

Quality in pancreatic endoscopic ultrasound: what's new in 2020?

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Abstract

Quality assessment and improvement of an endoscopic service has emerged as a basic component of everyday gastrointestinal endoscopy. In order to ensure a high level of quality, a series of actions must be adopted when performing an endoscopic examination. Nonetheless, quality still remains a qualitative parameter; thus, implementation of specific indicators of quality is warranted. Irrespective of the nature of the endoscopic procedure, quality indicators usually refer to either structural properties of an endoscopy unit (e.g., examination availability), procedural factors (e.g., diagnostic accuracy), or patient outcomes (e.g., occurrence of an adverse event related to performance of an endoscopic procedure). Moreover, they are usually classified into 3 distinct sections, according to the phase of the procedure they relate to: i.e., before, during, and after the examination. The aim of this review is to present measures that need to be adopted in order to reach an optimal quality level during an endoscopic ultrasound examination and to provide up-to-date data regarding the respective quality indicators implicated.

Keywords Endoscopic, ultrasound, quality, quality indicators

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Introduction

Endoscopic ultrasound (EUS) remains the cornerstone of the diagnostic and staging algorithm for various lesions of the gastrointestinal (GI) tract, the abdomen and the mediastinum,

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assisting in the preoperative staging and restaging of GI tumors. The introduction of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA), revolutionized the examination's nature, adding an interventional aspect to its diagnostic core, allowing acquisition of tissue samples even from lesions outside the GI tract (e.g., in the pancreas). This particular feature differentiates EUS from other diagnostic modalities, including computed tomography or magnetic resonance imaging (MRI) [1]. On the other hand, quality indicators have been integrated into everyday GI endoscopy (GIE) practice, aiming to improve endoscopic services, each time taking into account the specific aspects of each patient's disease and pursuing the ultimate goal: to provide optimal medical care [2]. In order to clarify the essence of quality, the Department of Health and Human Services Institute of Medicine (USA), has defined it as "the degree to which healthcare services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge" [3]. During recent years, quality has undergone significant changes, evolving over time into a significant prerequisite that should be met in all endoscopic procedures, implicating not only patients and physicians but also the services of healthcare systems. Interestingly, even among these 3 pillars, quality has a completely different orientation: patients desire to receive high-quality services regardless of cost, whereas clinicians pursue the best possible management, combined with a minimum risk of associated complications, and healthcare systems adopt an internal policy to ensure that the quality of

the services provided remains high. The American Society of Gastrointestinal Endoscopy (ASGE) published the first series of guidelines regarding quality measures in GIE, updated in 2015 [4]. Outside the USA, in a recent publication the European Society of Gastrointestinal Endoscopy (ESGE) has also highlighted quality in GIE, and particularly EUS [5].

Moreover, quality, being *per se* a qualitative parameter, renders any attempt at its objective evaluation rather problematic. Thus, there is a need for surrogate markers that will allow an accurate assessment of any measures taken to enhance GIE and EUS performance in particular. In order to achieve this goal, we have used the so-called quality indicators (QIs), which are tools that enable us to quantify our effort to ascertain quality by evaluating the efficacy of the quality measures implemented during the procedure or, as stated elsewhere, to allow performance of a comparison “between an individual or a group and an ideal or benchmark” [6,7]. QIs may reflect structural conditions of an endoscopy unit (e.g., examination availability), procedure-related factors (e.g., diagnostic accuracy of a given procedure), or final outcomes (e.g., an adverse event related to the procedure) [8]. They are usually classified according to the phase of the procedure with which they are related: pre-procedure, during the procedure and post-procedure (Fig. 1). This classification helps us comprehend the potential impact of the implementation of quality measures in the various aspects of the EUS examination. Approaching these measures, and their respective QIs, using this prism (i.e., pre-, during and post-endoscopy) also allows their critical appraisal, another issue addressed within this review.

QIs in the pre-procedure phase

This heading refers to all potential physician–patient interactions occurring prior to the beginning of the endoscopic procedure. In this phase, the following QIs are included:

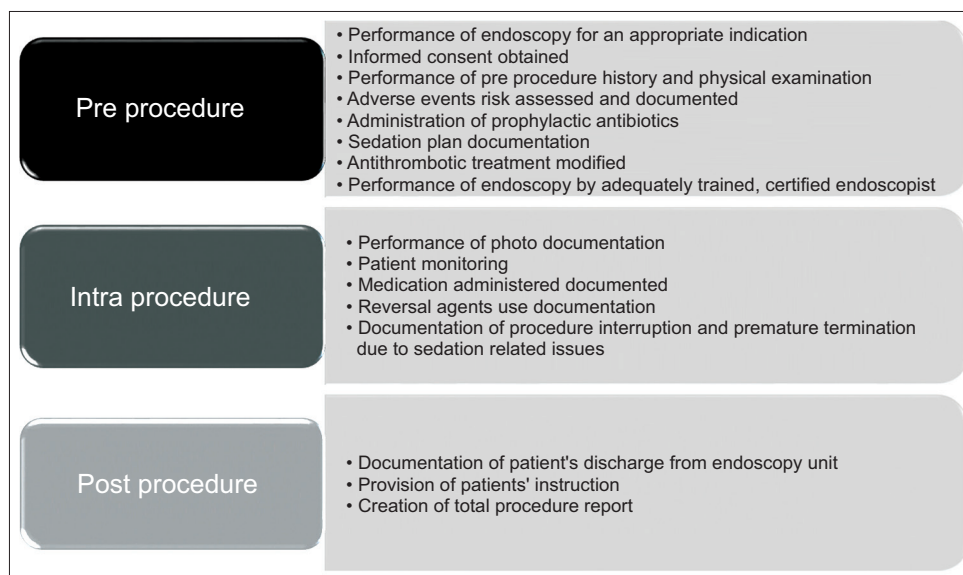


Figure 1 Classification of quality indicators regarding endoscopic ultrasound

Indications for EUS

As a first step, the physician must thoroughly inform patients regarding the procedure's indications, as well as the availability of alternative diagnostic modalities. Not only must an appropriate indication be included in a published standard list and be present in at least 80% of all EUS procedures performed in an endoscopic unit or by an individual, but this indication should also be clearly documented [8]. It should be noted that performing EUS for an indication outside those listed in the aforementioned literature may, under certain circumstances, be an acceptable strategy. However, in that case scenario, the patient should be offered a detailed explanation regarding the rationale that led to this decision and this should also be documented in the report [9,10]. In light of these statements, one apparent condition necessitating the performance (or avoidance) of EUS without strict adherence to an appropriate indication is the issue of local availability, which can exert significant impact on physicians' decision-making according to the availability of resources. For example, EUS could replace MRI when local availability dictates it, e.g., when assessment for potential vascular invasion of a pancreatic head mass comes into question. In case the lesion is deemed operable, EUS-FNA should not be performed, as advocated by the current literature, and the EUS should serve only for diagnosis and/or staging [1,2].

Informed consent form

This phase usually involves a detailed step-by-step discussion between patients and physicians regarding the EUS procedure (this should ideally be conducted for all endoscopic procedures, irrespective of their diagnostic or interventional nature, including informing patients about potential complications). All procedure stages, including

the merits and—equally significant—the potential caveats and complications of EUS, and particularly EUS-FNA, such as bleeding (0-0.5%), infection (<1%) and pancreatitis (0-2%) should be discussed in detail, taking into account the patient's capability to truly comprehend the information provided [11,12]. Although the rates of tumor seeding [13-19] and perforation [20-22] are very low, the possibility of their rare occurrence does exist, and thus should be also known. The patient must not only be aware of all the information related to the examination, but, equally important, should be provided with enough time to raise queries before finally signing the informed consent form (ICF). It is important to note that withdrawal of consent should always be possible, and physicians should anticipate this by providing their patients enough time to do so if this is their wish. A signed ICF should be obtained in at least in 98% of cases [8]. In case specific EUS-techniques are planned, e.g., celiac plexus neurolysis or radiofrequency tumour ablation, additional explanations regarding the specific complications directly linked to these interventions should also be provided [2]. The endoscopist's level of expertise regarding the procedure is also another significant QI. Nowadays, patients deserve the right to know the level of expertise of the performing endoscopist, including his/her complication rate. Although the rate of examinations performed by a fully-trained and certified endoscopist to perform this procedure should reach the cutoff of 98% [8], an optimal and validated threshold that will define the precise level of expertise for EUS remains yet to be determined.

Management of medications

Physicians should always obtain an in-depth medical history, focusing particularly on the use of anticoagulant and/or antiplatelet medication. Specific questions regarding the exact type and dosage of these drugs need to be asked, in order to carry out the appropriate changes on time, prior to the procedure. In case of anticoagulant use, a vulnerable equilibrium must be preserved, where the patient is stratified according to the presumable risk of bleeding associated with the endoscopic procedure, weighed against the potential cardiovascular risk. Moreover, each endoscopic procedure is awarded a low or high risk for complications [12,23,24]. While EUS *per se* is considered a low-risk procedure, EUS with the addition of FNA is listed among the high-risk ones. When performing simple diagnostic EUS, anticoagulants can be safely continued, while only the morning dose on the day of the procedure should be skipped in the case of direct oral anticoagulants (DOACs). Patients receiving warfarin should have their international normalized ratio (INR) checked prior to the procedure; when this is within a therapeutic range the EUS procedure can be performed safely. On the contrary, in cases when EUS-FNA is planned, the severity of the underlying cardiovascular disease will guide the dosing modifications of anticoagulation and antiplatelets. Clopidogrel and prasugrel must be withdrawn 5 days prior to the examination provided the cardiovascular risk is deemed low. If this risk is considered high,

the endoscopist should liaise with the responsible cardiologist to reach the best decision about the patient's favorable outcome. On the other hand, DOACs must be discontinued for 48 h (or 72 h in elderly patients with creatinine clearance <30-50 mL/min). Warfarin can be withheld until the INR returns to the normal range in case of low cardiovascular risk, or replaced by low molecular weight heparin, whenever the cardiovascular risk is high [25]. Puncture of cystic lesions is usually followed by antibiotic administration, acting as prophylaxis for infectious complications. Although this policy has been integrated into everyday worldwide clinical practice, its efficacy remains questionable, given the fact that the actual risk for infection remains very low (less than 1%) [26]. The latest ASGE guidelines suggest the use of prophylactic antibiotics only in cases of EUS-FNA of mediastinal and pancreatic cystic lesions; however, this was merely a weak recommendation, underlining the fact that data from prospective, randomized studies were lacking [27]. Indeed, the very first randomized trial evaluating the effect of antibiotic prophylaxis on the incidence of pancreatic cyst infection after EUS-FNA was only published very recently [26]. In this multicenter, randomized, non-inferiority trial conducted in Spain, prophylaxis with ciprofloxacin was compared against placebo administration in patients undergoing EUS-FNA for pancreatic cystic lesions. Among the 226 patients randomized, only 1 patient (in the placebo group) developed an infection (0.87%), while the incidence of infections did not differ significantly with or without ciprofloxacin prophylaxis. This finding is in line with the results reported in previous retrospective studies, all of which confirmed that antibiotic prophylaxis is not necessary [28-31]. In light of this emerging evidence, forthcoming guidelines should perhaps reappraise this particular statement. On the other hand, studies of the need for antibiotic prophylaxis before through-the-needle biopsy of pancreatic cystic lesions are warranted and welcome.

QIs during the procedure

This period is usually defined as extending from the time sedation is administered until the endoscope is removed from the patient [2]. EUS is usually performed in the context of special indications, aiming to provide specific answers. Besides the delineation of subepithelial tumors, which is a major indication for EUS, though not of the pancreas, EUS is most frequently performed for tissue sampling and tumor staging, when pancreatobiliary malignancies are in question [32]. Therefore, QIs concerning this time interval involve successful lesion sampling rates, accurate malignancy staging and identification of all anatomical structures [8]. Adequate tissue sampling can be evaluated only by rates of successful lesion sampling. Diagnostic rates for malignant tumors should be at least 71% in the case of adenocarcinoma of the pancreas [33,34] and even higher for nodal involvement (percentages up to 87% have been reported for nodal sampling in esophageal cancer) [35-37]. Although difficult to measure, the endoscopist's personal performance should be at least non-inferior to the abovementioned targets. To

facilitate this, the ROSE (rapid-on site evaluation) method can be adopted, which involves an immediate in-room first evaluation of the samples by a present cytopathologist to ensure adequate material has been obtained. In case ROSE is not available, a minimum number of punctures from the lesion evaluated should be performed (e.g., 5-7 needle passes for pancreatic adenocarcinoma) [9]. However, the latter might be refuted by recent, real-world data suggesting that even 2 needle passes in EUS-FNA of solid pancreatic lesions can provide sufficient tissue to facilitate a diagnosis, with no significant incremental tissue yield if 3 passes are performed [38]. To make things even more challenging, evidence regarding the superiority of any specific technique for sampling pancreatic masses is currently limited and somewhat conflicting. In a recent network meta-analysis, no specific EUS-guided tissue sampling technique was found to be superior in terms of diagnostic accuracy, sample adequacy, or histologic procurement rate for solid pancreatic masses, irrespective of different needle types (FNA vs. fine-needle biopsy [FNB]), or needle sizes (19-G vs. 22-G vs. 25-G) that were compared [39], although FNB has been proven to outperform standard FNA when it comes to the sampling of sub-epithelial lesions [40]. Thus, this statement is likely to be reappraised with the advent of newer FNB end-cutting needle designs (i.e., Acquire, Boston Scientific Corp, Natick, Massachusetts, United States or SharkCore, Medtronic, Minneapolis, Minnesota, United States) [41,42].

Another significant issue is tumour staging, where depth of invasion and presence of pathological lymph nodes must be adequately clarified. The TNM staging system should be always used and documented, as EUS is the optimal diagnostic modality to evaluate the “T” and “N” parameters of this classification, at the cost of low sensitivity for distant metastases (i.e., the “M” parameter) [43-45]. Documentation percentage of the relevant structures (those representing the target of each specific procedure) is the first QI. The endoscopist should be able to accurately recognize relevant structures in at least 98% of the cases and, if possible, to provide images that illustrate the findings (Fig. 2, 3A,B). Moreover, the use of the Doppler feature, with which modern electronic echoendoscopes are endowed, provides us with the possibility to better demonstrate such structures. For example, Doppler ultrasound can clearly differentiate a vessel from a dilated duct and thus provide reliable and non-questionable image documentation (Fig. 4A,B). As far as subepithelial masses are concerned (as stated above, this is a less common indication when it comes to the pancreas) the specific layer from which the lesion arises should always be identified and recorded in appropriate images. In these images, the size and specific morphological features of the mass under evaluation should be clearly delineated [8]. Provision for adequate sedation holds a cardinal role in any type of GIE, as it increases patient compliance, facilitating the performance of a detailed procedure, and contributes to better patient satisfaction and willingness to undergo endoscopic procedures. QIs regarding sedation include evaluation of the following parameters: frequency of routine vital signs monitoring during sedation,

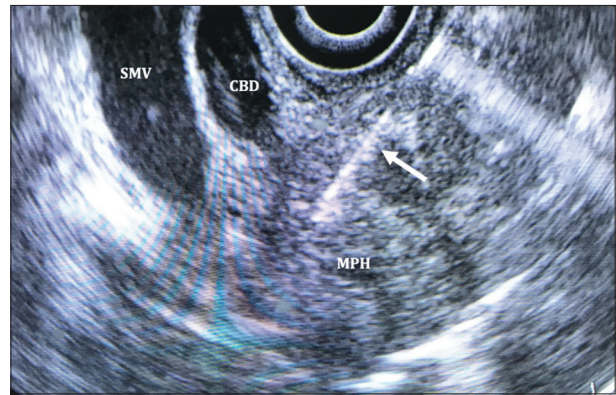


Figure 2 Endoscopic ultrasound-guided fine-needle aspiration of a mass in the head of the pancreas of a patient with lung cancer. The image clearly demonstrates the needle located within the mass (arrow), as well as relevant structures, including the mass in the head of the pancreas (MPH), the dilated common bile duct (CBD) and the superior mesenteric vein (SMV). Cytological examination of the acquired specimen revealed metastatic lung cancer

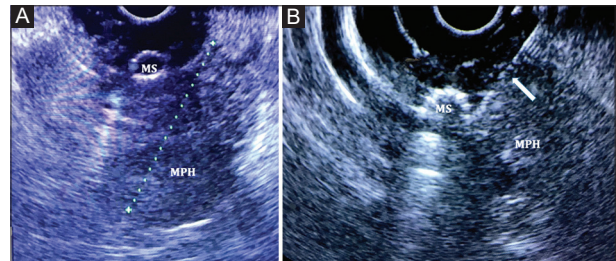


Figure 3 (A) Endoscopic ultrasound demonstrating a 3.5-cm hypogenic mass in the head of the pancreas (MPH). Because of obstructive jaundice, a metal stent (MS) had been placed in the patient’s common bile duct a few days before. (B) Endoscopic ultrasound-guided fine-needle aspiration of the mass in Fig. 3A. Note the needle located within the mass (arrow), as well as relevant structures, including the mass (MPH) and the biliary metal stent (MS). Cytology of the acquired specimen revealed pancreatic adenocarcinoma

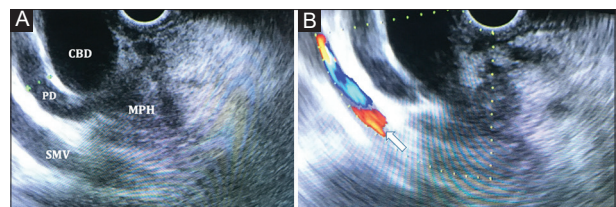


Figure 4 (A) Endoscopic ultrasound demonstrating a 2-cm hypogenic mass in the head of the pancreas (MPH) causing dilation of the common bile duct (CBD) and the pancreatic duct (PD) (double-duct sign). Note the superior mesenteric vein (SMV), which is clearly differentiated from the dilated PD by the flow depicted in color (arrow) when Doppler ultrasound is used (B)

recording of dose and administration route of medication(s) being administered, use of reversal agents, and interruption or premature termination of the examination due to sedation-derived complications [8].

QIs after the procedure

Several measures equally important to all previous QIs are included here, contributing to the procedure's quality: (a) identification and proper management of potential adverse events; (b) explaining the examination's findings to the patient and providing informative and adequate instructions for the direct post-endoscopy timeframe; (c) management of medications, and particularly antiplatelets/anticoagulants, after the examination; and (d) in case of histology/cytology acquisition, information regarding its follow up.

Adverse events related to EUS remain relatively rare, especially if no EUS-FNA or EUS-guided biopsy has been undertaken [12,46]. Nevertheless, endoscopists should always be able to recognize them promptly and deal with them effectively. The saying that "the worst complication in GIE is non-recognition or denial of a complication" seems to fit perfectly in this setting, and especially for pancreatobiliary GIE, including EUS: complications like bleeding and pancreatitis are usually mild and self-limiting, requiring no specific management. Although perforation seldom occurs, actions must be taken immediately, in order to ensure the best outcome for the patient [47,48]. As with all other endoscopies, patients must be informed in detail by the endoscopist regarding the examination's findings, as well as the impact these findings could have on their subsequent diagnostic and/or therapeutic path. This measure may seem relatively simple and straightforward; however, existing evidence points in the opposite direction. Various reasons could be held accountable for this phenomenon, primarily linked to organizational factors; it is commonplace among large referral centers that, because of an immense workload, there is literally "no time to explain" the findings to the patient. Moreover, the organization of healthcare systems could also contribute. For example, patients in several systems may be referred for GIE from general practitioners, who also theoretically carry the burden of informing the patient. This, however, can be rather burdensome for the non-specialist, especially when it involves providing further clarifications of complex and sophisticated examinations, as is the case for EUS. From the patient's point of view, rapid doctor-patient communication concerning the results of cytopathology or histology has demonstrated its value as an extremely important QI, even more significant than a good long-term relationship with the endoscopist [49]. However, real-world experience has shown that in everyday practice, things can be totally different. Moreover, providing the patient with fundamental postprocedural information is mandatory, including the avoidance of driving and/or intense physical activity, given their potentially fatal consequences. The vast majority of medications can usually be resumed safely in most cases of EUS or EUS-FNA after the examination, although when bleeding is suspected, following an individualized approach seems to be a sound practice [50,51]. As well as informing the patient about the procedure's findings, as mentioned above, the endoscopist also has the responsibility for receiving and interpreting the pathology/cytology results. As already outlined, EUS is performed with a specific clinical

question in mind. The answer to this question can be rather challenging in many cases; for instance, EUS-FNA has a low negative predictive value for differentiating pancreatic cancer from chronic pancreatitis with a pseudotumoral mass, which reaches almost 73.9% [52]. Here, the endoscopist is the one who should be called upon to interpret the findings in a particular context and to decide whether repeating the negative EUS-FNA, recommending another diagnostic modality, or simply performing clinical follow up accompanied with imaging could be the best strategy in a given case. When a repeat procedure is decided upon, EUS-guided core biopsy, instead of "classical" EUS-FNA aiming at cytology sampling, could also be considered as an attractive alternative (e.g., in the aforementioned study, EUS-guided core biopsy led to an increase of the examination's negative predictive value up to 87%). Cooperation with the cytopathologist/pathologist, as well as other medical specialists involved in each and every case (radiologists, internists or surgeons) may also lead to improvement in the clinical decision. Finally, a QI that usually remains underrated is that of the patient's satisfaction. This QI is indeed a pivotal one, that in many cases is totally neglected by endoscopists or other physicians involved in the patient's management. This attitude however, should change and actually is being reconsidered. In fact, this QI not only refers to sedation and post-procedural pain issues, but at some point also reflects the effect of most of the quality measures applied during the entire procedure, as well as the general management by the attending physician [53,54].

Concluding remarks

This review has presented a point-by-point description regarding the definition of the various quality measures that should be taken when performing EUS and has discussed the QIs related to them. Moreover, it has highlighted some of the most important ones, especially those most commonly used in everyday clinical practice. Clinicians should at all times keep in mind that these QIs are not part of a theoretical check-list for research studies only, but should rather be considered as a useful roadmap to guide us through uncharted areas of our everyday clinical practice, in an attempt to improve our patients' outcomes.

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