ANSWERING REVIEWERS

Dear Editor:

Please find enclosed the revised manuscript 21523, titled "Malignant Biliary Obstruction: From Palliation to Treatment."

The reviewers' comments are addressed as follows:

Reviewer 1:
No comments, acceptable for publishing.

Reviewer 2:
Major comments:
The approach to distal biliary strictures (either for resectable or advanced disease) mostly focus on pancreatic cancer patients. The approach to strictures from distal cholangiocarcinoma is not adequately described. In my opinion, each section should be divided in these 2 conditions and the management of each condition further described (mostly adding information to distal cholangiocarcinomas).
On additional literature review based on the above comment, we have found little evidence to differentiate the approach to strictures from distal cholangiocarcinoma from that of pancreatic cancer. Both types of malignancy are managed similarly and often grouped together in large studies. We have added a paragraph on page 5 (highlighted) to address this point.

A table or chart summarizing the management of each situation should be added to the manuscript.
Two figures have been created detailing the algorithms for management of both distal and hilar obstruction.

Minor comments:
Double spaces after some words and after "." are very frequent and should be corrected.
We have sought to locate and correct each instance of double spacing between words, though we have preserved the double space between sentences.

Change the sentence "Adams et al. in a retrospective cohort of 52 patients, described a the complication rate nearly 7 times higher with plastic stents, with a 3 times higher rate of hospitalization (20)." to "… described a complication…"
Corrected per request.

Change the sentence "Percutaneous stent placement has been another option to relieve malignant biliary obstruction, with recent trials of percutaneous SEMS placement demonstrating food safety and effectiveness (38-40)" to "… demonstrating good safety…"
Corrected per request.

In the sentence "After 48 hours laser irradation is then used to treat the tumor, leading to selective apoptosis within the tumor mass via generation of oxidative radicals" correct "irradiation".
Corrected per request.

In the sentence "The body of literature supporting RFA for biliary malignancies is not as robust as that for PDT, consisting mostly of retrospective se (77)" correct to "…retrospective series"
Corrected per request.

Reviewer 3:
I would like the authors to comment on the section: "Hilar cholangiocarcinoma: Surgically treatable disease", the "ideal approach" to determine the proximal extension of the tumor for treatment planning.
A new paragraph describing the possible imaging modalities for determining proximal extension has been added on page 10-11.

In the section "Malignant distal biliary obstruction," there is an error (puritis)
Corrected per request.

Reviewer 4:
This study discussed the endoscopic treatments of malignant obstructive jaundice, but the associated topics have been published in WJG recently, such as World J Gastroenterol 2014 July 28; 20(28): 9345-9353; World J Gastrointest Endosc 2015 June 10; 7(6): 582-592. After reading this review, I found that there were numerous minor problems with the English plus some structural issues. I suggested that this paper should be restructured to make it more relevant to the clinician reader. For example, the author could restructured this review according to the clinical scenario, such as the 1. for patients with resectable disease; 2. for patients with locally advanced disease; 3. for patients with advanced disease; and discuss the appropriate strategy for endoscopic treatment according to the obstructive locations, such as biliary drainage in hilar obstruction and in distal bile duct obstruction.
The reviewer's point regarding the recent publication of a similar review article is well taken. We have attempted to differentiate this manuscript by including a focus on the novel shift in the endoscopist's role to include therapeutic treatment of these cancers, in addition to the traditional palliative role.

We are somewhat confused by the suggestion to structure the treatment according to stage and clinical scenario, since this was already the manner in which we have presented the review. See the headings on page 6 for example. To clarify our intent, we have changed the title of the subsection on page 8 to reflect the stage of disease being discussed. If the suggestion is to consider the stage as the primary focus and then the site of obstruction as a secondary factor, I would respectfully disagree and argue that the site of obstruction is a logical starting point in the algorithm for how to provide biliary decompression, though the stage obviously influences the approach as detailed in the manuscript.

Moreover, the authors should further discuss the role of preoperative biliary drainage for malignant obstructive jaundice based on the recent RCTs and Meta analysis.
We also find this comment somewhat confusing, given that the goal of the article is to discuss exactly this topic. Our literature search was geared towards the most recent studies, including the well-designed study types mentioned above.

Some new endoscopic techniques for relief of malignant obstructive jaundice should be further introduced such as EUS-guided biliary drainage, the development of new stents, etc.
Novel stent designs are discussed on page 7. EUS-guided biliary drainage is discussed on page 9. Given the fairly broad scope of this review, we elected not to go into greater depth on either topic.

Reviewer 5:

I would suggest including: "Before the final choice of treatment is made, the possibility of a malignant transformation must be assessed with endoscopic retrograde cholangiography, brush biopsy, and core biopsy" reference: Biliary papillomatosis in the common bile duct. Kassir R, Barabino G, Bageacu S, Ferrari G, Abboud K, Dumas O, Peoc'h M, Porcheron J. Endoscopy. 2013;45 Suppl 2 UCTN:E197-8

This information has been added on page 3.