1.7 cm (range, 0.8–11.3 cm). The lesion's localization was the head/neck in 161 patients, body in 63 patients, and tail in 26 patients. A repeat biopsy was required in 12 patients (4%) because the initial result did not concord with the high clinical suspicion of malignancy.

Of the 250 initial biopsy samples, there were 201 true positive results for malignancy, 1 false positive result, 36 true negative results, and 12 false negative results. One biopsy sample was incorrectly diagnosed as a pancreatic adenocarcinoma; the final diagnosis was a neuroendocrine tumor, which was confirmed by the surgical pathology result. This sample was accepted as a false positive result because the alternative diagnosis had a different treatment protocol. False negative pathology results included chronic pancreatitis (n = 5), extrapancreatic fibroadipose tissue (n = 3), normal parenchyma (n = 2), chronic inflammatory disease (n = 1), and insufficient material (n = 1).

After initial biopsies, histopathological results were adenocarcinoma (n = 166), chronic pancreatitis (n = 21), nondiagnostic results (n = 20), metastasis (n = 11), neuroendocrine tumor (n = 9), chronic active inflammatory disease/granulomatous inflammatory disease (n = 4), necrotic tissue/fat

necrosis (n = 4), diffuse large cell lymphoma (n = 2), malignant mesenchymal tumor (n = 2), mucinous adenocarcinoma (n = 2), small blue round cell tumor (n = 2), serous cystadenoma/microcystic serous cystadenoma (n = 2), adenosquamous carcinoma (n = 1), anaplastic carcinoma (n = 1), acinic cell tumor (n = 1), biliary papillomatosis (n = 1), and pancreatic intraepithelial neoplasia (n = 1). The overall diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of all 250 biopsies were 94.8%, 94.3%, 97.2%, 99.5%, and 75%. It changed to 98.4%, 99%, 94.7%, 99%, and 94.7%, respectively, after the repeat biopsy in 12 patients.

The procedure was well tolerated by most patients. Twenty-seven patients (10.8%) experienced abdominal pain and nausea during or after the procedure. Appropriate analgesic and antiemetic drugs were administered when required, and symptoms resolved rapidly. Four major complications (1.6%) including gastroduodenal artery pseudoaneurysm in one patient (0.4%), acute pancreatitis in three patients (1.2%), and a minor complication (vaso-vagal syncope) in one patient (0.4%) were observed The gastroduodenal artery pseudoaneurysm was treated by endovascular embolization using microcoils through the right femoral artery access. Other complications were managed medically. Postprocedural amylase levels were available in 103 patients, and elevated serum amylase level without clinical symptoms was observed in 15 patients (14.5%). Biopsy-related death did not occur.

DISCUSSION

Biopsy techniques for pancreatic mass include surgical biopsy, percutaneous biopsy, and endoscopic US (EUS)-guided fine-needle aspiration (FNA) biopsy.[3,5,8–13] Surgical biopsy has high rates of morbidity and mortality and should be avoided. CT, US, and EUS can be used to guide a pancreatic mass biopsy.[5,6,10,14] The choice of the imaging modality depends on the availability and expertise of an interventional radiologist or endoscopist, and the lesion's and patient's characteristics, such as size and localization of the lesion, patient's obesity, and presence of excess bowel gas.

Core needle biopsy and FNA both provide tissue samples from a lesion/organ.[6,10,14–18] Core needle biopsy is more sensitive than FNA in the diagnosis of a pancreatic mass.[14,19] The sample quality of core needle biopsy is sufficient and of superior diagnostic quality than that of FNA and provides more tissue for further histopathological testing. Typically, 14–20-gauge cutting needles of the Tru-cut type are used. FNA is performed with smaller-gauge (20–25 gauge) needles. In our department, we routinely do percutaneous US-guided core needle biopsies of solid pancreatic masses using an 18-gauge semi-automatic Tru-cut biopsy needle.

CT-guided percutaneous pancreatic biopsy has shown a high diagnostic accuracy rate of $\geq$90%.[14–17] However, CT-guided biopsy is more time-consuming and involves radiation exposure. EUS-guided FNA is another method for sampling of pancreatic masses, which is increasing in popularity and availability. However, it has a lower sensitivity of 55%–97%.[6,7,10,20,21] A major advantage of this technique is the detection of small pancreatic lesions. However, this method may not be feasible for a biopsy of a mass located in the body or tail.

US-guided percutaneous biopsies of pancreatic solid masses are widely performed and have been shown to be a safe and effective method of biopsy.[5,11–13,19,22,23] This method has the advantages of greater availability, a higher success rate, lower cost, shorter procedure time, real-time visualization of the biopsy needle, and absence of ionizing radiation.[6,14] An anterior access is typically used to obtain a sample from the pancreatic lesion. However, a lesion located in the pancreatic head and uncinate process may be obscured by the colon, stomach, or duodenum. In such cases, a transhepatic, transgastric, or even transenteric access can be used, as in our study.[5,14,16,19] Although it is generally possible to access lesions located in any portion of the pancreas by percutaneous US-guided biopsy, accessing a small lesion located in the tail of the pancreas, particularly in obese patients with bowel gas distention, can be challenging. CT-guided biopsy is an alternative method for those patients. In our department, patients with a pancreatic mass that was not visible on US examination were referred for CT-guided biopsy. There were less than 10 such cases over the last 5 years.

Our final results showed high sensitivity and diagnostic accuracy of all 250 biopsies, which were consistent with the results of previous studies.[5,11–13,19,22,23] The causes of false-negative biopsy results include severe desmoplastic reaction induced by the pancreatic adenocarcinoma that limits the histopathological interpretation, needle misplacement, sampling errors, and small-size lesions.[19,22,23] Our initial false negative results were corrected by the repeat biopsies. Negative biopsy results should be carefully correlated with

clinical and imaging findings and the biopsy repeated if there is a suspicion of malignancy.

Complications of the pancreatic mass biopsies, which range from 0% to 21.4%, include self-limiting mild reactions, transient fever, duodenal perforation, abscesses, right gastric artery laceration, retroperitoneal hematoma, subcapsular hepatic hematoma, and tumor cell seeding to retroperitoneum.[5,11–14,16,19,20,22] We experienced an overall complication rate of 2%, which was consistent with the reported rates in the literature. Complications were mainly managed medically. However, one patient required an interventional radiologic procedure.

The limitations of this study include the retrospective nature of the study design, the absence of comparison with other image-guided techniques such as CT-guided biopsy or EUS-guided FNA, and the inability to analyze our results by the location and size of the masses. In conclusion, our study showed that percutaneous US-guided core needle biopsy in the diagnosis of solid pancreatic masses is a safe and effective method that can be used as the first-choice method for the histopathological diagnosis of solid pancreatic masses. Repeated pancreatic mass biopsy should be considered in patients with negative biopsy results with a high clinical suspicion of malignancy.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7.
2. Malvezzi M, Bertuccio P, Rosso T, et al. European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? Ann Oncol 2015;26:779.
3. Hartwig W, Schneider L, Diener MK, et al. Preoperative tissue diagnosis for tumours of the pancreas. Br J Surg 2009;96:5.
4. Tempero MA, Arnoletti JP, Behrman SW, et al. National Comprehensive Cancer Networks. Pancreatic adenocarcinoma, version 2.2012: featured updates to the NCCN guidelines. J Natl Compr Canc Netw 2012;10:703.
5. Yang RY, Ng D, Jaskolka JD, et al. Evaluation of percutaneous ultrasound-guided biopsies of solid mass lesions of the pancreas: a center's 10-year experience. Clin Imaging 2015;39:62.
6. Baek HW, Park MJ, Rhee YY, et al. Diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration cytology of pancreatic lesions. J Pathol Transl Med 2015;49:52.
7. Gupta S, Wallace MJ, Cardella JF, et al. Society of Interventional Radiology Standards of Practice Committee. Quality improvement guidelines for percutaneous needle biopsy. J Vasc Interv Radiol 2010;21:969.
8. Chang KJ, Nguyen P, Erickson RA, et al. The clinical utility of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of pancreatic carcinoma. Gastrointest Endosc 1997;45:387.
9. Garre Sánchez MC, Rendón Unceta P, López Cano A, et al. [Ultrasound-guided biopsy of the pancreas: a multicenter study]. Rev Esp Enferm Dig 2007;99:520.
10. Bergeron JP, Perry KD, Houser PM, et al. Endoscopic ultrasound-guided pancreatic fine-needle aspiration: potential pitfalls in one institution's experience of 1212 procedures. Cancer Cytopathol 2015;123:98.
11. Paulsen SD, Nghiem HV, Negussie E, et al. Evaluation of imaging-guided core biopsy of pancreatic masses. AJR Am J Roentgenol 2006;187:769.
12. Elvin A, Andersson T, Scheibenpflug L, et al. Biopsy of the pancreas with a biopsy gun. Radiology 1990;176:677.
13. Matsubara J, Okusaka T, Morizane C, et al. Ultrasound-guided percutaneous pancreatic tumor biopsy in pancreatic cancer: a comparison with metastatic liver tumor biopsy, including sensitivity, specificity, and complications. J Gastroenterol 2008;43:225.
14. Tyng CJ, Almeida MF, Barbosa PN, et al. Computed tomography-guided percutaneous core needle biopsy in pancreatic tumor diagnosis. World J Gastroenterol 2015;21:3579.
15. de Bucourt M, Busse R, Zada O, et al. CT-guided biopsies: quality, complications and impact on treatment: a retrospective initial quality control. Rofo 2011;183:842.
16. Amin Z, Theis B, Russell RC et al. Diagnosing pancreatic cancer: the role of percutaneous biopsy and CT. Clin Radiol 2006;61:996.
17. Clarke DL, Clarke BA, Thomson SR, et al. The role of preoperative biopsy in pancreatic cancer. HPB (Oxford) 2004;6:144.
18. Zamboni GA, D'Onofrio M, Idili A, et al. Ultrasound-guided percutaneous fine-needle aspiration of 545 focal pancreatic lesions. AJR Am J Roentgenol 2009; 193:1691.
19. Brandt KR, Charboneau JW, Stephens DH, et al. CT- and US-guided biopsy of the pancreas. Radiology 1993;187:99.
20. Tomonari A, Katanuma A, Matsumori T, et al. Resected tumor seeding in stomach wall due to endoscopic ultrasonography-guided fine needle aspiration of pancreatic adenocarcinoma. World J Gastroenterol 2015;21:8458.
21. Qian X, Hecht JL. Pancreatic fine needle aspiration. A comparison of computed tomographic and endoscopic ultrasonographic guidance. Acta Cytol 2003;47:723.
22. Zech CJ, Helmberger T, Wichmann MW, et al. Large core biopsy of the pancreas under CT fluoroscopy control: results and complications. J Comput Assist Tomogr 2002;26:743.
23. Karlson BM, Forsman CA, Wilander E, et al. Efficiency of percutaneous core biopsy in pancreatic tumor diagnosis. Surgery 1996;120:75.