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Ultrasound-guided percutaneous pancreatic tumor biopsy in pancreatic cancer: a comparison with metastatic liver tumor biopsy, including sensitivity, specificity, and complications

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Background. The aims of this study were to investigate the diagnostic value and safety of ultrasound-guided percutaneous pancreatic tumor biopsy (pancreatic biopsy) in patients with suspected unresectable pancreatic cancer, and to compare the data with those obtained by metastatic liver tumor biopsy (liver metastases biopsy). ***Methods.*** Data were collected retrospectively from 388 patients (398 procedures) for whom a final diagnosis was available and who underwent ultrasound-guided pancreatic or liver metastases biopsy with a 21-gauge needle (core biopsy) or a 22-gauge needle (fine-needle aspiration biopsy: FNAB). The sensitivity, specificity, and accuracy of pancreatic and liver metastases biopsies were evaluated. Biopsy-related complications were collected and analyzed. ***Results.*** Data from 271 pancreatic and 112 liver metastases biopsy procedures were available. For pancreatic core biopsy and FNAB, the sensitivity, specificity, and accuracy were 93%, 100%, and 93%, and 86%, 100%, and 86%, respectively, all of which were comparable to those of liver metastases biopsy. The complication rate in pancreatic biopsy was 21.4%, including a 4.4% incidence of post-biopsy ephemeral fever. The complication rate in liver metastases biopsy was 38.7%, including an 8.0% incidence of ephemeral fever. Fever and infection occurred more frequently among patients who underwent liver metastases biopsy (4.4% vs. 11%: $P = 0.038$). In pancreatic biopsy cases, a prebiopsy high serum total bilirubin level was a statistically significant predictor of ephemeral fever. ***Conclusions.*** Ultrasound-guided percutaneous pancreatic biopsy is an effective and safe modality for confirming the pathologic diagnosis in patients with unresectable pancreatic cancer.

Key words: pancreatic cancer, biopsy, sensitivity, complications, fever

Introduction

The majority of patients with pancreatic cancers have metastatic or locally advanced disease at the time of diagnosis, and are not candidates for surgical resection. In such patients with unresectable disease based on imaging findings, it is important to verify the histopathologic diagnosis of cancer before starting nonsurgical treatment, so as to exclude patients with pseudotumors or benign diseases from inappropriate aggressive therapies such as chemotherapy and radiotherapy. It is also important to distinguish pancreatic cancer with predominantly exocrine differentiation from others, such as cancer with endocrine differentiation or lymphoma, because their treatment strategy and tumor biology are completely different.

Pancreatic biopsy is a common procedure for obtaining histological specimens for diagnosis of a pancreatic mass. It can be performed endoscopically, intraoperatively, or percutaneously with computed tomographic (CT) or ultrasound (US) guidance. In our department, US-guided percutaneous pancreatic tumor biopsy (pancreatic biopsy) is the preferred method in patients whose tumors are suggested to be unresectable from preoperative abdominal imaging, because it allows accurate placement of the biopsy needle tip during real-time imaging and is less invasive than an endoscopic procedure or diagnostic laparotomy.

However, the diagnostic value and safety of US-guided percutaneous pancreatic biopsy have not yet been fully evaluated in patients with unresectable pancreatic cancer. In the present study, we aimed to assess the sensitivity, accuracy, complication rate, and risk factors of this procedure in comparison with US-guided

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metastatic liver tumor (liver metastases) biopsy, a common diagnostic procedure both in Japan and in other countries.

Patients and methods

Patients

We conducted a retrospective review of US-guided pancreatic or liver metastases biopsies performed during a 5-year period from January 1999 through December 2003. All patients were inpatients in whom preoperative abdominal imaging (dynamic CT or angiography) suggested that their pancreatic tumors were unresectable. Tumors encasing the celiac or superior mesenteric arteries or obstructing or bilaterally invading the portal vein were considered to be unresectable. Exclusion criteria were postoperative recurrence and pathological confirmation of cancer from biliary cytology, ascites cytology, or exploratory laparotomy.

For patients with both pancreatic tumor and liver metastases, the decision about which organ was to be targeted for biopsy was made by physicians on the basis of visualization of the lesion by transabdominal US, the patient's anatomy, and the physician's preference. The technique used for biopsy and the incidence of complications were reviewed from the clinical records. Coagulation measurements were performed before biopsy when the patient's history or presentation suggested an increased risk of bleeding, and we did not perform a biopsy if the results showed a bleeding tendency. We did not routinely use antibiotics prophylactically. A blood culture was routinely performed if patients had fever of ≥38.0°C after biopsy. All patients provided written informed consent for the biopsy procedures.

Biopsy techniques

In the case of both pancreatic biopsy and liver metastases biopsy, we used a convex probe or a linear-array probe, both of which were equipped with a guide attachment, and we performed biopsy with continuous real-time monitoring. The most appropriate approach was chosen after local sterilization with povidone–iodine, which was also used as the contact medium for the US probe. Local anesthesia was administered in all cases. The medial approach was always used for pancreatic biopsies. For liver metastases biopsies, in principle, the intercostal approach was used for tumors located in the right lobe and the medial approach for tumors in the left lobe. In pancreatic biopsies, the needle occasionally passed through the stomach. All patients who underwent pancreatic biopsy fasted from the night before the biopsy until after the biopsy itself to obtain good visualization of the pancreatic mass and to reduce the risk of peritonitis as a complication.

We used two types of needle, a 21-gauge needle (Sonopsy-C1; Hakko, Tokyo, Japan) for tissue core biopsy to obtain both pathologic and cytologic materials, and a 22-gauge needle (15 cm PTCD needle; Top, Tokyo, Japan) for aspiration biopsy to obtain cytologic material. The physician who performed the biopsy selected the more appropriate needle on the basis of US imaging and tumor size. The number of passes varied, but one or two passes were common. Biopsy material obtained from one pass was always checked macroscopically for adequacy before making the next pass.

When we performed core biopsies with the 21-gauge needle, the needle was advanced gently and withdrawn within the tumor lesion several times to obtain enough tissue for histologic diagnosis. Tissue core specimens were immediately preserved in 10% formalin, then the residual mucus was expressed onto glass slides, thin smears were prepared, and these were immersed in 95% ethanol. The needle tip was also cleansed in heparin-containing saline, and the wash-through fluid was examined cytologically.

We performed fine-needle aspiration biopsy (FNAB) with the 22-gauge needle. Once the needle had been placed within the lesion, the stylet was removed and suction was applied to the needle with a 20-ml disposable syringe. During the application of suction, the needle was gently advanced and withdrawn in the lesion several times. The aspirates were expressed onto glass slides and the needle tip was cleansed, as in the case of core biopsies.

Each pathologic diagnosis was determined by two or three pathologists specialized in pancreatic cancer and other cancers. A core sample was defined as tissue with preserved histologic structure. The final diagnosis was determined on the basis of autopsy or the clinical course of the patient. A diagnosis of benign pancreatic tumor was made together with a follow-up of at least 1 year during which there was no evidence of malignancy. The clinical course of the patient was used to confirm the histologic and cytologic diagnoses of malignancy.

Complications

We examined the clinical records of all patients in this study, and identified all complications such as pain, fever, and some infections. We defined pain as the need for additional analgesics after biopsy. Fever was classified into two categories: ephemeral fever and persistent fever. Ephemeral fever meant that patients had fever of ≥38.0°C within 24 h after the biopsy, but just once and never again (without antibiotics). Persistent fever meant that patients had fever of ≥38.0°C of unknown origin for more than 2 days after the biopsy, without any clini-

cally or microbiologically documented infection. Antibiotics were not used for ephemeral fever, but they were used for persistent fever.

Statistical analysis

The biopsy procedure for each organ was analyzed with regard to its ability to accurately diagnose malignancy or a benign tumor, and its safety in terms of the incidence of post-biopsy complications. The sensitivity, specificity, and accuracy of biopsies were calculated including specimens inadequate for diagnosis that were considered negative for malignancy. Biopsy specimens of both exocrine and endocrine carcinoma, including those diagnosed pathologically as neuroendocrine tumor, were considered positive for malignancy. For continuous variables, comparisons were made by *t* test. For categorical data, frequency comparisons were performed by χ-squared test. Logistic regression analysis was used to identify potential predictors of complications. Statistical significance was established at the $P < 0.050$ level.

The sensitivity of biopsies was calculated as the ratio of [true positives] / [true positives + false negatives]. The specificity of biopsies was calculated as the ratio of [true negatives] / [true negatives + false positives]. The accuracy of biopsies was defined as the ratio of [true positives] + [true negatives] divided by the total number of biopsy procedures.

Results

Patient characteristics

The study comprised 388 patients with suspected pancreatic cancer (Fig. 1); 170 had an unresectable pancreatic mass alone, 178 had liver metastases, and 40 had metastases to sites other than the liver. Among them, 274 patients underwent US-guided pancreatic biopsy, 110 underwent US-guided liver metastases biopsy, and four underwent both procedures on two separate occasions (Fig. 1). Six patients underwent biopsy of the same organ on two separate occasions (pancreas in five patients, liver in one); these were counted as two separate procedures. Among a total of 398 biopsy procedures, 15 (12 pancreas, 3 liver) that were performed with both types of needle during the same procedure were

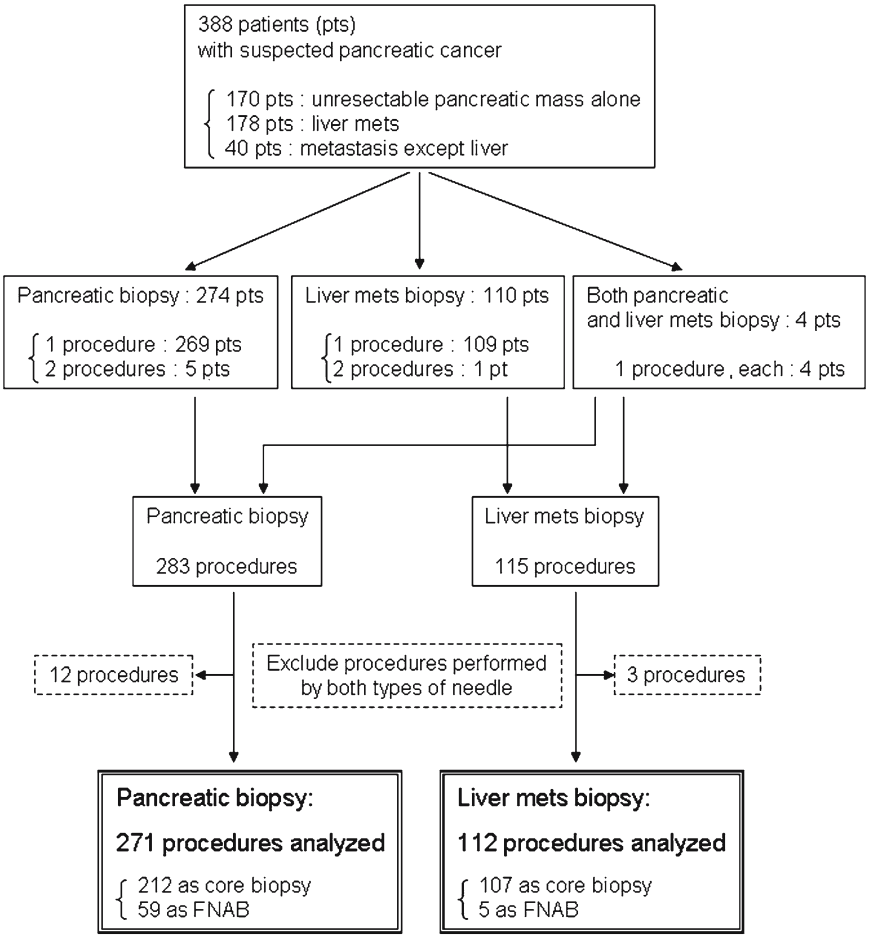

Fig. 1. A procedure-counting flow chart. "1 procedure" means that a patient underwent one organ biopsy on one occasion; "2 procedures" means that a patient underwent biopsy of the same organ on two separate occasions. We excluded procedures performed with both types of needle because it was impossible to determine which type provided the pathologic diagnostic material and produced the complications. Consequently, 271 (71%) pancreatic biopsy and 112 (29%) liver metastases (*mets*) biopsy procedures were performed. A total of 383 procedures were investigated and analyzed in this study. FNAB, fine-needle aspiration biopsy

Table 1. Patient demographics and clinical characteristics of targeted tumors

	Pancreatic biopsy			
	Total	Head	Body/tail	Liver metastases biopsy
No. of patients	266			111
Male	149			71
Female	117			40
Age, median years (range)	62 (32–86)			58 (37–79)
No. of biopsies, procedures	271			112
		106	165	
Mean tumor size, mm (SD)	42.2 (14.7)			26.2 (13.1)*
		37.0 (11.5)	45.6 (15.5)**	
Mean no. of passes	1.6			1.8
Core biopsy	1.6			1.8
FNAB	1.8			1.8

FNAB, fine-needle aspiration biopsy
* $P < 0.001$ vs. pancreatic biopsy
** $P < 0.001$ vs. pancreatic head biopsy

Table 2. Diagnostic value by site of biopsy in all 383 procedures

	Pancreatic biopsy	Liver metastases biopsy	*P* value
Final diagnosis			
Carcinoma, no. of procedures (patients)	266 (262)	112 (111)	
Benign disease, no. of procedures (patients)	5 (4)	0 (0)	
True positive, no. of procedures	244	109	
False positive, no. of procedures	0	0	
Sensitivity (95% CI)	92% (87.8–94.7)	97% (92.4–99.4)	0.713
Specificity (95% CI)	100% (47.8–100)	NE	
Accuracy (95% CI)	92% (88.0–94.8)	97% (92.4–99.4)	0.720

CI, confidence interval; NE, not evaluable

excluded because it was impossible to determine which type of needle had obtained the specimen from which pathologic diagnosis was made and which had caused any complications. Therefore, a final total of 383 biopsy procedures (271 pancreatic biopsy and 112 liver metastases biopsy procedures) were examined in the present study (Fig. 1).

At the time of analysis, 278 of the patients (73%) had died. The median follow-up time (from biopsy to death or the day to be censored) was 276 days.

In the pancreatic biopsy group, there were 149 men and 117 women with a median age of 62 years (range, 32–86 years) (Table 1). In the liver metastases biopsy group, there were 71 men and 40 women with a median age of 58 years (range, 35–79 years). In the pancreatic biopsy group, 106 targeted tumors were located in the pancreas head and 165 in the pancreas body and/or tail. The targeted tumors for pancreatic head biopsy were significantly smaller than those for pancreatic body/tail biopsy (37.0 mm vs. 45.6 mm; $P < 0.001$). The targeted tumors for liver metastases biopsy were significantly smaller than those for the pancreatic biopsies (26.2 mm vs. 42.2 mm; $P < 0.001$). There were no significant differences among the patient groups according to the site of biopsy with respect to the mean number of passes for core biopsies and FNABs.

Diagnostic value

Except for five procedures (four patients), the final diagnosis in all patients was pancreatic carcinoma (Table 2). The diagnoses of the four patients with benign pancreatic tumors were chronic pancreatitis (one), autoimmune pancreatitis (two), and retroperitoneal fibrosis (one). There were no false-positive histologic or cytologic interpretations in these four patients. The diagnosis of benign pancreatic tumor was confirmed again by long-term follow-up without anticancer treatment and without disease progression (median, 815 days; range, 322–1030). The sensitivity, specificity, and overall accuracy of the pancreatic biopsies were 92%, 100%, and 92%, respectively (Table 2). The sensitivity and overall accuracy of the liver metastases biopsies were both 97%. The specificity of liver metastases biopsies was not evaluated, because all patients who underwent liver metastases biopsy were finally diagnosed as having pancreatic carcinoma. There were no significant differences in sensitivity ($P = 0.713$) or accuracy ($P = 0.720$)

Table 3A. Diagnostic value of the core biopsy (21-gauge) by site and by type of specimen

Core biopsy (21-gauge) procedures	Pancreatic biopsy			Liver metastases biopsy (n = 107)
	Total (n = 212)	Head (n = 78)	Body/tail (n = 134)	
Tissue core specimen for histology				
Sensitivity (n)	77% (161/209)	68% (52/77)	83% (109/132)	84% (90/107)
Specificity (n)	100% (3/3)	100% (1/1)	100% (2/2)	NE (—)
Thin smears and needle-tip washing for cytology				
Sensitivity (n)	89% (187/209)	87% (67/77)	91% (120/132)	94% (101/107)
Specificity (n)	100% (3/3)	100% (1/1)	100% (2/2)	NE (—)

Table 3B. Diagnostic value by site and by type of biopsy needle

	Pancreatic biopsy			Liver metastases biopsy
	Total	Head	Body/tail	
Core biopsy (21-gauge) procedures[a]	n = 212	n = 78	n = 134	n = 107
Sensitivity (n)	93% (195/209)	90% (69/77)	96% (126/132)	97% (104/107)
Specificity (n)	100% (3/3)	100% (1/1)	100% (2/2)	NE (—)
Accuracy (n)	93% (198/212)	90% (70/78)	96% (128/134)	97% (104/107)
FNAB (22-gauge) procedures	n = 59	n = 28	n = 31	n = 5
Sensitivity (n)	86% (49/57)	85% (22/26)	87% (27/31)	100% (5/5)
Specificity (n)	100% (2/2)	100% (2/2)	NE (—)	NE (—)
Accuracy (n)	86% (51/59)	86% (24/28)	87% (27/31)	100% (5/5)

[a] Final diagnosis of core biopsy was defined as positive based on histological or cytological results

between pancreatic biopsy and liver metastases biopsy (Table 2).

Pancreatic biopsies yielded a sufficient amount of tissue to allow diagnosis in 93% of core biopsies, and an adequate yield of cells was obtained in 90% of FNABs. Liver metastases biopsies yielded a sufficient amount of material in 97% of core biopsies and in 100% of FNABs.

For procedures using the 21-gauge core biopsy needle, the sensitivity of the tissue core specimen for histology was 77% for pancreatic biopsy and 84% for liver metastases biopsy (Table 3A). The sensitivity of thin smears and needle-tip washing for cytology was 89% for pancreatic biopsy and 94% for liver metastases biopsy (Table 3A). When the result of the core biopsy procedure was defined as positive by histology or cytology, the total sensitivity, specificity, and accuracy were 93%, 100%, and 93%, respectively, for pancreatic biopsy and 97%, not evaluable, and 97%, respectively, for liver metastases biopsy (Table 3B).

For procedures using the 22-gauge aspiration biopsy needle (FNAB), the sensitivity, specificity, and accuracy were 86%, 100%, and 86%, respectively, and for pancreatic biopsy, and 100%, not evaluable, and 100%, respectively, for liver metastases biopsy (Table 3B).

There were no significant differences in sensitivity (core biopsy, $P = 0.810$; FNAB, $P = 0.819$) or accuracy (core biopsy, $P = 0.814$; FNAB, $P = 0.825$) between pancreatic biopsy and liver metastases biopsy according to the type of needle employed.

Complications

Regardless of the biopsy needle used, the proportion of patients with no complications was 79% for pancreatic biopsy and 75% for liver metastases biopsy (Table 4). There were no significant differences in the incidence of no complications ($P = 0.742$) or pain ($P = 0.999$). The total incidence of fever and infection, including ephemeral fever, cholangitis, and persistent fever, was significantly lower for pancreatic biopsy than for liver metastases biopsy ($P = 0.038$). None of the blood cultures collected from patients with fever and infection were positive.

For the core biopsy procedures, the incidence of pain was almost the same between pancreatic biopsy and liver metastases biopsy (Table 4). The incidence of ephemeral fever was lower for pancreatic biopsy (4.2%) than for liver metastases biopsy (7.5%), but not to a significant degree ($P = 0.252$). Cholangitis and persistent fever occurred only after liver metastases biopsy. For FNAB procedures, pain occurred only after pancreatic biopsy (15%). Cholangitis and persistent fever did not occur after either pancreatic or liver metastases FNAB.

There were no biopsy-related deaths, or life-threatening complications such as biopsy-related pan-

Table 4. Complications by site of biopsy

	Pancreatic biopsy	Liver metastases biopsy	*P* value
Core biopsy (21-gauge)	*n* = 212	*n* = 107	
No complication	168 (79%)	80 (75%)	
Pain[a]	38 (18%)	20 (19%)	
Ephemeral fever[b]	9 (4.2%)	8 (7.5%)	
Cholangitis	0	2 (1.9%)	
Persistent fever[c]	0	1 (0.9%)	
FNAB (22-gauge)	*n* = 59	*n* = 5	
No complication	47 (80%)	4 (80%)	
Pain[a]	9 (15%)	0 (0%)	
Ephemeral fever[b]	3 (5.1%)	1 (20%)	
Total	*n* = 271	*n* = 112	
No complication	215 (79%)	84 (75%)	0.742
Pain[a]	47 (17%)	20 (18%)	0.999
Fever and infection[d]	12 (4.4%)	12 (11%)	0.038*

* Statistically significant
[a] Patients needed additional analgesics after biopsy
[b] Patients had a single episode of fever of ≥38.0°C within 24 h after biopsy (without antibiotics).
[c] Patients had fever of ≥38.0°C of unknown origin for more than 2 days after biopsy, without clinically or microbiologically documented infection
[d] Includes ephemeral fever, cholangitis, and persistent fever

creatitis, macroscopic or symptomatic hematoma, or obvious needle-tract seeding.

Since ephemeral fever was the only clinically problematic complication of the pancreatic biopsy procedure that could reduce a patient's performance status, a logistic regression analysis was performed to examine the potential predictors of ephemeral fever in pancreatic biopsy cases. Potential predictors were the serum levels of total bilirubin (T-bil), aspartate aminotransferase, alanine aminotransferase (ALT), alkaline phosphatase, amylase, and C-reactive protein before biopsy, age, and size and location of the targeted pancreas tumor, which were considered to be related to retention of bile or pancreatic juice, or inflammation. Univariate analysis showed that T-bil ($P = 0.008$) and ALT ($P = 0.048$) before biopsy were significant predictors of ephemeral fever (Table 5). Multivariate analysis showed that only T-bil was a statistically significant predictor of ephemeral fever ($P = 0.006$, relative risk = 2.45; 95% confidence interval, 2.01–66.39).

Discussion

Because of dramatic developments in the technology of imaging diagnosis in the past decade, the resectability of pancreatic cancer can now be determined very accurately purely on the basis of diagnostic imaging techniques such as high-resolution spiral CT scan. However, histopathologic confirmation is necessary in patients deemed to have inoperable tumors or those who are medically unsuitable for surgery. In the National Comprehensive Cancer Network (NCCN) guidelines for pancreatic adenocarcinoma,[1] it is strongly recommended that all patients with unresectable pancreatic cancer should have cancer confirmation prior to nonsurgical treatment, and that a negative biopsy result should be confirmed by at least one repeat biopsy. Our present retrospective study demonstrated that US-guided percutaneous pancreatic biopsy is an effective modality for confirmation of the pathologic diagnosis in patients with unresectable pancreatic cancer. We also confirmed that it is as safe as liver metastases biopsy in these patients.

The reported sensitivity of US- or CT-guided percutaneous pancreatic biopsy procedures ranges from 80% to 97% with various types of needle.[2–6] The sensitivity observed in our study (92%, Table 2) is slightly higher than that reported in studies of US-guided biopsy studies.[5,6] This may be attributable to the design of our study, which yielded a high level of sensitivity for US-guided pancreatic biopsy. This was a retrospective study of all patients who underwent attempted biopsies of pancreatic masses by US, preselecting only those individuals in whom the mass could be seen, although in general US is often unable to visualize the pancreas completely.

Another selection bias was the fact that we usually selected FNAB from the viewpoint of safety when US visualization of the targeted pancreatic lesion was poor or unclear, and this may have lowered the sensitivity and accuracy of pancreatic biopsies in FNABs compared with core biopsies (86% vs. 93%, Table 3B), although not to a significant degree.

The complication rate associated with US- or CT-guided percutaneous pancreatic biopsy procedures is extremely low, ranging between 0% and 2%.[4,7–10] The

Table 5. Correlation of prebiopsy clinical data with ephemeral fever[a] after pancreatic biopsy

	Fever positive	
	No. of procedures (%)	*P* value*
Total bilirubin		**0.008**
≥2.0 mg/dl (*n* = 15)	3 (20%)	
<2.0 mg/dl (*n* = 256)	9 (3.5%)	
AST		0.995
≥40 IU/l (*n* = 45)	2 (4.4%)	
<40 IU/l (*n* = 226)	10 (4.4%)	
ALT		**0.048**
≥40 IU/l (*n* = 67)	6 (9.0%)	
<40 IU/l (*n* = 204)	6 (2.9%)	
Alkaline phosphatase		0.113
≥300 U/l (*n* = 98)	7 (7.1%)	
<300 U/l (*n* = 173)	5 (2.9%)	
Amylase		0.842
≥100 IU/l (*n* = 79)	4 (5.1%)	
<100 IU/l (*n* = 178)	8 (4.5%)	
CRP		0.095
≥0.5 mg/dl (*n* = 76)	6 (7.9%)	
<0.5 mg/dl (*n* = 195)	6 (3.1%)	
Age, years		0.571
≥65 (*n* = 114)	6 (5.3%)	
<65 (*n* = 157)	6 (3.8%)	
Size of targeted pancreas tumor		0.261
≥4.0 cm (*n* = 160)	9 (5.6%)	
<4.0 cm (*n* = 111)	3 (2.7%)	
Location of targeted pancreas tumor		0.853
Head (*n* = 106)	5 (4.7%)	
Body/tail (*n* = 165)	7 (4.2%)	

AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein
*Univariate analysis with logistic regression; statistically significant *P* values are shown in bold
[a]Single episode of fever of ≥38.0°C within 24 h after biopsy (without antibiotics)

most serious complications are postbiopsy pancreatitis, hemorrhage, and peritoneal dissemination.[4,7] Although a review of the literature has reported six deaths resulting from pancreatic biopsy,[7] there were no deaths or cases of biopsy-related pancreatitis in our series. Although acute pancreatitis after pancreatic biopsy is rare, it can be serious and sometimes fatal when it occurs, and this may be the main reason why the procedure is not commonly performed. The reported rate of postbiopsy pancreatitis ranges from 0% to 1.7%.[4,5,8,11–13] In patients with unresectable pancreatic cancer, the tumors are large and usually located just under the surface of the pancreas, allowing percutaneous puncture of the tumor without penetrating the normal pancreatic tissue. This is probably why biopsy-related pancreatitis is unlikely to develop, as Smith[7] has suggested.

Although the exact frequency of pancreatic biopsy-related peritoneal dissemination is not known, it may not have any influence on the prognosis of patients with unresectable pancreatic cancer, which is invariably poor.[14] On the other hand, in patients with resectable pancreatic cancer, preoperative percutaneous pancreatic biopsy is regarded as controversial because some studies have suggested a high frequency of procedure-related peritoneal dissemination (16.3%–75%).[15,16] The NCCN guidelines state that biopsy proof of malignancy is not required before surgical resection and that a non-diagnostic biopsy should not delay surgical resection, which is the only curative therapy for pancreatic cancer.[1]

In the present study, no cases of clinically or microbiologically documented infection were associated with pancreatic biopsy. There were, however, 12 cases (4.4%) of postbiopsy ephemeral fever, a lower incidence rate than that following liver metastases biopsy. We are not aware of any other published data on this type of fever. We routinely checked the serum level of amylase, but not that of lipase. Among 12 patients with postbiopsy ephemeral fever, two had amylase levels higher than the upper normal limit after pancreatic biopsy. Since leakage of pancreatic juice can occur after pancreatic biopsy, ephemeral fever could be an initial sign of pancreatitis, which has the potential to become life-threatening.

Pancreatic tumor biopsy can be performed using CT guidance with a complication rate ranging from 3.8% to 7%,[4,17,18] and our data showed a very similar rate. It can also be performed under endoscopic ultrasound guidance with a complication rate similar to that observed in our study.[19–22] However, we consider that US-guided pancreatic biopsy may be most useful in patients with unresectable pancreatic cancer, because their tumors are usually large enough to warrant a safe US-guided biopsy (mean size in our study, 42.2 mm, Table 1). Furthermore, although we did not perform a cost and patient satisfaction analysis, the procedure for US-guided pancreatic biopsy is obviously more time-saving and less stressful to patients than other biopsy modalities.

In conclusion, in patients with unresectable pancreatic cancer, US-guided percutaneous pancreatic biopsy is an effective and safe modality for confirmation of the pathologic diagnosis. If US visualization is obtained with enough care, pancreatic biopsy is as accurate and safe as liver metastases biopsy, which is well established and commonly perceived as safer. Another important conclusion is that even if a mass in the pancreas seems to be cancer and is large enough to warrant US-guided biopsy, 1.5% (4/266, Table 2) of such cases are not cancer. This indicates that all patients with unresectable pancreatic cancer should have cancer confirmation prior to nonsurgical treatment. Our study was a retrospective analysis, which precludes any firm conclusion. Therefore, a prospective study is needed for adequate evaluation of US-guided pancreatic biopsy as a diagnostic tool.

References

1. NCCN clinical practice guidelines in oncology. Pancreatic adenocarcinoma, vol. 2. National Comprehensive Cancer Network; 2006.
2. Bret PM, Nicolet V, Labadie M. Percutaneous fine-needle aspiration biopsy of the pancreas. Diagn Cytopathol 1986;2:221–7.
3. Hajdu EO, Kumari-Subaiya S, Phillips G. Ultrasonically guided percutaneous aspiration biopsy of the pancreas. Semin Diagn Pathol 1986;3:166–75.
4. Brandt KR, Charboneau JW, Stephens DH, Welch TJ, Goellner JR. CT- and US-guided biopsy of the pancreas. Radiology 1993; 187:99–104.
5. Tillou A, Schwartz MR, Jordan PH Jr. Percutaneous needle biopsy of the pancreas: when should it be performed? World J Surg 1996;20:283–6; discussion 7.
6. Mallery JS, Centeno BA, Hahn PF, Chang Y, Warshaw AL, Brugge WR. Pancreatic tissue sampling guided by EUS, CT/US, and surgery: a comparison of sensitivity and specificity. Gastrointest Endosc 2002;56:218–24.
7. Smith EH. Complications of percutaneous abdominal fine-needle biopsy. Review. Radiology 1991;178:253–8.
8. Linder S, Blasjo M, Sundelin P, von Rosen A. Aspects of percutaneous fine-needle aspiration biopsy in the diagnosis of pancreatic carcinoma. Am J Surg 1997;174:303–6.
9. Zech CJ, Helmberger T, Wichmann MW, Holzknecht N, Diebold J, Reiser MF. Large core biopsy of the pancreas under CT fluoroscopy control: results and complications. J Comput Assist Tomogr 2002;26:743–9.
10. Di Stasi M, Lencioni R, Solmi L, Magnolfi F, Caturelli E, De Sio I, et al. Ultrasound-guided fine needle biopsy of pancreatic masses: results of a multicenter study. Am J Gastroenterol 1998;93:1329–33.
11. Eloubeidi MA, Chen VK, Eltoum IA, Jhala D, Chhieng DC, Jhala N, et al. Endoscopic ultrasound-guided fine needle aspiration biopsy of patients with suspected pancreatic cancer: diagnostic accuracy and acute and 30-day complications. Am J Gastroenterol 2003;98:2663–8.
12. Gines A, Wiersema MJ, Clain JE, Pochron NL, Rajan E, Levy MJ. Prospective study of a Trucut needle for performing EUS-guided biopsy with EUS-guided FNA rescue. Gastrointest Endosc 2005;62:597–601.
13. Ryozawa S, Kitoh H, Gondo T, Urayama N, Yamashita H, Ozawa H, et al. Usefulness of endoscopic ultrasound-guided fine-needle aspiration biopsy for the diagnosis of pancreatic cancer. J Gastroenterol 2005;40:907–11.
14. Balen FG, Little A, Smith AC, Theis BA, Abrams KR, Houghton J, et al. Biopsy of inoperable pancreatic tumors does not adversely influence patient survival time. Radiology 1994;193:753–5.
15. Warshaw AL. Implications of peritoneal cytology for staging of early pancreatic cancer. Am J Surg 1991;161:26–9; discussion 9–30.
16. Micames C, Jowell PS, White R, Paulson E, Nelson R, Morse M, et al. Lower frequency of peritoneal carcinomatosis in patients with pancreatic cancer diagnosed by EUS-guided FNA vs. percutaneous FNA. Gastrointest Endosc 2003;58:690–5.
17. DelMaschio A, Vanzulli A, Sironi S, Castrucci M, Mellone R, Staudacher C, et al. Pancreatic cancer versus chronic pancreatitis: diagnosis with CA 19-9 assessment, US, CT, and CT-guided fine-needle biopsy. Radiology 1991;178:95–9.
18. Rodriguez J, Kasberg C, Nipper M, Schoolar J, Riggs MW, Dyck WP. CT-guided needle biopsy of the pancreas: a retrospective analysis of diagnostic accuracy. Am J Gastroenterol 1992;87: 1610–3.
19. Binmoeller KF, Thul R, Rathod V, Henke P, Brand B, Jabusch HC, et al. Endoscopic ultrasound-guided, 18-gauge, fine needle aspiration biopsy of the pancreas using a 2.8 mm channel convex array echoendoscope. Gastrointest Endosc 1998;47:121–7.
20. Williams DB, Sahai AV, Aabakken L, Penman ID, van Velse A, Webb J, et al. Endoscopic ultrasound guided fine needle aspiration biopsy: a large single centre experience. Gut 1999;44:720–6.
21. Voss M, Hammel P, Molas G, Palazzo L, Dancour A, O'Toole D, et al. Value of endoscopic ultrasound guided fine needle aspiration biopsy in the diagnosis of solid pancreatic masses. Gut 2000;46:244–9.
22. Itoi T, Itokawa F, Sofuni A, Nakamura K, Tsuchida A, Yamao K, et al. Puncture of solid pancreatic tumors guided by endoscopic ultrasonography: a pilot study series comparing Trucut and 19-gauge and 22-gauge aspiration needles. Endoscopy 2005;37: 362–6.