

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 61865

Title: Resection of Pancreatic Cystic Neoplasms in Recurrent Acute Pancreatitis Prevents Recurrent Pancreatitis but does not Identify More Malignancies

Reviewer's code: 02591964

Position: Peer Reviewer

Academic degree: FACS, MBBS, MCh, MS

Professional title: Professor, Surgeon

Reviewer's Country/Territory: India

Author's Country/Territory: United States

Manuscript submission date: 2020-12-21

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-12-21 10:41

Reviewer performed review: 2020-12-29 06:49

Review time: 7 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**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>

SPECIFIC COMMENTS TO AUTHORS

This retrospective study reports an expected outcome. Details of surgical intervention are not provided. Was chronic pancreatitis also ruled out on histopathological examinations. How many patients underwent surgery only for RAP.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 61865

Title: Resection of Pancreatic Cystic Neoplasms in Recurrent Acute Pancreatitis Prevents Recurrent Pancreatitis but does not Identify More Malignancies

Reviewer's code: 05429162

Position: Peer Reviewer

Academic degree: MD

Professional title: Academic Fellow, Doctor, Research Fellow

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2020-12-21

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-12-23 01:50

Reviewer performed review: 2021-01-05 01:22

Review time: 12 Days and 23 Hours

Scientific quality	<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
Language quality	<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
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Summary Muniraj et al. performed a retrospective analysis to determine the efficacy of pancreatic cystic neoplasms' resection for patients with recurrent acute pancreatitis. Although the manuscript well described, there are some major point to be revised.

Major points 1) Overall, the authors only performed univariate analysis of the possible factors determining recurrent acute pancreatitis. However, the multivariate analysis based on the result from univariate analysis and known risk factors for recurrent acute pancreatitis (RAP) should be performed. [Abstract] 1) As the authors described, the primary outcome is the incidence of RAP post-resection. The main result of this study should clearly describe in the conclusion of the abstract. [Introduction] 1) Page 5; While the term "pseudocyst" is widely used in the clinical setting, this term includes multiple cystic lesions. According to the revision of the Atlanta classification 2012 (Banks et al. Gut. 2013 Jan;62(1):102-11. doi: 10.1136/gutjnl-2012-302779), they stated that the development of a pancreatic pseudocyst is extremely rare in acute pancreatitis. The authors should mention at least about Acute necrotic collection (ANC) and Walled-of necrosis (WON) when they discuss about the pancreatic cysts in the setting of acute pancreatitis. [Methods] 1) Page 6; The definition of acute pancreatitis is not clear. Please describe the definition of the acute pancreatitis (Banks et al. Gut. 2013 Jan;62(1):102-11. doi: 10.1136/gutjnl-2012-302779). 2) Page 6; The authors stated that "those who had RAP, defined as 2 or more episodes of acute pancreatitis without an identifiable cause prior to resection". The definition of the "identifiable cause" is not clear. Please specify what is the "identifiable cause". 3) Page 6; There should be references of the definition of recurrent acute pancreatitis which is 2 or more episodes of acute pancreatitis (Testoni et al. World J Gastroenterol. 2014 Dec 7; 20(45): 16891-16901. doi: 10.3748/wjg.v20.i45.16891). 4) Page 6; The imaging used to diagnose is not clear.

Please specify the diagnostic modality used to determine the cystic lesions. Also, please mention the diagnosis is double checked. 5) Page 6; The preoperative diagnostic criteria of the IPMNs, both branch-duct and main-duct is not clear. Please specify whether the branch-duct and main-duct IPMNs were clinically diagnosed or pathologically proven. It is also important to interpret the result of this study. 6) Page 6; The pathological differential diagnosis of the subtypes of IPMNs is not clear. Please specify how to distinguish the subtypes of IPMNs (i.e. performing MUC staining or gene sequencing; Patra et al. Clin Transl Gastroenterol. 2017 Apr 6;8(4):e86. doi: 10.1038/ctg.2017.3.; Furukawa et al. Gut. 2011 Apr;60(4):509-16. doi: 10.1136/gut.2010.210567.). [Methods; Statistical analysis] 1) Page 7; The authors stated that "Statistical analysis was performed by using the statistical algorithms in Review Manager 5.3". The software used for this analysis (it may be Cochrane Review Manager Software 5.3) and its manufacturer should be described. [Results] 1) Page 7; If the preoperative diagnosis was made by using radiologic modalities, the final diagnosis may change according to the pathological diagnosis. Please mention about this possibility. 2) Page 7; Please describe the numbers of macrocystic type serous cystic neoplasms and microcystic type serous cystic neoplasms, as it may contribute having malignant potential (Kimura et al. Pancreas. 2012 Apr;41(3):380-7. doi: 10.1097/MPA.0b013e31822a27db.). 3) Page 8; The severity of RAP is not clear. Please specify the severity of the RAP (Banks et al. Gut. 2013 Jan;62(1):102-11. doi: 10.1136/gutjnl-2012-302779; Jang et al. J Gastroenterol Hepatol. 2013 Apr;28(4):731-8. doi: 10.1111/jgh.12121.). Comparison of Pre-Resection and Post-Resection Period in the RAP Cohort 4) Page 8; It is not clear that the reason of surgical intervention. The pancreatitis episodes per patient prior to resection in the RAP cohort was 2.2. This may indicate that the reason for the surgical intervention may not due to the RAP. Comparison of RAP and Control Cohort 5) Page 8; According to the table 3, there is a

difference of the location (tail: $p=0.02$). Please reconsider the main text. 6) Page 8; According to the table 3, there is a difference of the pathological subtype. There is also statistical difference the numbers of total IPMN patients. This result indicates both cohorts include non-IPMN patients. If the authors would like to perform the statistical analysis about pathological subtype, the different incidence of the BD-, MD-IPMN and non-IPMN should be taken care of. The specific statistical calculation method should be clarified (please reconsider about statistical subpopulation). 7) Page 8-9; In table 3-5, the multivariate analysis should be performed. Please take care of the multicollinearity.

[Discussion] 1) Page 11; the authors stated that “We found that episodes of recurrent acute pancreatitis are rare following surgical resection of pancreatic cystic neoplasms, suggesting that the pancreatic cystic neoplasms were indeed the cause of RAP in almost all cases”. Indeed, the article clearly shows the risk reduction of RAP after the pancreatic resection, it seems further investigation with large population prospective study is needed to prove causal relationship between the cause of RAP and pancreatic resection. Please reconsider this sentence. Minor points [Introduction] 1) Page 5; The authors stated that IPMN are the most common cystic pancreatic tumors. The IPMN is “neoplasm”, as its name suggests, not a tumor (Intra-ductal papillary mucinous tumor, known as “IPMT” was used before the term of IPMN has been developed). [Methods] 1) Page 6; The definition and numbers of patients in control cohort, experimental cohort both with IPMN and without IPMN is not clear. Please make a figure to explain entire cohort. Especially, the definition of control cohort is not clear. Please clarify whether the patients with resection who did not have prior RAP but have pancreatic cyst (or cystic neoplasm) served as control cohort. [Result] Comparison of RAP and Control Cohort 1) Page 8-9; In the table 3-5, not only showing the median age but also the IQR (interquartile range) of age in each cohort should be described. 2) Page 8-9; In the table 3-5; the median cyst size with IQR should be described, as it may affect to the



**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>

malignant potential (Sadakari et al. Pancreas. 2010 Mar;39(2):232-6. doi: 10.1097/MPA.0b013e3181bab60e). 3) Page 8-9; In the table 3-5, the number of IPMN patients with worrisome features and high-risk stigmata should be described.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 61865

Title: Resection of Pancreatic Cystic Neoplasms in Recurrent Acute Pancreatitis Prevents Recurrent Pancreatitis but does not Identify More Malignancies

Reviewer's code: 03358964

Position: Editorial Board

Academic degree: MD

Professional title: Chief Doctor, Director, Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2020-12-21

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-12-24 09:51

Reviewer performed review: 2021-01-08 05:12

Review time: 14 Days and 19 Hours

Scientific quality	<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
Language quality	<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
Conclusion	<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
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**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>

SPECIFIC COMMENTS TO AUTHORS

In this paper, the authors a retrospective analysis to determine the efficacy of pancreatic cystic neoplasms' resection for patients with recurrent acute pancreatitis.. The paper is interesting,; anyway some issues that needs to be addressed: - how they exclude other causes of acute pancreatitis? -The definition of acute pancreatitis is not clear. - How many patients underwent surgery only for RAP? REFERENCES are OK LANGUAGE: OK

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 61865

Title: Resection of Pancreatic Cystic Neoplasms in Recurrent Acute Pancreatitis Prevents Recurrent Pancreatitis but does not Identify More Malignancies

Reviewer's code: 03883464

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Attending Doctor, Doctor, Research Scientist

Reviewer's Country/Territory: Portugal

Author's Country/Territory: United States

Manuscript submission date: 2020-12-21

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-03 12:26

Reviewer performed review: 2021-01-22 00:36

Review time: 18 Days and 12 Hours

Scientific quality	<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
Language quality	<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
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I would like to congratulate the authors for this interesting paper. There are a few suggestions and a few questions that I would request the authors to clarify: Introduction

1. Page 5 line 91- I would suggest authors to include in introduction that the presence of a pancreatic cyst in imaging at diagnosis of pancreatitis is probably the cause of pancreatitis, while the detection of a cyst in the follow-up of pancreatitis with a normal first imaging exam. Methods 2. Were all cysts resected or there were surgeries without resection where preoperative classification using imaging and FNA was used? Please clarify in how many patients classification was based on pathology specimens. 3. Please specify what where the criteria evaluated to exclude other identifiable causes of recurrent acute pancreatitis besides cystic lesions. 4. Please specify follow-time after surgery (mean value, and interval of follow-up). Discussion 5. Please further discuss that, although there is no global increase in malignancy in RAP cysts, malignancy risk is increased in branch-duct IPMNs (n=59). Please further explore by multivariate analysis if it is related to pathological subtype of intestinal type? 6. Please discuss possible reasons why bd-IPMNs have higher risk of RAP than md-IPMNs in this series? Is it related to histological type (bd-IPMNs are predominantly intestinal type in this series). What is the case for md-IPMNs in this series? In the literature md-IPMNs are predominantly of intestinal type. Thank you for the opportunity to review this article.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 61865

Title: Resection of Pancreatic Cystic Neoplasms in Recurrent Acute Pancreatitis Prevents Recurrent Pancreatitis but does not Identify More Malignancies

Reviewer's code: 02591964

Position: Peer Reviewer

Academic degree: FACS, MBBS, MCh, MS

Professional title: Professor, Surgeon

Reviewer's Country/Territory: India

Author's Country/Territory: United States

Manuscript submission date: 2020-12-21

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-01-25 03:16

Reviewer performed review: 2021-01-25 06:10

Review time: 2 Hours

Scientific quality	<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
Language quality	<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
Conclusion	<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
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS



**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>

Page 6, lines 113-116. Introduction: "We therefore performed a retrospective study to assess the characteristics of patients with IPMN who present with unexplained RAP and the effect of surgical resection on the natural history. " However, the study has included other cystic neoplasms as well in the analysis. Aim needs to be modified in view of this and the title of the paper.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 61865

Title: Resection of Pancreatic Cystic Neoplasms in Recurrent Acute Pancreatitis Prevents Recurrent Pancreatitis but does not Identify More Malignancies

Reviewer's code: 05429162

Position: Peer Reviewer

Academic degree: MD

Professional title: Academic Fellow, Doctor, Research Fellow

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2020-12-21

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-01-25 06:15

Reviewer performed review: 2021-01-26 03:49

Review time: 21 Hours

Scientific quality	<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
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript has been revised well. I agree that the manuscript described the significance of pancreatic resection for recurrent acute pancreatitis in patients with pancreatic cystic lesion. I think this manuscript will be potentially acceptable after some correction have been done. I hope my comments would help to improve the quality of this article.

1) Please describe the surgical outcome and complications by surgical procedures. The pancreaticoduodenectomy (“Whipple procedure”) has a high mortality and complication rate. It may affect the patients outcome (Paolini et al. Surg Oncol. 2021 Jan 5;37:101515. doi: 10.1016/j.suronc.2020.12.009.)

2) The term “Whipple surgery” is not a standard term both in Asia and Europe. The term “pancreaticoduodenectomy” or “pancreatoduodenectomy” is more appropriate.

3) In table 1, please consider to add the following variables in entire cohort; • Age • Sex ratio • Location of cyst • Frequency of worrisome features, high-risk stigmata and malignancies • IPMN’s pathological subtypes

4) In the discussion section, the authors stated that the RAP was more often associated with BD-IPMN. As the authors described, there is a discrepancy from prior report. Please discuss this difference.

5) In the discussion section, the authors stated that “We found that episodes of recurrent acute pancreatitis are rare following surgical resection of pancreatic cystic neoplasms, suggesting that the pancreatic cystic neoplasms were indeed the cause of RAP in almost all cases”. I think the sentence is over-interrupted. As pancreatic exocrine function decreases after the pancreas resection (Moore et al. J Gastrointest Surg. 2021 Jan 22. doi: 10.1007/s11605-020-04883-1.), the pancreatic resection itself may decrease the frequency of RAP.