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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 03479389

**Reviewer's country:** Japan

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-02-28

**Review time:** 4 Hours

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 Grade E: Do not publish	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

### SPECIFIC COMMENTS TO AUTHORS

Thank you for giving me an opportunity of the review. This is a good systematic review and meta-analysis focused on adverse events of ERCP in cirrhosis patients. My comments and questions are as follows. Major comments: Is EST a risk factor for



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hemorrhage and post-ERCP pancreatitis (PEP) in cirrhosis patients? In general, endoscopic papillary balloon dilation (EPBD) has a higher risk of PEP than EST. Do you conclude that EPBD is better than EST in patients with cirrhosis? Minor comments: Please correct the text according to the guidelines for authors submitting manuscripts. Definition of adverse events (mainly bleeding and PEP) is not clear. Can you show the criteria for each article?

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 01430761

**Reviewer's country:** Japan

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-02-28

**Review time:** 6 Hours

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

### SPECIFIC COMMENTS TO AUTHORS

This is a well written meta-analysis of adverse events during ERCP in patients with cirrhosis. 1. As the authors discussed, clinical outcomes of ERCP might differ according to its indications and severity of cirrhosis. I understand severity of cirrhosis



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are not available in most studies but please add patient characteristics such as ERCP indications, severity of cirrhosis and severity of adverse events especially PEP etc. to understand the characteristics of studies included in the analysis. 2. I believe publication bias exists. Studies showing a higher incidence of AE are likely to be reported and published.

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 03261315

**Reviewer's country:** Romania

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-02-28

**Review time:** 17 Hours

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

### SPECIFIC COMMENTS TO AUTHORS

I am concern regarding the power of the meta-analysis. Majority of the studies included were retropective. Only a few studies were prospective (was included one study with only 7 patients). The heterogenity is high also the risk of bias. The authors should select



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more powerful studies and exclude the studies with small number of patients , cohort study....

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 01804189

**Reviewer's country:** India

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-03-02

**Review time:** 2 Days

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

### SPECIFIC COMMENTS TO AUTHORS

There are many deficiencies in this review. 1. Details of etiology of the cirrhosis is available only in 11% patients. In the remaining no details given regarding etiology. 2. In patients with CBD stones, no details are available whether these were large or small



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stones, whether mechanical lithotripsy was done or not and in how many patients CBD was cleared. All these factors have important bearing on complications. 3. In 26% patients, strictures have been reported. No details are available whether these strictures were due to portal cholangiopathy/malignancy/benign. This information and the nature of management are important as far as complications are concerned 4. No information is available why ERCP was done in gall stone pancreatitis group. 5. information regarding severity of pancreatitis and which group of patients had pancreatitis not available

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 01559599

**Reviewer's country:** Japan

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-03-05

**Review time:** 5 Days

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

### SPECIFIC COMMENTS TO AUTHORS

Authors demonstrated meta-analysis that patients with cirrhosis have increased risks after ERCP. Higher rates of hemorrhage are understandable due to the bleeding tendency with cirrhosis. However, the reasons of post ERCP pancreatitis (PEP) are as yet



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poorly understandable. Relations between PEP and cirrhosis have not been explained in detail. First, in discussion, PEP has a close relation with EST than EPBD. In general, EPBD has a higher risk of PEP more than EST. Park et al. noted that PEP rates are comparable in EST and EPBD on the basis of small number of patients with cirrhosis. Are there any articles in this problem? Second, how liver dysfunction can increase a risk of PEP? Inamdar et al. made a suggestion that many of physicians may hesitate to administer sufficient amount of infusion solution to patients with decompensated cirrhosis in consideration of volume overload. However, this hypothesis only explains the difficulties in management PEP with decompensated cirrhosis, not its higher frequency.

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##### ***Google Search:***

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 00503834

**Reviewer's country:** Taiwan

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-03-05

**Review time:** 5 Days

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

### SPECIFIC COMMENTS TO AUTHORS

The manuscript is a meta-analysis of ERCP in cirrhosis. The authors aimed to determine complications of ERCP in cirrhosis compared with non cirrhotic patients. Finally, the authors concluded that ERCP in cirrhosis carried higher risk of bleeding and post ERCP

pancreatitis. There are several points to be clarified. 1. Diagnostic and therapeutic ERCP are highly technique dependent. Multiple ERCP operators meaned great hidden bias. 2. It is reasonable that bleeding risk is higher among cirrhosis patients receiving ERCP. Only bleeding may be differences between liver cirrhosis and non-cirrhosis patient, if procedures was performed by single operator. Thus, the bias may be depend on the endoscopic and the intervention. Besides, the severity of cirrhosis is also need to be considered. The authors may describe these points or add in limitations. 3. Authors made great efforts on meta-analysis, but did not mention deeply on EST-induce bleeding and how to prevent this common complication in case of liver cirrhosis. This is the "soul" of the paper. May the authors discuss this. 4.pre-medication, such as NSAID or not, even rectal prophylaxis or not, may affect the risk of pancreatitis. How could the authors think about the bias. I also suggest that the authors may provide their clinical experience in the discussion section. Minor: 1. reference may be added to table 1 2. percentage of complications may be added to table 2. 3. According to flow chart, conference consensus should be excluded in the 2nd steps?

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##### ***BPG Search:***

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 02897448

**Reviewer's country:** China

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-03-05

**Review time:** 5 Days

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

### SPECIFIC COMMENTS TO AUTHORS

Very interesting topic! So far, we are still lack of consensus about adverse effects related to ERCP with Cirrhosis. So, a well-designed meta-analysis may help a lot in the clinical practice. However, the main concern about this manuscript is that most of the



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studies included in the meta-analysis are case-series, which are considered as low-level evidences and may directly influence the out-come of the analysis.

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**Manuscript NO:** 38087

**Title:** ERCP in Cirrhosis: A systematic review and meta-analysis focused on adverse events

**Reviewer's code:** 03316921

**Reviewer's country:** Mexico

**Science editor:** Li-Jun Cui

**Date sent for review:** 2018-02-28

**Date reviewed:** 2018-03-06

**Review time:** 6 Days

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

### SPECIFIC COMMENTS TO AUTHORS

I suggest to do some changes in grammar, i especific the localization in the manuscript. I dont have any other conflict of interest. GRAMMAR CORRECTIONS First paragraph - second line: change "paucity" for "a paucity". Introduction First paragraph -

second line: change "high risk" for "high-risk". First paragraph - third line: change "high risk" for "high-risk". First paragraph - eighth line: change "poor" for " a poor". Third paragraph - sixth line: change "comparison" for "a comparison". Materials and Methods Seventh paragraph - seventh line: change "number" for "a number". Nineth paragraph - sixth line: change "score method" for "scoring method". Nineth paragraph - eighth line: change "random effects" for "random-effects". Results Fifth paragraph - fourth line: change "comparison" for "a comparison". Discussion Second paragraph - third line: change "poor" for "a poor" Second paragraph - eighth line: change "smaller" for "a smaller" Second paragraph - tenth line: change "specifically" for "the specifically" Second paragraph - eleventh line: change "advanced" for "the advanced" Fourth paragraph - fourth line: In th sentence "these bleeds were clinically significant or not was not provided" delete the second "not" Sixth paragraph - first line: change "in" for "of" Sixth paragraph - twelfth line: change "similar" for "similarly" Seventh paragraph - Eighth line: change "rate" for "the rate" Eighth paragraph - thirteenth line: change "higher" for "the higher" Nineth paragraph - third line: change "similar" for "a similar" Nineth paragraph - sixth line: change "post procedure" for "post-procedure. Tenth paragraph - sixth line: change "was" for "were". Tenth paragraph - nineth line: change "are" for "is". Twelfth paragraph - sixth line: change "low" for "the low". CORE TIP First paragraph - second line: change "paucity" foe "a paucity"

## INITIAL REVIEW OF THE MANUSCRIPT

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