Introduction

Endoscopic ultrasound (EUS) currently has an important role in the diagnosis and management of gastroenteropancreatic and biliary diseases. However, prospective data on the morbidity and mortality related to its use are sparse and often retrospective. We attempted to assess the acute and immediate complications of both diagnostic and interventional EUS.

Patients and Methods: At our university-affiliated tertiary care referral center, immediate (occurring during the procedure) and acute (occurring within 24 hours) complications of EUS were prospectively investigated. Over a first period, spanning 10 years, complications of diagnostic EUS involving 3207 consecutive patients were assessed. During the second period of 3 years, complications observed after EUS-guided fine-needle aspiration (FNA) biopsy were evaluated from 224 procedures. EUS was mostly done with the patient under sedation with intravenous propofol and spontaneous ventilation, and complications were evaluated by both the operator and the anesthesiologist.

Results: There were no deaths, and no surgery was required over the two periods of assessment. Three mild complications occurred among patients who underwent standard diagnostic EUS: two immediate complications were related to anesthesia and one to the procedure. There were five complications associated with interventional EUS; all were related to the procedure (acute pancreatitis, duodenal perforation, upper digestive bleeding, cyst, and mediastinal infection), with a mean delay of occurrence of 30 hours, and mean duration of hospitalization of 7 days.

Conclusion: In our experience, which is the longest reported in Europe, the morbidity rates of diagnostic EUS and EUS-guided FNA biopsy were 0.093% and 2.2%, respectively, with no mortality.

Background and Study Aim: Endoscopic ultrasonography (EUS) now has an important place in the diagnosis of gastroenteropancreatic diseases. However, prospective data on the morbidity and mortality related to its use are sparse and often retrospective. We attempted to assess the acute and immediate complications of both diagnostic and interventional EUS.

Patients and Methods: At our university-affiliated tertiary care referral center, immediate (occurring during the procedure) and acute (occurring within 24 hours) complications of EUS were prospectively investigated. Over a first period, spanning 10 years, complications of diagnostic EUS involving 3207 consecutive patients were assessed. During the second period of 3 years, complications observed after EUS-guided fine-needle aspiration (FNA) biopsy were evaluated from 224 procedures. EUS was mostly done with the patient under sedation with intravenous propofol and spontaneous ventilation, and complications were evaluated by both the operator and the anesthesiologist.
Standard EUS and EUS-guided FNA are both performed using moderate anesthesia (using narcotics or anxiolytics) or deep anesthesia (with propofol) for several reasons: for example, the patient must remain completely still during the examination; and the echo endoscopes have a rigid tip and are larger than standard endoscopes. Also, the average procedure time needed for EUS is longer than that of gastroscopy [10]. All these requirements, together with the performance of FNA or therapeutic procedures, can increase the morbidity of this endoscopic technique. However, there is only sparse information on the complication rate for EUS as documented prospectively. Complications of diagnostic EUS have been mostly evaluated retrospectively, without precise inclusion or exclusion criteria. These studies report morbidities of 0.05% to 0.6% [11–14]. In addition, complications of interventional EUS have been evaluated in other separate studies, with reported morbidities ranging from 1% to 3% and a mortality of around 0.1% [5,14–17].

We initiated a prospective study, 14 years ago, to assess the acute and immediate complications of both diagnostic and interventional EUS, at our university-affiliated tertiary care referral center.

**Patients and Methods**

**Patients**

Our prospective single-center study covered two periods.

The first period, from January 1990 to September 2000, included 3207 consecutive patients (1760 men, 1447 women; mean age 58±10.3 years, range 19–89 years) who underwent diagnostic EUS (of whom 2% had more than two EUS examinations). The indications for EUS were: staging of cancers, of the esophagus and cardiac region (8%; among these one-third were classified as uST3-T4 tumors with stenosis), of the stomach (3%), of the ampulla, pancreas, and bile ducts (8%), and of the anus and rectum (1.7%); confirmed or suspected chronic pancreatitis (5%); idiopathic acute pancreatitis, unexplained cholestasis, and cystic lesions of the pancreas (56%); examination of mediastinal lesions, submucosal tumors, giant fold gastritis, and benign gastrointestinal lesions, and other reasons (18.3%).

During the second period, from October 2001 to September 2004, the study focused only on interventional EUS. The same trained endoscopist (L.B.) carried out 224 interventional EUS procedures consecutively in 221 patients (120 men, 101 women; mean age: 61±10.7 years, range 25–81 years); the FNA procedure was performed twice in three patients. EUS-guided FNA biopsy was done for 105 solid pancreatic tumors (three were sampled twice), 74 pancreatic cystic lesions, and 34 extrapancreatic solid lesions. These 34 lesions included recurrent rectal and esophageal cancers (n=8); neoplastic or infectious (due to tuberculosis) lymph nodes (n=12); and mediastinal or abdominal solid tumors (n=14). In addition, eight celiac plexus blocks were applied.

**Methods**

**Diagnostic and EUS-guided FNA.** Standard diagnostic EUS procedures were carried out using different echoendoscopes, that is, the EUM3 and EUM20 devices (Olympus, Hamburg, Germany) linked to UM3 and UM20 ultrasound devices (Olympus), respectively. EUS-guided FNA was done, by a single endoscopist (L.B.), using the GF-UC30P (Olympus) or FG36UX (Pentax, Argenteuil, France) linked to the Envision (Dornier, Epagny, France) and EUB 525 (Hitachi, Wiesbaden, Germany) ultrasound devices, respectively.

When esophageal stenosis was observed, EUS was performed without prior dilation. In addition, no water was added into the stomach for gastric EUS examinations.

All patients had a preoperative assessment for anesthesia, with verbal and written information regarding the procedure. Standard information, produced by the French Societies of Gastroenterology (SNFGE) and Digestive Endoscopy (SFED), was given to all patients, who also gave their written informed consent to EUS examination.

Blood samples were routinely assessed for hemostasis parameters before each interventional EUS. In addition, any curative or preventive treatment with aspirin or warfarin was stopped at least 8 days before interventional EUS and replaced by short-lasting anticoagulants.

All the procedures, except for rectal EUS, were done with the patients under anesthesia and extended in the left lateral position. Before, during, and 1 hour after anesthesia, the patient’s oxygen saturation, and respiratory rate were measured, blood pressure was determined using a noninvasive method, and an electrocardiogram was recorded. Anesthesia was administered by an anesthesiologist, using intravenous propofol sedation and with spontaneous ventilation (air and oxygen by nasal tube). The propofol dose was titrated; the first bolus was between 1.5 and 2 mg/kg, adjusted to the patient’s physiological status on the American Society of Anaesthesiologists (ASA) scale to obtain unconsciousness. Further injections were given depending on patient movement and monitoring data.

In addition, patients scheduled for FNA of a pancreatic cystic tumor or a perirectal lesion received antibiotic prophylaxis with 1 g of intravenous cefazoline before examination. Antibiotics were also administered in patients with cardiac lesions or conditions that confer an increased risk of endocarditis. EUS-guided FNA and celiac plexus block were performed with 22-gauge and 19-gauge needles, respectively (EUS-N1; Wilson Cook, Wilson-Salem, North Carolina, USA).

A maximum of three to four needle passes were generally done for solid tumors while only one needle pass was done for cystic tumors. The mean time for EUS-guided FNA, as measured over 50 procedures at our center, was 24.7±5 minutes (including anesthesia time).

From 1990 to 1997 diagnostic EUS procedures were done by a single endoscopist. This endoscopist began to use EUS after 5 years’ experience in standard endoscopy. Thereafter, diagnostic
EUS was done by four different endoscopists until 2000. The three other endoscopists had 5 years’ experience of standard endoscopy and had been trained in EUS by the first endoscopist (L.B.).

**Evaluation of complications.** At our institution, patients remain in hospital for 12 hours after standard EUS (unless they need other investigations) in a so-called ambulatory setting. However, during the present study all the patients who underwent interventional EUS stayed in hospital for 24 hours after the procedure. Whatever the type of EUS examination, complications were defined as any deviation from the expected clinical course during or after EUS or EUS-guided FNA, including complications resulting from anesthesia (such as severe hypoxemia, heart failure, or shock). We thus defined as “immediate” complications that occurred during EUS, and as “acute” those complications that occurred within 24 hours following the procedure. No follow-up call to the patient or referring medical doctor was routinely planned. Therefore, even though the patient might have been given information about contacting the endoscopist or the anesthesiologist if any events had occurred after hospital discharge, only early complications (i.e. occurring within 24 hours) have been completely assessed during the present study.

The following protocol was used systematically for patients who underwent EUS examination at our center.

1. During anesthesia, vital signs were monitored as described above.
2. After EUS, all patients were monitored in the recovery room until they were awake, conscious, pain-free, and with stable vital signs. We particularly checked for neck, thoracic, or abdominal pain, or hypoxemia or hypotension, that might have led to a suspicion of perforation or bleeding.
3. Patients then transferred to the ambulatory unit and were re-examined 6 hours later, with checking of vital, abdominal, pulmonary, and neurological signs. If criteria for home-readiness for discharge were fulfilled (vital signs stable over 1 hour, conscious, no bleeding, no edema, no vertigo, no nausea or pain, and spontaneous urination), patients were discharged, except for EUS-guided FNA patients who stayed in hospital for 24 hours.

**Results**

**Mortality**

There were no deaths over the two periods of assessment of EUS complications.

**Morbidity of Standard Diagnostic EUS**

A complication was observed in three of the 3207 patients who underwent diagnostic EUS over the 10-year period. The first complication was observed in a 75-year-old woman during an EUS examination carried out because of suspicion of common bile duct stone. She became severely hypoxic under propofol sedation, which led to an unplanned tracheal intubation after EUS was started and until the end of examination. The EUS examination was completed and extubation was done rapidly. There was no subsequent pulmonary infection or fluid, but the patient was kept under supervision for 1 day.

The second complication occurred in a 71-year-old man, also during investigation for suspicion of a residual common bile duct stone. This patient had no history of cardiovascular disease but during the induction of anesthesia by propofol, a supraventricular tachycardia was diagnosed. EUS was quickly halted and the patient stayed for 3 days in the hospital’s cardiology department to normalize his cardiac rhythm.

The last case involved a 27-year-old woman with a suspected huge gastric stromal tumor. A persistent abdominal pain was noted 1 hour after the EUS procedure that required delivery of an intravenous class 1 analgesic. A computed tomography (CT) scan excluded any complications such as perforation or hemorrhage. The patient was treated by fasting and analgesia (paracetamol 3 g per day) during a 24-hour hospitalization. The only explanation seems to be mobilization of the huge tumor during EUS examination.

None of these three patients had any late complication after discharge from hospital. In addition, over this period, fewer than 0.5% of patients experienced moderate temporary pharyngeal pain immediately after EUS examination. After the first 4 years of the study period, this event was rare because of the decrease in the diameter of EUS endoscopes. Finally, surgery was never required and the morbidity of diagnostic EUS in our series was 0.093%, with no mortality.

**Morbidity of EUS-Guided Interventional Procedures**

The population included 221 consecutive patients over a 35-month period. EUS-guided FNA was done for 216 cystic, solid or mixed lesions (with 182 being located in the pancreas) and there were eight EUS-guided celiac plexus blocks.

There were five occurrences of complication, of which four were encountered during FNA of a pancreatic lesion (one cystic lesion, two solid masses, and one mixed lesion; 2.2% of all pancreatic lesions) (Table 1). One complication occurred after EUS-guided FNA of a mediastinal lesion (2.9% of the 34 extrapancreatic lesions).

A 60-year-old woman (case 1) had acute pancreatitis after EUS-guided FNA of a solid endocrine tumor (12 mm in diameter) located in the body of the pancreas. The symptoms resolved within 3 days after fasting and class 1 analgesia (paracetamol).

Upper digestive bleeding occurred in a 56-year-old woman (case 2), with formation of melena, 2 days after EUS-guided FNA of an adenocarcinoma in the head of the pancreas. This patient had no gastric or duodenal mucosal lesion and we suspected hemorrhage from the main pancreatic duct (no endoscopic treatment was needed). No blood transfusion was required and the bleeding stopped spontaneously.

Duodenal perforation occurred in a 59-year-old woman (case 3) after EUS-guided FNA of a malignant intraductal papillary mucinous tumor in the isthmus of the pancreas. Fever and abdominal pain was noted 6 hours after the procedure, and soluble barium
transit radiography and CT allowed diagnosis of a punctiform perforation of the third part of the duodenum accompanied by a small pneumoretroperitoneum. Given the small size of the perforation, we speculate that the needle was responsible rather than the echo endoscope itself. The patient was treated successfully with antibiotic and fasting within 4 days of EUS-guided FNA.

A 60-year-old woman (case 4) was readmitted, because of fever and abdominal pain, 2 days after an EUS-guided FNA. She had undergone the procedure for a mucinous cystadenoma of the pancreatic body. The symptoms were resolved within 3 days, after antibiotic and analgesic treatment.

The final complication (case 5) occurred after EUS-guided FNA of a mediastinal mass in a 72-year-old man. The mass appeared solid initially but was eventually found to be a bronchogenic cyst. The patient was readmitted 4 days after the procedure for thoracic pain and arrhythmia. A diagnosis of pleuropericarditis and auricular fibrillation was established. Treatment involved pleural drainage over a 21-day hospitalization.

All the five patients with complications related to EUS-guided FNA had no further sequelae over a follow-up of at least 9 months. Three of these five patients had developed complications after discharge from the hospital (cases 2, 4, and 5; Table 1). The mean delay between the EUS-guided FNA procedure and clinical signs of complications was 30 hours and the mean length of hospitalization after these complications was 6.8 days (Table 1).

During this study period we met with no complications related to EUS-guided celiac block procedures performed under EUS guidance.

The overall morbidity rate for interventional EUS procedures was 2.23% (five complications in 224 interventional EUS procedures), no surgery was required, and there was no mortality.

Discussion

In the present study, the overall complication rate for standard EUS, assessed during the first 10-year period and for more than 3000 examinations, was 0.09%, with no mortality, and therefore we conclude that EUS is a safe technique. Complications may occur with any endoscopic procedure and are mainly represented by perforation, hemorrhage, and specific cardiopulmonary episodes due to sedation. Previous observations and large retrospective reports (involving between 32,000 and 43,000 EUS procedures) have described some major complications of standard EUS. Complication rates of 0.05% to 0.03% have been encountered and there have been perforations of the pharynx, esophagus or duodenum, and major bleeding requiring transfusion and endoscopic hemostasis [11,12]. In France, a national study conducted over a single day revealed that the rate of complications with standard EUS was 0.6%. The majority of these complications were related to conscious anesthesia [13]. In addition, a recent single-center report involving over 582 examinations that included both standard and interventional EUS described a complication rate of 0.7% [14]. A recent Danish experience also mentions a complication rate of 0.2% among 2654 diagnostic EUS examinations [17].

It is noteworthy that we do not dilate an esophageal stenosis before EUS and we do not fill the stomach with water to establish the necessary fluid interface for gastric wall examination. This may avoid perforation and aspiration pneumonia in patients anesthetized without tracheal intubation.

Overall, EUS has a low morbidity rate, even though the instrument used is more rigid and has a larger diameter than an upper endoscope. Moreover, this rate seems to be lower than that of upper gastrointestinal endoscopy which has a risk of 0.03% for haemorrhage, of 0.03% to 0.1% for perforation, and a risk of death [18]. Indeed the overall morbidity rate for upper gastrointestinal endoscopy has been evaluated at 0.2% in a recent prospective French study involving 8167 procedures [19]. However, no formal comparison between the two procedures has been clearly done that included follow-up to assess long-term complications.

Finally, the principal complications seem to be related to conscious anesthesia (cardiovascular complication, hypoxemia, and aspiration pneumonia). In some western countries, sedation for endoscopic procedures is responsible for 0.54% of morbidity and 0.03% of deaths [20], and is occasionally administered by the gastroenterologist himself [21]. In France, the complication rate due to anesthesia is around 0.01%, but anesthesia is invariably carried out by an anesthesiologist. This might partly explain the discrepancies.

### Table 1 Details of complications in 224 consecutive interventional endoscopic ultrasound (EUS) procedures

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Lesion</th>
<th>Location</th>
<th>Complication</th>
<th>Diagnosis</th>
<th>Delay *, hours</th>
<th>Hospitalization †, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Solid tumor</td>
<td>Body of the pancreas</td>
<td>Pancreatitis</td>
<td>Endocrine tumor</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Solid tumor</td>
<td>Head of the pancreas</td>
<td>Upper gastrointestinal bleeding</td>
<td>Pancreatic carcinoma</td>
<td>48</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>Mixed tumor</td>
<td>Body of the pancreas</td>
<td>Duodenal perforation</td>
<td>Intraductal papillary mucinous tumor (IPMT) of the pancreas</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>Cyst tumor</td>
<td>Body of the pancreas</td>
<td>Infection</td>
<td>Mucinous cystadenoma</td>
<td>48</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Mixed tumor</td>
<td>Mediastinum</td>
<td>Pleuropericarditis</td>
<td>Bronchogenic cyst</td>
<td>96</td>
<td>21</td>
</tr>
</tbody>
</table>

* Delay between fine-needle aspiration (FNA) biopsy and first symptoms of complication.
† Hospital stay for complicated cases.
Obviously, interventional EUS can bring additional complications compared with diagnostic EUS. The rate for these complications is low and has been evaluated as being from 1% to 3%, according to different published experiences, mortality being close to 0.1% [4,5,8,9,15–17]. The rate of 2.2% observed in the present study was thus in accordance with the literature.

One case of perforation occurred in our study, and was related to fine-needle aspiration as the needle penetrated the normal pancreas and perforated the third part of the duodenum. The patient was managed medically. In general, perforation is related to the passage of the echoendoscope rather than the fine needle itself, and surgery is then necessary because of the size of the perforation [5,12].

One case of pancreatitis was noted, and the calculated rate of 0.7% is similar to that described by other investigators, the reported incidence varying from 0.5% to 2% [5,15,16,22]. This complication is essentially due to a biopsy of a benign lesion within healthy pancreas (a cystic or endocrine tumor). In order to decrease the risk of post-biopsy acute pancreatitis, it is recommended that passage of a needle through pancreatic duct or through normal pancreatic parenchyma is avoided. This situation occurs frequently if the target lesion is less than 1 cm in diameter.

In the present study, 74 pancreatic cystic lesions were punctured, and all the patients received antibiotic prophylaxis. We suspected an infection in one case because of pain and fever that appeared 2 days after EUS-guided FNA and thus despite antibiotic administration. As we did not continue prophylactic treatment, an occurrence of infection beyond the 24-hour period cannot be excluded. Bacteremia may be observed with 5.8%–6% of EUS and EUS-FNA procedures [23–25], whatever the indication, but it has not been proven whether these bacteremias are clinically relevant. A subgroup analysis of patients with cysts who underwent FNA demonstrated a 14% risk of infectious complications [5]. However, the use of prophylactic antibiotic administration in EUS-guided FNA of pancreatic cysts has not been clearly studied in randomized, controlled trials. 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 confer an increased risk of endocarditis. We finally observed one case of upper gastrointestinal bleeding, with a wound of the main pancreatic duct being suspected. The literature suggests that bleeding is a rare event, estimated to occur in no more than 1% of EUS-guided FNA procedures [5,26].

Considering our experience and that of other groups, EUS-guided FNA is a safe technique. The morbidity rate should be no more than 1%–3% if simple rules are respected. These rules might include: systematic pre-anesthesia evaluation, avoiding needle passage through the main pancreatic duct and normal pancreatic parenchyma, a single needle pass with pancreatic cystic lesions, and antibiotic prophylaxis with high-risk patients and lesions. However these rules should be prospectively evaluated.

Until now, routinely, all our patients have stayed in hospital during the 24 hours following EUS-guided FNA, but given the low complication rate, EUS-guided FNA can certainly be performed in ambulatory conditions as several teams have already advocated. However, from our experience, the first symptoms of complications may appear 24–48 hours after discharge (this happened in three out of five cases of complication). Therefore, both the patient and the referring clinician should be informed about a possible need to return to the hospital.

To our knowledge, the present study is the longest reported European experience in which EUS-related complications have been assessed, and we conclude that both standard and interventional EUS are safe procedures with no mortality and a low complication rate. In the case of EUS-guided FNA, this rate should be no more than 2% in experienced hands. These immediate complications are easily detected and treated. It can therefore be suggested that EUS-guided FNA could be done in an ambulatory setting, with probably lower costs. However, this proposition should first be supported by multicenter experience. In addition, both patient and referring clinician would have to be informed about a possible need to return to hospital after discharge.

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Competing interests: None

References

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