

June 26, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 01806455-OLT-Sleeve Gastrectomy WJH Editorial 6-26-15.doc).

**Title:** Liver Transplantation and Sleeve Gastrectomy in the Medically Complicated Obese: New Challenges on the Horizon

**Authors:** Diego C. Reino, Keri E. Weigle, Erik P. Dutson, Adam S. Bodzin, Keri E. Lunsford, Ronald W. Busuttil

**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 19716

The manuscript has been improved according to the suggestions of reviewers.

1. Contextual revisions have been made as follows and have been highlighted within the manuscript:

(1) a. In paragraph 2, we further clarified that the incidence of NASH cirrhosis as a primary indication for liver transplant has risen from 1.2% in 2001 to 9.7% in 2009.

b. On page 8, the sentence structure was revised such that the two major findings within the referenced Heimbach article were more clearly delineated as per the reviewers suggestions.

c. Similar to b above, the following paragraph at the bottom of page 8 going onto page 9 was revised. The two paragraphs were combined so as to allow for a better paragraph construct in order to highlight the message that the timing of sleeve gastrectomy within the spectrum of liver disease is crucial.

d. In the final paragraph prior to the conclusion, we made several changes to better illustrate the importance of timing of sleeve gastrectomy in relation to liver transplant. We agree with the reviewers that most patients with NASH and grade 2 fibrosis or perhaps even Child's A cirrhosis should tolerate major abdominal surgery without overt decompensation of their liver disease. However, we simply wanted to highlight the findings of the Weingarten article to illustrate that we have already been performing weight reduction surgery on patients with NASH/Fibrosis and perhaps even low grade cirrhotic patients, though we do not have any evidence to support the latter. Therefore, we can extrapolate from this data and use it to identify the appropriate subset of patients who could be offered sleeve gastrectomy prior to liver transplant.

e. The conclusion paragraph was adjusted and articles cited to support the statement that NASH will likely be the major indication for liver transplant in the future based on the projection that 25 million Americans will develop NASH by 2025, with 20% of these patients progressing to cirrhosis and HCC.

(2) a. In Paragraph 2 of page 9, revisions were made to discuss the alterations to the surgical

field that can occur after sleeve gastrectomy which can affect the technical conduct of the ensuing liver transplant. This is an important consideration with respect to the added risk that would be attributable to the pretransplant sleeve gastrectomy. Thank you.

b. The term “Reverse transcriptase inhibitors” in the conclusion was changed to “direct acting antivirals.”

(3)

a. Page 8 paragraph 1 was revised to include the BMI of 35 as the minimal cutoff for inclusion into the Heimbach study. At our institution we follow BMI of 35 as our cutoff for consideration for LT and sleeve gastrectomy if patients exhibit evidence of having metabolic syndrome.

b. Within the conclusion section, the 3<sup>rd</sup> sentence beginning with “Our review of the literature...” summarizes our viewpoint when it comes to the optimal timing of sleeve gastrectomy in relation to liver transplant. The critical concept is that sleeve gastrectomy can be offered pre-transplant, during transplant or post-transplant. However, the timing will largely be dependent on center and regional variables. For instance, high acuity centers in regions with scarce organ availability are unlikely to offer their NASH patients with physiologic MELD of 40 a combined LTSG as the risk may be prohibitive. In these centers, patients with MELD exceptions may be the main target for combined LTSG or perhaps patients who have been diagnosed with early stage, compensated liver disease (Child’s A) and a diagnosis of NASH can potentially undergo sleeve gastrectomy in the pretransplant setting.

2. Formatting was revised as follows:

a. All acronyms throughout the editorial were specifically defined according to the reviewer’s suggestions (ie. ICU = intensive care unit)

3 References were corrected in paragraph 1 and they are now in the appropriate sequential order.

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,

Ronald W. Busuttil, MD, PhD, FACS

Response  
7/23/2015

Letter

Regarding editorial suggestions for the following submission:

Name of journal: World Journal of Hepatology  
ESPS Manuscript NO: 19716

Manuscript Type: EDITORIAL

Liver transplantation and sleeve gastrectomy in the medically complicated obese: New challenges on the horizon

Ronald W Busuttil, Diego C Reino, Keri E Weigle, Erik P Dutson, Adam S Bodzin, Keri E Lunsford

Dear Sir or Madam,

The following changes have been made to our manuscript, as requested. The changes are highlighted on the resubmitted draft.

1. The order of authors is confirmed as correct
2. The mailing code was added to the address for each author
3. The full address for correspondence to Dr. Busuttil is added
4. The core tip is added
5. The audio core tip will not be included
6. The reference section was updated with all names of authors and PMID/DOI numbers where available.

Please accept our manuscript for resubmission. Thank you for your time and effort in making this possible. Please respond with any further concerns or corrections.

Best Regards,  
Ronald W. Busuttil, MD, PhD