

Original Article

Endoscopic Ultrasound-Guided Fine Needle Aspiration versus Percutaneous Ultrasound-Guided Fine Needle Aspiration in Diagnosis of Focal Pancreatic Masses

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Abstract

Objective: Pancreatic carcinoma is one of the leading cancer morbidity and mortality world-wide. Controversy has arisen about whether the percutaneous approach with computed tomography/ultrasonography-guidance fine needle aspiration (US-FNA) or endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is the preferred method to obtain diagnostic tissue. Our purpose of this study is to compare between the diagnostic accuracy of EUS-FNA and percutaneous US-FNA in diagnosis of pancreatic cancer.

Patients and Methods: A total of 197 patients with pancreatic masses were included in the study, 125 patients underwent US-FNA (Group 1) and 72 patients underwent EUS-FNA (Group 2).

Results: EUS-FNA has nearly the same accuracy (88.9%) as US-FNA (87.2%) in diagnosis of pancreatic cancer. The sensitivity, specificity, positive predictive value and negative predictive value for EUS-FNA was 84%, 100%, 100%, 73.3% respectively. It was 85.5%, 90.4%, 94.7%, 76% respectively for US-FNA. EUS-FNA had a lower complication rate (1.38%) than US-FNA (5.6%).

Conclusion: EUS-FNA has nearly the same accuracy as US-FNA of pancreatic masses with a lower complication rate.

Keywords: pancreatic cancer; ultrasound; endoscopic ultrasound; fine needle aspiration

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INTRODUCTION

Pancreatic cancer is a well-known cause of morbidity and mortality world-wide. Pancreatic cancer has one of the lowest at 5-year survival rates of all cancers.¹ This low survival rate is mainly due to the late presentation of patients with pancreatic cancer and limited treatment modalities for advanced disease; the average survival time after diagnosis is only 6 months.² Therefore, early and precise diagnosis is very important for improving the results of surgery.

Surgical resection remains the only potentially curative treatment for pancreatic adenocarcinoma and is associated

with momentous perioperative morbidity and mortality.³ Accurate pre-operative diagnosis is critical to avoid unnecessary laparotomy in those with benign disease. Furthermore precise pre-operative staging to those with malignant lesions is vital, because only 10% of patients have the chance of surgical cure at the time of diagnosis. Correct staging of patients with pancreatic malignancy will allow accurate identification of those who may benefit from surgery.⁴

The ability to obtain high quality images and perform fine needle aspiration (FNA) has led endoscopic ultrasound (EUS) to become the recommended procedure for diagnosis and staging of pancreatic tumours with a low rate of complications (<2%).⁴ Previous studies aimed to evaluate EUS-FNA in diagnosis of solid pancreatic lesions reported a range of diagnostic accuracy between 62% and 96%.^{5,6}

Ultrasonography (US) guided percutaneous FNA biopsy is a well-established method for obtaining tissue for cytological

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examination since the 1970s. US-FNA of the liver and pancreas has been shown to be an accurate method for the cytological diagnosis of malignancy; the diagnostic yield has been reported to be from 84% to 95%.⁷ Moreover, US-FNA has very low rate of complications if contraindications are followed.⁸ To reach the highest accuracy of diagnosis, US-FNA must be performed by well-experienced sonographers and cytopathologists.⁹

Controversy has arisen about whether the percutaneous approach with computed tomography (CT)/US-FNA or EUS-FNA is the preferred method to obtain diagnostic tissue.^{10,11}

PATIENTS AND METHODS

After being approved by the Local Scientific Ethical Committee and obtaining written informed consent from all participants, this multicenter prospective study was conducted on 197 consecutive patients presented with pancreatic head masses based on CT, magnetic resonance imaging (MRI) and/or EUS confirmation from September 2008 to January 2013. According to accessibility and feasibility, they were sub-classified into two main groups: Group 1 included 125 patients, underwent percutaneous US-FNA. Group 2 included 72 patients, underwent EUS-FNA.

Inclusion criteria for enrolment were accessibility of the tumor, platelet count $>50 \times 10^3$ and prothombin concentration $>50\%$.

US-FNA

US examination was done using Hitachi machine, EUB 7500, Japan. FNA was done using Chiba needles, 20 and 22G. It was done under complete sonographic guidance with a biopsy attachment. Local xylocaine 2% was given in most patients and deep sedation by propofol was given in few irritable patients.

EUS-FNA

EUS examination was done using a Pentax EG-3830UT machine connected to a Hitachi machine EUB-7500, Japan. FNA was done using 19 and 22-G Echotip needles (Cook Endoscopy, Winston-Salem, NC). One to three passes were done to every patient. Deep sedation with propofol was used in all patients.

On-site cytopathology was done in only 15 patients, as it wasn't available until recently and this small group only benefited from such maneuver. Biopsy samples were preserved in formalin after preparing at least two dry slides.

Follow-up and final diagnosis

A final diagnosis was based on definitive cytopathology, surgical pathology and clinical follow-up for more than 18 months. Cytology that was "suspicious" for malignancy was repeated for confirmatory purpose.

Statistical analysis

Data were statistically described in terms of frequencies (number of cases) and percentages. Accuracy was represented using the terms sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy. All statistical calculations were performed using computer programs Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

RESULTS

A total of 197 patients were included in the study; of these, 152 were males and 45 females. Patient characteristics and final diagnosis of Groups 1 and 2 are summarized in (Tab. 1).

Accuracy of US-FNA and EUS-FNA

Out of 125 diagnosed by US-FNA, 83 were malignant pancreatic head masses, 71 cases were true positive and four cases were false positive. 42 cases were benign, 38 cases were true negative and 12 cases were false negative, with sensitivity of 85.54%, specificity of 90.48%, PPV of 94.67%, NPV of 76% and accuracy of 87.20% (Tab. 2).

Out of 72 cases diagnosed by EUS-FNA, 50 were malignant pancreatic head masses, 42 cases were true positive and no cases showed false positive results. 22 cases were benign, 22 cases were true negative and eight cases were false negative, with sensitivity of 84%, specificity of 100%, PPV of 100%, NPV of 73.33% and overall accuracy of 88.89% (Tab. 3).

Table 1. Patient's characteristics and final diagnosis of both groups

Patients' characteristics	Group 1 (US-FNA)	Group 2 (EUS-FNA)	Total
Number of patients	125	72	197
Age (mean±SD)	53.7±10.7	55.7±8.97	—
Gender (M:F, no./%)	98:27 (78.4:21.6)	54:18 (75:25)	—
Final diagnosis			
Benign (no./%)	42 (33.6)	22 (30.56)	64 (32.49)
Malignant (no./%)	83 (66.4)	50 (69.44)	133 (67.51)

US-FNA: Ultrasonography-guided fine needle aspiration; EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration; SD: Standard deviation

Table 2. Effect of the number of passes on the accuracy of both US-FNA and EUS-FNA in diagnosing pancreatic cancer

Number of passes	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
One pass (92 patients)	60.00	100	100	63.64	76.47
Two passes (84 patients)	89.66	100	100	75.00	92.11
Three passes (21 patients)	90.91	100	100	83.33	93.75

US-FNA: Ultrasonography-guided fine needle aspiration; EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration; PPV: Positive predictive value; NPV: Negative predictive value

Effect of the presence of on-site cytology on the accuracy of EUS-FNA in diagnosing pancreatic cancer

Within the EUS-FNA group, the sensitivity was 81.82% in those cases where no on-site cytology was available, while the sensitivity reached 92.85% when on-site cytology was available. The overall accuracy also increased from 88.57% to 93.33% (Tab. 4). No on-site cytopathology was available for any of the US-FNA group.

Effect of the number of passes on the accuracy of both US-FNA and EUS-FNA in diagnosing pancreatic cancer

The sensitivity was 60% in those cases where one pass was used while the sensitivity reached 90.91% when three passes was used. The overall accuracy increased from 76.47% with one pass to 93.75% as shown in Tab 2.

Complications occurred in eight patients (4.06%), one of the 72 patients underwent EUS-FNA (1.38%) and 7 of the 125 patients underwent US-FNA (5.6%). The patient who underwent EUS-FNA had severe epigastric pain due to acute pancreatitis requiring hospitalization for 3 days with improvement. 3 of patients underwent US-FNA had severe epigastric pains that responded to non-steroidal anti-inflammatory drugs within 1-3 days without hospitalization. Three patients had seeding of malignant cells in the peritoneal cavity in two cases and in the subcutaneous tissue at the biopsy site in one case 1 year after radical surgical excision of the pancreatic head mass. The last case has severe infection in the form of pancreatic abscess requiring surgical debridement and drainage. None of our patients

Table 3. Sensitivity, specificity, PPV, NPV and accuracy of US-FNA/ EUS-FNA in diagnosing pancreatic cancer

Statistical data	US-FNA (n = 125)	EUS-FNA (n = 72)
True positive	71	42
False negative	12	8
True negative	38	22
False positive	4	0
Sensitivity %	85.54	84
Specificity%	90.48	100
PPV	94.67	100
NPV %	76	73.33
Accuracy %	87.2	88.89

PPV: Positive predictive value; NPV: Negative predictive value; US-FNA: Ultrasonography-guided fine needle aspiration; EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration

Table 4. Effect of the presence of on-site cytology on the accuracy of EUS-FNA in diagnosing pancreatic cancer

On-site cytology	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
No (57 patients)	81.82	100	100	76.47	88.57
Yes (15 patients)	92.85	100	100	50	93.33

EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration; PPV: Positive predictive value; NPV: Negative predictive value

experienced clinically significant hemorrhage, perforation, or death.

DISCUSSION

Pancreatic malignancy is one of the leading cancer morbidity and mortality world-wide. Sometimes the ordinary imaging tools like CT and MRI don't provide a paved way for definite diagnosis and a necessity for cytopathological diagnosis is mandatory to define the protocol of therapy. US-FNA and EUS-FNA has been established during the last decades as a diagnostic tool for many hepatobiliary and pancreatic malignancies. In 2012, Hewitt *et al.*⁴ pooled 4984 patients in his wide meta-analysis research and demonstrated that EUS-FNA has a sensitivity of 85%, specificity of 98%, PPV of 99% and a NPV of 72% in diagnosis of solid pancreatic masses. These results are very similar to the results of the current study that showed a sensitivity of 84%, specificity of 100%, PPV of 100% and NPV of 73%.

The results of the current study showed that US-FNA and EUS-FNA of pancreatic masses have a nearly similar diagnostic accuracy (87.20% and 88.89% respectively). In 2011, Dumonceau *et al.* published the guidelines of the European Society of Gastrointestinal Endoscopy regarding the clinical impact of EUS-guided sampling in gastroenterology and reported that EUS-FNA seems to present a higher diagnostic accuracy than US-FNA.¹²

Eloubeidi *et al.*¹³ studied major complications in a total of 355 consecutive patients with a solid pancreatic mass underwent EUS-FNA. Major complications were encountered in nine patients (2.54%). Examples of complications included acute pancreatitis, severe pain after the procedure, fever and surgical debridement for necrosis. Only seven patients (1.97%) required hospitalization (range: 1-16 days). They reported no haemorrhage, perforation or death.

In the present study, complications occurred in eight patients (4.1%). Only 1 of the 72 patients underwent EUS-FNA (1.38%) had acute pancreatitis requiring hospital admission. 7 of the 125 patients underwent US-FNA (5.6%) had complications, three patients (2.4%) had tumor seeding, 3 (2.4%) had severe epigastric pains and 1 (0.8%) had a pancreatic abscess.

This was also the conclusion of Hewitt *et al.*⁴ who demonstrated that the observed complication rate of EUS-FNA was also low, at 1%-2%, with complications occurring more commonly when EUS-FNA was performed on cystic lesions than on solid lesions. Examples of complications include bleeding, infection, self-limiting pancreatitis, and tumour seeding; however, there are similar risks for CT-guided biopsy.

All masses underwent US-FNA were larger than 20 mm, because lesions less than 20 mm were not easily visible or accessible for US-FNA, while EUS-FNA could be done in masses as small as 9 mm and more.

In the developing country like Egypt, US-FNA is much cheaper than EUS-FNA (170 vs. 750 € i.e., about one-

fifth of the cost), with nearly similar diagnostic accuracy (87.2% vs. 88.89%), so it is more cost-effective. However, the main drawbacks of US-FNA that: It needs larger tumour sizes, not all tumours were accessible or even visible by such modality and it had a higher incidence of complications.

CONCLUSION

(1) EUS-FNA has nearly similar diagnostic accuracy as US-FNA of pancreatic masses with a lower complication rate. EUS-FNA of pancreatic masses should be the first-line procedure, but since US-FNA is much cheaper and nearly as accurate, may be considered an acceptable alternative when EUS is not available, but in rather larger masses (i.e., >20 mm) and more complications rate. (2) On-site cytopathological examination increases the sensitivity and accuracy of the procedure. However our limitations were that such maneuver became available only recently. Further studies with application of on-site cytology on a larger number of patients are needed to yield better results.

REFERENCES

1. Walters S, Rachet B, Westlake S, et al. Cancer Survival, England, Patients Diagnosed 2001-2006 and followed up to 2007: One Year and Five Year Survival for 21 Common Cancers, by Sex and Age. London: Office for National Statistics; 2009. p. 1-11.
2. Bornman PC, Beckingham IJ. ABC of diseases of liver, pancreas, and biliary system. Pancreatic tumours. *BMJ* 2001; 322: 721-3.
3. Greenblatt DY, Kelly KJ, Rajamanickam V, et al. Preoperative factors predict perioperative morbidity and mortality after pancreaticoduodenectomy. *Ann Surg Oncol* 2011; 18: 2126-35.
4. Hewitt MJ, McPhail MJ, Possamai L, et al. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: A meta-analysis. *Gastrointest Endosc* 2012; 75: 319-31.
5. Gress F, Gottlieb K, Sherman S, et al. Endoscopic ultrasonography-guided fine-needle aspiration biopsy of suspected pancreatic cancer. *Ann Intern Med* 2001; 134: 459-64.
6. Ardengh JC, Lopes CV, Campos AD, et al. Endoscopic ultrasound and fine needle aspiration in chronic pancreatitis: Differential diagnosis between pseudotumoral masses and pancreatic cancer. *JOP* 2007; 8: 413-21.
7. Hovdenak N, Lees WR, Pereira J, et al. Ultrasound-guided percutaneous fine-needle aspiration cytology in pancreatic cancer. *Br Med J (Clin Res Ed)* 1982; 285: 1183-4.
8. Mitty HA, Efremidis SC, Yeh HC. Impact of fine-needle biopsy on management of patients with carcinoma of the pancreas. *AJR Am J Roentgenol* 1981; 137: 1119-21.
9. Hartwig W, Schneider L, Diener MK, et al. Preoperative tissue diagnosis for tumours of the pancreas. *Br J Surg* 2009; 96: 5-20.
10. Mallery JS, Centeno BA, Hahn PF, et al. Pancreatic tissue sampling guided by EUS, CT/US, and surgery: A comparison of sensitivity and specificity. *Gastrointest Endosc* 2002; 56: 218-24.
11. Horwhat JD, Paulson EK, McGrath K, et al. A randomized comparison of EUS-guided FNA versus CT or US-guided FNA for the evaluation of pancreatic mass lesions. *Gastrointest Endosc* 2006; 63: 966-75.
12. Dumonceau JM, Polkowski M, Larghi A, et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2011; 43: 897-912.
13. Eloubeidi MA, Tamhane A, Varadarajulu S, et al. Frequency of major complications after EUS-guided FNA of solid pancreatic masses: A prospective evaluation. *Gastrointest Endosc* 2006; 63: 622-9.