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PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 52999

Title: Polycystic liver disease: Classification, diagnosis, treatment process, and clinical management

Reviewer's code: 03477653
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Attending Doctor, Research Scientist, Surgeon
Reviewer's country: Spain
Author's country: China

Manuscript submission date: 2019-11-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2019-11-29 17:55

Reviewer performed review: 2019-12-03 19:07

Review time: 4 Days and 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [Y] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

Well researched narrative review on polycystic liver disease. I found the review to be complete, however, it did not present almost nothing novel that has not been mentioned in the multiple review articles on the subject. The English in this paper is just not acceptable on its current format. Some comments: - If the review performed was not a systematic one, please state this fact. - "However, the effectiveness of these therapies except liver transplantation are still uncertain". You detailed afterwards some proofs of the effectiveness of medical, percutaneous, and other surgical options. - Please clarify: "while the mechanisms of cysts in PLD and polycystic kidney disease (PKD) are complicated". - The diagnosis of PLD is made with 4 or more cysts if familiar precedents exist. What you stated is incorrect. - Please reorganize the different treatments by type (medical, percutaneous, surgical). - You stated: "a study showed the benefits of lanreotide still persisted 4 months after cessation of the drug", clarify that this study only showed improvement on volumetrics, not in symptoms relief. - You stated: "A meta-analysis showed that the recurrence rate through open surgery was lower than through laparoscopic approach (5% vs 6%), and most recurrent cysts do not require second surgery". The reference you put is from an Italian series of laparoscopic cyst fenestrations. Disregarding this, a reduction of 1% on the recurrence based on this evidence is clinically insignificant. - I would recommend this be rewritten with someone who has a mastery of the English (scientific) language to make it more legible.

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PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 52999

Title: Polycystic liver disease: Classification, diagnosis, treatment process, and clinical management

Reviewer's code: 05059707
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's country: Japan

Author's country: China

Manuscript submission date: 2019-11-28

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2019-12-27 01:08

Reviewer performed review: 2019-12-29 08:02

Review time: 2 Days and 6 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[Y] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced
			[ ] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

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SPECIFIC COMMENTS TO AUTHORS

This review was well written, but there are some concerns. 1. (Page 5, Line 28~Page 6, Line 5) The authors described "global incidence of about 1% to 2%". However, incidence described by the authors seems to be higher than that described recent literature, such as a 2018 Nature Disease Primer by Bergmann et al.. In addition, the frequency of mutations in PKD1 and PKD2 gene also seems to be inadequate. Therefore, the authors should need the correction. 2. (Page 6, Line 20) The authors described GANAB gene. However, mutations of GANAB gene often involve polycystic kidney, like ADPKD. The authors should consult a 2018 Nature Disease Primer by Bergmann et al.. Therefore, the authors should classify GANAB mutations to ADPKD. Table 1 also need the correction. 3. (Page 13, Line 20) Junichi may be the first name, so the authors should correct this to Hoshino.

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PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 52999

Title: Polycystic liver disease: Classification, diagnosis, treatment process, and clinical management

Reviewer's code: 01567543
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Doctor, Professor
Reviewer's country: Netherlands
Author's country: China
Manuscript submission date: 2019-11-28
Reviewer chosen by: Jin-Zhou Tang
Reviewer accepted review: 2019-12-27 06:23
Reviewer performed review: 2019-12-31 22:08
Review time: 4 Days and 15 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[Y] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced
			[ ] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

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SPECIFIC COMMENTS TO AUTHORS

Polycystic liver disease: classification, diagnosis, treatment process, and clinical management Zeyu Zhang, Zhiming Wang, Yun Huang Dr Zhang and collegues have produced a seminal paper on polycystic liver disease. This is a narrative review centered on the classification, diagnosis, treatment process, and clinical management. This paper aims to provide a better understanding of progress in the field as well as obtain potential directions for future research. As such they have achieved their goals, and the authors have to be commended with this feat. The core tips, abstract ad paper contains the line that "However, unfortunately, there is no significant breakthrough in the treatment of PLD so far". I am not sure what the authors would consider as a "significant breakthrough" and what would be needed for that. I think that this would be more interesting for the readership than a general, rather sobering, message. The authors contrast the mechanisms of cysts in PLD and polycystic kidney disease (PKD): the primary cilia of biliary epithelial cells vs congenital bile duct dysplasia through multiple mechanisms. I am not sure whether these statements are actually contrasting with each other. The disorders described in this review are broadly termed fibrocystic diseases. Fibrocystic liver disease is a collective definition of a group of congenital and rare diseases affecting the biliary tree deriving from a perturbed development of the embryonic ductal plate. Together with fibrocystic renal disease, they are often part of the multisystemic hepatorenal fibrocystic diseases in which dysgenesis of the biliary structures is associated with the fibrocystic malformation of the kidneys. The paper opens up the discussion on PKD3 , the third ADPKD gene and cites a paper that revisited this issue. (Kidney Dis (Basel)). I think that it would be worthwhile to mention that 8 genes have been associated with ADPKD (PKD1 and PKD2), ADPLD (PRKCSH, SEC63, LRP5, ALG8, and SEC61B), or both (GANAB). Thus GANAB (although rare) is

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considered to be the bonafide 3rd PKD gene. J Am Soc Nephrol. 2018 Jan;29(1):13-23 The authors are right in stating that there is "no widely accepted international guideline for treatment of PLD". Kidney Health Australia – Caring for Australasians with Renal Impairment Guidelines have attempted to formulate guidance in the field, and I think that it would be useful to look that up. http://www.cari.org.au/CKD/CKD%20adpkd/12.%20PLD.pdf It would be interesting to know how computerized three-dimensional imaging contributes to the design of the treatment plan as this is not a routine product from radiological imaging. If it would be helpful it would be necessary to convince imaging specialists, and to do so you need arguments why this would be beneficial. The discussion on the two clinical classifications on PLD is helpful, but a picture / cartoon depicting the affected / non affected liver would be probably useful here. I do not agree that "organ malfunction" is needed to trigger treatment in PLD. In fact in the majority of patients who are in need of treatment suffer from incapacitating symptoms and a lower quality of life, not "organ malfunction". United European Gastroenterol J. 2018 Feb;6(1):81-88 The authors mention that "Frederik et al. increased the therapeutic dose of lanreotide non-responder from 90mg to 120mg, which led to stopping liver volume growing". I think that what this study shows is that both lanreotide 90 as well as 120 mg are effective in terms of reducing liver volume, and that the dose can be reduced from 120 to 90 mg in case side effects occur. Perhaps it would be useful to mention the effect of stopping somatostatin analogues (so called drug holiday) here. Therap Adv Gastroenterol. 2018 Oct 3;11:1756284818804784. I think that the statement that wraps up the paragraph on the efficacy of somatostatin analogue therapy could be sharper formulated. Somastatin analogues have a rapid onset of effect (within first months of therepay), the effect persists while patients are on therapy (there is evidence that the effect is there up to 3 or even 4 years), that cessation of treatment results in a significant increase of liver

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volume (rebound effect with re-emergence of symptoms) and that re-introduction of the drugs replicates the success of initial treatment (or the effect is probably similar in treatment experienced vs previously non-exposed patients). I think that the safety profile of mTOR inhibitors is well known (contrasting the authors statement "is not totally understand at present"). There have been a number of excellent reviews detailing on the safety profile of these drugs Expert Opin Drug Saf. 2013 Mar;12(2):177-86 The authors cite the paper on "Alcohol sclerotherapy of hepatic cysts: its effect in relation to ethanol concentration Hepatol Res. 2000;17(3):179-184. to support a statement on a meta analysis on aspiration sclerotherapy. The data cited do not come from this paper published in Hepatol Res. I looked for a meta analysis in this field but could only identify a systematic review (AJR Am J Roentgenol. 2017 Jan;208(1):201-207.). I stand to be corrected. The authors devote a paragraph on transcatheter arterial embolization. It would be great if they could cite their own personal experience as this would be useful for the readership. I am not sure whether the statement "incidence of complications after liver transplantation is 41%, and the mortality rate is 17%." Is currently correct. I think that a mortality rate of 17% would be a contra indication to perform this procedure in this population. The cited paper mentions " Estimates of 3- and 5-year survival probability for LT recipients with PCLD were 88.8% and 85.1% compared to 79.3% and 70.8% with HCC, and 80.5% and 74.2% with CLF, respectively (Table 3)".I suggest that the authors cite their own data or refer back to more recent data.

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PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 52999

Title: Polycystic liver disease: Classification, diagnosis, treatment process, and clinical management

Reviewer's code: 02671773
Position: Peer Reviewer
Academic degree: MD, PhD

Professional title: Chairman, Professor

Reviewer's country: Greece

Author's country: China

Manuscript submission date: 2019-11-28

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2019-12-27 11:15

Reviewer performed review: 2020-01-02 10:51

Review time: 5 Days and 23 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

No specific comments to authors.

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