



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32681

Title: Para-aortic node involvement is not an independent predictor of survival after resection for pancreatic cancer

Reviewer's code: 03548113

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-01-21 15:55

Date reviewed: 2017-01-23 13:19

Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, SCIENTIFIC MISCONDUCT, CONCLUSION. It contains checkboxes for various criteria like 'Grade A: Excellent', 'Priority publishing', 'Google Search', etc.

COMMENTS TO AUTHORS

1. Authors described that all patients underwent standard lymph node dissection and para-aortic sampling and they also described "Para-aortic nodes were excised by harvesting the lymphocellular aortocaval tissue located below the left renal vein until the origin of inferior mesenteric artery ". Regarding station 16b1, were all patients undergo the complete dissection of 16b1? Were some patients undergo just the sampling? 2. What is LFN ratio, LFN status, and Para-aortic LFN status in Table 4 and 5? LFN is lymph node? 3. I agree that a few patients with PALN metastases can survive and this results are interesting. However, this study has a crucial problem about the statistical analysis. Authors showed that there were significantly correlations between lymph node status and PALN involvement, radicality and PALN involvement. And there is a significantly correlation between stage and lymph node status, certainly. Therefore, these factors can't be included to the variables for multivariate analysis simultaneously. Furthermore, although lymph node ratio was not associated with poor survival by univariate analysis, why was lymph node ratio included to the variables for multivariate analysis? If the statistical analysis is performed correctly, PALN status



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may be the independent factor.



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 32681

**Title:** Para-aortic node involvement is not an independent predictor of survival after resection for pancreatic cancer

**Reviewer's code:** 00001832

**Reviewer's country:** Germany

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-01-21 15:55

**Date reviewed:** 2017-01-23 14:45

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"/> 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 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 type="checkbox"/> No	

**COMMENTS TO AUTHORS**

The manuscript by Sperti and colleagues analyzes the prognostic impact of para-aortic lymph node involvement on survival in resected pancreatic cancer patients. 151 patients that underwent pancreaticoduodenectomy were included in this retrospective study. Besides others, the authors show that para-aortic lymph node involvement was associated with reduced survival, yet this was not an independent prognostic marker. It is concluded that "the decision to perform pancreatic resection should not be only taken on the basis of lymph node status". This is an interesting and well-written analysis of a relevant topic. Drawbacks are the retrospective study design and the relatively small patient cohort. If I have two further minor comments: Was para-aortic node sampling done routinely in all patients or only in those with suspected metastasis? I would change the term "radicality" to margin involvement, since the resection is not more or less radical depending on margin status (at least in most cases).



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 32681

**Title:** Para-aortic node involvement is not an independent predictor of survival after resection for pancreatic cancer

**Reviewer’s code:** 01804834

**Reviewer’s country:** Germany

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-01-21 15:55

**Date reviewed:** 2017-01-23 16:04

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"/> 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 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 type="checkbox"/> No	

**COMMENTS TO AUTHORS**

The authors report on their experience of 151 pancreatic resections and the influence of PALN on overall and disease-free survival. On multivariable analysis, PALN+ was no independent risk factor reducing overall- and disease-free survival. Generally, the manuscript deals with an interesting and relevant topic. The influence of PALN metastases on survival and the indication / contraindication to surgery is still under debate, and the presented study supports the theory that a suspected PALN involvement should not per se be considered a contraindication for surgery. Please find my specific comments below: The Results section should be sub-headed in e.g. Univariable Analysis and Multivariable Analysis. Some phrase- and language polishing should be done throughout the text, for example: Abstract: AIM: ? Lymph node involvement is an important prognostic factors for pancreatic cancer.." should read "Lymph node involvement is an important prognostic factor for pancreatic cancer" Methods: "...with para-aortic nodes dissection .." should read: "... with para-aortic node dissection" "Mean and median number of pathologically assessed lymph nodes were 28 and 26, respectively (range 14-63)." Range of mean or median? Only give the median number



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“One-hundred forty-one patients recurred and died” should read (as I understand) “Died after tumor recurrence” Conclusion: “, but they were not independent prognostic index.” Should read “ .. were not independent prognostic factors” In the discussion section, the following sentence: “Unfortunately we have inadequate data on the number of lymph nodes removed, and their metastasis rate within 16a1, 16a2, 16b1 and 16 b2 stations.” Should be explained / is difficult to understand in the context (at least to me)..



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 32681

**Title:** Para-aortic node involvement is not an independent predictor of survival after resection for pancreatic cancer

**Reviewer’s code:** 00053888

**Reviewer’s country:** United Kingdom

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-01-21 15:55

**Date reviewed:** 2017-01-23 19:49

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 checked="" 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**

This is a good study worthy of publication and reports 151 patients undergoing pancreaticoduodenectomy for pancreatic adenocarcinoma. The histological data on resection margins, lymph node status, etc is reproducible across other data sets. The authors have chosen to concentrate on the presence or absence of LN metastases in the para-aortic lymph node groups. In doing so they have inevitably ended with very small sub-set analysis from which it is difficult to make firm conclusions. The authors have wisely acknowledged the short comings of their own study, they then go on to tell us the strengths of the study which are far out weighed by the weaknesses and this sentence can be removed. The authors have wisely been limited with their conclusions and are essentially correct in saying that no real conclusion regarding resection in the presence of para-aortic LN metastases can be made from these data.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 32681

**Title:** Para-aortic node involvement is not an independent predictor of survival after resection for pancreatic cancer

**Reviewer's code:** 02976802

**Reviewer's country:** Germany

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-01-21 15:55

**Date reviewed:** 2017-01-24 15:48

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 checked="" 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"/> 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 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

Sperti et al. report results on a retrospective series of pancreatoduodenectomy for pancreatic cancer including para-aortic lymph node resection (LN16b1). From 151 patients with PALN resection, 16.5% patients had positive PALN. However, PALN metastasis was not a multivariate determinant of survival. The study is important, although there are two recent meta-analysis on this topic. However, the authors should underline the novel aspects of their study. What do pancreatic surgeons learn from this additional study? Moreover, I have some questions, that should be addressed. - Do the authors have data on the morbidity of PALN resection, i.e. do they have cases without PALN resection for comparison. The potential benefit of the PALN resection regarding survival must be outweighed against the associated morbidity. - Why do the authors not have the number of positive (tumor-infiltrated) PALN? This would be an important measure tumor biology. - What is meant by radicality of resection? Do the authors mean the R status? - What was the follow-up time of the study? - What was the median survival time of patients with PALN+ status? Can the authors provide data on palliative patients and compare the survival outcome? - 151 patients in 12 years



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means approximately 12 patients per year. The Padua center probably had more pancreatoduodenectomies within this period. Was there a selection of cases, or did not all patients had a PALN dissection? If so, could there be a bias regarding the selection of cases for PALN dissection? - there are some misspellings typos throughout the manuscript (e.g. Introduction: However, some Authors reported ...), so that the paper should undergo language revision.



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## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 32681

**Title:** Para-aortic node involvement is not an independent predictor of survival after resection for pancreatic cancer

**Reviewer's code:** 00069105

**Reviewer's country:** Spain

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-01-21 15:55

**Date reviewed:** 2017-01-27 02:33

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 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"/> 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 checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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"/> No	

### COMMENTS TO AUTHORS

I have enjoyed the paper. The weakness of the paper (retrospective) is commented by you. Some more information about morbidity and relationship with survival could be interesting. Mistake in reference 6 (no year included). Interesting review of the literature



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32681

Title: Para-aortic node involvement is not an independent predictor of survival after resection for pancreatic cancer

Reviewer's code: 03261792

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-01-21 15:55

Date reviewed: 2017-02-01 19:59

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 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
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<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" 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

First of all I have a comment about multivariate analysis. I think LN status or LN ratio and Para-aortic LN status were possible to be confounding factor each other because PLAN+ cases are all node positive cases. You may need perform multivariate analysis using selected factor "Grading, Radicality, LFN status" or "Grading, Radicality, Para-aortic LN status". These factors not likely to be confounded each other. I think that there is critical mistake in the data of table 3. Is this data of table 3 right? It's impossible that MST of all factor are exactly same between OS and DFS. Usually MST of DFS is shorter than that of OS. In fact the MST value of Para-aortic lymph nodes status in the Table 3 is different from that derived from survival curve shown in Fig 2. If the data in table 3 are correct, all tumor recurrent cases died on the same day when recurrence is found. Is it possible? How about the results of multivariate analysis in the tumor grade 1-2 group? Is PLAN status independent prognostic factor or not? There is wrong spelling in the chapter "Statistical analysis". Fischer's exact test =>Fisher's exact test