Interventional Endoscopic Ultrasound in Pancreatic Diseases

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Endoscopic ultrasound • Fine-needle aspiration biopsy • Pancreatic cancer • Celiac plexus neurolysis • Pancreatic pseudocyst drainage

Introduction
During the past 15 years, endoscopic ultrasound (EUS) has become an important imaging technique for diagnosis and management of pancreatic diseases. The clinical interest of EUS is now enhanced by interventional procedures. Noteworthy, fine-needle aspiration biopsy is one of the most important contributions of EUS, in particular for the investigation of patients with pancreatic cancer and cystic tumors. EUS-guided fine-needle aspiration appears to be a safe and reliable technique to obtain tissue from pancreatic masses with a low risk of complications. EUS became also a therapeutic procedure, especially applied for celiac plexus neurolysis, pseudocyst drainage, and pancreaticogastrostomy. Further developments are expected by improvement of needle devices such as pancreatic pseudocyst drainage kits. In the future, EUS might be also a support for local application of new treatments of pancreatic tumors, such as gene or cellular therapy products. In this review, we discuss the current clinical applications of interventional EUS and the future development for diagnosis and management of pancreatic diseases.
**Materials and Equipment**

*Ultrasound Endoscopes*

Two types of ultrasound endoscopes are available, using either radial- or linear-array transducers. The linear-array assembly uses an electronic device of multiple transducers that are sequentially activated, producing a sector ultrasound beam parallel to the long axis of the endoscope. Biopsy performed under EUS requires this linear array, because the full length of the needle can be tracked in real time into the lesion. Olympus/Aloka, Pentax/Hitachi, and Fuji/Toshiba companies produce electronic curved linear-array ultrasound endoscopes, equipped with real-time and color Doppler (as well as Color Flow Angio). The diameter of the working channel varies between the endoscopes (2.8–3.8 mm). A working channel with the largest diameters allows the use of stenting kits. Some have an elevator assembly which allows a useful variation in the direction of needle puncture.

*Needle Biopsy*

The system of single-use needles comprises three elements: (1) a protective plastic cover of the working channel; (2) a handle at the proximal end of the needle connected to the entry of the working channel (this handle allows the needle to move out from the protective cover to get into a lesion), and (3) a needle with a stylet that prevents contamination of samples from the gut wall mucosa. Needles present a sliding handle to adjust the maximum distance for the needle to move out from the endoscope (8 cm). The needles are designed so as to have a tip (echo tip) visualized by ultrasound. Several diameters are available (22–19 gauges) [3]. A 22-gauge diameter allows generally to collect cytological samples and satisfactory microbiopsy. In addition, single-use needles provide hygienic safety. For solid pancreatic masses, Trucut needles (19-gauge) are now available. EUS-guided Trucut needle biopsy, when performed transgastrically, is safe and accurate with results equivalent to standard FNA. Histological assessment of core specimens obtained by EUS Trucut needle biopsy may improve tumor identification [4–6].

**Technique**

The needle is positioned so that the target lesion is located on the top right of the ultrasound image. The needle assembly is introduced into the working channel of the ultrasound endoscope and is guided into the targeted lesion using the elevator device. The echo tip needle is visualized during ultrasound which allows to check in real time the correct position of the needle within the target lesion (fig. 1). The stylet is completely withdrawn, and an aspiration is operated back and forward using a 20-ml syringe. Three to four needle passes are generally required to obtain a correct diagnosis of solid pancreatic masses [7]. However, a recent report [8] recommended that seven needle passes would be necessary to ensure a high-degree diagnosis after EUS-guided biopsy of the pancreas. It is usually possible to obtain small samples of tissue in about 85–90% of the cases using a 22-gauge needle. Thin Prep preparation using a bench cell sorter may enhance results for the diagnosis of pancreatic solid tumors. According to preliminary studies [9], the procedure could reduce the number of needle passes and the frequency of false-negative results.

The main limits of this technique are: the small size of the lesion (<5 mm), the depth of the lesion (>6–7 cm), and the presence of hemostasis disorders (prothrombin level <60%, platelet number <80,000/mm$^3$).

**Role of EUS-Guided FNA/Biopsy in Diagnosis and Staging of Solid Pancreatic Tumors**

*EUS in Diagnosis and Staging of Solid Pancreatic Tumors*

Since its introduction, EUS had a significant impact on the diagnosis of pancreatic diseases. Indeed, diagnosis of obstructive jaundice and detection of small solid or
cystic pancreatic lesions and endocrine pancreatic tumors have been improved by means of EUS. For the detection of small pancreatic tumors <2 cm in diameter, EUS appeared to be the most sensitive method [10–12]. Besides its diagnosis performance, EUS is also accurate for the preoperative staging of pancreatic adenocarcinomas. Even if resectability is evaluated at the time of surgery, preoperative criteria of resectability, such as the presence of major peripancreatic and/or vascular involvement by the tumor, are currently used. A good preoperative staging could not only decrease the rate of laparotomies without resection, but also improve the quality of surgical resection, without evidence of residual disease (i.e., Ro mass) that determines the rate of recurrence and survival.

Thus, EUS appears to be a reliable technique to assist the medical and surgical management of pancreatic cancer patients. Comparison between different imaging techniques for predicting resectability has been extensively evaluated, and both helical CT and EUS are effective. Recent studies included comparative evaluation of multidetector CT scan, the resolution of which highly increases pancreatic visualization. Resectability of pancreatic carcinomas can be predicted in 71–90% and in 61–86% of the cases for CT scan and EUS, respectively. The performances for predicting unresectability range from 64 to 90% and from 70 to 100% for CT scan and EUS, respectively [13–19]. As other specialized imaging procedures, the EUS performance depends on the material availability and on the operator training. The latter is particularly crucial for pancreatic cancer staging. Even if new-generation high-resolution CT scans can equally assess pancreatic cancer resectability, EUS may be useful for small tumors or for doubtful findings after CT scan. This is represented in figure 2 as a staging algorithm for patients clinically suspected of having pancreatic cancer, including first clinical and current (CT scan) imaging procedures and secondly EUS evaluation. Previous studies (including our experience) led to propose this decisional algorithm, taking into account the high performance of helical CT (fig. 2) [13, 15].

**Indications, Results, and Position of EUS-Guided FNA in Diagnosis and Staging of Pancreatic Carcinomas**

FNA is now considered a safe and reliable procedure for the histological diagnosis of pancreatic neoplasms. Foremost studies that evaluated the performances of the procedure for the final diagnosis of solid pancreatic masses are detailed in table 1. The feasibility varies from 90 to 98%, and the efficiency in terms of collecting analyzable biopsy specimens varies from 80 to 95% (fig. 3). For the diagnosis of pancreatic adenocarcinomas, the sensitivity of EUS-guided FNA varies from 75 to >90%, the specificity being 82–100%, with a mean accuracy of 85% [7, 9, 20–26] (table 1). The presence of a trained cytopathologist at the time of the procedure may increase the total yield and decrease the rate of unsatisfactory samples

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**Table 1. Performance of EUS-guided FNA for the positive diagnosis of pancreatic solid masses**

<table>
<thead>
<tr>
<th>Authors, year of publication [ref.]</th>
<th>Number of FNA procedures</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>Accuracy %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang et al., 1994 [20]</td>
<td>46</td>
<td>91</td>
<td>100</td>
<td>87</td>
</tr>
<tr>
<td>Giovannini et al., 1995 [21]</td>
<td>141</td>
<td>77</td>
<td>100</td>
<td>79</td>
</tr>
<tr>
<td>Gress et al., 1997 [22]</td>
<td>208</td>
<td>89</td>
<td>100</td>
<td>87</td>
</tr>
<tr>
<td>Wiersema et al., 1997 [23]</td>
<td>145</td>
<td>88</td>
<td>95</td>
<td>90</td>
</tr>
<tr>
<td>Williams et al., 1999 [24]</td>
<td>144</td>
<td>82</td>
<td>100</td>
<td>85</td>
</tr>
<tr>
<td>Voss et al., 2000 [9]</td>
<td>99</td>
<td>75</td>
<td>88</td>
<td>75a</td>
</tr>
<tr>
<td>Raut et al., 2003 [25]</td>
<td>233</td>
<td>91</td>
<td>100</td>
<td>92</td>
</tr>
<tr>
<td>Afi fy et al., 2003 [26]</td>
<td>65</td>
<td>80</td>
<td>82</td>
<td>–</td>
</tr>
<tr>
<td>Eloubeidi et al., 2003 [7]</td>
<td>101</td>
<td>94</td>
<td>100</td>
<td>–</td>
</tr>
<tr>
<td><strong>Total/mean</strong></td>
<td><strong>1,182</strong></td>
<td><strong>85</strong></td>
<td><strong>96</strong></td>
<td><strong>85</strong></td>
</tr>
</tbody>
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a Accuracy for adenocarcinomas 81%, for endocrine tumors 47%.
for evaluation [27, 28]. The learning curve of the endosonographer has been recently evaluated, and about 25 supervised EUS-guided FNA procedures for the diagnosis of pancreatic carcinomas appear reasonable [29]. False-positive results remain an exception, and, therefore, the positive predictive value of this procedure is close to 100%. On the other hand, the negative predictive value for the diagnosis of malignant lesions varies from 25 to 85%. This is due to a difference in the prevalence of benign lesions in the series of studied patients. One can conclude that a negative biopsy specimen does not prevent a diagnosis of pancreatic cancer.

It has been demonstrated that EUS-guided tissue sampling of pancreatic masses is as accurate as CT/US-guided sampling and surgical biopsies [30]. However, feasibility and accuracy of EUS-guided FNA are high, even for difficult or unreachable regions via the percutaneous access. In particular, EUS-guided FNA can be performed in the celiac mesenteric region, in the hepatic peduncle, and in the entire pancreas (hook and tail included) [23–27]. EUS allows also a Doppler analysis to visualize and characterize the collateral venous system in case of splenic or mesenteric portal vein thrombosis and then to perform FNA with a low risk, when the percutaneous route is not indicated [9]. In addition, EUS-guided biopsy may identify an invasion of lymph nodes located in the celiac, lumboaortic, retroduodenal, or superior mesenteric regions. EUS-guided FNA is the only preoperative procedure which can demonstrate invasion of such lymph nodes [24]. Early diagnosis of peritoneal carcinomatosis (trace of ascites) might also be performed following the same protocol. Aspiration of ascitic fluid with a cytological study done by EUS can validate a carcinomatosis that could not be revealed using conventional imaging [31]. Finally, the use of EUS recently demonstrated that small metastases of the left liver lobe could be found and were easily accessible to biopsy by means of EUS with a sensitivity close to 100% [32]. The finding of such lesions modifies considerably the management of supposed resectable cancer. Finally, EUS-guided FNA can take a special place when nonresectability of a pancreatic carcinoma has been proven by abdominal US or CT scan: EUS may thus play a role in the confirmation of the histological diagnosis. Indeed, neoadjuvant radio- and/or chemotherapy allows under certain conditions an increasing rate of tumor resectability and/or patient survival. Conversely, in case of a resectable tumor, a histological diagnosis is not necessary, and a laparotomy in a curative way is generally proposed. The position of EUS-guided FNA in the staging strategy of pancreatic carcinomas is also detailed in figure 2.

EUS-Guided FNA in the Differential Diagnosis of Pancreatic Carcinomas

Malignant pancreatic tumors comprise in 5–10% of the cases lymphomas, endocrine carcinomas, or metastases. All these lesions can be also confirmed by EUS-guided FNA [33, 34]. The treatment and sometimes the prognosis can differ from those of adenocarcinomas, and it is thus important to obtain a histological confirmation. On the other hand, solid ‘incidentalomas’ of the pancreas raise the question of benefit and risk of a surgical procedure: the preoperative histological diagnosis of these often small lesions is also essential to help in the therapeutic decision, and EUS can be also helpful in these cases.

The presence of a solid mass within the pancreas does not necessarily imply the diagnosis of pancreatic cancer. It concerns the difficult problem of pseudotumor chronic pancreatitis which is sometimes difficult to differentiate from a pancreatic cancer, even by means of all available imaging procedures, including standard EUS. EUS-guided FNA can thus be the key examination to solve such a paradigm. Nevertheless, in these cases the histological diagnosis is often difficult, and only a positive biopsy specimen must be taken into account (i.e., the only proof of cancer) [35]. Analysis of pancreatic juice (cytology and search for a K-ras mutation) obtained during endoscopic retrograde cholangiopancreatography can also facilitate such a diagnosis. Nevertheless, the sensitivity of mutant K-ras detection in pancreatic juice for the diagnosis of pancreatic cancer remains low with a rate of 60% [36, 37].
Conversely, the high negative predictive value of this method might exclude a pancreatic cancer in nearly 95% of the cases (personal results). Recent reports [38] indicate that EUS-guided FNA coupled with molecular analysis could improve the sensitivity (81%), the specificity (100%), and the accuracy (85%) of the diagnosis of pancreatic carcinomas in comparison with cytology or K-ras mutation analysis alone. The amount of cellular material sampled by EUS-guided FNA is indeed more appropriate to perform DNA extraction and amplification for restriction fragment length polymorphism as well as for sequencing. By means of EUS-guided FNA, the combination of cytopathologic analysis and K-ras mutation detection may improve the diagnosis to differentiate pancreatic cancer from chronic pancreatitis.

Cost Analyses of EUS-Guided FNA

Cost analyses of EUS to determine unresectable disease have been evaluated. Decision analysis was used by Tierney et al. [39] to simulate alternative staging strategies. A decision model found that EUS when performed in all patients, followed by laparoscopy in patients supposed to have resectable tumors, reduced the number of unnecessary surgical exploration by 61% as compared with laparoscopy alone. This combination of procedures (EUS followed by laparoscopy) resulted in the lowest cost per surgical resection [39]. In another cost analysis comparing EUS-guided FNA versus CT-guided FNA versus surgery in the management of nonmetastatic adenocarcinomas of the head of the pancreas, EUS was the most economical strategy [40].

Pancreatic Cystic Tumors

Cystic pancreatic tumors are uncommon lesions, representing only 10–15% of all pancreatic cysts and only 1% of all pancreatic cancers. It is sometimes difficult to distinguish them from pancreatic pseudocysts. Cystic lesions in the pancreas are frequently found in asymptomatic patients. The key dilemma is how to accurately distinguish lesions with no malignancy potential (such as pancreatic pseudocysts and serous cystadenomas) from lesions with a high malignancy potential (such as mucinous cystadenomas and intraductal papillary mucinous tumors) or already transformed lesions (cystadenocarcinomas). This risk implies a precise pretherapeutic diagnosis in order to select patients with premalignant or malignant lesions for surgery. Occasionally, pancreatic cystic lesions can be distinguished by EUS morphological criteria alone. For instance, serous cystadenomas are typically multilocular and multimicrocystic tumors, while mucinous cystadenomas are uni- and macrocystic tumors [41, 42]. In addition, some features such as solid component, size (>3 cm), septa, and lymph nodes can be predictive of malignancy. However, in several situations, the simple EUS examination is not sufficient [42]. There is a macrocystic variant of serous cystadenomas [43], and some asymptomatic small cysts <2 cm can be malignant or premalignant lesions [44]. EUS-guided FNA of pancreatic cystic lesions with cystic fluid analysis can be helpful in these cases (fig. 4). Cytology is a relatively insensitive test, even if cytological analysis of pseudocysts often demonstrates inflammatory cells such as histiocytes or leukocytes, while positive mucin staining is detected in

Fig. 4. A Transgastric EUS visualization of a 2-cm macrocystic tumor (T) of the body of the pancreas. B FNA of the same lesion under EUS. The echo tip of the needle within the cystic tumor is shown (arrow).
mucinous cystadenomas. Cyst fluid tumor markers such as carcinoembryonic antigen (CEA) have been used to improve the sensitivity for the detection of the malignancy. CEA values are uniformly low in serous cystadenomas (<5 ng/ml) and markedly elevated in mucinous cystadenomas and cystadenocarcinomas. Other markers have been also prospectively tested (CA 19-9, CA 72-4, CA 125, and CA 15-3), but CEA remains the most accurate test available to differentiate mucinous from nonmucinous lesions. The optimal cutoff CEA value ranges from 192 to 400 ng/ml [43, 45–48], and its sensitivity ranges from 79 to 97% [45, 46, 48] for the diagnosis of mucinous cystadenomas. However, in the subgroup of intraductal papillary mucinous pancreatic tumors, cytology and/or histology obtained by FNA displays a low sensitivity: estimated at 44% in a recent work performed by Maire et al. [49].

Therapeutic Approaches of EUS

EUS-Guided Celiac Plexus Neurolysis

Pancreatic cancer and chronic pancreatitis commonly produce pain that is difficult to control. When the pharmacological therapies are inadequate, infiltration of the splanchnic nerves or celiac plexus neurolysis may improve pain control and quality of life, while reducing the risk of drug-related side effects. Up to the present time, celiac plexus neurolysis is performed under radiological guidance or surgically, with sometimes important side effects (abscess, spleen injury, and paraplegia). Recently, EUS-guided celiac plexus neurolysis has been developed, because needle localization and feasibility of celiac plexus injection can be clearly visualized by EUS.

Using echoendoscope and color Doppler, the celiac trunk is easily visualized at the exit from the aorta. A 19-gauge needle is passed through the biopsy channel and inserted into the celiac region via a transgastric approach. At this point, an injection over the celiac axis can be performed. In malignant diseases, a combination of a long-acting local anesthetic, such as bupivacaine or ropivacaine, and absolute alcohol is generally used. In chronic pancreatitis, steroids such as triamcinolone, are also applied [50, 51].

EUS-guided celiac plexus neurolysis is more successful in patients with pancreatic carcinomas as compared with those having chronic pancreatitis [52]. In a large-scale study including 58 patients [50], the pain scores decreased in 78% of the patients with nonrespectable pancreatic cancer. The pain scores were lower 2 weeks after EUS-guided celiac plexus neurolysis, and this effect was sustained for up to 24 weeks, when the patients were adjusted for morphine use and adjuvant therapy. In chronic pancreatitis, a higher proportion of patients remained free from pain for a longer period of time after EUS-guided celiac plexus neurolysis when compared with CT-guided celiac plexus neurolysis (median postblock pain scores 1 vs. 9) [51]. The main complications (2.5%) observed were peripancreatic abscess and bleeding of the celiac artery due to ethanol-induced pseudoaneurysm [50–53]. The risk of causing paraplegia by involuntary injection into the artery of Adamkiewicz is theoretically negligible, because the celiac axis is accessed via an anterior transgastric approach (1% risk of paraplegia with the posterior percutaneous approach). EUS-guided celiac plexus neurolysis seems to be a relatively simple, safe, and reproducible method to decrease chronic plexus pain. The results of the above studies are promising, but they do not allow any definitive conclusions. Considering chronic pancreatitis, further data are needed to clarify the painful phases of the disease.

EUS-Guided Pancreatic Pseudocyst Drainage

A pancreatic pseudocyst is the most common cystic lesion of the pancreas. A pseudocyst is a fluid collection, rich in amylase, which is enclosed by a nonepithelialized wall and localized within or adjacent to the pancreas after acute or chronic pancreatitis. The timing of drainage is a controversial issue. Recent literature suggests that the traditional criteria 6 cm/6 weeks for intervention should be a relative rather than an absolute indication. Pancreatic pseudocysts can be drained radiologically, surgically, or endoscopically by way of cystogastrostomy or cystoduodenostomy. Endoscopic drainage of pancreatic pseudocysts is less invasive than surgery, but is not possible in all cases. A bulging in the digestive lumen should be detectable to determine the appropriate puncture site. The main risks associated with endoscopic treatment are hemorrhage (6–10%) and perforation [54]. EUS might theoretically facilitate a pancreatic pseudocyst drainage, because the optimal puncture site can be chosen whether the bulge is detectable or not.

EUS is first performed to determine pseudocyst location, size, number, wall thickness, presence of septation or debris (that might increase the risk of infection), and the distance from the pseudocyst to the enteric wall (a distance >1 cm is considered a relative contraindication) [54]. Power Doppler of duodenum or stomach zone shows lack of vessels or gastric pseudoaneurysm in this zone. A needle knife is introduced through the working channel and used to carry out EUS-guided transgastric or trans-
duodenal puncture of the cyst. Contrast medium may be injected into the cyst through the needle knife catheter, and then a guidewire is positioned. Below the guidewire, a nasocystic drain or stent is placed within the cyst to establish complete drainage of the pancreatic pseudocyst or abscess. Sometimes single or double pigtail stents are placed through the guidewires. New kits are available that deliver an endoprosthesis system that can be inserted into a pancreatic pseudocyst in one step (i.e., without changing endoscopes, catheters, or guidewires), guided exclusively by ultrasound endoscopes with a large channel [55–59].

Endoscopic methods for pancreatic pseudocyst drainage are associated with low mortality and acceptable success rates. EUS-guided drainage is associated with a low rate of complications [58–60]. Thus, this technique has the theoretical advantage of reducing the risks of bleeding, perforation, and, potentially, infection. However, this efficient method should be further evaluated in large-scale studies.

**Other EUS-Guided Diagnostic and Therapeutic Procedures**

EUS-guided puncture of common bile duct and/or pancreatic duct following an unsuccessful endoscopic retrograde cholangiopancreatography has been reported. The common bile duct is usually punctured via the duodenum and the pancreatic duct via the stomach. The main problem with the common bile duct is the risk of bile leakage into the peritoneum. In the future, the introduction of a covered biliary stent under EUS guidance using a therapeutic echoendoscope might decrease this risk [61–64]. EUS could be used to access a dilated pancreatic duct that cannot be drained by conventional endoscopic retrograde cholangiopancreatography because of complete obstruction. The fistula created endoscopically might be maintained by stent placement, thus performing a real pancreaticogastrostomy. EUS-guided pancreaticogastrostomy, in selected cases, is a new interesting technique that necessitates further evaluation and a longer-term follow-up of the patients [65]. However, these techniques are currently restricted to expertise centers dedicated to biliopancreatic therapy [66].

**Future Prospects**

The quality and the amount of cellular sampling using FNA (and more recently the Cytolite cell sorter system) may allow to extract sufficient quantities of RNA or DNA to perform amplification and/or hybridization with new analysis of the results of micro- or macroarray technology. This provides some future prospects for the identification of potential molecular markers for pancreatic diseases using real-time polymerase chain reaction analysis [67].

Pilot studies of cellular and gene therapy have been conducted in nonresectable pancreatic cancer, targeting pancreatic tumors by means of EUS-guided FNA. Gene therapy was applied by EUS-guided intratumoral injection of the replication-selective adenovirus ONYX-015 in combination with gemcitabine without major toxicity [68]. No significant therapeutic effect has been observed, but this study demonstrated the feasibility of the EUS route to locally inject therapeutic principles. Allogenic lymphocytes mixed (cytointplant) and recently IL-12 gene driven by an adenovirus vector have been also injected into pancreatic carcinomas using EUS without substantial toxicity [69, 70]. Finally, preclinical studies underline the possibility to reach the pancreas under EUS guidance for radiofrequency treatment [71]. Application of other ablation therapies, such as laser, microwave, and cryogenic approaches, is also conceptually feasible.

**Complications and Morbidity**

As with any endoscopic procedure, perforation, hemorrhage, and specific cardiopulmonary complications due to sedation might occur. EUS and EUS-guided FNA are both performed under moderate (narcotics or anxiolytics) or deep (propofol) anesthesia for various reasons: the patient must stay stock-still during the examination, and the endoscopes have a rigid tip and are larger than standard endoscopes. Finally, the EUS procedure requires an average time longer than gastroscopy, and thus complications, in case of conscious anesthesia without tracheal intubation, such as hypoxemia and aspiration pneumonia may occur. Interventional procedures can bring additional complications that have been mostly evaluated in monocentric studies with a morbidity ranging from 1 to 3% and a mortality ranging from 0 to 0.1% [9, 23, 72–74]. The incidence of acute pancreatitis varies from 0.5 to 2% [23, 74]. This complication is essentially due to biopsies of small lesions (cystic or endocrine tumors) with a needle pass through healthy pancreas or pancreatic duct. Bacteremia can be observed in 5.8–6% of EUS procedures and EUS-guided FNA [75–77], whatever the indication. However, it is not proven whether these bacteremias are clinically relevant. A subgroup analysis of patients with cysts undergoing FNA demonstrated a 14% risk of infectious complications [23]. However, the use of prophylactic antibiotic administration in EUS-guided FNA of pancreatic cysts has not been clearly studied by randomized,
controlled trials. As compared with solid masses, a single needle pass is recommended due to the higher risk of complications (infections and hemorrhages). On the other hand, regarding this risk of bacteremia during EUS-guided FNA, antibiotic prophylaxis is recommended in patients with cardiac lesions or conditions that are associated with an increased risk of endocarditis. In addition, bleeding is a rare event, estimated to occur in no more than 1% of the EUS-guided FNA [23, 78]. Finally, the above-mentioned risk of peritoneal dissemination in biopsies of pancreatic tumors is difficult to appreciate. This risk of percutaneous biopsy procedures has never been really quantified. Its clinical importance is still controversial and must be considered in case of potentially resectable pancreatic tumors.

Taking together our experience and that of others, EUS-guided FNA is a safe technique [79]. The morbidity rate should be no more than 1–3%, if simple rules are observed such as: systematic preanesthetic evaluation, avoidance of needle passes through main pancreatic duct and normal pancreatic parenchyma, one single needle pass for pancreatic cystic lesions, and antibiotic prophylaxis in high-risk patients and lesions (pancreatic cysts, perirectal lesions).

Conclusions

The clinical interest of EUS is now enhanced by these interventional procedures. FNA is the most important advance, especially for the diagnosis (cytology and/or histology and/or molecular marker analysis) of pancreatic cancer and cystic tumors, with an accuracy ranging from 85 to 90%. EUS-guided FNA appears as a safe and reliable technique to obtain tissue from pancreatic masses with a low risk of complications (1–3%). The role of EUS in therapeutic procedures continues to expand, especially in celiac plexus neurolysis and in pseudocyst drainage. In the future, EUS might also be a support to local delivery of new treatment modalities of pancreatic tumors, especially gene or cellular therapy.

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