

# Format for ANSWERING REVIEWERS

Sep, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 19038-review.doc).

**Title:** Vascular complications after adult living donor liver transplantation: Evaluation with ultrasonography

**Author:** Lin Ma, Qiang Lu , Yan Luo

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 19038

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

**1. Format has been updated**

**2. Running title, core tip and conflict-of-interest have been added.**

(1) Running title : Ultrasonographic evaluation of LDLT vascular complications

(2) Core tip: Vascular complications are some of the most severe complications after living donor liver transplantation (LDLT), which may lead to graft loss and death of death of the recipients. Conventional gray-scale and Doppler ultrasound, contrast-enhanced ultrasound (CEUS) play important roles in identifying vascular complications in the early postoperative period and during follow-up. This review focuses on the current applications of conventional ultrasound and CEUS in the diagnosis of vascular complications in the early period after adult LDLT, including the diagnostic efficacy, controversial diagnostic criteria and current issues requiring further investigations.

(3) Conflict of interest: The authors declare no conflicts of interest.

**3. Revision has been made according to the suggestions of the reviewer**

(1). The punctuation (;) have been replaced by full stop (.).

(2). Figures of ultrasound in various vascular complications of LDLT have been added and the illustrations have been edited by AJE.

(3). What are the false positive and false negative rates of Doppler US in detecting HAT?

False positive results of Doppler US in detecting HAT are mainly due to reduced hepatic arterial flow caused by hypotension, small hepatic artery caliber, early postoperative vasospasm, rejection reaction, improper adjustment of ultrasound machine or scanning. Reported false-positive rates are relatively high<sup>[1-4]</sup> and Hom BK *et al* <sup>[5]</sup> reported the false positive rate even reaching as high as 75%. False negative results arise mainly from collateral circulation, with a reported false-negative rate of 4%-29%<sup>[4,6]</sup>. These contents have been added in the revised manuscript (on page 5).

#### Reference:

- 1). **Luo Y**, Fan YT, Lu Q, Li B, Wen TF, Zhang ZW. CEUS: a new imaging approach for postoperative vascular complications after right-lobe LDLT. *World J Gastroenterol*. 2009; **5**: 3670-3675 [PMID: 19653347]
- 2). **Tamsel S**, Demirpolat G, Killi R, Aydin U, Kilic M, Zeytunlu M, Parildar M, Oran I, Ucar H. Vascular complications after liver transplantation: evaluation with Doppler US. *Abdom Imaging* 2007;**32**:339-347 [PMID: 16967253]
- 3). **Dodd GD 3rd**, Memel DS, Zajko AB, Baron RL, Santaguida LA. Hepatic artery stenosis and thrombosis in transplant recipients: Doppler diagnosis with resistive index and systolic acceleration time. *Radiology* 1994;**192**: 657-661 [PMID:8058930]
- 4). **Nolten A**, Sproat IA. Hepatic artery thrombosis after liver transplantation: temporal accuracy of diagnosis with duplex US and the syndrome of impending thrombosis. *Radiology* 1996; **198**: 553-559 [PMID: 8596865]
- 5). **Hom BK**, Shrestha R, Palmer SL, Katz MD, Selby RR, Asatryan Z, Wells JK, Grant EG. Prospective evaluation of vascular complications after liver transplantation: comparison of conventional and microbubble contrast-enhanced US. *Radiology* 2006;**241**:267-274 [PMID: 16990679]
- 6). **García-Criado A**, Gilabert R, Nicolau C, Real I, Arguis P, Bianchi L, Vilana R, Salmerón JM, García-Valdecasas JC, Brú C. Early detection of hepatic artery thrombosis after liver transplantation by Doppler ultrasonography: prognostic implications. *J Ultrasound Med* 2001; **20**: 51-58 [PMID: 11149529]

(4). Grammar mistakes pointed out by the reviewer have been corrected:

1) Page 5, paragraph 2:

“which may result in reduce use of angiography” ➔ “which may reduce use of angiography”.

2) Page 6:

“anastomosis stoma” ➔ anastomotic site.

3) Page 8, under PVT:

“PVT may be lead to liver function” → “PVT may lead to liver function”.

4) “the drainage areas” → “the drained area”.

**4. In order to make it easy to understand, I change some words on the premise that the original meaning .All of the revision have been highlighted in red in the revised manuscript.**

(1) Page 1:Vascular complications after liver transplantation remain a major cause of morbidity and mortality for recipients, especially those receiving LDLT owing to the slender vessels and complex vascular reconstruction. → Vascular complications after liver transplantation remain a major threat to the survival of recipients. LDLT recipients are more likely to develop vascular complications because of their complex vascular reconstruction and the slender vessels

(2) Page 1: Contrast-enhanced ultrasound (CEUS) has been applied gradually in recent years and has provided a significant improvement in diagnosing postoperative vascular complications because of its fine vascular tracing and perfusion visualization. → Recently, owing to the detailed vascular tracing and perfusion visualization, contrast-enhanced ultrasound (CEUS) has provided a significant improvement in diagnosing postoperative vascular complications.

(3) Page 4:Furthermore, ultrasound contrast agent is non-nephrotoxic, and with very rare adverse reactions because the gas within micro-bubbles is eliminated from circulation by exhalation. → CEUS usually causes rare adverse reactions and can be applied in the recipients with renal insufficiency, because the gas within micro-bubbles is metabolized by respiration

(4) Page 5: Bile ducts are supplied by hepatic artery only and the biliary epithelium is more sensitive to ischemic injury than hepatocytes. Ischemia resulted from HAT initially affects the bile ducts, which may lead to biliary necrosis, cast formation, subsequent scarring and multifocal stenosis. →Ischemia resulting HAT initially affects the bile ducts because bile ducts are supplied only by the hepatic artery and the biliary epithelium is more sensitive to ischemic injury than hepatocytes. Biliary ischemia may lead to biliary necrosis, cast formation, abscesses, non-anastomotic bile leak and bilomas.

(5) Page 6: Recently, CEUS has been used to show the perfusion of the hilar bile ducts, since detection of severely impaired perfusion may facilitate the early diagnosis of biliary complications. →Recently, CEUS has been used to show the perfusion of the hilar bile ducts, facilitating the early diagnosis of biliary complications.

**5. The language have been edited by professional English language editing companies (AJE). The**

**revisions have been highlighted in yellow and blue in the revised manuscript.**

**6. References and typesetting have been corrected.**

I deleted the 86th reference because it is the same as the 80<sup>th</sup> and the 11st reference was instead of another better one.

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

Sincerely yours,  
Lin Ma