

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 6766

**Title:** Aetiology and risk factors of post-transplant ischaemic cholangiopathy

**Reviewer code:** 00505331

**Science editor:** Qi, Yuan

**Date sent for review:** 2013-11-01 19:50

**Date reviewed:** 2013-11-22 11:06

| CLASSIFICATION  | LANGUAGE EVALUATION   | RECOMMENDATION                      | CONCLUSION   |
|---|---|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)            | <input type="checkbox"/> Grade A: Priority Publishing                 | Google Search:                      | <input type="checkbox"/> Accept                        |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input checked="" type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed    | <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"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)                 |   | BPG Search:                         | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)                 | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input type="checkbox"/> Major revision                |
|   |   | <input type="checkbox"/> No records |  |

## COMMENTS TO AUTHORS

This is a thorough review of what is known about the causes and risk factors of ischemic cholangiopathy in DCD liver transplantation. The manuscript is well written and seems accurate except in one area. Specifically, Section Title: "Donor, graft characteristics, procurement and preservation process and IC" Pg 11, paragraph 5 The discussion about higher viscosity preservation solutions causing higher incidents of IC by less capillary perfusion is not accurate. At best, the data overall show that the viscosity of the preservation solution is irrelevant to IC. In fact, some of the references cited as supporting the high viscosity hypothesis show no change between UW (high) and HTK (low). This section should be deleted or modified to reflect the correct conclusions about viscosity of flush solutions, as reflected by the prevailing data.

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 6766

**Title:** Aetiology and risk factors of post-transplant ischaemic cholangiopathy

**Reviewer code:** 02861134

**Science editor:** Qi, Yuan

**Date sent for review:** 2013-11-01 19:50

**Date reviewed:** 2013-12-16 16:11

| CLASSIFICATION  | LANGUAGE EVALUATION  | RECOMMENDATION                      | CONCLUSION   |
|---|--|-------------------------------------|--|
| <input checked="" type="checkbox"/> Grade A (Excellent) | <input checked="" type="checkbox"/> Grade A: Priority Publishing     | Google Search:                      | <input checked="" type="checkbox"/> Accept             |
| <input type="checkbox"/> Grade B (Very good)            | <input type="checkbox"/> Grade B: minor language polishing           | <input type="checkbox"/> Existed    | <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"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)                 | <input type="checkbox"/> Grade D: rejected                           | <input type="checkbox"/> Existed    | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)                 |  | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

## COMMENTS TO AUTHORS

The paper makes original contribution The paper is well organized Author Guidelines has been followed properly in preparing the manuscript The paper is based on sound methodology Literature review is adequate

**ESPS Peer-review Report**

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

**ESPS Manuscript NO:** 6766

**Title:** Aetiology and risk factors of post-transplant ischaemic cholangiopathy

**Reviewer code:** 02861019

**Science editor:** Qi, Yuan

**Date sent for review:** 2013-11-01 19:50

**Date reviewed:** 2013-12-17 17:10

| CLASSIFICATION                                     | LANGUAGE EVALUATION  | RECOMMENDATION                      | CONCLUSION   |
|--|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)       | <input checked="" 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"/> Existed    | <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"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)            |  | BPG Search:                         | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)            | <input type="checkbox"/> Grade D: rejected                           | <input type="checkbox"/> Existed    | <input type="checkbox"/> Major revision                |
|  |  | <input type="checkbox"/> No records |  |

**COMMENTS TO AUTHORS**

Dear Authors, I have read with great interest Your manuscript entitled Aetiology and risk factors of post-transplant ischaemic cholangiopathy in which the authors reviewed the natural history of this serious post-OLT complication. The review is clinically exhaustive and well written; it takes a clinical overview over this condition. Despite the good quality of the paper, I suggest to improve some sections of the text: - in the "Definition, incidence, and types of IC" the authors report the difference among anastomotic and non-anastomotic strictures, describe the NAS, but not the anastomotic ones and give a brief paragraph on the pathogenesis. The incidence of IC, ranging 2-20%, is referred to old studies (1993 and 1995); I would suggest to update the references, if available. I also suggest to include the pathogenesis of anastomotic strictures. Finally, the paragraph is entitled definition and types of IC, but in the text different types of ICs are not mentioned. - "clinical presentation" is quite descriptive, reporting only "increase" incidence of complications (gallstone formation, cholestasis, cholangitis, etc). Are there any data on the incidence and prevalence of these complications among patients with un-complicated OLT and ICs? Are there any histologic diagnostic criteria to perform diagnosis? - the risk of IC is increased in graft with prolonged cold ischemia; could the authors reported this relative risk, reported in the studies cited [12,13,41-3]; - does the underlying liver disease could play a role or represents a risk factor for ICs? - the management section could be improved; I suggest to describe first the possible therapeutic options available to prevent or reduce the risk of IC development; after that, I would stress the endoscopic (ERCP) and percutaneous trans-hepatic management of bile duct stenosis and gallstones. Minor: In the introduction, in my opinion, biliary and vascular complications are not the only issues in post-OLT setting; I would cite also graft reinfection and immune disease (rejection).

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 6766

**Title:** Aetiology and risk factors of post-transplant ischaemic cholangiopathy

**Reviewer code:** 02861170

**Science editor:** Qi, Yuan

**Date sent for review:** 2013-11-01 19:50

**Date reviewed:** 2013-12-18 19:24

| CLASSIFICATION                                     | LANGUAGE EVALUATION  | RECOMMENDATION                      | CONCLUSION   |
|--|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)       | <input checked="" type="checkbox"/> Grade A: Priority Publishing     | Google Search:                      | <input checked="" type="checkbox"/> Accept             |
| <input type="checkbox"/> Grade B (Very good)       | <input type="checkbox"/> Grade B: minor language polishing           | <input type="checkbox"/> Existed    | <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"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)            | <input type="checkbox"/> Grade D: rejected                           | <input type="checkbox"/> Existed    | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)            |  | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

## COMMENTS TO AUTHORS

The paper is a clinically exhaustive review and represent an innovative contribution. in the text (section of types of IC ) different types of ICs are not described. References updating is recommended.

**ESPS Peer-review Report**

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

**ESPS Manuscript NO:** 6766

**Title:** Aetiology and risk factors of post-transplant ischaemic cholangiopathy

**Reviewer code:** 02861035

**Science editor:** Qi, Yuan

**Date sent for review:** 2013-11-01 19:50

**Date reviewed:** 2013-12-23 00:06

| CLASSIFICATION  | LANGUAGE EVALUATION  | RECOMMENDATION                      | CONCLUSION   |
|---|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)            | <input checked="" type="checkbox"/> Grade A: Priority Publishing | Google Search:                      | <input type="checkbox"/> Accept                        |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing       | <input type="checkbox"/> Existed    | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good)                 | <input type="checkbox"/> Grade C: a great deal of                | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)                 | language polishing   | BPG Search:                         | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)                 | <input type="checkbox"/> Grade D: rejected                       | <input type="checkbox"/> Existed    | <input type="checkbox"/> Major revision                |
|   |  | <input type="checkbox"/> No records |  |

**COMMENTS TO AUTHORS**

This is generally a good review that covers most aspects of ischaemic cholangiopathy. However, there are some minor corrections or points the authors might consider to mention or alter. In the abstract, authors had accidentally typed DCD as 'after donation circulatory death' instead of 'donation after circulatory death'. In the DCD and ischaemic cholangiopath section, the authors mentioned Taner et al showed that DWIT was not a significant factor. However, Taner et al showed the different case when considering individual time points like the asystole-to-crossclamp duration, which includes the mandatory waiting time in DWIT. Maybe the authors want to explain this clearer.

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 6766

**Title:** Aetiology and risk factors of post-transplant ischaemic cholangiopathy

**Reviewer code:** 02861012

**Science editor:** Qi, Yuan

**Date sent for review:** 2013-11-01 19:50

**Date reviewed:** 2013-12-23 02:29

| CLASSIFICATION  | LANGUAGE EVALUATION   | RECOMMENDATION                      | CONCLUSION   |
|---|---|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)            | <input type="checkbox"/> Grade A: Priority Publishing                 | Google Search:                      | <input type="checkbox"/> Accept                        |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input checked="" type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed    | <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"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)                 | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input checked="" type="checkbox"/> Minor revision     |
| <input type="checkbox"/> Grade E (Poor)                 |   | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

## COMMENTS TO AUTHORS

This review article contains a large amount of information that has been reported in the literature regarding the incidence, risk factors and management of ischaemic cholangiopathy after liver transplantation. Minor modifications would be necessary prior to acceptance of this article. 1) The authors should give the full name and not the abbreviated name in the introduction. Some abbreviated words i.e CIT and WIT have been described in the abbreviations list but they should be reported in the text as well. 2) In the "Introduction" section paragraph three the authors write "...hepatic artery thrombosis or stenosis 16" is the 16 a typo or has a meaning? 3) The authors need to conclude whether it should be "ischaemia" or "ischemia" 4) Similar to comment 2, in the section "Blood supply of the biliary tree" paragraph 2 " 28 hepatic artery damage..." what is the meaning of 28? 5) In the section "other risk factors" paragraph 2: the authors should consider expanding the mechanisms by which the bile ducts are lost. "(1) a direct immunological destruction of the biliary epithelium" which immune cells have been reported to be responsible for this destruction? "(2) an indirect, ischemic damage" what is the actual mechanism of this?