

**ESPS Peer-review Report**
**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 9198

**Title:** Operative strategy for Nonfunctioning Pancreatic Neuroendocrine Tumors

**Reviewer code:** 00001832

**Science editor:** Na Ma

**Date sent for review:** 2014-02-08 14:00

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

In their current manuscript, Furukori et al. report on the results of a small case series (n=9) of surgically treated nonfunctional (NF) pancreatic neuroendocrine tumors (pNETs), with particular focus on lymph node positivity rate after regional lymphadenectomy. Among these 9 patients, the authors identified 7 patients with G1, one patient with G2 and one patient with G3 (neuroendocrine carcinoma-NEC) differentiation status. 6 out of 7 patients with G1 tumors, and the only patient with a G2 tumor had no lymph node metastasis. In the only NEC case, the tumor size was 22mm (compared to approx. 10mm for the G1 tumors), and this patient also had lymph node metastasis. Interestingly, in the only G1 case in which the tumor was unusually large (i.e. 32mm), the authors detected direct invasion of the tumor to a regional lymph node. Therefore, the authors concluded that, in the surgical treatment of NF-pNETs, regional lymphadenectomy could be omitted if the tumor is smaller than 10mm in size. The study addresses a question of high clinical interest and actuality, and there are an increasing number of studies that try to elucidate whether a regional lymphadenectomy is indeed necessary for small pNETs. The question has not yet been sufficiently answered, making such studies further necessary. With regard to the study of the authors, though, I have some fundamental concerns, which are listed as follows: 1) In a recent study by Hashim et al., even low-risk pNETs were shown to have the potential of positive lymph node status and to bear a worse survival rate if positive lymph nodes are detected (4.5 versus 14.6 years). Indeed, some authors (e.g. Tsutsumi et al.) also favoured regional lymphadenectomy for tumors greater than 15mm in size and for those located in the pancreatic head. However, the currently available, relative large case series do now allow conclusions on the omission of lymphadenectomy in pNETs. Rather, current literature seems to favor



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regional lymphadenectomy in the treatment of pNETs, regardless of the tumor size and G status, due its prognostic role. The authors should definitely discuss the implications of the findings of Hashim et al. (Annals of Surgery, 2014) and Tsutsumi et al. (J Gastroenterol 2012) for their study. 2) As also noted by the authors, the very small case load in their study does not allow reliable conclusions, at least not at the extent as put forward by the authors. For example, the case no. 3 on the Table 1 had a tumor size of 22mm but still had no lymph node metastasis. In the presence of such a small number of patients, it is possible to draw a big spectrum of conclusions, the majority of which may be wrong. Therefore, the authors should certainly consider including more patients and/or more carefully/conservatively formulating their conclusions.

**ESPS Peer-review Report**
**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 9198

**Title:** Operative strategy for Nonfunctioning Pancreatic Neuroendocrine Tumors

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

The present manuscript by Furukori et al. focuses on the need of lymphadenectomy in NF-pNETs <10mm and suggests that in these tumors the lymphadenectomy can be omitted. The concept is very challenging. Minor points: 1) How the authors characterize "free of recurrence"? Is it only radiologically (which modality?) and/or biochemically (CgA and/or PP and/or other related hormones)? The biochemical values before the operation and during follow up should also be reported. 2) I suggest that the authors will clearly state that the well differentiated cases were sporadic NF pNETs (except the vHL case). 3) It is recommended that the authors will include only well differentiated sporadic cases. NECs have a different pathophysiology and even small tumors can be aggressive including a potential of giving hematogenous seeding. Furthermore, by including only one NEC case it is not appropriate to draw safe conclusions. Major points: 1) The number of well differentiated sporadic NF pNETs cases that are less than 10 mm is limited and no reliable conclusions can be drawn. More cases should be included. On the other hand I understand that identifying NF pNETs <10mm has its limitations. 2) The identification of LN metastases may be a late event for pNETs due to their slow growing nature especial for tumors with a Ki67<3%. A longer (radiological and biochemical) follow up in the cases that did not undergo lymphadenectomy (eg cases 1 and 9) would strengthen the manuscript especially when the authors' postulation opposes the to date literature trend that favors lymphadenectomy. 3) Other factors eg neural/angio-invasion and not only size may determine the malignant potential of a lesion.