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EDITORIAL

Endoscopic ultrasonography and pancreatic cancer – close companions

P. Fockens

Department of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands, e-mail: p.fockens@amc.uva.nl

The first description of endoscopic ultrasonography (EUS) in the Lancet dates back almost 25 years ago. In an editorial in 1987 the conclusion was that there was probably not much future for EUS. The authors stated in their last sentence: *'echoendoscopy will remain a somewhat uneasy marriage of two techniques, best restricted to research centres.'*[1] The future turned out to be different as it almost always does. EUS is currently an important technique for the detection, diagnosis and therapy of a variety of gastrointestinal and also pulmonary diseases. In the Netherlands around 30 to 40 hospitals are using EUS on a daily or weekly basis for indications such as staging of oesophageal cancer, diagnosing submucosal lesions in the gastrointestinal (GI) tract, detecting common bile duct stones, detecting early chronic pancreatitis, detecting and staging pancreatic tumours, treating pancreatic pseudocysts, staging rectal tumours and last but not least for biopsying mediastinal lymph nodes in patients with lung cancer, sarcoidosis and other diseases. The biggest advance in the technique of EUS has been the EUS-guided fine needle aspiration (FNA) biopsy. With the help of EUS-guided FNA biopsy it is now relatively easy to image but also to puncture lesions just outside the GI tract (such as mediastinal lymph nodes). The procedure can be performed under mild sedation and has a very low complication risk.

In this issue of the *Netherlands Journal of Medicine*, Meijer and colleagues provide an excellent illustration of one of the important applications of EUS.[2] They report on a group of patients that had a clinical suspicion of pancreatic cancer and a negative computed tomography (CT) scan. CT scanning has become the first-line imaging technique for these patients and it has markedly improved in the past decades. Twenty years ago we were looking at lightboxes with films containing 24 pictures per film, made with 1-cm slices through the body. Nowadays we scroll through the same body on a large computer screen with 2-mm slices and a resolution of around 1 mm. Advances in computer technique have made it possible to quickly scroll up and down and also allow reconstructions in multiple planes. CT scan is clearly the current gold standard for imaging of the pancreas. The pancreas, however, is a difficult organ to image. Tumours are quite often only slightly hypodense or even isodense compared with the normal parenchyma. And therefore many tumours are detected because of secondary changes to the organ such as distortion of the normal contours of the pancreas, obstruction of the pancreatic duct or invasion into surrounding tissues.

The resolution of EUS is about ten times higher then that of CT. Ultrasonography additionally has a different tissue interaction compared with X-ray and thus provides a completely different way of imaging of the pancreas making EUS complementary to CT. When looking for relatively small (<2.5 cm) tumours the sensitivity of CT drops dramatically to around 50% whereas the sensitivity of EUS remains high at around 90%.[3] EUS is therefore an important second-line imaging technique since a negative CT scan clearly does not rule out the presence of a tumour. In the article from the University Medical Center in Groningen, a tertiary referral centre, 34 patients are described over an 18-month period who underwent EUS because of a negative or inconclusive CT. The authors have carefully followed these 34 patients and conclude that EUS assisted in a correct final diagnosis in 30 of these 34 patients. Exactly in line with the size limitation of CT discussed above, the average size of the lesions the authors found with EUS was 22 mm. It would be interesting to know how many patients with a suspicion of pancreatic cancer overall were seen in the study period as this would help further define the place of EUS in this patient group. It is our impression that around 20% of all patients referred for evaluation of a possible pancreatic mass undergo an EUS.

EUS is rather difficult to learn and requires a substantial annual volume to warrant quality. It is therefore logical that EUS is centralised in referral centres. Calculations have been made in the past that at least one EUS centre should be available for every one million inhabitants in

the Netherlands. With the growth of pulmonary EUS indications, this figure should probably be somewhat higher but in general one could state that we probably do not need more than around 30 active EUS centres. Dilution of EUS to more hospitals could endanger the good results as achieved in the current article. EUS is almost never an emergency procedure and this is another argument to call for concentration in larger hospitals.

In the current study, EUS was combined with EUS-guided FNA biopsy in almost 60% of patients. One could question why this was not done in all patients and this is a matter of continuous debate around the world. Let's look at sensitivity and specificity before drawing conclusions. EUS-guided FNA biopsy of pancreatic tumours has a sensitivity of maximally 90% and a very high specificity, approaching 100%.[4] In our opinion a sensitivity of 90% is not good enough to demand a positive biopsy for every patient before considering surgery. Therefore, at the current time a positive imaging study (CT or EUS) in a patient with a clinical suspicion of pancreatic cancer is considered an indication for surgery in the absence of signs of irresectability or metastases. This algorithm implicates that in our current practice about 5% of patients that are operated on because of suspected pancreatic cancer, end up with a postoperative diagnosis of focal pancreatitis. This 5% of patients being overtreated seems acceptable in view of the fact that 10% patients would be undertreated in case of limiting surgery to patients with a positive biopsy. Biopsies are therefore currently reserved for patients with inconclusive imaging studies, patients in whom a biopsy is considered a prerequisite because of high operative risk, and irresectable patients who will receive radiotherapy and/or chemotherapy. With neoadjuvant therapy on the horizon for pancreatic cancer, we seem to be only years away from a preoperative biopsy in almost every patient since neoadjuvant chemotherapy and/or radiotherapy can only be administered in patients with a positive cytological or histological diagnosis.

Thirty years after its introduction, EUS has achieved a strong position in the workup of patients with pancreatic cancer and this position is likely to grow in the future. Pancreatic EUS nevertheless remains difficult because of the necessary expertise and expensive because of the manpower involved. An endoscopy room is blocked for 45 to 60 minutes with involvement of two nurses, one endoscopist and an available cytopathologist or cyto-technician in case of a biopsy. CT and EUS are therefore never in competition but in close cooperation. The marriage of inconvenience from the Lancet in 1987 has changed into a close companionship in 2010.

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