Format for ANSWERING REVIEWERS

February 10, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15555-review.doc).

Title: The role of ALPPS in colorectal liver metastases – a review

Author: Kristina Hasselgren, Per Sandstrom, Bergthor Björnsson

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15555

The manuscript has been improved according to the suggestions of reviewers and editor:

Point from reviewer 1

"Are there any data about the combination of intervention radiologic methods like radio-frequent ablation (RFA) or percutaneous etahnole infiltration (PEI) with ALPPS. This aspect should also be discussed."

Thank you for this important point. Although ablation has become a significant part of the treatment arsenal for malignant liver tumors this has not been described in the context of ALPPS. This is now clarified in "Discussion" with the following text "An aspect where data is lacking is ablative therapies, such as radio frequency ablation (RFA) and percutaneous ethanol infiltration (PEI), combined with ALPPS. In none of the included reports was local ablation described as a complement to resection. On the other hand, data combining local ablation in classical two staged resection are also scant. One possible explanation might be that resection is the procedure of choice when it comes to curative treatment and that local ablative treatment has a larger place for patients who are assessed as non-operable. Local ablative therapies have higher recurrence frequency compared to resection [50, 51]."

Points from reviewer 2

1 "It will be better to describe a little bit more details in the procedure of ALPPS. Acturally, the method may vary in different patients or centers, is there any indivadulized standards exist? "

2 "What the indications for the second stage surgery?"

3 "What they did in the first procedre and wait for how long to do the second step?"

The details of the surgical procedures are now included....XXX

As regarding the interval between the two steps of ALPPS treatment this is already stated under the heading "Volumetry" by the following text: "The interval between step 1 and step 2 range from 6 to 40 days with median interval 6-15.3 days."

4 "Laproscopic or open surgery?"

These important issues, points 1-2 and 4, are explained in the following text that has been added as a separate chaper.:

"Surgical technic

All of the procedures was conducted with open surgery, except in two patients there both steps was conducted laparoscopic (37). Common principles during the first step are examination of the abdominal cavity to rule out metastases and intra operative ultrasound of the liver. Thereafter identifying the portal vein, hepatic artery and bile duct. The right portal vein is divided and hepatic artery and bile duct marked with vessel loops to ensure identification during step 2. The liver parenchyma is thereafter transected.

The differences in technic are in essence how the mobilization of the liver is conducted. The hanging manoeuvre during mobilisation is described in tree papers (21, 25, 40). There are also differences whether hepatic veins are transected during the first step. Transection of the middle hepatic vein are described in two papers (21, 37), were as dividing retrohepatic veins are described in one (25)and transection of minor hepatic veins are described in one paper (24). Whether portal vein, hepatic artery and bile duct to segment 4 was transected is depending on the resection is an extended right hemihepatectomy or not is conducted which is described in all papers. How the parenchymal dissection is conducted is specified in tree papers. The transection is describes as total or nearly total in two papers (20, 37) and complete in one (25). To prevent adhesion between the two hemilivers a plastic bag (20, 25, 40), collagen (25) or silicon (21)sheet, a bioactive sealant (24) or omentyplasty (41) is used. The use of drain after step 1 is described in four of the papers (21, 24, 37, 38).

After evaluation with CT and when FLR has gain sufficient volume, step 2 is conducted. The exact criteria for FLR size to perform step 2 are described in three papers (21, 24, 38). The common principle is transection of right hepatic artery, bile duct and hepatic vein and regarding this step no significant difference are described."

Points from the editor

Author contributions are now stated as follows

"Björnsson B initiated the paper, Hasselgren K did the literature search. Hasselgren K, Sandström P and Björnsson B wrote the paper."

A Confilct-of-interest statement is now included
"The authors declare no conflict of interest"

Telephone- and faxnumber to corresponding author are now included

An audio Core Tip has now been uploaded

Abbrevated author names and manuscript title is now included after the Core Tip

The language has been edited by American journal experts (www.aje.com), please find the certification attached

Reference format has been changed to fit the format of WJG

DOI and PMID is now included in the reference list and all authors are listed

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

Sincerely yours,

Bergthor Björnsson, MD, PhD
Department of Surgery, County Council of Östergötland
Department of Clinical and Experimental Medicine,
Faculty of Health Sciences, Linköping University,
58185 Linköping, Sweden
bergthor.bjornsson@liu.se