PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	The risk of pyogenic liver abscess and endoscopic sphincterotomy:
	A population-based cohort study
AUTHORS	Peng, Yen-Chun; Lin, Cheng-Li; Sung, Fung-Chang

VERSION 1 – REVIEW

REVIEWER	Professor Ross Smith University of Sydney, Australia
REVIEW RETURNED	27-Aug-2017

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GENERAL COMMENTS	Yen-Chun Peng has made excellent use of a community data base established in Taiwan allowing for long term follow up after endoscopic sphincterotomy. The results appear convincing and it is perhaps surprising that this association is not more widely known. There was a smaller study in 1998(Tanaka et al. 465-69) but the issue has been largely ignored. It is well known that hepatic ablation of tumours is likely to be followed by abscesses after an endoscopic sphincterotomy. Reference List Tanaka, M., et al. "Long-term consequence of endoscopic
	sphincterotomy for bile duct stones." Gastrointest.Endosc. 48.5 (1998): 465-69

REVIEWER	Chang-Min Cho Department of Internal Medicine
	Kyungpook National University School of Medicine
	Kyungpook National University Chilgok Hospital Deagu, South Korea
REVIEW RETURNED	14-Sep-2017

GENERAL COMMENTS	I would like to respect your study of large cohort comparison for the association of pyogenic liver abscess and endoscopic sphincterotomy. In my knowledge, there were no previous studies that whether endoscopic sphincterotomy may cause the risk of
	pyogenic liver abscess. Your result is relatively important as endoscopic sphincterotomy is a risk factor of pyogenic liver abscess. I put some comments and questions before decision for acceptance.
	Major comments 1. In sampled participants, subjects with any PLA within 1 year after the index date were excluded. However, you mentioned the number of event cases and rate in table 3.

Would your explained that situation?
2. In table 4, the case number of event in subjects with
cholangitis and no ES was 8, which was lower than that of subjects
without both of ES and cholangitis. However, rate is higher. Would
you show the PY?
3. Would you put references for the association of endoscopic
sphincterotomy and pyogenic liver abscess? Although your
hypothesis that the disruption of barrier in biliary tree may cause
ascending infection and pyogenic liver abscess, there was
insufficient to explain that. If possible, please put references such as
case report or clinical data.
Minor comments
1. An error in table 1 – the number of women with ES
(n=28232).
By peer-reviewer

REVIEWER	Jose M. Ramos
	Department of Internal Medicine
	Hospital General Universitario de Alicnate
REVIEW RETURNED	10-Dec-2017

GENERAL COMMENTS	The risk of pyogenic liver abscess and endoscopic sphincterotomy:
	A population-based cohort study bmjopen-2017-018818
	The authors have made an interesting manuscript
	Title the risk of pyogenic liver abscess and endoscopic
	sphincterotomy: A population-based cohort study
	The authors present a well-written and argued scientific article.
	The introduction is clear,
	the material and methods are well written,
	the results are synthetic,
	the discussion is well argued
	The limitations were no included
	The reference is OK, but shout be improve
	The tables are clear
	The article must be accepted for publication but we considered to
	include the limitation of the study and review of References 18, 20
	that are incomplete

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Professor Ross Smith

Institution and Country: University of Sydney, Australia

Please state any competing interests or state 'None declared': nil declared

Please leave your comments for the authors below

Yen-Chun Peng has made excellent use of a community data base established in Taiwan allowing for long term follow up after endoscopic sphincterotomy. The results appear convincing and it is perhaps surprising that this association is not more widely known. There was a smaller study in 1998(Tanaka

et al. 465-69) but the issue has been largely ignored. It is well known that hepatic ablation of tumours is likely to be followed by abscesses after an endoscopic sphincterotomy.

Reference List

Tanaka, M., et al. "Long-term consequence of endoscopic sphincterotomy for bile duct stones." Gastrointest. Endosc. 48.5 (1998): 465-69

Reply:

Thanks for your suggestion. The reference paper by Taneka, M., et al. is indeed an important manuscript, and we have added it in the revised manuscript.

Reviewer: 2

Reviewer Name: Chang-Min Cho

Institution and Country: Department of Internal Medicine, Kyungpook National University School of

Medicine, Kyungpook National University Chilgok Hospital, Deagu, South Korea Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below Dear authors,

I would like to respect your study of large cohort comparison for the association of pyogenic liver abscess and endoscopic sphincterotomy. In my knowledge, there were no previous studies that whether endoscopic sphincterotomy may cause the risk of pyogenic liver abscess. Your result is relatively important as endoscopic sphincterotomy is a risk factor of pyogenic liver abscess. I put some comments and questions before decision for acceptance.

Major comments

1. In sampled participants, subjects with any PLA within 1 year after the index date were excluded. However, you mentioned the number of event cases and rate in table 3. Would your explained that situation?

Reply: Thanks for your comments in details. We indeed excluded PLA within 1 year to exclude cholangitis or short-term effect related PLA in the initial design. In table 3, we have revised the time as 1-2 instead of <1.

2. In table 4, the case number of event in subjects with cholangitis and no ES was 8, which was lower than that of subjects without both of ES and cholangitis. However, rate is higher. Would you show the PY?

Reply:

Thanks for your comments in details. Your comment that adding PY is a good suggestion. We have added PY in table 4. It is be reasonable about rate and case number in cholangitis no ES, and both cholangitis with ES.

3. Would you put references for the association of endoscopic sphincterotomy and pyogenic liver abscess? Although your hypothesis that the disruption of barrier in biliary tree may cause ascending infection and pyogenic liver abscess, there was insufficient to explain that. If possible, please put references such as case report or clinical data.

Reply:

Thanks for your comments; After literature review, indeed, most studies concerned that ES related to recurrent stone. There are case reports about the PLA and EST. As another reviewer suggest and our searching, we add references and add a paragraph in discussion.

Minor comments

1. An error in table 1 – the number of women with ES (n=28232).

Reply:

We have corrected this point in revised manuscript table 1.

Reviewer: 3

Reviewer Name: Jose M. Ramos

Institution and Country: Department of Internal Medicine, Hospital General Universitario de Alicnate

Please state any competing interests or state 'None declared': NOne declared

Please leave your comments for the authors below

The risk of pyogenic liver abscess and endoscopic sphincterotomy: A population-based cohort study bmjopen-2017-018818

The authors have made an interesting manuscript

Title the risk of pyogenic liver abscess and endoscopic sphincterotomy: A population-based cohort study

The authors present a well-written and argued scientific article.

The introduction is clear,

the material and methods are well written,

the results are synthetic,

the discussion is well argued

The limitations were no included

The reference is OK, but shout be improve

The tables are clear

The article must be accepted for publication but we considered to include the limitation of the study and review of References 18, 20 that are incomplete

Reply:

Thanks for your detail comments. We have list two limitations in the discussion section and completed the references 18 and 20.