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Endoscopic Ultrasound in Pancreatic Disease – Its Influence on Surgical Decision-Making

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Abstract

Endoscopic ultrasonography (EUS) was introduced about 25 years ago with the primary aim of better visualization of the pancreas as compared to transabdominal ultrasonography. This review discusses the current evidence in 2008 concerning the role of EUS in the clinical management of patients, with a special emphasis on its impact on surgical therapy. According to the literature, good indications are detection of common bile duct stones (e.g. in acute pancreatitis), the detection of small exo- and endocrine pancreatic tumors, the performance of fine-needle aspiration in pancreatic masses depending on therapeutic consequences. In other areas such as diagnosis of chronic pancreatitis and cystic pancreatic lesions, the contribution of EUS seems limited. Pancreatic cancer staging is discussed controversially due to conflicting evidence and certainly has lost grounds due to improvements in CT technology. Therapeutic EUS is, however, more widely accepted and may replace other techniques, e.g. in pancreatic cyst drainage and celiac plexus neurolysis; further techniques of interest are being developed.

Endoscopic ultrasonography (EUS) was introduced into the diagnostic armamentarium of gastroenterology some 25 years ago for superior visualization of the pancreas as compared to transabdominal ultrasonography, where intervening air often hampers clear and full demonstration of the organ. In fact, no systematic study has since evaluated the real ability of EUS to fully cover the pancreas, perhaps mostly due to the absence of an easy gold standard. However, the best model may be detection of small focal lesions such as pancreatic endocrine tumors in various areas of the organs. Some clues as to a lower accuracy in the tail came with some of the early studies [1, 2] as well as from an analysis of missed cancers [3]. Image quality may also play a role in the detection of subtle pancreatic malignancy, and finally, all modern echoendoscopes work on the basis of electronic (instead of mechanical) ultrasound imaging. In a randomized study blindly comparing image quality and time to common bile duct (CBD) visualization between the electronic and the mechanic scanner, electronic images were rated better and also the time until CBD visualization was significantly shorter [4]. Electronic EUS scanning may in addition provide the expanded diagnostic possibilities of modern ultrasound technologies: the clearer images obtained by harmonic imaging techniques were appreciated in the subjective assessment of examiners [5]. In the difficult issue of differential diagnosis between benign and malignant pancreatic mass lesions, good sensitivity and speci-

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ficity values were reported for the clinical use of power Doppler as well as contrast-enhanced EUS [6, 7]. Whether these results will withstand the test of time and further studies with different patient populations, has to be seen. The latest development of sophisticated ultrasound technology – elastography – is discussed below in the section on differential diagnosis of pancreatic tumors.

This review aims at summarizing the current evidence on the role of EUS in the clinical management of patients with special emphasis on surgical therapy. Most recent evidence including recent congress abstracts is preferred.

Acute Pancreatitis: Role of EUS

Challenges in the assessment of patients with acute pancreatitis are diagnosis of severity of the disease – CT is considered to be the gold standard here – and the recognition of a biliary cause, with the consequences of early endoscopic retrograde cholangiopancreatography (ERCP) performance. The diagnosis of CBD stones is probably one of the best indications for EUS, and accuracy results have been consistently very good over the last 15 years, more or less independent of the level of stone likelihood, stone size and echoendoscope type [8]. Recently, a prospective randomized study assessed outcomes in patients with an intermediate likelihood for bile duct stones and compared an EUS-directed strategy with primary ERCP performance: use of EUS led to significantly fewer negative outcomes (10%) as compared to the ERCP group (40%) [9]. In the setting of acute pancreatitis, EUS seems to be similarly accurate in the diagnosis of CBD stones [10–12].

Acute recurrent pancreatitis without an obvious cause on conventional imaging and work-up is another potential indication for EUS, and several papers have shown some value [13–15]. A similar recent prospective study from Spain included 21 cases with biliary colics or recurrent pancreatitis with normal transabdominal ultrasound results performed twice. For the diagnosis of cholelithiasis including sludge in both CBD and gallbladder, ceruletide-induced bile aspiration and analysis were used as gold standard. With 100% of cases showing microlithiasis on the aspiration test, EUS was very sensitive since it correctly diagnosed all but one. Specificity data can however not be derived from this study [16]. There are very limited data on the assessment of the pancreas itself when EUS is done (e.g. for diagnosing CBD stones) in the setting of acute pancreatitis [17].

Conclusion. EUS is helpful for diagnosis of common bile stones in acute pancreatitis with a low to moderate likelihood. For surgical decision-making, CT is still the test of choice.

Chronic Pancreatitis: Aspects of Making the Diagnosis

EUS has been shown to be quite accurate in the diagnosis of chronic pancreatitis in a variety of comparative studies [18, 19]. However, in the moderate to advanced form of the disease, most alternative tests are also quite sensitive and specific, and may be less invasive compared to EUS. A lot of attention in the gastroenterologic literature has centered around the question of whether EUS would be capable of diagnosing the disease earlier than other tests. Results have been somewhat variable, but a good sensitivity was sometimes contrasted by a weaker specificity [20, 21]. Image parameters have been developed and linked to a scoring system to make the diagnosis of early chronic pancreatitis more or less likely [22]. In studies assessing patients with abdominal pain of possible pancreatobiliary origin, the rates of early pancreatitis have been quite high [23], so that some skepticism with regard to the potential to generate many false positive diagnoses has been raised. This question could perhaps be answered by long-term follow-up of cases positive on EUS but negative on other tests. A recent retrospective analysis from Milwaukee reviewed 37 cases diagnosed as early chronic pancreatitis on EUS between 1993 and 1998; these patients had had negative findings on CT and secretin function testing. After a mean follow-up of 8.5 years, signs of chronic pancreatitis were found in 67% of these patients on either CT or secretin testing or both [24]. This confirms a previous study on a group of 32 patients with normal ERCP but slightly abnormal EUS, 69% of whom developed signs of chronic pancreatitis during follow-up of a mean of 18 months including repeated pancreatic tests [25]. The selection bias of these studies may, however, be substantial, since cases presenting again for assessment in retrospective studies are probably those with a higher likelihood to have the disease, and furthermore, the studies were done in centers highly specialized in pancreatobiliary endoscopy, which may introduce some referral bias.

These aspects are probably less likely to be relevant for surgical decision-making. Operative management of painful chronic pancreatitis rests on the diagnosis of a dilated duct as well as of inflammatory tumors, and cal-

cifications, all of which are sufficiently delineated on CT. The differential diagnosis of inflammatory from malignant masses, or, even more difficult, the recognition of malignancy in patients known to have chronic pancreatitis, is still problematic on EUS [26–28], even when involving fine-needle aspiration (FNA) [29], so that EUS may play a limited role in the setting of chronic pancreatitis from a surgical perspective.

Another area in chronic pancreatitis where the role of EUS in patients' work-up could prove important is chronic autoimmune pancreatitis; in a retrospective review of 3 cases, Levy et al. [30] highlighted that the use of a Trucut biopsy with positive immunohistochemistry for IgG4 could, in the appropriate clinical setting, spare the affected patient an unnecessary surgical intervention. However, as clearly shown by the small number of patients, it must be noted that data on this field remain rather insufficient to make definite conclusions.

Conclusion. For surgical decision-making, EUS plays a very limited role. Even with FNA, a reliable differential diagnosis of inflammatory and malignant tumors cannot be provided.

Pancreatic Endocrine Tumors

Another quite consistent indication for EUS is the localization of pancreatic endocrine tumors [2, 31–33], although limitations of EUS were also recently analyzed [34]. The clinical scenario here is mostly quite different, since in functioning endocrine tumors, the diagnosis is made on the basis of laboratory tests, and imaging is used to localize the tumor for subsequent surgical removal. Problems can arise if EUS is the only method to show a tumor, other preoperative tests are negative, palpation during surgery is doubtful and intraoperative imaging is inconclusive. Preoperative marking of the tumors has recently been suggested as a helpful adjunct [35] but has not been extended beyond case report status.

The other setting are non-functioning endocrine tumors which are mostly found incidentally, e.g. on transabdominal ultrasound. They present – similarly to the functioning lesions – as well-demarcated, echo-poor lesions in the pancreas. FNA has been assessed to establish a tissue diagnosis [36–38], and further analyses from the specimens such as microsatellite loss analyses were recently performed and could be correlated to prognosis [39].

Conclusion. EUS is still the test of choice in localizing pancreatic endocrine tumors. In incidental lesions, FNA may be considered, depending on the possible influence on management. Whether individual patients thought not to be candidates for surgery can benefit from EUS-guided therapy using alcohol injection [40] has to be seen and has to be weighed against potential complications which have not fully been explored.

Pancreatic Cancer: Hereditary Forms

Patients with familial risk for pancreatic cancer undergo special screening programs in order to detect cancers at an early stage which usually include CT and EUS, followed by ERCP with tissue sampling and/or EUS-FNA in case of abnormalities. Using such an approach in 78 high-risk patients, 8 patients with pancreatic neoplasia were detected (10% yield) and confirmed by surgery or FNA over a 4-year period; 6 of these 8 were, however, mucinous intraductal neoplasias [41]. Another recent paper dealt with interpretation variability of pancreatic abnormalities found in these patients by using expert video assessment, but with rather disappointing results also after a consensus phase [42]. In conclusion, EUS has been included into the armamentarium of these patients, without definitive evidence of its precise role, but its accuracy shown in other settings gives some credit to its usefulness in the surveillance of hereditary pancreatic cancer. A better definition of criteria for abnormalities to be further followed has to be achieved.

Conclusion. Mostly under study conditions, EUS is used together with CT in the surveillance of patients with familial pancreatic cancer. The dilemma of recognizing cancer in familial chronic pancreatitis is reviewed below.

Pancreatic Cancer: 'Diagnosis' and Differential Diagnosis

Endosonographic diagnosis of sporadic pancreatic cancer has been evaluated in numerous studies. Tumor 'detection' accuracy has been consistently high [43–45]. It should be pointed out here that accuracy of EUS staging in pancreatic cancer is also dependent on other factors influencing good visualization, e.g. the logical recommendation that an optimal EUS-based T- and N-staging of pancreatic head neoplasms should be performed prior to biliary stent placement was recently supported by a study performed in a consecutive series of 65 patients who underwent preoperative EUS for diagnosis and stag-

ing of suspected pancreatic cancer, some of whom had biliary stents in situ and some of whom did not. According to multivariate analysis, patients with stents were 6.55 times more likely to be incorrectly T-staged and 3.71 times more likely to be incorrectly N-staged than patients without stents [46]. However, caution has to be exercised since pretest likelihood was usually quite high in all studies, which mostly came from referral centers, and the value of EUS in a primary care setting is difficult to analyze since indications may be ill defined, and EUS is rarely performed outside of specialty units. Clues as to a somewhat lower detection rate by EUS come from analyses of small tumors [47] as well as from a focused analysis of missed cancers [3]. Another question is the negative predictive value of a negative EUS when a tumor suspicion is raised clinically or by other imaging tests. This question was again evaluated in a recent retrospective study including 412 patients either without a clear mass lesion or those with lesions, but negative on FNA. The overall negative predictive value of EUS was 95.4%. Two patients in the group of 253 cases without visible lesions were later diagnosed to have cancer, both had concomitant diffuse chronic pancreatitis being diagnosed. In the other group, i.e. those with masses negative on EUS-FNA (n = 159), 17 cancers were finally detected [48]. The latter certainly represents a group of cases in whom a negative FNA should be doubted and put into perspective with clinical likelihood. This study confirmed previous experience from other centers, partially also focusing on indeterminate CT findings in which the rate of missed cancers by EUS was excessively low [49–51]; they nevertheless exist [3]. It can, however, be concluded that – with indeterminate CT or transabdominal ultrasound findings – an EUS examination negative for a tumor mass appears to be quite reliable. However, it should be emphasized here that many of the studies displaying comparative data between EUS and other cross-sectional imaging techniques are characterized by absence of blinding amongst examiners, and therefore an objective assessment of superiority of one test over another is hard [52]. In everyday clinical practice the role of CT and EUS in the diagnosis and staging of pancreatic cancer is rather complementary.

A far more difficult problem for EUS as well as for almost all other imaging tests is differential diagnosis of a pancreatic mass lesion. Despite a clinical and imaging likelihood for either malignancy or an inflammatory mass, there is still a substantial percentage of cases in which the final conclusion remains ambiguous. EUS imaging has repeatedly been shown not to reliably provide this differential diagnosis. Whether with new 'functional' imaging such as elastography, which evaluates tissue hardness, this will substantially change remains open. After an initial report on EUS-based elastography in lymph node and pancreatic tumor differentiation with moderate results [53], the same group, using modified criteria, assessed 101 cases with enlarged lymph nodes as well as 121 patients with pancreatic masses. For the latter, sensitivity and specificity values were 81 and 92% [54]. However, the pretest likelihood by clinical or imaging data as well as blindness of assessment is not known. Thus, at the present state of knowledge, EUS cannot provide this differential diagnosis, similarly to other tests. Some years ago, we could show that clinical assessment including knowledge of laboratory values and transabdominal ultrasound results was as accurate in the differential diagnosis of pancreatic masses as were CT, ERCP and EUS, when the latter were evaluated blindly [55].

Conclusion. A negative EUS seems to be quite reliable in excluding a pancreatic tumor in indeterminate cases. Differentiation of focal chronic pancreatitis from cancer on the basis of EUS imaging alone (but also using FNA) is not possible.

Pancreatic Masses: When Do We Need FNA?

It was hoped that tissue diagnosis might help to improve the differential diagnostic dilemma described above. This may be true in the case of positive results, but a negative result does not rule out malignancy. A large number of studies, recently reviewed, confirmed an almost 100% specificity with 80–90% sensitivity [56], although the pretest likelihood may vary from study to study. Most series have utilized EUS-derived cytology and cytologic analysis, but recently, larger and newer needles were developed with the purpose to gain larger specimens for a histologic analysis. The Trucut needle was, however, shown to offer only limited benefit [57–59]. In a retrospective as well as a prospective analysis, we could show that in two-thirds of cases, a small histologic cylinder could be gained. Sensitivity – even if adjusted for only cases with sufficient material – was, however, not superior to that of cytology in general [60, 61].

In addition, some larger prospective series have appeared on EUS and EUS-FNA complications. In a prospective study on 224 FNA examinations a complication rate of 2.2% (n = 5) was found [62]. The 2 fatalities of another large prospective series on both EUS and EUS-FNA (overall complication rate: 0.3%) were both related to

FNA [63]. Pancreatitis is a feared complication of pancreatic EUS-FNA, but the incidence is obviously low [64]. This was shown by a prospective study on 100 pancreatic FNA in which a 12% rate of hyperamylasemia and a 2% rate of clinical pancreatitis was found [65]. A warning was issued from 2 cases who underwent same-day EUS-FNA and ERCP of pancreatic head lesions, and it seemed that inadvertent biliary puncture during EUS-FNA was aggravated by biliary manipulation during ERCP, and subsequent leakage had to be treated surgically [66]. Cyst puncture has been associated with the risk of infection following EUS-FNA since an initial complication study [67]. Later studies did not find any significant complications in 111 such patients [68], whereas another study in 50 patients specifically looking at intracystic hemorrhage found 3 such cases (6%) [69]. In the largest (retrospective) study on this topic, 603 patients with 651 cysts were analyzed; complications were identified in 13 patients (2.2%): 6 patients developed pancreatitis, 4 patients had abdominal pain, 1 patient suffered from a retroperitoneal bleed, 1 patient had a cyst infection, and 1 patient had bradycardia. 12/13 patients required hospitalization. Type of cyst, size, presence of septations or mass, and same-day ERCP were not predictive factors of these complications [70].

Conclusion. Quite simply, EUS-FNA in pancreatic cancer should only be used if the results will influence management. This is mostly not the case with resectable pancreatic adenocarcinoma. Neoadjuvant regimes might alter this approach, but are far from being established.

Pancreatic Malignancy: Staging and Assessment of 'Resectability'

As far as pancreatic cancer staging is concerned, many studies have appeared in the past 20 years, with some of them tuning down initial enthusiastic results even by the same group [71, 72], confirmed by other studies [73, 74] including careful endosonographic-histologic correlations [69], but objected by others who consistently show superiority of EUS over helical CT [75–79]. Own experience, published in abstract form only, and using expanded criteria of resectability (only retroperitoneal and major arterial invasion) found EUS to be quite inaccurate in predicting resectability [submitted]. In line with these inconsistent results, a recent review concluded that all studies published up to now are too heterogeneous in study design, quality and results, so that definitive conclusions on the relative value of EUS and CT cannot be given [80]. A recent study thus concluded that both tests should be used since both together they had the highest accuracy to predict irresectability [81].

Conclusion. Due to very inconsistent results of comparative studies on EUS versus CT which use different criteria of resectability, partially ill-defined and unclear gold standards especially with regard to diagnosis of irresectability, the role of EUS is still ill defined. This is disappointing in the light of so many papers published, but may also mean that if a method requires so many studies to be shown to be useful, its value may be limited for pancreatic cancer staging. In the authors' personal opinion, good-quality high-standard helical CT should be given preference if interpreted by experienced radiologists.

The Dilemma of Pancreatic Cystic Lesions

Pancreatic cystic lesions pose several diagnostic and therapeutic challenges: (1) Differential diagnosis of cystic tumors and pseudocysts. (2) Differential diagnosis and management of cystic tumors or cystic lesions presumed to be neoplastic (i.e. serous vs. mucinous types). It is assumed that the risk of malignancy is very low for serous cystadenoma, which was confirmed recently in a series of 158 such cases undergoing surgery, with only two malignancies, one diagnosed initially, the other one on follow-up due to metastases after an initial benign diagnosis from the resection specimen [82]. (3) Management of pancreatic pseudocysts (see below). (4) Management of intraductal papillary mucinous neoplasms (IPMNs).

The diagnosis of a pancreatic cystic lesion without a clear association to acute or chronic pancreatitis (unequivocally diagnosed) should always raise a tumor suspicion, reinforced by other factors such as female gender, higher age and location in body/tail. Among the tumors, the mucinous types have to be taken more seriously with surgery being considered in all of them, whereas the rate of malignancy in serous cystadenomas seems to be very low; this has led others to suggest a more conservative approach for patients with small and asymptomatic cystic lesions (including asymptomatic, branch duct IPMN <3 cm in size) [83–85].

Early papers suggested specific EUS image features to be more frequent in pseudocysts versus cystic tumors [86], but this may not be helpful in the individual case. Furthermore, agreement among endosonographers was only fair (κ value 0.24) in this differential diagnosis [87]. In a large multicenter study on 341 patients, 112 of which

had histologic proof by resection, the accuracy of EUS to differentiate mucinous from non-mucinous lesions was only 51% [88]. However, the group of non-mucinous lesions (n = 44) included both pseudocysts (n = 27) and neoplasias (7 serous cystadenomas, 5 endocrine tumors, 5 others), so that the differentiation between pseudocysts and cystic tumors was not assessed, and since only operated cases were included in the analysis, there was a selection bias towards neoplasia [88].

Studies evaluating EUS-FNA with different parameters to be assessed from the aspirated fluid (amylase, mucin, CEA, cytology) also reached contradictory conclusions. In the multicenter study cited above [88], the accuracy was best with CEA determination (79%), although the cut-off value was determined on the same patient population; cytology (59%) or any combination of the above tests were less accurate. In contrast, a French study using similar definitions (need for surgery, which was not given for pseudocysts and serous cystadenomas) had sensitivity/specificity rates of 71/91% for EUS and 40 and 100% for EUS-FNA, with very limited value for CEA (54/77%) [89]. In a small study on 34 operated cases, EUS alone had a 91% sensitivity and 60% specificity; cytology and CEA were not done on all cases and fared less well [90]. Other studies had even smaller subgroups with definitive tissue confirmation [91, 92], and may not contribute substantially to the evidence we need clinically, especially since they were retrospective. Another recent study called *prospective* in the title, but already called *retrospective* in the abstract [93], used combinations of viscosity measurements, CEA and amylase levels reaching excellent results (sensitivity/specificity rates 85–100%), but did not mention pretest likelihood or the problem of test hierarchy [93]. The complication rate of cyst puncture (2%) seems to be moderate [70], but whether more aggressive puncture methods such as Trucut puncture of the cyst wall [94] will really increase accuracy, but not complications, has to be seen.

To get around the problem of differential diagnosis, EUS-guided treatment including alcohol lavage was proposed and presented in an initial series of 25 cases, with no complications but with a complete cyst resolution of 35% only [95]. While this may be regarded if anything than as palliative therapy, the authors went on with a randomized study comparing alcohol with saline lavage including 39 patients. Complete and partial (25% size reduction) cyst resolution was reported in 22 versus 8% and in 61 versus 17% of patients, respectively. In the alcohol group, the complication rate (pancreatitis rate) was 4%. Two patients were operated on later: in 1 case an intraductal mucin-producing tumor showed 50–75% epithelial ablation while the other patient had a mucinous cystic tumor in which complete epithelial ablation was achieved [96]. Another study added paclitaxel, a chemotherapeutic agent to alcohol, as shown in a series on 10 such patients, where 3 cases each had complete and partial resolution [97]. Similar results were also presented in a series of 11 cystic tumors (here, taxol was added to ethanol) with good success rates (8/11, but with a summary of all results in the abstract yielding 12 instead of 11 cases) [98]. Further studies should concentrate on the potential long-term benefit of cystic tumors as their malignant potential is low and any effect can only be assessed from long-term follow-up.

EUS is being increasingly employed in the management of IPMNs due to its ability to image predictors of malignancy (i.e. mural nodules) and the possibility to obtain tissue diagnosis [99]. Pais et al. [100] in a series of 65 patients who underwent preoperative EUS for IPMNs (out of a total of 74 patients) showed that EUS features of a solid lesion, a dilated main pancreatic duct, ductal filling defects, and thickened septa were predictive of malignancy in patients with IPMNs. EUS-FNA cytology proved helpful with sensitivity, specificity and accuracy of EUS-FNA for the diagnosis of malignancy of 75, 91 and 86%, respectively, but cyst fluid CEA and CA19-9 did not differ between the groups with malignant or benign IPMNs [100]. The role of EUS in the work-up of patients with intraductal papillary mucinous tumors was also assessed in a French study presented at the United European Gastroenterology Week (UEGW) 2007. In 103 surgical patients, about half of whom had malignancy, EUS predicted malignancy with 70% accuracy. Predictive features were dilated main duct >10 mm and a mass lesion [101].

Conclusion. In general, EUS potentially with FNA contributes limited information to the management of patients with indeterminate cystic lesions. Clinical parameters (absence of pancreatitis, gender, age) add at least as much important information as morphology (EUS and/or CT) and FNA results do. Surgery could be considered in all operable patients with incidental cysts; however, other parameters could be taken in account, e.g. location (head) or morphology suggesting serous cystadenoma which may lead to FNA in individual cases if the results have an impact on the patient's management. Alcohol lavage of cysts is clearly experimental; the concept itself will certainly raise opposition.

Pancreatic Cysts and Necroses: EUS-Guided Endotherapy

Cyst drainage of pancreatic pseudocysts, long done and still performed under endoscopy guidance (as well as radiologic control) [99], is – when indicated – now performed under direct EUS targeting in most larger endoscopy units. In case of bulging lesions, drainage can also be done by endoscopy alone, radiologic monitoring being an integral part of all cyst drainage procedures [103]. A new echoendoscope with forward-viewing optics, EUS image, and puncture canal was used in a pilot series on 5 patients for cyst drainage [104]. A series from Rome on 110 cases with pseudocysts found a better efficacy of transmural compared with transpapillary drainage [105]. EUS may have some additional advantages for cyst drainage in the situation of portal hypertension [106]. Due to a relatively high rate of cyst persistence with the risk of abscess formation [107], close follow-up after cyst drainage has to be performed in order to detect insufficient effects and to reintervene early. Unfortunately, prospective comparative studies (not to speak about randomized ones) comparing the endoscopic (endosonographic), the percutaneous and the surgical approach do not exist [108].

The next step after gaining transluminal access to the retroperitoneal space via cyst drainages has been the transluminal endoscopic removal of infected *pancreatic necroses*; EUS allows for initial access into the cavity and the tract is then expanded by balloon dilatation, followed by endoscope introduction and debris removal with various ERCP accessories. After pilot data with good clinical success [109, 110], a larger multicenter retrospective German study with long-term follow-up was recently presented. Initial clinical success was 73% with 15% significant morbidity and 6% mortality. Of these cases with initial good endoscopic outcome, 77% had good long-term results [111]. Another retrospective study from the same first author (not overlapping) was focused on complications in 50 cases: a rate of 28% severe complications with 12% mortality was reported [112]. Smaller studies presented at DDW 2007 showed similar outcomes [113–115]. Naturally, comparative data with surgical necrosectomy do not exist. Thus, selection of patients for either form of treatment may be biased. Nevertheless, surgical complication and mortality rates after surgery are also substantial and often much higher [116, 117].

Conclusion. Endoscopic/endosonographic cyst drainage is mostly considered as standard for primary cyst drainages in the pancreas if the cysts are adjacent to the upper gastrointestinal wall. Surgery is mostly considered as salvage therapy or for complicated cases. Percutaneous drainages are often used complementary. Due to the complexity of cysts after pancreatitis, a uniform approach cannot be recommended for all cases. Furthermore, there is no comparative evidence from randomized trials. Despite our preference of transluminal drainage, decisions should be made in an interdisciplinary approach, and the limits of this approach clearly be borne in mind.

Therapeutic EUS Helps the Pancreatobiliary Endoscopists

Finally, EUS has developed into an important therapeutic tool in case of conventional ERCP failures [45]. This applies for a small minority of cases in each interventional pancreatobiliary center and requires considerable experience in pancreatobiliary endoscopy and EUS. Recent reviews and case series described this salvage treatment with good, but somewhat variable success rates [118–124]; complication rates were also variable, but in one study up to 31% [122]. Thus, this approach should be weighed against surgical options. In contrast, celiac plexus neurolysis performed under EUS control has been rather well established [125]. In a randomized study presented at DDW 2007, one versus two injections were compared in 51 patients with painful chronic pancreatitis without overall difference between both groups; only in the subgroup of responders was the response longer lasting with two injections [126].

What the role of *EUS-guided radiotherapy* will be is difficult to foresee. In a pilot trial from China [127], radioseed implantation into pancreatic cancer in combination with chemotherapy was reported (not detailed) on 28 cases, with 3 partial remissions, 10 stable diseases and 10 progressions (8 died) [128]. EUS-guided injection of antitumor factors seems to be hampered by the lack of effective new substances and has not yet made substantial progress after the first trials with mixed results [129]. However, scientific interest in this field remains and might show better results in the future [130].

Conclusion. Interesting new options for the pancreatobiliary endoscopists have to be appropriately evaluated and weighed against surgical options. However, it must be kept in mind that these options do not always lead to guaranteed success: sometimes persistence on methods over years may finally also lead to unpleasant (but not totally unexpected) surprises for endoscopists (as seen elsewhere, e.g. endotherapy of chronic pancreatitis) [131, 132].

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