



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** bpgoffice@wjgnet.com  
**https://www.wjgnet.com**

## PEER-REVIEW REPORT

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

**Manuscript NO:** 72007

**Title:** Microbiologic Risk Factors of Recurrent Choledocholithiasis Post-Endoscopic Sphincterotomy

**Provenance and peer review:** Unsolicited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05910688

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-09-29

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-10-01 22:28

**Reviewer performed review:** 2021-10-20 06:25

**Review time:** 18 Days and 7 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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**Peer-reviewer  
statements**

Peer-Review: [  ] Anonymous [  ] Onymous

Conflicts-of-Interest: [  ] Yes [  ] No

## SPECIFIC COMMENTS TO AUTHORS

This manuscript revealed the significance of the analysis of microbiomes using NGS. Lactobacillales is very promising risk factor of recurrent choledocholithiasis. It was very interesting that the results of culture might be different from those of NGS. According to one explanation, EST breaks the barrier of invasion of intestinal (duodenal) bacterium into biliary tract and might increase retrograde biliary infection. In this study, the source of analysis was taken at the time of EST. So, alteration of microbiomes might occur. It would be more appreciated that these considerations might add into discussion. Among the recurrent cases, verification of microbiome might be useful at the time of re-intervention. Cholecystectomy is preferred after EST or lithotomy of choledocolithiasis. The most frequent cause of choledocolithiasis is spilled gallstones. In the population of this study, how many cases cholecystectomy after EST was performed? The influences of cholecystectomy into the microbiome should be included in consideration. Other cause is infection in biliary tract. The infection rate varies depending on regions. The incidence is assumed to be low in areas with good hygiene. So, the differences between regions might be taken into consideration. In the abstract, "RA" lacks annotation.



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**Reviewer's code:** 05752663

**Position:** Peer Reviewer

**Academic degree:** MD, MSc

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** South Korea

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-09-29

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-10-28 09:12

**Reviewer performed review:** 2021-11-05 21:15

**Review time:** 8 Days and 12 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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Peer-Review: [  ] Anonymous [  ] Onymous

Conflicts-of-Interest: [  ] Yes [  ] No

## SPECIFIC COMMENTS TO AUTHORS

The authors tried to identify the microbiome factors for CBD stone recurrence. The study idea is very intriguing and manuscript is relatively well-written. However, the method especially in bile sampling and clinical outcome measurement (stone recurrence) is somewhat ambiguous and not clear.

1. The authors mentioned that the patients who were diagnosed with cholelithiasis using CT or MRCP were included. In general, "cholelithiasis" means GB stones, and "choledocholithiasis" means CBD stones. Thereby, did the authors mean to say that the patients with GB stones were enrolled? Not the patients with CBD stones?

2. How many patients who had acute cholangitis were included in this study? Or what is the number of just GB stone patients who were not accompanied by acute cholangitis? As you know, the presence of gallstones does not always mean that patients have got inflammatory conditions such as acute cholangitis or cholecystitis.

3. Furthermore, I think the term of "cholelithiasis" in this manuscript was not used appropriately, and a bit confusingly used. So, please check the word usages once again in entire manuscript.

4. I am wondering about the timing of bile juice sampling. Did the authors do sample firstly from the beginning of ERCP procedure? or the bile sample was done at the last time of ERCP procedures after EST and CBD stone extraction had been done?

5. Please show whether the enrolled patients have GB stone or not because CBD stone can be developed by migration of GB stones (secondary CBD stone). How do you define the CBD stone recurrence in this study? How do you discriminate the residual CBD stone or secondary CBD stone due to migration of GB stone from true CBD stone recurrence?

6. Please, show the results of stone characteristics of enrolled patients. For example, cholesterol stone, mixed



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stone, black pigmented stone or brown pigmented stone. And is there any differences of  
bile microbiome composition according to the stone nature? Thank you.