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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35716

Title: Characteristics of Fecal Microbial Communities in Patients with Non-anastomotic Biliary Strictures after Liver Transplantation

Reviewer's code: 01221925

Reviewer's country: Greece

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-05

Review time: 8 Hours

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is an interesting paper looking into the relationship between microbial population and non-anastomotic biliary strictures in patients after liver transplantation. Could the authors please respond to the following: 1) Have the authors considered additional groups, such as patients with biliary strictures but no liver transplantation, and patients with anastomotic strictures? 2) How firm do the authors consider the association to be between fecal microbes and those present in the biliary system, ie are these necessarily the same? 3) How do the authors know that the changes seen with the microbial population are not a result, rather than a cause of the stricture? 4) The authors report that all the donors were DCDs which could certainly account for the presence of non-anastomotic biliary strictures. 5) Please define "subacute liver failure". What was the cause? 6) Did all patients with HCC have cirrhosis? 7) The authors provide an



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excellent discussion regarding the potential role of endotoxins and TLRs regarding the microbial population. Is there any data available in this experimental setting? 8) Could the authors provide some more information on the quality of the donors?



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35716

Title: Characteristics of Fecal Microbial Communities in Patients with Non-anastomotic Biliary Strictures after Liver Transplantation

Reviewer's code: 00039518

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-13

Review time: 8 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The paper "Characteristics of Fecal Microbial Communities in Patients with Non-anastomotic Biliary Strictures after Liver Transplantation" deals with the changes of intestinal microbiota after liver transplantation comparing the data of transplanted patients with and without non anastomotic biliary strictures (NAS). The main result is that NAS patients showed decreases of Firmicutes, Bacteroidetes and increases of Proteobacteria at the phylum level and this could be a pathogenic factor for NAS occurrence. The study is original and provides potentially useful pathogenic and clinical information. I have some criticisms that should be addressed by the Authors Major points This a pilot study with a limited number of cases from which no firm conclusion can be drawn; this is highlighted by the Authors in the Conclusion but should be also reported in the Abstract Were the patients included in the study consecutively enrolled?



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This must be specified by the Authors. Were there any differences in term of hepatic artery inflow between uncomplicated transplanted patients and patients with NAS? In other words, the Doppler ultrasound pattern of hepatic artery was normal in all patients of the two groups of patients undergone OLT? This is essential to rule out alterations of the arterial inflow in the pathogenesis of NAS. The Authors should specify that the healthy subjects had not taken antibiotics during the 30 days before the inclusion in the study and assess if there were any differences in the antibiotic intake during the period elapsed from OLT to the inclusion in the study between the group of uncomplicated OLT patients and the group of NAS OLT patients. The Discussion is too much long and should be shortened; furthermore, I think that the Authors should highlight that the alteration of intestinal permeability could play an essential role in the pathogenic model of NAS induced by the imbalance of intestinal microbiota in OLT patients. For this reason, in my opinion, future studies in this field should include a thorough assessment of intestinal permeability.

Minor points

Introduction: Actually, the relationship between dysbacteriosis and postoperative complications including acute rejection, early-stage infection and graft loss have been totally realized [15, 16]. Account for all of these, we hypothesized that.... Write as follows: Actually, the relationship between dysbacteriosis and postoperative complications including acute rejection, early-stage infection and graft loss are under investigation [15, 16]. We hypothesized that....

Introduction: Remove the phrase "But so far, the detailed relationship between them has never been explored".

Introduction: Remove the phrase "We hope the study may contribute to the possible mechanism research about NAS after LT, also shed some light on its prevention in future".

Discussion: "While Firmicutes and Bacteroidetes were intestinal predominant bacterium, playing a major role in host's intestinal homeostasis. Their losses always indicated the deterioration of intestinal barrier function and increased the risk of bacterial translocation". I do not understand the meaning of this phrase. Please, change. Use the abbreviation OLT instead of LT throughout all the paper. Use undergone OLT instead of underwent OLT throughout all the paper.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35716

Title: Characteristics of Fecal Microbial Communities in Patients with Non-anastomotic Biliary Strictures after Liver Transplantation

Reviewer's code: 00054255

Reviewer's country: South Korea

Science editor: Ze-Mao Gong

Date sent for review: 2017-08-05

Date reviewed: 2017-08-16

Review time: 11 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This study “characteristics of fecal microbial communities in patients with non-anastomotic biliary strictures(NAS) after liver transplantation” is unusual retrospective study regarding differences of bacterial species among three groups, 10 patients with NAS after LT, 10 patients with no complications after LT and 10-non-LT healthy individuals. There are significant different bacterial changes among groups and authors interpreted that this derangement of bacteriosis may affect biliary stricture by systemic effect of the bacterial change. So, bacterial change in NAS might affect on biliary stricture. However, reviewer interpret it conversely, so that, biliary stricture might affect on bacterial change. The common causes of biliary stricture are surgical result such as deficient hepatic arterial blood flow, prolonged cold ischemic times, delayed rearterialization of the graft and ischemia/reperfusion injury. And injury of the



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biliary epithelium by direct effect of cold ischemia or damage to the biliary tree microvasculature affect on NAS. And also arterial back-table perfusion. Anatomical variation of hepatic artery make more chance to arterial blood flow deficiency by cutting of important arteriol such as posterior superior pancreaticoduodenal artery that provide supraduodenal bile duct. Other causes of NAS described above rather than bacterial change of the colon should be speculated. Liver function markers are different among groups as shown in the Table 1. The amount of bile acid excretion into the bowel lumen can change of the bacteriosis. There are no data regarding antibiotics use of each group. Antibiotics use itself may affect more on the bacterial change.