

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16547

Title: Advantage of endoscopic mucosal resection with a cap for rectal neuroendocrine tumors

Reviewer's code: 01714224

Reviewer's country: Italy

Science editor: Ya-Juan Ma

Date sent for review: 2015-01-23 07:55

Date reviewed: 2015-01-30 20:36

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The article by Park Sb et al reports on a retrospective study comparing endoscopic mucosal resection (EMR) versus endoscopic submucosal resection (ESD) of neuroendocrine tumors located in the rectum. Thus, being retrospective, it is possible that all endoscopic procedures and findings emerging from the study are related with the routine clinical practice. Several important points should be clarified. 1. Was NET histotype established prior to or following endoscopic resection? How many NETs were malignant and how many benignant? Did patients with a malignant NET undergo other staging investigations or chemotherapy or other treatments? How patients were followed up, performing clinical visit, radiological investigations, other? Authors should take into account all these points to reach a conclusion about adequacy of endoscopic procedures they compared. 2. Authors reported that all polyps were examined by EUS. Is EUS assessment a their routine policy for all polyps, especially when the lesions is <5 mm in size? Such a policy seems to be time consuming, especially in the clinical practice when a diminutive polyp is generally removed by a biopsy forcep. Authors should explain this choice in a non prospective setting study. 3. More than half of all

polyps (63/116) were <5 mm in size, and 13/63 were removed by ESD. Authors should clarify the reason why these diminutive polyps have been removed by ESD. Did Authors reach a pre-procedure histological diagnosis of NET or EUS show an invasive neoplasm in such 13 diminutive polyps? 4. Authors should explain the reason why endoscopic resection was complete in 100% versus histological resection in 53% of the lesions <10 mm in size. This discrepancy seems to be particularly surprising when ESD was adopted. 5. Authors should furnish data regarding outcome of patients (metastases and survival rate) treated with EMR in comparison to those undergone ESD. Data should be stratified according to lesion size. 6. In Table 2 Authors reported that ESD allowed to reach a complete histological resection in 40/51 (78.4%) of lesions, 35 of them having <10 mm in size (see Table 4). Thus, ESD failed in two lesions >10 mm in size. Authors should furnish possible reasons of incompleteness in all occurred cases, above all with lesions >10 mm. 7. Majority of polyps (109/116, 94%) measured <10 mm and only 7 were >10 mm. As Authors reported in Introduction, the risk of metastases has been reported to be 0-10% (but differently in Discussion they stated 1.7-10%) for tumors <10 mm and 4-30% for tumors 10-19 mm in diameter. As requested in point 1, how many NETs were malignant? It is possible that the number of malignant NETs, together with the number of lesions >10 mm, is too small to reach a conclusion regarding the possible advantage of EMR compared to ESD in the resection of NET.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16547

Title: Advantage of endoscopic mucosal resection with a cap for rectal neuroendocrine tumors

Reviewer's code: 02823396

Reviewer's country: Spain

Science editor: Ya-Juan Ma

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

I have revised the article, focused on 114 patients with endoscopic resection of NETS with a mean diameter of 4-7mm. The authors performed a retrospective study comparing the efficacy of EMR-C vs ESD. They conclude that efficacy (complete resection were similar, 100% in both groups), being EMR-C faster (and cheaper) than ESD for NETs <10mm. I have any comment. Results and conclusion are robust.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16547

Title: Advantage of endoscopic mucosal resection with a cap for rectal neuroendocrine tumors

Reviewer's code: 02544032

Reviewer's country: Norway

Science editor: Ya-Juan Ma

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The paper is an observational, comparative study of two endoscopic techniques for resection of rectal neuroendocrine tumours, limited to rectal mucosa/submucosa. Endoscopic Mucosal Resection with a Cap (EMR-C) is compared with Endoscopic Mucosal Resection with rate of complete histological resection as main endpoint. A significant difference in favor of EMR-C was found (93.3% versus 78.4%), and these data support the conclusion that the preferable method is EMR-C. The study has important limitations: It is retrospective and not randomized. But these facts are underlined in the discussion, which is appropriate. The paper is well written and brings forward some new information.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16547

Title: Advantage of endoscopic mucosal resection with a cap for rectal neuroendocrine tumors

Reviewer's code: 00068723

Reviewer's country: Japan

Science editor: Ya-Juan Ma

Date sent for review: 2015-01-23 07:55

Date reviewed: 2015-02-06 06:15

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This study focused on EMR-C. The aim of this study was clear and interesting. EMR-C showed better outcome than ESD. Mean tumor size was smaller in EMR-C group than ESD group. This point was one major concern about the study. It seemed that smaller tumor were easier to treat. Another concern was that selection criteria of EMR-C or ESD to NET <10mm. Patient selection might affect the results. Introduction. Not all the readers are familiar with NET. More information on NET is necessary. For example, brief introduction of rectal submucosal tumor, percentage of NET against all the rectal SMT, clinical course of NET, pathological feature of NET. Above information would illustrate the clinical significance of this study. Brief introduction of EMR with a cap is necessary. Merit and demerit would be helpful comparing EMR-C and ESD.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16547

Title: Advantage of endoscopic mucosal resection with a cap for rectal neuroendocrine tumors

Reviewer's code: 02438888

Reviewer's country: China

Science editor: Ya-Juan Ma

Date sent for review: 2015-01-23 07:55

Date reviewed: 2015-02-10 17:09

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> [] High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> [] Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> [Y] No	<input type="checkbox"/> [] Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> [] Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> [Y] No	

COMMENTS TO AUTHORS

This study enrolled 114 patients with rectal NETs and 116 lesions were found and resected with EMR-C or ESD. The authors analyzed endoscopic complete resection rate, pathologic complete resection rate, procedure time, and adverse events in the EMR-C and ESD groups to compare the outcomes of EMR-C with those of ESD for the resection of rectal neuroendocrine tumors. They also performed a subgroup analysis by tumor size. The results showed that mean tumor size was 4.62 ± 1.66 mm in the EMR-C group and 7.73 ± 3.14 mm in the ESD group ($P < 0.001$). Endoscopic complete resection rate was 100% in both groups. Histologic complete resection rate was significantly greater in the EMR-C group than in the ESD group ($P = 0.042$). Mean procedure time was significantly longer in the ESD group than in the EMR-C group ($P < 0.001$). Rates of histologic complete resection without complication were similar for tumor diameter ≤ 5 mm as well as in cases of $5 \text{ mm} < \text{tumor diameter} \leq 10$ mm. Finally, the authors concluded that EMR-C may be simple, faster, and more effective than ESD in removing rectal NETs and may be preferable for resection of small rectal NETs. In clinical practice more and more NETs have been diagnosed because of the recognition about this disease,



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improvement of endoscopic technique and increased screening rate. EMR-C and ESD have been used to treat NETs for decade and the reported results were obviously variable. Until now there is no consensus about which modality is superior as to endoscopic complete resection rate, pathologic complete resection rate, procedure time, and adverse events. The different conclusions may be the results of various subgroup patients, specific maneuvers and the preference of endoscopists in different units. So it is not easy to compare the two methods in clinical work with perfectly statistical ways. For example, this manuscript is a non-randomized retrospective study performed in one hospital and its results and conclusions have definite limitations. However, the experience the authors shared in this manuscript is beneficial for further study in this field.