

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45047

Title: Clinical outcomes of ampullary neoplasms in resected margin positive or uncertain cases after endoscopic papillectomy

Reviewer's code: 03475728

Reviewer's country: Italy

Science editor: Ruo-Yu Ma

Date sent for review: 2018-12-13

Date reviewed: 2018-12-18

Review time: 21 Hours, 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 checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

We really enjoyed the opportunity to review the manuscript titled, "Clinical outcomes of ampullary neoplasms in resected margin positive or uncertain cases after endoscopic papillectomy". The article focuses on a interesting and controversial topic: the

endoscopic management of ampullary tumors. Despite its retrospective character, it is an interesting and timely study. I would suggest to bring some minor revisions, which I will try to list below:

1. Considering such a hot topic, widely debated in the literature, I would enrich the reference list, discussing some interesting papers that have already faced this theme, e.g.:
 - Ardengh et al. "Endoscopic papillectomy: The limits of the indication, technique and results". *World J Gastrointest Endosc.* 2015;7(10):987-94.
 - De Palma et al. "Endoscopic snare papillectomy: a single institutional experience of a standardized technique. A retrospective cohort study" *Int J Surg.* 2015.
 - Nam K. et al. "Usefulness of argon plasma coagulation ablation subsequent to endoscopic snare papillectomy for ampullary adenoma" *Dig Endosc.* 2018
 - Ridditid Wet al. "Endoscopic papillectomy: risk factors for incomplete resection and recurrence during long-term follow-up". *Gastrointest Endosc.* 2013;79(2):289-96.
2. Pancreatoduodenectomy is considered to be too invasive for benign neoplasms, so endoscopic papillectomy is proposed as an alternative: the differences in complications, morbidity/mortality, between the two procedures should probably be better emphasized.
3. You assert that "main" indications for EP was adenoma. Do you use other selection criteria, e.g. the lesion size? ... this should be discussed.
4. In the RESULTS section, the authors say that 12 lesions were diagnosed as adenocarcinoma; follow-up was selected for 5 adenocarcinoma, while additional PD was performed in 4 cases: what about the other 3 adenocarcinoma?
5. With regard to technical details, the authors say that they "tried to insert both bile duct and pancreatic stent after the EP procedure"; it might be interesting to discuss this attitude and current evidence for it. More, regarding the resection technique, it would be interesting to understand if they tried to attempt an en block resection in all the cases and, eventually, which were the reasons for failure.
6. Regarding the follow-up protocol, it would be nice to discuss a bit if there are any current established recommendation.
7. Some evidence from literature regarding the



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role of APC after EP should be probably discussed. 8. The retrospective nature of the study along with the small sample size should be emphasized before concluding that positive or uncertain resected margin could be managed by APC. Prospective and comparative data are probably required.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45047

Title: Clinical outcomes of ampullary neoplasms in resected margin positive or uncertain cases after endoscopic papillectomy

Reviewer's code: 03476031

Reviewer's country: Sweden

Science editor: Ruo-Yu Ma

Date sent for review: 2019-01-08

Date reviewed: 2019-01-09

Review time: 21 Hours, 1 Day

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 checked="" type="checkbox"/> Grade D: Fair	<input checked="" 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 type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Nice retrospective study but with only 45 cases over almost 12 years so quite a small case load to draw conclusions from and no really new conclusions are drawn except that the utility of determining radical resection is probably of no use. The study aims at



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determining the clinical outcome of patients that has gone thru EP were the resected specimen has undetermined or positive resection margins. They show that the outcome is probably the same as if the margins were negative, at least for adenomas with recurrence 1/18 or 2/15. Adenocarcinomas were found in both study groups and the authors do not present in what degree the preinterventional biopsies showed adenocarcinoma or adenoma. EP is an established treatment method for the treatment of adenomas in the major duodenal papilla. One question that still remains is at what level of adenocarcinoma invasion is it safe to treat these patients. And how to stage this correctly before any resection is made? No prospective study has to my knowledge been made where patients with biopsy proven adenocarcinoma and thorough staging is allocated to either EP or PD. Instead conclusions regarding the resectability of early adenocarcinomas (Tis or T1a) is made from retrospective studies. The feasibility and results regarding adenoma resection have been shown several times previously in several papers. To make the paper a bit more interesting I would prefer that more data regarding the preinterventional investigations where included. • What did the preinterventional biopsies show? • How many had adenoma or adenocarcinoma already before the EP? • How did that correlate with the results from the resected specimen? • Estimated size of the lesions before the resections? • What clinical signs did the patients have? Jaundice? Abdominal pain? • Define more precisely a super-elderly? How many were they? • What was the performing endoscopists impression regarding the radicality of the resection? Did they believe that the resection was complete or not? • Were all patients examined with EUS and IDUS? At what level of invasion did they have a cutoff to deem them irresectable with EP? • Were there no changes in their approach to these patients over the 12 years? • How did they define their complications? I would also like them to discuss and hopefully present at what rate they succeed with pancreatic stenting and if that correlated to the relatively high rate of post interventional



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pancreatitis. One of the few conclusions that can be made from this study is that the issue of negative resection margins or not is probably of little interest. Instead, that a strict follow-up regimen is applied to find any signs of recurrence and the bit question still remains, if one dares (or finds it ethically appropriate) to randomize between EP or PD in patients with biopsy proven adenomcarcinoma and a strict preinterventional staging.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

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- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45047

Title: Clinical outcomes of ampullary neoplasms in resected margin positive or uncertain cases after endoscopic papillectomy

Reviewer's code: 00069105

Reviewer's country: Spain

Science editor: Ruo-Yu Ma

Date sent for review: 2019-01-25

Date reviewed: 2019-01-25

Review time: 22 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 type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear sirs: You have great experience in the endoscopic treatment of ampullar tumors. Comments. Introduction: you do not mention surgical ampullectomy that is an alternative between endoscopic treatment and PD Material and Methods. IDUS explanation should



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be improved. What do you mean if it is feasible. How many patients biopsy was positive for adenocarcinoma but they were unfit for surgery. Exclusion criteria for surgery was age, Charlson Index,... why surgery was not done after relapse? Hemorrhage and pancreatitis were severe/mild? mortality? need for surgery or endoscopy treatment due to complications? The decision of follow up or PD after positive margin on adenocarcinoma was based ??? Mean follow up and free disease and total survival 1 year 2 year and 5 year of ampullectomy done in malignant tumors? Hospital stay?

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BPG Search:

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- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45047

Title: Clinical outcomes of ampullary neoplasms in resected margin positive or uncertain cases after endoscopic papillectomy

Reviewer's code: 03388124

Reviewer's country: United States

Science editor: Ruo-Yu Ma

Date sent for review: 2019-01-27

Date reviewed: 2019-01-27

Review time: 14 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	(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 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 checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a very nice study that evaluated the clinical outcome of endoscopically resected ampullary tumors with positive/equivocal margins. It has potential implications for patient management and prognostication. This manuscript is well-written and appears

acceptable for publication. 1. Recommend to include statistical analysis (e.g. Fisher's exact test) between adenoma and adenocarcinoma to strengthen the manuscript. 2. Recommend to include representative microscopic histopathologic images (adenoma and adenocarcinoma with positive/equivocal margins). 3. For the follow-up period, recommend to use "months" instead of "days". 4. Recommend to spell out the full word for "PD" at first appearance in the abstract. 5. Is there any difference between a positive HM and positive VM? 6. Based on your study, would you recommend endoscopic therapy only for T1a or T1b adenocarcinoma? 7. During the study time period, have you treated any neuroendocrine tumors with endoscopic resection? Any comments on the clinical outcome of those tumors with positive margins, compared to adenoma/adenocarcinoma?

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- ☐ No