Response

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Considerations on intraductal fully covered self-expandable metal stent in treatment of biliary anastomotic strictures after liver transplantation

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To the Editor:

We read with great interest the recent study by Sissingh et al[1] and congratulate the authors on publishing impressive results on the advantages of intraductal fully covered self-expandable metal stents (ID-FCSEMSs). The study comprised a sample size of 80 patients from 2 large centers with long follow-up times of 3 and 5 years. It provided important evidence that ID-FCSEMSs could reduce patient burden in comparison with multiple plastic stents and achieve earlier stricture resolution with fewer ERCPs and fewer admission days. However, we have several concerns about the results.

First of all, stent migration is an endoscopist's great concern. The ideal stent could spontaneously migrate or dissolve after stricture resolution.[2] Not every stent migration should be considered an adverse event, and the definition needs further refinement. We suggest that only migrations occurring before stricture resolution and demanding further stent treatment should be regarded as clinically related adverse events. However, the authors failed to distinguish clinical-related migration from natural migration resulting from stricture resolution. The results were simply based on endoscopic reports, which may contribute to overestimation of stent migration.

Second, a cost-effectiveness analysis is lacking. Although the study indicated that ID-FCSEMSs had the advantages of fewer ERCPs and fewer admission days, they were also more expensive than plastic stents. Given the lack of cost-effectiveness analysis, it is too early to recognize ID-FCSEMSs as a favorable alternative.

Third, the statistical analysis is incomplete. A nonparametric test was used to compare recurrence time differences between the 2 groups. Kaplan-Meier curves were used to describe recurrence, but a further analysis (log-rank test) was absent. What is more, if an additional analysis of short-term and long-term recurrence rates after primary stent resolution had been provided, it would help readers have a better understanding of the role of ID-FCSEMS.

DISCLOSURE

All authors disclosed no financial relationships.

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Response:

We would like to express our gratitude for the letter to the editor by Chen et al[1] related to our article "Intraductal fully covered self-expandable metal stent versus multiple plastic stents for treating biliary anastomotic strictures after liver transplantation"[2] published in the April issue. We appreciate their feedback and would like to provide a response.

Chen et al[1] stated that not every stent migration in the treatment of anastomotic strictures after liver transplantation should be considered an adverse event, a point with which we fully agree. In fact, this is precisely why we provided details about the specific context in which stent migration was detected (ie, elective vs nonelective ERCP) and the occurrence of adverse events such as cholangitis and progressive cholestatic liver enzymes. Inasmuch as Chen et al[1] raised the suggestion to distinguish between migrations that occurred before stricture resolution and

at the time of stricture resolution, we went back to the data. After the exclusion of stent migrations that occurred at the time of stricture resolution, 3 out of 8 cases in the intraductal fully covered self-expandable metal stent (ID-FCSEMS) group (n = 3 patients, 7%) versus 18 out of 21 cases in the multiple plastic stent (MPS) group (n = 13 patients, 36%) remained. The majority of patients in the MPS group required additional treatment after stent migration because the stricture was still present. This implies that the majority of stent migrations in the MPS group were clinically relevant and contributed to a suboptimal treatment and persistence of the stricture. For ID-FCSEMS, one could argue the opposite, inasmuch as only a minority of the stent migrations occurred before stricture resolution. It is possible that in ID-FCSEMS, migration can be seen as a result of successful stricture resolution. These differences in clinically relevant migration, however, only confirm the benefit of ID-FCSEMS over MPS.

We agree with Chen et al[1] that a cost-effectiveness analysis is an important issue. Costs were previously evaluated in 3 randomized trials evaluating anastomotic strictures after liver transplantation to compare (intraductal or transpapillary) FCSEMS and MPS.[3-5] Although 2 of 3 studies observed reduced procedural costs favoring (ID-)FCSEMS,[3,4] none of these studies performed a cost-effectiveness analysis.[6] Owing to the retrospective nature of our study, we were unable to evaluate the costs of all intramural health care use, and we therefore thought that an accurate cost comparison between ID-FCSEMS and MPS was not possible. Nonetheless, previous studies have shown that stent costs are only a minor cost driver compared with the total health care costs, including hospital stay and the need for reinterventions, in patients with distal malignant biliary obstruction,[7] biliary strictures related to chronic pancreatitis,[8] and infected necrotizing pancreatitis.[9] On the basis of this information, it is reasonable to speculate that the reduced number of ERCPs and admission days observed in our study compensate, or even outweigh, the price of an ID-FCSEMS. Moreover, and perhaps more importantly, such outcomes may contribute to a reduction in carbon emissions. However, we agree with Chen et al[1] that future trials with an extensive health economic analysis should be performed to confirm whether ID-FCSEMS placement is truly cost effective over MPS.

Concerning the comments on the statistical analysis, we performed a log-rank test for both time to stricture resolution ($P = .004$) and time to stricture recurrence ($P = .455$).

Again, we appreciate the interest of Chen et al[1] in our study. In the future, well-designed randomized controlled trials should be performed to validate the findings of our study.

DISCLOSURE

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EUS-guided prophylactic drainage of the gallbladder: a bridge too far

To the Editor:

We read with interest the study by Robles-Medranda et al[1] regarding the utility of EUS-guided prophylactic drainage in patients with malignant bile duct obstruction undergoing palliative metal stenting. Although EUS-guided gallbladder drainage is a good option for nonsurgical candidates with acute cholecystitis, proposing routine prophylactic drainage in malignant bile duct obstruction seems like a bridge too far. We believe some issues require further clarification.

1. What is the explanation for the inordinately high number of acute cholecystitis cases in this series compared with those in existing reports on ERCP-related adverse events?[2,3]
2. Why did the authors choose to define the main outcome measure, called "definitive cholecystitis," in accordance with the Tokyo criteria for "suspected cholecystitis," where only 2 out of 3 diagnostic criteria are required? According to the authors, a patient presenting with right upper quadrant pain and systemic inflammation would meet the criteria for their main study outcome, when, in fact, cholangitis might be just as likely a diagnosis, according to the Tokyo criteria.[4]
3. Did the authors consider the possibility that the intervention in the control group (ie, cholangioscopy and/or forceful [over]injection of contrast medium to identify the cystic duct) might constitute a significant risk factor for post-ERCP cholecystitis, similar to mechanisms identified in post-ERCP pancreatitis,[5] thus introducing a significant bias in the analysis?
4. In everyday practice it seems unlikely that the gallbladder will always be sufficiently distended to allow EUS-guided drainage, as was the case for all patients in the study's active arm. A sufficiently distended gallbladder, favorable for EUS-guided drainage, is more likely to be associated with a patent cystic duct implanted above the site of the malignant stricture.

Although prophylactic gallbladder drainage might be a reasonable option in a highly selected population, we believe that routine EUS-guided drainage should not be encouraged until additional data are available.

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Response:

We have read with great interest the letter written by Voiosu et al.[1] In the mentioned letter to the editor, the authors demonstrate a cautious attitude toward the proposed procedure prophylactic EUS-guided gallbladder drainage (EUS-GBD) in patients with unresectable malignant biliary obstruction (MBO) and occlusion of the cystic duct orifice (CDO).[2]

Their first concern was the high number of acute cholecystitis (AC) cases in our series of cases compared to other existing reports on ERCP-related adverse events. Existing reports on ERCP-related adverse events have not evaluated tumor involvement of the CDO as a risk factor for post-ERCP cholecystitis (PEC). In their study, Cao et al[3] mentioned the following as PEC risk factors: history of chronic cholecystitis, previous acute pancreatitis, gallbladder opacification, biliary stent placement, high leukocyte count before ERCP, and biliary metallic stent placement. However, according to their report, occlusion of the CDO was not evaluated for PEC risk.[3] Additionally, another study evaluated tumor involvement in the occlusion of the CDO as a risk factor for cholecystitis after placement of self-expandable metallic stents. Cholecystitis was observed in 16.8% of 95 patients with tumor involvement to the CDO and in 25% of patients with CDO tumor involvement in whom a metallic stent with a high axial force was placed.[4,5] This number