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# Percutaneous Needle Biopsy of the Pancreas: When Should It Be Performed?

Areti Tillou, M.D.,[1] Mary R. Schwartz, M.D.,[2] Paul H. Jordan, Jr., M.D.[1]

[1]Department of Surgery, Baylor College of Medicine, The Methodist Hospital, 6550 Fannin, Suite 1639, Houston, Texas 77030, U.S.A.
[2]Department of Pathology, Baylor College of Medicine, The Methodist Hospital, 6550 Fannin, Houston, Texas 77030, U.S.A.

**Abstract. Is it appropriate for a good risk patient with a clinical history or imaging studies suggestive of an operable pancreatic neoplasm to undergo a percutaneous fine-needle aspiration biopsy (FNAB) prior to operation? A group of 118 patients who underwent percutaneous FNAB of the pancreas between 1987 and 1993 were evaluated retrospectively. The initial readings of the biopsies were positive for neoplasm in 78 patients and negative in 32. Four suspicious biopsies were included with the positive biopsies for analysis, and four unsatisfactory biopsies were added to the negative biopsies. Operation was performed on 57 of the 118 patients; 39 of these patients had a positive and 18 a negative FNAB. Of the 18 patients with a negative biopsy, 12 were proved to have neoplasia at operation. No operation was performed on 61 patients; 43 of these patients had a positive and 18 a negative FNAB. Three patients with a negative biopsy were treated with chemotherapy, and three subsequently died of pancreatic cancer. It was concluded that because the sensitivity of percutaneous FNAB is only 84% the procedure should be limited to patients suspected of having pancreatic cancer deemed technically inoperable or medically unsuitable for operation.**

Errors in diagnosis of pancreatic masses by an experienced surgeon using inspection and palpation range from 3% to 25% [1, 2]. To avoid errors in diagnosis, intraoperative biopsies of the pancreas are used. Their use is controversial because of the associated morbidity and mortality. In 1975 Hancke et al. [3] and Smith et al. [4] recommended percutaneous fine needle aspiration biopsy (FNAB) of the pancreas using ultrasound guidance. The complication rate associated with this method was low, and results suggested that the technique might prevent operations for suspected, but nonexistent, carcinoma of the pancreas.

Percutaneous FNAB of the pancreas has become a common procedure for evaluating pancreatic masses discovered by various imaging techniques. Although FNAB is associated with low morbidity, its reported sensitivity has varied from 45% to 100% [5, 6]. In most reports the sensitivity ranges from 60% to 86% [7–14]. The smaller the lesion, the more difficult it is to make a correct FNAB diagnosis [15]. The lesion can be so small it is difficult for the pathologist to find. Thus the more favorable a lesion for resection the less likely it is that percutaneous FNAB will yield the diagnosis. The variability and level of the sensitivity raises the question whether pancreatic FNABs are overused. The purpose of this paper is to review the results of FNABs in our institution and to evaluate the relevance of the procedure for patients with suspected pancreatic cancer.

*Correspondence to:* P.H. Jordan, Jr., M.D.

## Patients and Methods

We reviewed retrospectively 118 consecutive patients who had undergone pancreatic FNAB between 1987 and 1993 at The Methodist Hospital in Houston. All patients had either a pancreatic or peripancreatic mass demonstrated by a computed tomography (CT) scan and many had undergone endoscopic retrograde cholangiopancreatography (ERCP). The masses were located in the head of the pancreas in 68 patients, in the body in 20, in the tail in 16, and in the entire gland in 20. The exact location of the tumor was not recorded in 12 patients. There were 59 men and 59 women. The mean age of all patients was 65.2 years with a range of 19 years (islet cell tumor) to 93 years (mucinous adenocarcinoma). Jaundice and duodenal obstruction were the most characteristic signs and symptoms leading to patient evaluation; however, the most common presenting symptoms were pain and weight loss.

The FNABs were performed usually with 21 gauge Surecut needles under CT or ultrasound guidance. The number of passes varied, but three was the usual number. In some cases material obtained from a pass was checked for adequacy before making the next pass. The results of FNABs were classified as positive, suspicious, or negative for neoplasm or unsatisfactory. The four suspicious biopsies were analyzed with the positive biopsies because they did not provide adequate evidence to preclude the need for exploration. The final diagnoses in these four cases were pancreatic cancer in two, lymphoma in one, and pancreatitis in one. The four patients with unsatisfactory FNABs were analyzed with those having negative biopsies. The final diagnoses made at operation were pancreatic islet cell tumor in one patient and lymphoma in another. The pancreatic carcinoma in the other two patients who were not operated on was diagnosed during follow-up. Although the unsatisfactory biopsies were not negative from the pathologists' standpoint, they were negative from the point of view of the patient who had undergone the discomfort, risk, and cost of FNAB with no benefit. Others [15] have considered unsatisfactory *and* suspicious biopsies as negative FNABs. The final diagnosis for patients with FNABs who underwent operation

**Table 1.** Comparison of preoperative FNAB and postoperative diagnoses.

| FNABs | | Preoperative diagnosis | | Postoperative diagnosis | |
|---|---|---|---|---|---|
| Results | No. | Diagnosis | No. | Diagnosis | No. |
| Positive | 35 | Ductal adenocarcinoma | 30 | | 27[a] |
| Suspicious | 4 | Mucinous carcinoma | 4 | | 4 |
| | | Islet cell tumor | 3 | | 3 |
| | | Adenosquamous carcinoma | 2 | | 2 |
| | | | | Pancreatitis | 1[b] |
| | | | | Carcinoma of stomach | 1 |
| | | | | Lymphoma | 1[b] |
| Negative | 16 | No tumor | 18 | Ductal adenocarcinoma | 10 |
| Unsatisfactory | 2 | | | Islet cell tumor | 1[c] |
| | | | | Lymphoma | 1[c] |
| | | | | No tumor | 6 |

[a]Two suspicious FNABs.
[b]Suspicious FNAB.
[c]Unsatisfactory FNAB.

was confirmed, either by intraoperative biopsies or by histologic examination of the specimen.

## Results

Three major complications were attributed to the FNAB. One patient with pancreatic cancer died owing to acute necrotizing pancreatitis following FNAB with a 21 gauge needle. A second patient required operation to drain an abscess caused by the FNAB, and a third patient developed an extensive hematoma in the area of the pancreas that prevented resection. A fourth patient had a significant, but less severe, hemorrhage surrounding the pancreas. Some type of pancreatectomy was performed in 17 patients, palliative bypass in 32, and other procedures in 8. Most of the FNAB diagnoses were ductal adenocarcinoma. Other FNAB diagnoses were mucinous adenocarcinoma ($n = 4$), islet cell tumor ($n = 3$), adenosquamous carcinoma ($n = 2$), lymphoma ($n = 1$), microcystic adenoma ($n = 1$), and metastatic small-cell carcinoma ($n = 1$). The intraoperative biopsy diagnosis was different from the FNAB diagnosis in 15 patients (26%) (Table 1).

There were 82 patients with a positive FNAB (78 positive, 4 suspicious) diagnosis of malignancy. Operation was performed on 48% (57 of 118) of the patients who underwent FNAB. The FNAB was positive for neoplasm in 68% (39/57) and negative in 32% (18 of 57) of operated cases. Of the 39 patients with a positive FNAB, there were three incorrect diagnoses; and 12 of the 18 patients who had a negative FNAB were found to have a neoplasm at operation (Table 1). The diagnosis of pancreatic neoplasm was confirmed in 92% (36 of 39) of those with a positive FNAB undergoing operation. The other three patients had pancreatitis, cancer of the stomach, or lymphoma instead of pancreatic cancer. A pancreatic neoplasm was found in 61% (11 of 18) and a lymphoma in 1 of the 18 patients with a negative FNAB who were operated on. Thus a neoplasm was present in 88% (50 of 57) and a pancreatic neoplasm was present in 82% (47 of 57) of the patients operated. Of the 118 patients, 61 had no operation after the FNAB. The FNAB was positive in 43 patients of this group. Of these 43 patients, 35 underwent palliative irradiation, chemotherapy, or both; 8 patients had no further treatment. Of the 43 patients who had nonoperative treatment, 27 had lesions that were deemed unresectable, 6 were poor surgical candidates, 1 patient died of acute pancreatitis following FNAB, and 4 chose not to have any treatment. Two patients had nonoperative treatment for unknown reasons. One patient each had a lymphoma, metastatic small-cell carcinoma, and asymptomatic microcystic adenoma. These three patients were spared an unnecessary operation by having had an FNAB.

Of the 18 patients with negative biopsies who were not operated on, 3 had palliative therapy and 15 no further treatment. We were particularly interested to determine which patients with negative FNABs and who were unoperated might have had pancreatic cancer. Of the 18 patients, 7 (one received palliative treatment) were well (2–7 years) and were presumed to have had no cancer. The FNABs in these seven patients were considered true negatives and prevented unnecessary operations. Two patients died after FNAB from causes unrelated to the biopsies or cancer. Three patients (two were treated with palliative therapy) died of pancreatic cancer, two of them had had an unsatisfactory FNAB. No follow-up information was available on six patients (hypothetically true negatives).

It was assumed that patients with positive FNABs who were not operated had true positive biopsies although we have no proof. Thirty-seven patients with a positive FNAB who were operated on were true positives for neoplasia, 36 for pancreatic cancer, and 1 for carcinoma of the stomach. There were two false-positive FNABs. One patient had pancreatitis, and one had a lymphoma. Although the patient with lymphoma had neoplasia, the biopsy is considered a false positive because had the diagnosis of lymphoma been made the patient would not have been operated on. There were 12 false-negative FNABs among the operated group and at least three false negatives in the nonoperated group. If we assume that the six patients with negative FNABs lost to follow-up were truly negative, a total of 42% (15 of 36) of the patients with a negative FNAB had a falsely negative result. We conclude that the sensitivity in our series of FNABs was no greater than 84% [80/(80 + 15)]. If any of the six patients considered hypothetically to have true negative results actually had false-negative readings, the sensitivity might have been as low as 79%. The sensitivity range of 79% to 84% for the diagnosis of pancreatic cancer by FNAB is consistent with most reports.

## Discussion

Percutaneous FNAB of the pancreas is technically easy to perform on an outpatient basis in the radiology department under local anesthesia. The cost in our hospital is approximately $2000 for a CT-guided FNAB. The specificity of the test is high, but the sensitivity is lower because the accuracy of diagnosis depends not only on the expertise of the pathologist but on the adequacy of the samples provided. The morbidity and mortality of the procedure are low, although complications, including acute pancreatitis, hemorrhage, pancreatic fistula, abscess, pancreatic ascites, intraperitoneal seeding of tumor, and death [5, 16–20], do occur. The complication rate of FNAB in this series was 3.4%. This figure might be considered low if it were not for the demise of one patient who died of acute pancreatitis.

A CT scan is the most accurate, readily available method for determining the resectability of a pancreatic mass. Unresectable tumors are usually large, and tissue planes between surrounding structures, particularly the vascular structures, become less distinct or obliterated. FNABs of large tumors have fewer complications and are more likely to yield an accurate diagnosis of cancer [15, 18] than FNAB of small, circumscribed lesions [21]. Because the sensitivity of an FNAB of a pancreatic mass is sufficiently low that one would not exclude exploration on this basis, it seems reasonable that FNAB should be limited, with few exceptions, to patients considered inoperable for technical reasons or who have medical contraindications to operation.

Fine needle aspiration biopsy is not discouraged in patients who wish to undergo palliative therapy if cancer is present. Of the 43 unoperated patients with positive FNABs in our study, 35 were benefited because the biopsy provided prognostic information to the patients and tissue confirmation to the oncologist. In addition, FNAB established the diagnoses of lymphoma, small-cell carcinoma, and microcystic adenoma of the pancreas of three patients who were spared unnecessary operations.

In addition to the patients deemed inoperable or medically unsuitable for operation, FNAB is indicated in those suspected of having lymphoma or asymptomatic microcystic adenoma. With these exceptions, a pancreatic mass seen on CT scan is usually an indication for exploration and possible pancreatic resection without resorting to FNAB [22, 23]. Because 21 of 36 patients with negative FNABs were operated on or otherwise treated, it is difficult to believe that the 39 patients with a positive FNAB who were operated on would not have been if the FNAB had been negative. This point implies that the FNAB had little influence on the decision whether to operate on patients with pancreatic masses that appeared operable. In view of the cost, risk, and low sensitivity of FNAB, it seems inappropriate to perform the procedure except under the special circumstances enumerated above.

Some physicians, however, believe the risks are so high and the results of pancreatic surgery so poor that patients with cancer are best served by a period of expectant observation and supportive management [5]. In their opinion, FNAB is the best nonoperative method for establishing the diagnosis of cancer that permits chemotherapy, irradiation, or both. In contrast, the reported mortality for the Whipple procedure has been reduced to as low as zero [24, 25]. Not only is the Whipple procedure safe and potentially curative for cancer, it is an excellent palliative procedure for patients with jaundice, duodenal obstruction, and pain due to either inflammatory or malignant pancreatic disease [26].

Some patients or their primary care physicians refuse to commit to operative treatment unless a positive diagnosis has been established. It is clear that the sensitivity of FNAB is sufficiently low that a significant number of pancreatic cancers would go unoperated if operation depended on a positive FNAB. In our own study, 14.4% (14 of 97) of patients with known pancreatic neoplasia were not diagnosed by FNAB. This figure is similar to the average reported in the literature, although in some institutions the number of incorrect diagnoses is even higher. The number of cancers missed by FNAB would be increased if analysis were limited to small lesions of the size that is difficult for the surgeon and even the pathologist to recognize grossly—the lesions most likely to be cured by operation. Although six patients with a negative FNAB were lost to follow-up, we know that at least 42% (15 of 36) of the FNABs read as negative were falsely negative. Viewed in another way, 15% (18 of 118) of all biopsies performed in this review are known to have been incorrect. In all, the information obtained by FNAB in 18% (21 of 118) of the patients were disregarded when formulating patient management.

If a positive tissue diagnosis is required before a Whipple procedure is performed, it can be achieved more successfully by a needle core or wedge biopsy at operation than by an FNAB [2, 27, 28]. Even so, the diagnosis of cancer may be difficult or not forthcoming, particularly in patients with small, potentially curable lesions. It may be necessary for the surgeon to decide whether to perform a Whipple procedure when there is not tissue confirmation. Cohen et al. [26] and we have recommended resection when cancer is strongly suspected. The risk of performing an unnecessary Whipple operation is low if the patient has been properly evaluated before operation. The decision to perform a Whipple procedure without positive tissue diagnosis is also easier in patients with severe pancreatic pain because of its beneficial effect on the pain caused by cancer or chronic pancreatitis. Finally, if the decision to perform resection is based on pancreatic biopsy, one must remember the possible coexistence of cancer and chronic pancreatitis and the occasional difficulty of distinguishing pathologically one from the other.

In our opinion the reliability of a negative FNAB is sufficiently low that it should be omitted when evaluating a patient for suspected pancreatic cancer unless the patient is not expected to survive an operation or the tumor is considered unresectable. FNAB is recommended also in patients suspected of having a lymphoma or an asymptomatic microcystic adenoma or who will not commit to treatment unless there is a positive diagnosis. If the suspicion of cancer was great enough that an FNAB was performed, a negative FNAB should not preclude operation, which is the most accurate method for diagnosing pancreatic cancer. The requirement of a pathology diagnosis of cancer before performing a Whipple operation is more likely to result in leaving a small, possibly curable cancer unresected than resection of a normal pancreas.

## Résumé

Est-il raisonnable de proposer une biopsie percutanée du pancréas préopératoire chez le patient opérable avec une histoire clinique et/ou une imagerie typique de cancer du pancréas? On a évalué rétrospectivement les résultats chez 118 patients ayant eu

une biopsie percutanée entre 1987 et 1993. Les biopsies initiales étaient positives chez 78 patients et négatives chez 32. Quatre biopsies suspectes ont été analysées avec les résultats positifs alors que quatre autres non concluantes ont été analysées avec les résultats négatifs. Une intervention a été réalisée chez 57 de 118 patients; 39 avaient eu une biopsie positive, 18 avaient eu une biopsie négative. Douze des 18 patients ayant une biopsie négative avaient un cancer du pancréas à l'intervention. Aucune intervention n'a été réalisée chez 61 patients, 43 avaient une biopsie positive, 18 avaient une biopsie négative. Trois patients ont été traités par chimiothérapie, et trois patients sont décédés d'un cancer du pancréas. Conclusion: Puisque la sensibilité de la biopsie percutanée n'est que de 84%, elle ne doit être pratiquée que chez les patients suspectés d'avoir un cancer du pancréas inopérable soit techniquement soit médicalement.

**Resumen**

Es apropiado que un paciente en riesgo con historia clínica y/o imágenes diagnósticas que sugieren la presencia de un neoplasma pancreático operable sea sometido a biopsia por aspiración percutánea con aguja fina antes de la operación? Se efectuó la evaluación retrospectiva de 118 pacientes sometidos a biopsia del páncreas por aspiración con aguja fina entre 1987 y 1993. El diagnóstico inicial de las biopsias fue positivo para neoplasma en 78 pacientes y negativo en 32. Cuatro biopsias sospechosas fueron incluidas entre las positivas, para efectos de análisis, y cuatro biopsias no satisfactorias fueron añadidas al grupo de las biopsias negativas. Se practicó operación en 57 de los 118 pacientes; 39 habían tenido una biopsia positiva y 18 una biopsia negativa. Doce de los 18 pacientes con biopsia negativa demostraron tener un neoplasma en la operación. No se practicó operación en 61 pacientes; 43 de ellos tenían biopsia positiva y 18 negativa. Tres pacientes con biopsia negativa fueron tratados con quimioterapia y 3 murieron como consecuencia de cáncer pancreático. *Conclusión*: puesto que la sensibilidad de la biopsia por aspiración percutánea con aguja fina es de sólo 84%, parecería que este procedimiento debe ser limitado a los pacientes en que un probable cáncer pancreático aparezca técnicamente inoperable o con contraindicación médica para la operación.

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# Invited Commentary

A.R. Moossa, M.D.

Department of Surgery, University of California, San Diego Medical Center, San Diego, California, U.S.A.

The feasibility of a test or a procedure is not an indication for its performance. The available literature on pancreatic biopsy is often confusing, as contradictory recommendations are often made based on retrospective and inadequate data. Whenever the results of fine-needle aspiration (FNA) of pancreatic masses (preoperative or intraoperative) are reported, pertinent parameters of the tumors, such as size, stage, and resectability, are rarely if ever mentioned. Thus one cannot escape the impression that *routine* preoperative biopsy of pancreatic masses is a triumph of technology over reason.

What are the facts? The earlier the tumor, the less likely it is that any attempt at needle biopsy will yield a positive tissue diagnosis. In addition, every tumor induces a varying degree of acinar rupture with periacinar inflammation and fibrosis as well as distortion of ductal distribution. This situation leads to the coexistence of a surrounding area of histologic pancreatitis, compounding the problem of sampling error. A negative biopsy for cancer does not exclude cancer. Proponents of routine percutaneous biopsy of all pancreatic masses emphasize the need for making an exact tissue diagnosis preoperatively to "help the surgeon" plan an operative strategy and to obviate the need for time-consuming diagnostic maneuvers on the operating room table. This argument is no longer pertinent today, as the mortality associated with pancreatoduodenal resections is well under 1% in expert hands. Furthermore, the generally accepted surgical treatment for focal pancreatitis affecting the head and uncinate process of the gland is also some form of pancreatoduodenectomy. Thus the result of any biopsy is unlikely to influence the surgical decision process. Every surgeon should be prepared and delighted to accept an occasional benign pathology report to avert the tragedy of not resecting a potentially curable lesion.

Apart from the "sampling error" problem, complications from pancreatic biopsies by any technique ensue more frequently than is generally admitted or reported. Every surgeon can provide anecdotal experiences with biopsy-induced pancreatitis, pseudocyst, pancreatic fistula, and hemorrhage. I have seen three deaths resulting from complications of percutaneous biopsy over the last 5 years; and in two of these instances the pancreatic tumors were missed by the needle, providing an associated false-negative cytologic result. Although the absence of recorded cases in which puncture of the stomach or colon has resulted in an adverse outcome is often cited, I have also seen several abscesses and fistulas resulting from colon perforation and plead guilty for never having bothered to report such events. Seeding of the needle tract by cancer is also an often neglected issue because many of these patients already have advanced disease. The pancreas and peripancreatic tissues share a rich network of vascular and lymphatic plexuses. Common sense dictates that unnecessary needling for diagnosis has a risk of disseminating cancer. Although this situation is rarely reported in the literature, it is often acknowledged during panel discussions by experts.

"Interpretative errors" of needle biopsy specimens is another hazard that may plague even the most accomplished pathologist. Atypical hyperplasia occurring in conjunction with chronic pancreatitis is sometimes mistaken for cancer, especially on frozen section histologic analysis. The histologic differentiation between the benign cystic tumor (cystadenoma) and its malignant counterpart (cystadenocarcinoma) or between a benign and a malignant islet cell tumor may be impossible on needle biopsy unless the presence of distant metastases (in the lymph nodes or the liver) is documented.

The paper by Tillou and colleagues is long overdue. It emphasizes the irrationality and dangers of routine pancreatic biopsy. The technique should not be advocated in a casual, "knee-jerk" fashion. Before proceeding with FNAB the physician must ask himself or herself if the results of the procedure is likely to influence further management strategy. The patient should not be "biopsied to death" with no plan. Injudicious needle passes into the pancreas often induce an inflammatory response within the gland that make pancreatic resection more difficult for the surgeon and more hazardous for the patient.

During an era of informed consent, cost containment, and increasing medicolegal controversies, obsession with tissue diagnosis, in contrast to decision-making, should be curtailed. The FNAB technique is eminently suitable and appropriate for patients with unresectable or metastatic lesions of the pancreas diagnosed by CT scanning. It is largely applicable to masses in the body and tail of the pancreas, as these cancers are usually unresectable; and it is especially valuable in the frail, elderly patient in whom one wishes to avoid a purely diagnostic laparotomy when surgical palliation is not indicated or warranted. However, the technique should not be employed for small potentially resectable cancers because of sampling error and possible tumor dissemination.

An allied question often asked by surgeons is how to proceed if one incidentally finds an asymptomatic mass in the pancreas during the course of a laparotomy for some other procedure, such as cholecystectomy or hysterectomy. Unless surgeons are prepared (and they never are) to proceed with an immediate pancreatic resection if the biopsy is positive for cancer, they should never perform a biopsy at that time. A negative result for cancer does not help, and the inflicted trauma prevents accurate evaluation of the mass by imaging techniques postoperatively. In addition, the surgeon should refrain from mobilizing and assessing resectability at that operation. Such manipulations and dissections undoubtedly make evaluation by subsequent investigations difficult to interpret and render the second laparotomy technically more difficult and more dangerous.

We surgeons have the responsibility of emphasizing these issues to our nonsurgical colleagues. Ideally, radiologists and gastroenterologists are invited to the operating room to ascertain the difficulties first-hand and to examine the resected specimen with the surgical pathologist. The pros and cons of any preoperative and operative strategy must also be explained to the patient in simple terms. Only in this way will we be able to avoid the many unpleasant and expensive medicolegal problems that are becoming all too frequent.