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Endoscopic Ultrasonography: A Novel Procedure for the diagnosis of GI tract diseases

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ABSTRACT

Twenty years after the introduction of endoscopic ultrasonography, many papers on this topic are being published every year in the medical literature. Along with established clinical indications, such as gastrointestinal and pancreatic cancer staging and differential diagnosis of submucosal tumors, new applications have been suggested, such as meditational and liver tumor sampling with fine-needle aspiration. Improved accuracy and cost-effectiveness have been demonstrated in comparison with other imaging techniques. Reports of large series of fine-needle aspiration procedures have described a high level of accuracy for EUS in the diagnosis of lymph nodes and perivisceral masses. Pancreatic and ampullary tumors still represent a major challenge, as shown by numerous articles describing differential-diagnostic criteria and cytological sampling techniques. A few papers have also been published on the topic of portal hypertension, but it seems questionable whether there is any real advantage for endoscopic ultrasonography over traditional endoscopy here. New techniques such as radiofrequency tumor ablation are promising, while others such as three-dimensional imaging and the use of contrast enhancement have not yet met with routine clinical application. Finally, some of the papers published during the last year have studied the technique of endoscopic ultrasonography itself, dealing with issues of outcome, current clinical availability and use, and the learning curve. Evidently, endoscopic ultrasonography is still widely under used, not only among general practitioners and physicians in other specialties, but even by gastroenterologists. Although endoscopic ultrasonography is already 20 years old, considerable efforts are still needed, therefore, to ensure that it becomes more widely accepted in clinical practice.

Keywords: EUS, Tumor, Cancer, Eco-Endoscope,

1.0 INTRODUCTION

This paper focused on the most interesting aspects of clinical and basic research in endoscopic ultrasonography (EUS) that have been published during the last 12 months since the previous state-of-the-art review in Endoscopy, by Chak [1]. Publications on the purely technical aspects of EUS are rare, as the use of different instruments (radial scanning, linear scanning, miniprobes, and blind probes) at varying frequencies (principally 7.5, 12, and 20 MHz) has been extensively assessed. Fine needle aspiration (FNA) is no longer a new technique, and its use should be regarded as a routine extension of the diagnostic capabilities of EUS. However, EUS is now being investigated in different clinical contexts, and its role in diagnostic algorithms is being carefully assessed.

2.0 EUS in Established Indications of EUS

2.1 Esophagus

Esophageal cancer staging is probably the primary indication for EUS, as none of the alternative techniques can yield the same level of accuracy, and many papers have been published on this topic. Nevertheless, scientific debate is still continuing as new technical facilities become available.

The introduction of FNA led to a great improvement in the accuracy of staging, particularly with regard to lymph nodes. EUS alone is very sensitive for assessing lymph nodes, but it is not very specific, and false-positive results can occur. Giovanni et al. [2] reported very high sensitivity and specificity levels for FNA of distant lymph nodes in esophageal cancer. In 198 patients examined over a four-year period, they detected enlarged distant lymph nodes and sampled them with FNA in 40 cases (in the mediastinum or at the celiac axis). The results of cytological examination were positive in 31 patients, true-negative in eight (as confirmed by surgery), and nonspecific in one. The sensitivity and specificity of EUS-FNA were 97% and 100%, respectively. Subsequently, the 31 patients diagnosed as having M1 disease were excluded from surgery. If these very high accuracy figures can be replicated, FNA would provide an indispensable diagnostic tool, as it would influence treatment decision-making in a very high proportion of patients.

Approximately 30% of patients with esophageal cancer have malignant stenosis that cannot be traversed with the echo endoscope. In these cases, reliable tumor staging with conventional EUS is impossible, as the assessment of the depth of wall infiltration at the proximal margin of the tumor is inaccurate. Alternatives include endoscopic dilation before EUS, use of dedicated esophageal over-the-wire blind probes, and use of catheter ultrasound probes. Although previous reports have suggested that endoscopic dilation involves a risk of perforation, Wallace et al. [3] reexamined the issue, maintaining that less aggressive dilation up to 14–16 mm is sufficient for complete staging in almost all patients. The newer models of echo endoscope used in their study (Olympus GF-UM 20, GF-UM130, and GF-UC30P) have a more tapered tip, so that a smaller diameter is available to pass the stenosis in comparison with the older models (Olympus UM-2 or UM-3). The authors carried out 44 dilations in 42 patients with obstructing tumor, and were able to pass an echo endoscope and conduct complete staging in 74% of them, including FNA of the celiac lymph nodes when indicated. Advanced disease was detected in 19% of cases. No complications occurred. Interestingly, despite the malignant stenosis, 40% of the patients had early-stage tumors (T1–2, N0 or N1, M0 or MX). However, these results are in strong contrast to those of previous papers, in which it was reported that more than 90% of patients with stenosis finally proved to have advanced tumors; in these cases, dilation would have been useless [4,5].

Other reports on esophageal cancer have been published. Case series usually present cumulative staging accuracy rates without making a distinction between adenocarcinoma and squamous-cell carcinoma. Salminen et al. [6] focused on 26 patients with

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adenocarcinoma of the esophagus or esophagogastric junction, and compared their results with pathological staging after radical resection of the esophagus and proximal stomach. The ability to predict the T stage was 66%, and the ability to predict the N stage was 72%. Given this low level of accuracy, the authors believe caution must be exercised during judging a patient to be inoperable solely on the basis of EUS without confirmed distant metastases. Schlick et al. [7] pointed out the effect of the examiner's experience on the accuracy of esophageal cancer staging. In 139 patients examined over an eight-year period, there was a significant improvement in the T staging accuracy from 64% to 90%; by contrast, the N staging accuracy was similar from the beginning to the end of the same period. Thus, EUS preoperative staging of cancer of the esophagus is of value only if performed by an experienced endosonographer or under his or her supervision.

Small esophageal lesions are difficult to visualize using the dedicated echoendoscope, and the balloon mounted on its tip can create compression artifacts. In this case, catheter ultrasound probes can be of great value, as was shown by Wallace et al. [8], refining the condom water-filling technique first described by Inoue. A double-channel endoscope and a 20 MHz miniprobe placed within the water-filled condom were adequate for obtaining good images without air artifacts and without the risk of aspiration associated with filling the esophageal lumen with water. The best results were described with small esophageal submucosal tumors and early carcinoma. On the other hand, miniprobes allowed only incomplete study of advanced or bulky lesions, due to a limited depth of penetration and inaccuracy in detecting lymph nodes.

2.2 Mediastinum

The staging of lung cancer is a valuable application for EUS-FNA. Some clinical studies have shown that it is feasible, safe, and accurate in comparison with other modalities such as mediastinoscopy, mediastinotomy, and, more recently, positron emission tomography. Aabakken et al. have shown that it is also cost-effective [9]. They reviewed the performance data for mediastinoscopy/mediastinotomy and EUS from the literature, along with life expectancy data. The costs of the procedures were retrieved from their hospital's billing system. For patients with lymph nodes that were positive on computed tomography (CT) in stations accessible by EUS, the cost per year of expected survival was $1729 with the EUS strategy and $2411 with the mediastinoscopy/mediastinotomy strategy. EUS thus offers a favorable alternative to mediastinoscopic access.

Mediastinal lymph nodes can be detected in a variety of clinical conditions apart from lung cancer. The distinction between benign and malignant lymph nodes is crucial, but it is not always reliable using imaging alone, and cytological or histological confirmation is needed. Mishra et al. [10] were able to diagnose sarcoidosis in seven of 108 consecutive patients who underwent FNA of mediastinal lymph nodes for various indications. Interestingly, EUSFNA was not only easy and safe in these seven patients, but was also the only technique that led to the correct diagnosis of sarcoidosis, as transbronchial forceps biopsy and bronchoalveolar lavage were negative.

2.3 Stomach

Gastric EUS is a well-established method for staging cancer and lymphoma and for the differential diagnosis of large gastric folds. With regard to small or localized lesions such as submucosal tumors and early gastric cancer (EGC). EUS can reliably assist the gastroenterologist in planning endoscopic mucosal resection (EMR) with diagnostic and/or curative intent.

In Japan, where the incidence of gastric cancer is high, endoscopic screening of the population allows frequent diagnosis of EGC. Accurate staging by EUS is mandatory in these cases, as intramucosal cancer is likely to be cured by EMR alone, while cancer invading the submucosa is best cured by surgical resection (Figure 1). Ohashi et al. [11] published a study including 61 patients diagnosed with EGC over the past five years. The depth of tumor infiltration was assessed in 49 patients by EUS before EMR, and the results were correlated with the histological examination of the resected specimens. Forty-six patients showed no changes in the submucosa at EUS; histologically, these included 37 cases of mucosal cancer and nine of very slight submucosal infiltration. Three patients showed echo changes in the submucosa; histologically, two of these patients were confirmed as having submucosal cancer and one as having peptic ulcer scar within the tumor. The authors concluded that the combined use of EUS and EMR is useful in diagnosing the depth of infiltration in patients with EGC.

Another interesting study combining EUS and endoscopic resection was conducted by Kojima et al. [12]. They carried out EUS examinations in 54 patients with sub mucosal tumors (including 26 esophageal tumors and 23 gastric tumors), and then attempted en-bloc resection of lesions originating in the second or third layer of the gut wall. The strip biopsy technique with a double-channel endoscope was used. For lesions originating in the fourth layer, they carried out partial resection limited to the covering mucosa and then obtained standard biopsies from the exposed lesion. The histological samples were sufficient in all cases, and no serious complications occurred. The EUS and histopathological diagnoses matched in 74% of cases. Two lesions that did not present malignant features at EUS, originating in the muscularispropria of the stomach, were found to be leiomyoblastoma and leiomyosarcoma at histology. According to this study, EUS is the best method for guiding subsequent endoscopic partial or total resection. This is of great importance for diagnostic purposes in cases of submucosal tumor, particularly in tumors arising in the fourth layer, as EUS alone is still not sufficiently accurate to rule out malignancy, and other techniques such as jumbo forceps biopsies and FNA have been shown to be insensitive. On the other hand, endoscopic resection cannot be routinely suggested for all cases of submucosal tumor, particularly in small lesions originating in the second or third layer, with EUS findings compatible with benign lesions (Figures 2,3). Nevertheless, the systematic use of EMR adopted in this study is intriguing, as it provided adequate and immediate histological confirmation of the echo features described with EUS.

Palazzo et al. [13] also addressed this issue in a study describing EUS features suggestive of malignancy in 56 histologically confirmed cases of stromal-cell tumor. Stromalcell tumors originate from the muscularispropria of the gut wall (more rarely from the muscularis mucosae) and include leiomyoma, leiomyoblastoma, leiomyosarcoma, and leiomyoma of uncertain malignant potential. Irregular extraluminal margins, cystic spaces, and lymph nodes with a malignant pattern were most predictive of malignant or borderline stromal-cell tumors, and the combined presence of two of these three features showed a positive predictive value of 100%. On the other hand, regular margins, tumor size ≤ 30 mm, and a homogeneous echo pattern were most predictive of benign stromal-cell tumor. The low sensitivity is the main drawback with these criteria, as it is rare to find a stromal-cell tumor presenting all three features si-

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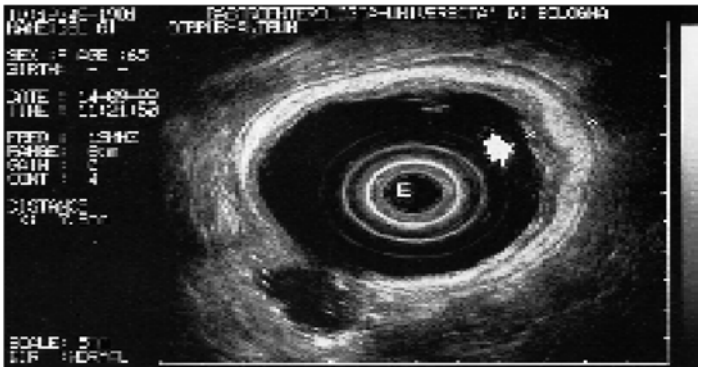

Figure 1 Early gastric cancer (12-MHz radial scan using the Olympus GF-UM130). Localized thickening of the second and third layer of the wall is visible (mucosa and submucosa). This lesion is not suitable for endoscopic mucosal resection multaneously.

Overall, EUS is still far from providing an accuracy of 100% in investigating submucosal tumors and stromal-cell tumors; further studies are still required in this area.

2.4 Pancreas

Pancreatic cancer still represents a diagnostic challenge, and the different imaging techniques are being compared to assess which offers the greatest accuracy in staging. In addition, pancreatic neoplasms cover a wide histological spectrum, ranging from types with uncertain malignant potential (e.g., some cystic and endocrine forms) to very aggressive ones; reliable preoperative diagnosis may help predict the best treatment in the individual patient.

Gress et al. [14] reported their experience comparing EUS and CT in 81 patients who underwent surgery for pancreatic cancer. They reported a striking difference between the two modalities, with an EUS accuracy for T and N staging of 85% and 72%, respectively, compared with a CT accu racy of 30% and 55%, respectively. In addition, the ability to predict vascular invasion was 93% for EUS and 62% for CT ($P < 0.001$). The authors also observed a learning phase effect, as seven of nine cases of mis-staging occurred before the examiner had performed his first 100 pancreatic EUS examinations. This study is interesting, as it presents a large prospective case series confirming that EUS is superior to axial thin-section CT in experienced hands. Further studies comparing EUS with spiral CT in large numbers of patients are warranted.

Figure 2 Ectopic pancreas (12-MHz radial scan using the Olympus miniprobe XUM- 2R). Localized thickening of the third layer is present, with internal hypoechoic pseudoacinar structures.

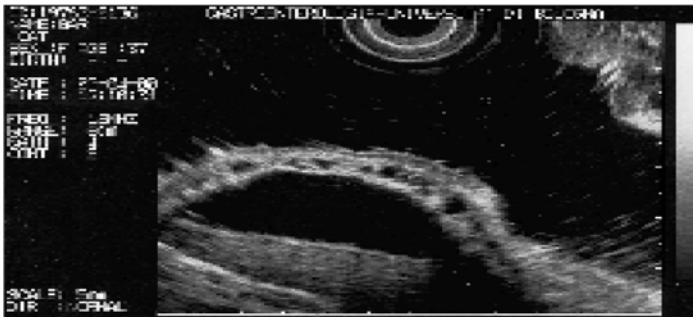

Figure 3 A case of multifocal cystic gastritis (12-MHz radial scan using the Olympus GF-UM130). There are numerous anechoic lacunae of various sizes, compatible with submucosal cysts, inside the third layer

EUS without FNA no longer appears to be reliable in the diagnosis of pancreatic malignancies. Erickson et al. [15] published a very well conducted prospective assessment of 109 FNA procedures, including 95 pancreatic masses, seven lymph nodes, and seven hepatic metastases. With the participation of a cytopathologist, they aimed to investigate whether any patient characteristic or EUS characteristic might be capable of predicting the number of needle passes needed to detect malignancy. This is an important aspect, since when FNA is performed without a cytopathologist being present, the number of passes is often too low, leading to poor diagnostic accuracy, or too high, leading to increased procedure times, numbers of needles used, and overall examination costs. Among a variety of factors studied, the differentiation of the primary tumor – which of course can only be assessed by the cytopathologist – was the strongest predictor for the number of passes. In particular, adenocarcinomas that were well differentiated required a significantly higher number of aspirations than moderately or poorly differentiated ones. If features assessable by the endoscopist alone were considered, only the type of lesion turned out to be helpful, as pancreatic masses required five or six passes compared to two or three passes for lymph nodes or hepatic metastases. Nevertheless, this approach resulted in a 10–15% reduction in definitive cytological diagnoses. The presence of a cytopathologist is therefore necessary for cytological yields greater than 90% and minimization of number of FNA passes.

Another case series of FNA in solid pancreatic masses was presented by Voss et al. [16]. They used EUS as a thirdline investigation, after ultrasound and spiral CT; this approach seems reasonable for routine clinical practice. They were able to obtain a biopsy core of tissue using a 22gauge needle, and carried out both histological and cytological examinations; however, a cytopathologist was not present in the examination room. They carried out FNA in 90 patients, but obtained analyzable material in only 73; in the latter subset, the overall diagnostic accuracy was only 74%. There was a lower diagnostic accuracy for neuroendocrine tumors than for adenocarcinoma. These results suggest that the technique of FNA requires further elaboration, and that the presence of a cytopathologist during the procedure is needed to achieve acceptable diagnostic accuracy.

Other interesting reports were published by Gress et al. [17], presenting some differential EUS features useful for characterizing pancreatic cystic neoplasms that have a more

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favorable prognosis than adenocarcinoma; and by Ardengh et al. [18], who reported a much higher sensitivity (83% vs. 17%) with EUS than with spiral CT for detecting small insulinomas of the pancreas.

Ampullary neoplasms have a better prognosis than pancreatic neoplasms (40% five-year survival), but due to the low prevalence of these lesions, there have been few studies of them. Diagnosis with endoscopic retrograde cholangiopancreatography (ERCP) is accurate, but does not allow TN staging. Kubo et al. [19] preoperatively examined by EUS 35 patients with ampullary tumors. The overall accuracy was 74% for the T stage and 63% for the N stage. In particular, they found that EUS was highly accurate in ruling out pancreatic infiltration – an essential aspect for the prognosis and therapy. However, EUS was not accurate in detecting nodal involvement, and it must therefore always be complemented by ultrasound and CT. In a study including 50 patients with ampullary neoplasms, Cannon et al. [20] found that EUS was more accurate than CT and magnetic resonance imaging (78% vs. 24% and 46%, respectively) for T staging. The accuracy of EUS for N staging was found to be low (68%). Interestingly, they observed that the presence of an endobiliary stent (25 patients), which is often positioned in these neoplasms for drainage purposes, was associated with a trend toward less accurate T and N staging. However, the most frequent error was EUS overstaging or understaging of pancreatic invasion (desmoplastic peritumoral pancreatitis can be difficult to differentiate from foci of invasive carcinoma).

It has been shown that EUS has a good level of accuracy for detecting chronic pancreatitis and that its findings correlate well with those of ERCP. Hastier et al. [21] assessed the prevalence of pancreatic abnormalities in 72 patients with alcoholic cirrhosis. EUS and ERCP were performed in all patients, and chronic pancreatitis was diagnosed in 14 using both methods independently (ductal and parenchymal lesions). In addition, isolated parenchymal lesions such as a honeycomb appearance were observed by EUS alone in a further 17 cases, and these patients underwent EUS and/or ERCP follow-up examinations. During the followup period of up to three years, these patients continued to consume alcohol, but the parenchymal abnormalities did not progress, and none of the patients developed clinical signs of pancreatic insufficiency. This clinical study confirmed the high accuracy of EUS for the study of pancreatic parenchyma. More intriguing was the demonstration that isolated parenchymal changes seen at EUS, which are more frequent than ductal changes and are usually thought to be representative of chronic pancreatitis, corresponded only to alcoholic diffuse fibrosis of the pancreas. This condition was associated with alcoholic liver cirrhosis, but did not necessarily imply a diagnosis of chronic pancreatitis.

Finally, Sahai et al. [22] suggested a putative role of EUS for patients with dyspepsia. They studied the pancreatic parenchyma in 156 patients with dyspepsia, and found a greater number of endosonographic abnormalities than in control individuals. Although this approach seems cumbersome in view of the large numbers of patients who present with dyspepsia and the availability of less invasive methods, the authors maintain that this syndrome may be an atypical presentation of pancreatic disease and that EUS may therefore be useful for screening patients with persistent symptoms.

2.5 Biliary Tree

Intraductal ultrasonography (IDUS) is now an established method of diagnosing bile duct abnormalities. Miniprobes for IDUS can be used during ERCP without the need for endoscopic sphincterotomy. Bile duct carcinoma, biliary strictures, and pancreatic strictures can be carefully assessed, and transverse-section imaging of the bile duct wall allows careful assessment of portal vein and hepatic artery invasion.

Tamada et al. [23] studied the local effects of radiotherapy, and used IDUS to predict the subsequent patency of metallic stents in 16 patients with bile duct carcinoma. They inserted small-caliber 20-MHz probes via a percutaneous transhepatic approach, and studied the thickness of the bile duct wall both before and after radiotherapy. After this, metallic stents were inserted through the tumor. When radiotherapy was deemed to be effective at the second IDUS examination (i.e., when a 30% reduction in the thickness of the bile duct wall was observed), the metallic stents were patent for a greater period of time compared with ineffective therapy. Stent obstruction occurred in 67% of patients with ineffective therapy, compared to 14% of patients with effective therapy ($P < 0.05$).

Chak et al. [24] described the use of a new over-the-wire probe (Olympus XUM-G20-29R) that can be used during ERCP without losing access to a cannulated duct. Twentyone patients with a variety of inflammatory and malignant pancreaticobiliary lesions were studied. Sixteen masses were identified, and in all cases the use of IDUS was judged to be very easy and fast. The authors considered that IDUS provided useful additional information in all cases; however, it remains to be shown whether IDUS can offer a real diagnostic yield additional to that of ERCP alone.

Menzel et al. [25] compared EUS and IDUS for predicting resectability in 56 patients with biliary obstruction. They found that IDUS was significantly better than EUS for T staging, with 19% of biliary obstructions being depicted by IDUS but not by EUS. However, the N staging was far from accurate with IDUS, and was significantly inferior to EUS in cases of pancreatic cancer. The authors report that the IDUS procedure was much faster than conventional EUS. It seems that these two techniques should still be regarded as complementary for reliable and complete TN staging.

A study by Polkowski et al. [26] compared helical CT cholangiography and EUS in the diagnosis of bile duct stones. The authors note that, although EUS and MRCP have already set a very high standard in this field, the two techniques are not widely available and suffer from high costs. The relatively low costs and wide availability of helical CT scanning mean that it may represent a useful alternative. Fifty-two non-jaundiced patients with suspected bile duct stones underwent both EUS and helical CT after intravenous administration of a cholangiographic contrast material. The sensitivity, specificity, and overall accuracy were very high, and no significant difference was detected between the two techniques. The greatest limitations of helical CT cholangiography, as the authors point out, lie in the fact that it is ineffective in jaundiced patients and that there is a risk of adverse reactions to the contrast material. However, as the latter were negligible in the present study, helical CT cholangiography represents a cheaper and more accessible alternative to EUS in individuals with normal serum bilirubin levels.

Liu et al. [27] published an interesting case series of 89 consecutive patients with acute pancreatitis. Sixty-four of them

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were diagnosed with cholelithiasis by conventional radiological methods, but 18 of them were classified as having idiopathic pancreatitis after evaluation by ultrasonography, CT, and ERCP. Interestingly, EUS identified small gallbladder stones in 14 of this subset of patients, and concomitant choledocholithiasis in three. In these cases, EUS allowed a biliary cause of the acute pancreatitis to be identified, and early treatment was started to reduce the risk of recurrences. Lachter et al. [28] reported that linear-scanning EUS is as good as radial scanning for detecting bile duct stones.

The differential diagnosis of small polypoid gallbladder lesions was carefully described by Sugiyama et al. [29]. They found that EUS was superior to ultrasonography in differentiating neoplastic from nonneoplastic lesions. Features such as tiny echogenic spots or microcysts and comet-tail artifact were predictive of benign lesions (cholesterol polyp and adenomyomatosis); when EUS did not produce findings of this type, neoplasia was suspected (adenoma and adenocarcinoma), and was subsequently confirmed by surgical resection. This approach seems to be of particular value as a second-line examination in patients with gallbladder lesions without unequivocally benign features at transabdominal ultrasonography.

Finally, Fujita et al. [30] reported good results for EUS in the preoperative staging of a large series, collected over a ten-year period, of 39 patients with gallbladder carcinoma.

2.6 Colon

The accuracy of EUS staging of rectosigmoid neoplasia is still a matter of debate, as many factors can affect its reliability. On the other hand, even when good accuracy is obtained, its influence on subsequent therapeutic management has not been unanimously recognized. McClave et al. [31] addressed the first of these issues, identifying some pathological EUS features that are deceptive. These included reactive peritumoral inflammation and microscopic spread without inflammation in the T staging, and large benign lymph nodes or small malignant lymph nodes in the N staging. These features accounted for almost half of the errors of overstaging or understaging, respectively. The accuracy of staging was good only when these deceptive features were absent.

Norton et al. [32] addressed the second issue in a study of 121 patients with rectosigmoid neoplasia. The overall accuracy of T staging, but not of N staging, was good (92% and 65%, respectively), and subsequent treatment using endoscopy, minimally invasive surgery, or open surgery could be planned accordingly. However, the authors concluded that the impact of the improved staging on patient management and outcome was unclear.

Several authors reported other interesting aspects in this field. Most local rectal cancer recurrences are extraluminal, but early detection using EUS and FNA surveillance, as described by Lohnert et al. [33], led to potentially curative repeat intervention in a significant proportion of cases. The accuracy of N staging in rectal cancer is still unsatisfactory; Spinelli et al. [34] showed that it is even worse, falling from 75% to 43%, if a special lymph-node dissection technique is adopted for pathological staging. The explanation for this lies in the larger number of lymph nodes harvested with the new technique, particularly those smaller than 5mm; the genuine diagnostic yield of EUS N staging should therefore be further investigated. Finally, Magdeburg et al. [35] reported that EUS in the staging and follow-up of anal carcinomas had a direct impact on the treatment of the great majority of patients.

3.0 EUS in Operative and Investigational Indications

3.1 Fine-Needle Aspiration and Drainage

As new and more refined CT and MRI techniques are now available, EUS is now facing tougher competition as a diagnostic modality. FNA, which is not easily performed under guidance with other imaging techniques, is therefore probably indispensable to the survival of EUS as a diagnostic technique. Williams et al. [36] published an impressive FNA case series, reporting the most complete results yet available. A total of 327 lesions were sampled, including lymph nodes, pancreatic masses, extra intestinal masses, and intramural tumors. The overall accuracy of FNA for the diagnosis of malignancy was 86%, with a sensitivity of 84% and a specificity of 96%. With respect to the lesion type, these figures were high for lymph nodes and for pancreatic and extra intestinal masses, but not for intramural tumors. FNA provided cytological diagnoses that were superior to EUS criteria alone for predicting malignancy. One complication occurred (streptococcal sepsis in a patient with a pancreatic cyst adenoma), and the authors therefore recommend the use of prophylactic antibiotics before puncturing cystic lesions in the pancreas. The detection of malignancy was crucial for determining patient management in most cases. The presence of the cytopathologist at the time of FNA procedure was essential, according to the authors, in obtaining such high levels of accuracy.

Another large FNA case series was reported by Sahai et al. [37]. This study aimed at verifying the safety, efficacy, and accuracy of the new Olympus GF-UM30P echo endoscope for FNA. This particular instrument, a mechanical linear scanning scope, proved to be inferior to the curved linear array system in terms of inferior resolution and needle visualization, as well as lack of Doppler capability. The figures for sensitivity and accuracy in assessing malignancy were also inferior to those reported using the curved linear array system. However, the authors concluded that GFUM30P is a reasonable second choice or alternative to the curved linear-array system. As its only advantage is that it uses the same processing unit as the radial scanning scope, it may be suitable for centers with limited financial resources.

Seifert et al. [38] described a one-step puncture and drainage technique for the treatment of peripancreatic fluid collections. The procedure was carried out in six patients (five with pseudo cysts and one with an abscess) under direct EUS guidance using the curved linear-array Pentax FG38UX scope, equipped with a 3.2 mm working channel. Drainage was successful in all patients.

3.2 Portal Hypertension, Liver, and Retroperitoneum

Although a definite clinical role has not been established for the use of diagnostic EUS in patients with portal hypertension, some authors have suggested a therapeutic application for the technique. Lahoti et al. [39] administered sclerotherapy in five patients with esophageal varices under continuous EUS color Doppler flow control. They reported that this technique is feasible and safe. Precisely targeted delivery of the sclerosant, particularly at the level of the perforating veins, was obtained until the varix was seen as completely thrombosed and the absence of flow was documented using color Doppler. As a result, the number of sessions required to achieve eradication was reduced, and no episodes of recurrent bleeding were observed. However, it is difficult to see this technique being used

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in routine clinical practice, as band ligation is a simple and safe technique that has replaced sclerotherapy for elective treatment of esophageal varices. Moreover, EUS sclerotherapy, if preferred to band ligation, would be very expensive and confined to a few highly specialized centers.

Lee et al. [40] carried out repeated sessions of gastric varicealsclerotherapy with cyanoacrylate until EUS, performed after sclerotherapy, demonstrated complete obliteration of all the varices. They documented a significant reduction in late recurrence of bleeding compared to the non-EUS–assisted technique. This particular condition seems a useful indication for EUS, as sclerotherapy needs to be repeated only when it is clearly demonstrated that the vein is still patent.

The liver is not routinely investigated by EUS, as simpler and more effective techniques are available. Nevertheless, in selected cases, EUS may be superior to other modalities, as shown by Nguyen et al. [41]. They carried out EUS guided FNA in 14 patients with focal liver lesions of uncertain nature, and were able to diagnose or rule out malignancy in all cases, with an overall accuracy of 100%. As a consequence, definitive M staging was obtained in all cases, and therapeutic management was changed accordingly.

Retroperitoneal tumors are uncommon, but the differential diagnosis is challenging. Erickson et al. [42] obtained a tissue diagnosis by EUS-FNA in 18 patients with retroperitoneal masses, and were able to differentiate between primary tumors, metastatic cancers, and nonmalignant lesions. The patient management was subsequently affected.

4.0 New Techniques and Instruments

The newest and most promising technique is probably EUS-guided radiofrequency ablation of pancreatic tumors. Goldberg et al. [43] reported their experience in animal models in which radiofrequency was applied to normal pancreatic tissue with specially modified 19-gauge needle electrodes. This produced discrete zones of coagulation necrosis in the pancreas. The authors believe that management of small neuroendocrine tumors and palliation of unresectable adenocarcinoma might be potential clinical applications of this technique.

Chak et al. [44] published a prospective evaluation of the use of the new Olympus GF-UM130 video echo endoscope in comparison with the traditional fiber optic echo endoscope. They found that the moderately improved optics and slightly better mechanical characteristics of the new scope allowed the performance of EUS without the need for concurrent diagnostic endoscopy. The ultrasonographic performance was comparable. The new instrument led to improved patient comfort, decreased the procedure time, and led to cost savings.

Better demarcation of gut wall tumors was reported by Nomura et al. [45] using contrast-enhanced EUS with intravenous injection of air-filled albumin micro spheres. Tamada et al. [46] used three-dimensional IDUS for the staging of extra hepatic bile duct carcinoma. They reported that three dimensional IDUS is superior to two-dimensional IDUS for assessing tumor invasion of the right hepatic artery, portal vein, and pancreatic parenchyma.

5.0 Outcomes of EUS

The good results obtained with EUS imaging in a wide variety of diseases often raises a further question – the issue of EUS outcomes. Does the use of EUS in real clinical protocols affect patient management, influence treatment decisions, and lead to cost savings? Allescher et al. [47] published a study on this issue that is well worth reading, along with an accompanying editorial by Nickl [48]. The authors studied the appropriateness of the indications for EUS and the potential influence of EUS on the outcome in 397 consecutive patients studied over a period of ten months, with data collected by contacting the referring physicians two months after the examination. The indications were appropriate in 81% of cases, and the referring physicians considered that the information provided by EUS was useful in 55% of the cases, but a change in treatment was believed to be directly due to EUS in only 6% of the cases. The latter result is somewhat surprising. It could be real, or it might be due to under appreciation of the real benefit of EUS, or to difficulties in recalling the patient's history two months after referral for EUS. In any case, these data require further careful evaluation.

Kim et al. [49] also reported rather discouraging results. They surveyed 100 gastroenterologists with regard to their use of EUS in patients with esophageal cancer. Surprisingly, only 41% judged EUS to be very useful or essential, and only 33% had referred a patient for an EUS examination. A lack of perceived usefulness and unavailability of the technique were independent predictors of non referral for EUS.

Not only general practitioners and physicians in other specialties, but even gastroenterologists, appeared to lack a full awareness of the potential value of EUS in clinical practice. Future efforts may need to be directed toward improving the general awareness among physicians of the real benefits and capabilities of EUS, to ensure that it becomes more widely accepted in clinical practice.

ETHICAL ISSUES

The authors declare no competing financial interest.

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