Follow-up of Barrett's epithelium after ablation by endoscopic argon plasma coagulation

To the Editor:

We read with interest the article by Schultz et al.1 on ablation of nondysplastic Barrett's epithelium by endoscopic argon plasma coagulation in combination with high-dose omeprazole. Using APC and acid suppression with 120 mg/day of omeprazole, they obtained complete ablation of Barrett's epithelium in all but 1 of their 70 patients and, adapting the acid suppression to obtain cumulative reflex time of less than 7% per 24 hours, they did not observe relapse of Barrett's epithelium after a median follow-up of 12 months.

We found these results impressive, especially in comparison with those of other studies2,3 of the same treatment modalities except for a lower dose of omeprazole during the treatment. One should be extremely careful before recommending APC as a promising new treatment modality for patients with nondysplastic Barrett's epithelium based on the fact that it is effective and safe with regards to short-term results. Indeed, having had the opportunity to treat 40 patients starting 6 years ago, we now observed in 1 of them, 18 months after eradication, the development of an adenocarcinoma that arose beneath the new squamous epithelium.4 There are therefore two major concerns about the use of this technique. First, we do not know the long-term outcomes of this treatment modality, which is not devoid of potential complication. Second, the new squamous epithelium might hide the development of a small cancer from the endoscopist, making the diagnosis at an early stage more difficult.

Therefore, we think that it is clearly too early to recommend this modality as a routine treatment, and it should still be performed only in the setting of well-designed clinical trials that include careful endoscopic follow-up.


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References


Response

We totally agree with Drs. Eisendrath, van Laethem, and Devière that at present endoscopic argon plasma coagulation (APC) cannot be recommended as a routine technique, and that the value of this technique should be evaluated in adequately designed clinical trials with long-term follow-up. We clearly stated in our discussion\textsuperscript{1} that APC—although it is without doubt a promising technique—has to be regarded as an experimental method at this point. We also discussed the critical issue of possible residual metaplastic epithelium underneath the regenerated squamous epithelium, and emphasized the importance of long-term surveillance endoscopies with rigorous biopsy procedures.

We read with interest the observation by Eisendrath et al. of a patient who developed intramucosal adenocarcinoma of the esophagus 18 months after APC treatment of nondysplastic Barrett's esophagus,\textsuperscript{2} which is the first report as far as we know. Others have shown in the meantime that genetic abnormalities in patients with Barrett's esophagus with low-grade or high-grade dysplasia may increase after photodynamic therapy.\textsuperscript{3} Interestingly, in the particular patient reported by van Laethem et al.,\textsuperscript{2} remaining metaplastic glands had been detected at the end of APC treatment, apparently in the area where the carcinoma had developed. Possible explanations for this finding include dysplastic epithelium that was missed at the initial endoscopy and later during follow-up examinations, although the investigators performed 4-quadrant biopsies at 2-cm intervals. It is also noteworthy that neither in the first publication\textsuperscript{4} nor in the recent case report\textsuperscript{2} was the applied energy of APC described. As in our study,\textsuperscript{1} others have shown\textsuperscript{5} in the meantime that a high-power setting for APC (70-90 W) in combination with high doses of omeprazole (60-120 mg daily) may lead to complete restoration of squamous epithelium without detection of underlying metaplastic epithelium. This supports our contention that a high-energy APC and complete acid suppression might be crucial to avoid residual metaplastic epithelium.

Meanwhile, our study population of patients with Barrett's esophagus treated with APC consists of 129 patients with endoscopic-histologic follow-up of up to approximately 6 years (median follow-up approximately 2.5 years). Endoscopies including quadrant biopsies are regularly performed at 12 month-intervals. So far, we have not detected any case of metaplastic glands underneath squamous epithelium (except the one patient described in the original report),\textsuperscript{1} nor any dysplasia or carcinoma (manuscript in preparation).


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References


EUS and the prediction of gallbladder neoplastic polyps: Are polyps of 5 to 15 mm diameter really a homogenous group?

To the Editor:

We read with interest the article by Choi et al.1 entitled, “A new strategy to predict the neoplastic polyps of the gallbladder based on a scoring system using EUS.” The messages of this study are that echo pattern rather than the size of polypoid lesions is important in the differential diagnosis of gallbladder polyps, and that EUS should be included in the work-up of the majority of patients with gallbladder polyps.

It has been our practice that a gallbladder polyp exceeding 10 mm in diameter is an indication for an elective cholecystectomy and that smaller polyps are subjected to regular follow-up. If we take the recommendation offered by Choi et al.,1 we can certainly avoid unnecessary cholecystectomies in patients with polyps larger than 10 mm in diameter and we may pick up some neoplastic lesions among polyps 10 mm or smaller in diameter.

We would like to make a point here. The chance that a polyp of 5 to 10 mm diameter is neoplastic is 28.9% (11 of 38) according to the data of Choi et al.1 and 19.1% (4 of 21) according to the data presented by Sugiyama et al.2 This means that 70% to 80% of patients having polyps of 5 to 10 mm in diameter could undergo an unnecessary EUS, which is expensive, operator-dependent, and uncomfortable for patients. Moreover, we do not know the natural history of small adenomas in the gallbladder. It may not be too late in the natural course of this lesion if EUS is selectively performed in patients with 5 to 10 mm polyps that exhibit growth and changes in echo patterns and shape on follow-up transcutaneous US examinations.

The cost effectiveness of this strategy should be compared with that of performing EUS as soon as a polyp of 5 to 10 mm in diameter is found. Choi et al.1 state in their results that there was no significant difference in the risk of neoplasia for polyps of 5 to 10 mm in diameter compared with those 10 to 15 mm in diameter, even when the results obtained from the reference group and the validation group were combined. The risk of polyps of 5 to 10 mm in diameter being neoplastic was 28.9% (11 of 38) and that of polyps of 10 to 15 mm was 54.8% (17 of 31). According to our statistical calculation, however, this difference was significant by Fisher exact test ($p = 0.048$) but not by chi-square test ($p = 0.053$). This may indicate that the risk of polyps being neoplastic is different between polyps 5 to 10 mm and those 10 to 15 mm in diameter. Therefore, it seems necessary to identify a high-risk group among patients with polyps between 5 to 10 mm in diameter by using clinical data in order to arrive at a more specific indication for EUS.

Another point concerns the design of the study of Choi et al.1 To validate the usefulness of their new EUS scoring system, all patients with EUS scores of 6 or more should have undergone surgery and all patients with EUS scores of 5 or less should have been followed. Then the accuracy of their EUS scoring system should have been determined by comparison with the histopathologic data for polyps with EUS scores of 6 or more and with the follow-up data for those with EUS scores of 5 or less, as was done by Sugiyama et al.2 In the study of Choi et al.,1 however, the data for the validation group were collected retrospectively.

Obviously, Choi et al.1 have provided us with a clinically relevant guide for the management of gallbladder
polyps. However, the management of polyps between 5 to 10 mm in diameter seems to remain controversial.


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References


Response

We appreciate the interest of Chung et al. in our article. Recent advances in US and its widening clinical application have made it possible to detect small polypoid lesions in the gallbladder. Although gallbladder cancers are associated with a poor prognosis, the outcome for early stage cancers has been favorable. An adenoma to carcinoma sequence has not been clearly demonstrated for gallbladder adenoma, unlike the sequence from polyp to cancer that occurs in the colon. But, a transition from benign adenoma into carcinoma has been detected histologically. Furthermore, Ishikawa et al. asserted that sessile polyps, even those less than 10 mm in diameter are likely to be malignant and occasionally invade the submucosal layer, and therefore these lesions should be resected. Therefore, it is important clinically to establish criteria for the diagnosis of neoplastic gallbladder polyps.

Sugyama et al. reported that EUS is highly accurate for the diagnosis of polypoid gallbladder lesions. These investigators recommended that EUS be used when transabdominal US cannot rule out a neoplastic lesion. Therefore, our study was designed to clarify the features of neoplastic and non-neoplastic polyps and to develop a method to predict neoplastic polyp of the gallbladder by EUS.

We agree that EUS is expensive, operator dependent, and uncomfortable for patients. Our data are based on EUS variables that can be assessed by conventional US. Thus if conventional US can provide sufficient resolution equivalent to EUS, it is not necessary to perform EUS in all cases. The scoring system can also be applied to transabdominal US. But EUS is considered to be superior to conventional US for imaging the gallbladder and has a low rate of complications. Furthermore, most of the referrals to tertiary centers are for precise evaluation of gallbladder polyps and therefore EUS is a valuable imaging technique in these cases in which the picture is not that of a typical cholesterol polyp or cancer by conventional US. In our institution, the cost of standard US and EUS is not so different. Moreover, EUS can provide information about the stomach and duodenum. Thus the cost of EUS and transabdominal US is comparable in some institutions. Nevertheless, EUS does cause discomfort for patients. After the initial EUS characterization of the polyp, however, it is possible to follow the patient with transabdominal US by using EUS-derived data and clinical findings.
We agree that because our data were collected retrospectively, bias is a possibility. As mentioned in our conclusions, the optimal treatment strategy for gallbladder polyps may not be settled conclusively until we have long-term follow-up of patients who do not undergo surgery.


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References


Self-expanding metal stents for the treatment of benign esophageal strictures

To the Editor:

Fiorrini et al. reported the use of self-expanding metal stents for the treatment of benign esophageal strictures. They concluded that self-expanding metal stents may be a useful alternative to repeated dilation in patients with refractory strictures. However, we would like to sound a note of caution.

The mean follow-up for their 10 patients was 17 months. However, only 2 patients were followed for more than 2 years and 1 of these patients developed a new stricture.

Are metal stents safe for long-term usage? We have used metal stents in 3 patients with benign esophageal strictures, which were resistant to conventional treatment with regular dilation and acid suppression. One of these patients, a 67-year-old man with diabetes and a benign peptic stricture, had an Ultraflex stent (Boston Scientific, Ltd., St. Albans, U.K.) inserted after we were unable to achieve reasonable swallowing with frequent dilations and acid suppression with proton pump inhibitors. Two years after insertion of the stent he was admitted with a torrential upper GI hemorrhage from which he exsanguinated. At post mortem the upper part of the stent was found to have eroded through the esophageal wall and into the aorta.
A further patient has redeveloped a stricture after insertion of an Ultraflex stent for a caustic stricture 2.5 years after the initial stent was inserted.

Clearly, metal stents may be useful in the management of refractory benign esophageal strictures. However, the need for these stents to remain in situ for much longer periods of time compared with stents that are placed for malignant stricture indicates that prolonged follow-up is necessary to determine whether metal stents may be used safely for long periods.


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Reference


Response

We read with interest the letter by Catnach and Barrison with their comments about the use of metallic stents in benign esophageal strictures. We have stressed in our article\(^1\) that this therapeutic approach must be used only in refractory cases in which conventional treatment is unsuccessful and the patient is not a candidate for surgery. We also have indicated that the etiology of the stricture must be considered when selecting patients because we found that the results of the use of metallic stents in postradiation strictures were better and there were no associated complications. The case of exsanguination presented by Drs. Catnach and Barrison is very impressive. However, in our series\(^1\) and in others\(^2\) no similar case was reported. Most complications were stent migration or restenosis. For our patients, mean follow-up is now around 26 months and although most patients have had their stents in situ for more than 2 years, no new complications have been encountered.

Are metal stents safe for really long-term usage? No one can answer this question. In our experience, it seems to be so. Most complications were treated successfully and it seems to us that complications are not time-related. Even the fatal complication reported by Drs. Catnach and Barrison was probably not related to time but probably related to other conditions that are not evident.

Again, we totally agree with Drs. Catnach and Barrison that caution should be exercised when considering the use of metal stents in benign esophageal strictures.


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Is ERCP a procedure for all, the majority, or just a few endoscopists? A dilemma

To the Editor:

I read with great interest the article by Choudari et al.\textsuperscript{1} on the experience of a referral center with respect to ERCP performed after a previously unsuccessful attempt at another institution. Emphasis must be placed on success and complication rate for ERCP procedures in this period of managed care, and selected patients should be referred to a center of excellence. Articles such as that by Choudari et al.\textsuperscript{1} that prospectively analyze data pertaining to referred patients in a leading pancreaticobiliary center are therefore welcome.

An important factor with respect to enhancing success rates and lowering complication rates is a reconsideration of the indication for the procedure. Because ERCP no longer has an important role in the diagnosis of biliopancreatic disease, most patients who require a diagnosis alone need not undergo the procedure. In fact, Choudari et al.\textsuperscript{1} report major and severe complications occurring in patients with the indication of abdominal pain or pancreatitis compared with the group with biliary obstruction or bile duct stones. A 14\% rate of normal ERCP findings is an unusual result for a second attempt at ERCP at a referral center. Moreover, the fact that sphincter of Oddi dysfunction was present in 44\% of patients may indicate selection bias with respect to the specific interests and expertise of this group. Therefore, the indications for the procedure may be questioned, and the case-mix reported by these investigators does not mirror that generally observed by other referral centers.

A prospective study would provide more information. Choudari et al.\textsuperscript{1} report factors contributing to failure of the prior ERCP in only 27\% of cases. It is surprising that duodenal diverticulum and overhanging duodenal folds, which are not considered to be especially difficult technical problems by experienced biliopancreatic endoscopists, account for almost all previous failures, whereas Billroth II or Roux-Y gastrojejunostomy were present in only 1.8\% of their referred patients.\textsuperscript{2-4} Choudari et al.\textsuperscript{1} do not provide information as to the number of referral sources, the level of experience with ERCP of the referring endoscopists, the number of such referrals per year, or the number of referrals sent by these referring physicians to other centers. Presumably, there may be more than one physician performing ERCP at a single referring institution, and the relative experience of these physicians, one compared with the others, is not given.\textsuperscript{5} It would also be helpful to know whether the referral was made after one or more than one unsuccessful ERCP because it is well known that a second attempt at the referring institution increases the success rate.\textsuperscript{6} It would also be important to know what type of sedation and/or analgesia was used for the initial attempt(s) at ERCP as well as for the successful ERCP at the referral center. Last, it would have been useful if Choudari et al.\textsuperscript{1} had included a difficulty level or scale for the referral procedures.

ERCP can be divided into 3 phases: reaching the papilla, diagnosis, and therapy. It is surprising that only patients in whom the first and second phases alone were unsuccessful were referred, and no referrals were made because of an unsuccessful therapeutic procedure. It is also surprising that access to the desired duct was achieved at the second attempt with a simple catheter rather than advanced techniques. This would

References


appear to confirm the usefulness of a second attempt at ERCP at the referral source institution before sending the patient to a center.\textsuperscript{6}

ERCP is increasingly becoming a complex therapeutic procedure. The increasing competition offered by other diagnostic or therapeutic procedures emphasizes the need to maintain optimal outcomes levels. ERCP should be performed by an endoscopist whose experience and success predictably will be the highest, especially in difficult cases. Both the number of ERCPs and the indications for the procedure have significantly changed over the last few years. But it is obvious that it is extremely important to perform sufficient numbers of ERCPs to ensure an acceptable outcome. The dilemma, then, is whether ERCP should be an endoscopic procedure for all endoscopists, the majority, or just a few highly experienced individuals. This dilemma continues to await resolution.\textsuperscript{9-11}


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References


Response

We thank Dr. Mosca for his comments about our work. When an attempt at ERCP is unsuccessful, there are several options to consider depending on the indication for ERCP. Our study focused only on the value of repeating the ERCP in a center where advanced skills in this technique are available. For patients presenting with biliary obstruction, some physicians might choose surgery, a primary percutaneous approach, or a combined percutaneous-endoscopic procedure to alleviate the obstruction. However, in the setting of pancreaticobiliary-type pain or idiopathic pancreatitis, sphincter of Oddi manometry performed at ERCP is the best-studied and most appropriate evaluation. Clearly a referral bias exists and will depend not only on the physician’s recommendations to the patient and the expertise in the referring physician’s center to perform alternative interventions, but also on the patient’s decision to travel (frequently) far from the support of family and friends. We would be surprised to find significantly different referral populations for a second-attempt ERCP in other centers where expertise in manometry is available.

Dr. Mosca suggests that a 14% rate of normal ERCP findings is high for a second-attempt ERCP at a referral center. However, 76% of the group of “normal studies” were referred for suspected sphincter of Oddi dysfunction. The published data are clear that 30% to 50% of patients undergoing manometric evaluation will have a normal study depending on their clinical presentation (pancreatitis or pancreaticobiliary pain), sphincter of Oddi dysfunction classification type, and whether one or both sphincters are studied. Thus, Dr. Mosca should not equate the 14% rate of no demonstrable pathology with a suboptimal indication for the procedure. We agree with Dr. Mosca that ERCP alone (i.e., without manometry) is rarely used to make a diagnosis given the safety and efficacy of competing imaging technologies. In virtually all patients referred for the second-attempt ERCP, our goal was a therapeutic intervention.

In the United States, endoscopists with variable training and experience perform ERCP. What may seem challenging to one endoscopist may not be so for another. The 27% rate of identified factors possibly contributing to ERCP failure was what we perceived as the potential difficulty for the referring physician. Most of our referring physicians do not attempt ERCP when there is complex altered surgical anatomy such as Billroth II, Roux-en-Y gastrojejunostomy, and Whipple procedures; these patients, therefore, would not be included in this study.

We would like to clarify the term “second-attempt ERCP.” Many patients referred for another ERCP already have had more than one attempt by one or more endoscopists with variable expertise. The difficulty of the procedure for us can be discerned by reviewing Table 3, which reveals that 41% of patients required advanced techniques for cannulation. More than 95% of the patients in this series were referred by physicians who refer all of their patients who require a second-attempt ERCP to our institution. However, it is important not to equate the number of referrals with the number of failures as a physician might choose an alternative to repeating the ERCP. With rare exception, the procedures were done with the patient under conscious sedation in both the referring institution and our institution. We agree that knowledge of the referring physician’s ERCP failure rate (as it relates to their experience and skill with ERCP), alternatives chosen, and patient outcomes would be of great interest. This is being addressed in an ongoing study by our group that looks at the ERCP practice patterns in the community.

Our study evaluated failures of cannulation rather than failures of therapy. It is obvious that without a successful cannulation, endoscopic therapy is not possible. We agree, however, that an equally important study would be one that addresses outcomes for the second attempt at endoscopic therapy.

Our main conclusion was that referral for a second-attempt ERCP to a center with expertise in ERCP warrants...
consideration given the high success rate with an acceptable complication rate. In the United States, it is highly unlikely that ERCP will ever be restricted to experts. Physician practice patterns and patient wishes will likely be the most important determinants in the “next step” for a patient with an unsuccessful ERCP.


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