Indetermination of indeterminate biliary strictures

To the Editor:

We have read with interest the study by Gerges et al[1] and would like to express our concerns.

The authors demonstrated a significantly higher sensitivity for malignant biliary stricture (MBS) diagnosed by digital single-operator peroral cholangioscopic (digital SOC)–guided biopsy over ERCP-guided brushing in patients with indeterminate biliary stricture (68.2% vs 21.4%; $P < .01$). Practically, indeterminate biliary stricture usually refers to a stricture that does not have an obvious mass on cross-sectional imaging, and ERCP with standard tissue sampling by transpapillary biopsy and/or brushing (TPB)[2,3] fails to confirm. Therefore, in this study, patients who had suspected MBS based on MRCP only without prior ERCP might not reflect the population referred with indeterminate strictures. In our perception, they should be called "highly suggestive for MBS" instead. Furthermore, the authors excluded those who underwent prior ERCP with TPB, and many previous studies have referred them as "true indeterminate structure."[4-6] Moreover, in their Table 3, there were 11 patients whom the authors reported as having "indeterminate" results after the determined procedure.[1] A previous review of fiberoptic SOC demonstrated a lower diagnostic odds ratio for MBS diagnosis in a "true indeterminate stricture" subgroup compared with the overall diagnostic odds ratio (46 vs 66).[7] Therefore, the results of this study might not be applicable to patients with "true indeterminate biliary stricture." Owing to the high cost of digital SOC, using it during the first ERCP session without an attempt at TPB may not be cost effective. Previous data showed the reported sensitivity of conventional TPB for MBS diagnosis to be as high as 59%,[8] compared with the much lower result in this study (21.4%). This, in turn, could make the performance of digital SOC–guided biopsy to appear relatively higher.[1] In our opinion, the decision to use digital SOC either after the indeterminate TPB result or during the first ERCP is still debatable.

DISCLOSURE

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Response:

We thank Drs Kulpafcharapong and Rerknimitr[1] for their important comments on our study.[2] An indeterminate biliary stricture can be defined on the basis of cross-sectional imaging appearance, on the basis of sampling, or on both. The aim of our study was to identify the comparative accuracies of single-operator cholangioscopy (SOC)-guided biopsies and ERCP-based transpapillary brushing (TPB) on the basis of an indeterminate stricture on cross-

sectional appearance alone. To determine which sampling modality has higher accuracy at first intervention, we excluded patients who had previously undergone TPB. Because of the major differences in treatments constituting endoscopic intervention, medical treatment, extensive surgery, and palliation, a correct diagnosis, preferably at first ERCP, is crucial for the patient's prognosis and treatment.[2] In addition, it may be unethical to randomize patients who have an indeterminate stricture after TPB to yet another round of TPB. Furthermore, the visual interpretation of digital SOC may potentially be affected if there has been prior intervention such as TPB. To clarify which diagnostic modality is superior at first intervention, we thought we needed to exclude patients with prior TPB/sampling. Furthermore, it is difficult to compare the sensitivity of TPB in our study with that in other studies because they were not necessarily controlled or prospective and were often based on an older-generation imaging platform.

We agree that ERCP with TPB may still be a standard procedure in many units in those cases, but we are not sure, looking at the currently published and very promising results of SOC-guided biopsy examinations, whether that will remain the case for this selected group of patients.[2-10] The pooled sensitivity in the review cited by Drs Kulpafcharapong and Rerknimitr[1] showed results below 50% with no significant difference between transpapillary brushing (45%) and biopsies (48%).[11] This review included several mixed populations (pancreatic cancer, ampullary adenocarcinoma, and cholangiocarcinoma), and the authors themselves stated that they could not tell "specific sensitivities of the modalities in detecting different malignancies…."[11] Therefore, the authors are concerned that we studied the wrong population, while at the same time referring to studies that combined many different populations. Looking even deeper into this review, we can see that the 2 largest patient cohorts included had a sensitivity for brushing of only 35% and 26%.[11] In addition, we believe that a procedure with a sensitivity that is lower than the chance of flipping a coin cannot determine or define a "true" indeterminate stricture. Thus, to be absolutely correct in our study, the stricture is indeterminate at the level of cross-sectional imaging, inasmuch as we already here cannot say whether it is malignant or benign and remains indeterminate if the first procedure fails (see Table 3 in the article by Gerges et al).[2]

Regarding the systematic review by Navaneethan et al,[8] we would like to emphasize several important points. A comparison of fiberoptic SOC data with digital SOC data is not really applicable because these are 2 very different devices, and the diagnostic odds ratio in that review mentioned by Kulpafcharapong and Rerknimitr[1] was applicable for only 4 of the investigated 10 studies. Besides, the authors of that review themselves state that only 1 included study compared the yield of SOC biopsies in a paired cohort design with standard brushings and biopsies. In this study, SOC biopsies had a sensitivity of 76.5% compared with brushings (5.8%) and biopsies (29.4%).[3,8] Looking at this study, in particular, one can ask what value a definition has if the results in 94.2% of the population still remain unclear after the defining procedure. Would it not be more correct to define it as indeterminate from the beginning?

Looking deeper into the published data, we believe that our findings reflect our personal experience in patients with intrinsic biliary strictures and confirm previous published experiences alike. We believe our study demonstrates that the utility of digital SOC for indeterminate strictures and that further studies, including those of cost effectiveness, will help to establish its exact role in the diagnosis of indeterminate strictures.

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Adverse events of lumen-apposing stents for pancreatic fluid collections: opening Pandora's box

To the Editor:

We read with great interest the article by Fugazza et al,[1] retrospectively evaluating the occurrence of adverse events (AEs) in 304 patients with pancreatic pseudocysts (PCs) (153) and walled-off necrosis (WON) (151) treated with lumen-apposing metal stents (LAMSs). Seventy-four (24.3%) patients experienced 79 AEs, of which bleeding (22), stent migration (20), stent occlusion (14), and infection (19) were the most frequently observed. At multivariate analysis, WON and lack of pneumatic tract dilation were the only statistically significant risk factors associated with AEs.[1]

The high rate of AEs observed raises some serious considerations about the use of LAMSs in patients with both PCs and WON, especially in view of the lack of well-designed studies that can guide their proper use in this clinical setting.[2-5] Indeed, it opens Pandora's box, with many unanswered questions suddenly coming out: (1) Which stent should be used in both PCs and WON? (2) Are LAMSs cost effective in the treatment of PCs and WON? (3) Which stent size should be used for both PCs and WON? (4) Which patients with WON should undergo direct necrosectomy through the LAMS? (5) Should a double-pigtail stent be placed through the LAMS to avoid bleeding once the collection is resolving?

In the only available randomized controlled study published so far comparing double-pigtail stents versus LAMSs in patients with WON, treatment success, clinical AEs, readmission, and length of hospital stay were similar in both groups.[6] However, stent-related AEs and procedural costs were significantly higher in the LAMS group.

The time for large randomized controlled studies has thus arrived to close back Pandora's box and find the best solutions to reach the highest clinical success rates with the lowest AEs, and in the most cost-effective way in patients with both PCs and WON.

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