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Digestive and Liver Disease

Digestive and Liver Disease 37 (2005) 142-152

www.elsevier.com/locate/dld

#### Review Article

# Present and future of endoscopic ultrasonography

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Available online 21 January 2005

#### Abstract

Endoscopic ultrasonography and endoscopic ultrasonography-guided fine needle aspiration are well-established techniques, encompassing a variety of diagnostic and therapeutic applications. Along with traditional indications that constitute everyday clinical practice in all endoscopic ultrasonography centres, new indications are emerging that resemble the continuing research carried on in this field. Some of these are innovative applications, developed by highly experienced endosonographers and with a putative role for clinical practice in the near future. Others are merely experimental applications, carried out on in animal models or in highly selected groups of patients, opening up new fascinating areas of research but not for imminent introduction in clinical practice. The purpose of this review, after summarising the present indications of endoscopic ultrasonography, is to focus on the future applications and try to establish their possible advent, either in the near or in the far future.

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Keywords: Endoscopic ultrasonography; EUS; Fine needle aspiration; Therapeutic EUS

#### 1. Diagnostic EUS: present

Main indications to endoscopic ultrasonography (EUS) can be explained by its ability to visualise the gut wall as a multi-layer structure corresponding to histological layers [1]. Both benign and malignant conditions are represented. For the former, differential diagnosis of submucosal tumours (SMT) should be cited. For the latter, staging of gastrointestinal neoplasms (oesophageal, gastric, and rectal) and lymphomas should be remembered.

Other important indications to EUS derive from its capability of visualising in detail structures and lesions surrounding the gut wall, such as the pancreato-biliary area, masses of uncertain origin and lymph nodes [2]. In this respect, EUS-fine needle aspiration (FNA) has become an indispensable adjunct to the technique since 1993, when it was shown to be feasible and safe to obtain tissue diagnosis in the majority of the lesions under the reach of EUS [3]. Again, both benign and malignant conditions should be cited. Among the former, study of the extrahepatic biliary tree for detection of stones and of pancreatic parenchyma for detection of chronic

pancreatitis has been shown to be very accurate. Among the latter, differential diagnosis of pancreatic lesions, both cystic and solid, and staging of pancreatic and lung cancer represent key applications of EUS.

In recent years, several authors dealt with the applications of EUS in real clinical practice, validating its use in many diagnostic and staging algorithms and showing that it is cost-effective and significantly affects patients' outcome [4,5].

All the indications cited above were addressed in detail in previous publications [6,7].

### 2. Diagnostic EUS: future

#### 2.1. Innovative indications

Several reports dealt with potential new indications of EUS that could become part of current EUS clinical armamentarium in the near future.

#### 2.1.1. Head, neck, and mediastinum

Wildi et al. [8] probably disclosed a new indication for EUS regarding head and neck diseases, such as tumours of the oropharynx, hypopharinx, larynx, and thyroid. They

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reviewed the EUS and EUS-FNA records of patients whose referral criteria were suspected invasion of the oesophagus or mediastinal lymphadenopathy. Out of 32 patients, EUS demonstrated direct primary tumour invasion of the oesophagus in four and of the pleura in one, and confirmed metastases in eight cases. Importantly, EUS changed the management in more than half of the patients preventing more invasive procedures such as mediastinoscopy.

Fritscher-Ravens et al. [9] studied 18 patients with EUS-FNA who had been admitted to an intensive care unit for suspected mediastinitis. They were able to detect mediastinal abscesses in 89% of the cases and detect an aetiological agent in all of them (mainly bacterial). EUS-FNA was more accurate than computed tomography (CT) and led to appropriate drug therapy in the majority of the patients.

Varadarajulu et al. [10] described the utility of EUS-FNA of lung masses after unsuccessful attempts by CT-guided or bronchoscopic tissue sampling. As EUS cannot penetrate air-filled structures, a prerequisite was that all the patients had a mass adjacent to or abutting the oesophagus. EUS-FNA provided a positive diagnosis of malignancy in 100% of the cases with a mean number of two needle passes in which no complications occurred. EUS significantly influenced subsequent treatment leading to palliative chemoradiation in the majority of the cases.

#### 2.1.2. Liver, biliary tree, and portal vessels

Liver exploration with EUS seems to be feasible and reliable as demonstrated by many studies [11–13]. Prasad et al. [11] reviewed the records of 222 patients who underwent staging of malignancies and had a complete examination of the liver. EUS of the liver was abnormal in 27 patients (12%), and EUS-FNA was performed in 21. Positive cytologic evidence of liver metastases was obtained in 15 patients, five of whom had normal non-invasive imaging. The opinion of the authors is that complete liver examination is warranted in those patients undergoing EUS for another indication but that EUS should not replace traditional imaging modality in any other case.

Several authors reported that EUS could help shed some light in lesions of the extrahepatic biliary tree that often represent a diagnostic challenge [14–18]. Fritscher-Ravens et al. [14] used EUS-FNA to characterise potentially operable hilar cholangiocarcinoma. They obtained adequate material for cytological examination in all the patients identifying hilar cholangiocarcinoma in 26, metastases in 5, and benign disease in 12. The overall diagnostic accuracy, sensitivity, and specificity were 91, 89, and 100%, respectively. EUS-FNA resulted in a major change of management in 20% of the patients in whom planned surgery was avoided. The authors concluded that EUS-FNA is a new, feasible and safe approach for hilar strictures of unknown origin significantly filling a diagnostic gap and affecting patients' outcome.

Lai et al. [19] determined the accuracy of EUS for the diagnosis of portal venous system thrombosis. The patients

had underlying evidence of malignancy, biliary obstruction or parenchymal liver disease. Using a linear echoendoscope with colour Doppler capability they were able to detect portal venous system thrombosis in the majority of the patients with an overall accuracy of 89%. As CT scan was falsely negative in a significant proportion of them, the authors maintain that linear EUS can significantly impact the decisions regarding resectability in this group of patients.

#### 2.1.3. Left adrenal gland and spleen

Scattered reports described that EUS-FNA of the left adrenal is feasible and safe. Eloubeidi et al. [20] published a systematic review of their experience in this field. Over a 3-year period they performed 31 procedures in patients with enlarged left adrenal gland on abdominal imaging and known or suspected malignancy. Tissue adequate for interpretation was obtained in all patients, the median number of needle passes was 4.5, and no complications were encountered. Malignant adrenal masses were detected in 42% and benign conditions in the remaining. Patients with benign masses were more likely to have preservation of the normal seagull shape of the gland than those with malignant conditions. According to the authors, this technique can help overcome the high rate of non-diagnostic aspirates with percutaneous approach. Nevertheless, the decision for EUS-FNA of the left adrenal gland should be individualised and based on potential clinical impact and indication.

The same author [21] described that the spleen could be properly identified and studied in a prospective series of 163 patients undergoing EUS with a linear echoendoscope. Moreover, in three cases of suspected lymphoma EUS-FNA was performed leading to correct diagnosis in two cases and to a false-negative result in the third one. No complications occurred. However, more studies are needed to assess the safety of transgastric EUS-FNA of the spleen.

## 2.2. Experimental indications

Imaging of the portal vein is readily obtained with EUS. Lai et al. [22] tested the feasibility of EUS-guided portal vein catheterisation with a 22-gauge needle in normal pigs and in pigs with portal hypertension. The results are very interesting. Baseline EUS-guided catheterisation was possible in all animals unlike transhepatic catheterisation; high quality portal vein pressure tracings were obtained in the majority of cases. No significant complications occurred: at necropsy there were small subserosal haematomas at the EUS puncture site; only in one anticoagulated pig a small periduodenal collection of blood was detected. According to the authors, the potential for the use of this technique in the management of patients with portal hypertension is promising. However, caution and a high level of expertise are warranted due to the significant risk of bleeding, particularly in coagulopathic patients.

Parasher et al. [23] assessed the feasibility of EUS identification and puncture of the thoracic duct in a swine model. The

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