

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7284

Title: Pain sensation in pancreatic diseases is not uniform -- the different facets of pancreatic pain

Reviewer code: 02467447

Science editor: Gou, Su-Xin

Date sent for review: 2013-11-13 13:45

Date reviewed: 2013-11-27 02:38

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 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 checked="" 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

D'Haese and colleagues have submitted a retrospective analysis of patients treated with pancreatic resection in order to evaluate 'pain patterns' in patients with various pancreatic pathologies. The authors present their manuscript as an evaluation of pain in patients with pancreatic diseases other than pancreatic cancer and pancreatitis since little is known about 'pain sensation and their mechanisms' in these patients and that it requires more characterization. The aim of the study was therefore to evaluate pain in patients with less common pancreatic neoplasms and how it compared to patients with pancreatic cancer and pancreatitis. There are some interesting findings in this paper from a large series of patients. Although the authors note that pain sensation and pain patterns in patients with rare neoplasms is not well known, it is unclear what these data would add to the literature. This reviewer has a few comments. General – there are too many abbreviations and it is confusing (e.g., Ptm, Pca, NEN, AmpC, IPMNI, NENh). None of these are used in the pancreas surgical or medical literature. Introduction – paragraph 2 – the authors discuss retrospective studies and different hypotheses for the etiology of pain in patients with chronic pancreatitis – the studies cited were not designed to evaluate the pathophysiology of pain. Furthermore, this paper is not designed to evaluate the pathophysiology of pain or develop an hypothesis about pain. Furthermore it is well known that these rare neoplasms are most often found incidentally. When they are symptomatic, they are more often malignant and therefore would be potentially in the cancer group. The authors should focus the discussion on what is known about pain in the rare neoplasms rather than the review of pancreatitis and cancer related pain. This can include pain as presenting symptoms, what it may or may not indicate, etc. This will help set the paper up much better since pain may be an indication to operate on patients with serous cysts but a marker of

malignancy in a patient with a mucinous cyst. Also, a patient with a mucinous cyst with pain may need resection vs one that does not have pain. A better foundation for the study should be provided. Methods – the authors cite previous reports on how the pain was assessed – this is not adequate for a study focused on pain as this was the primary methodology. Please provide more details in the Methods. Methods – the authors state that pain analysis was performed prior to the operation. When was it analyzed? In clinic, the day of surgery? Methods – was it determined whether patients were taking narcotics during the time of the pain assessment? This would impact pain scores. Results – the Tables are very difficult to interpret with all of the abbreviations. Furthermore, numbers should be provided in addition to percentages. Results – the data in Tables 3 and 4 could be provided in the text and are not informative and simply demonstrate the selection of patients who need or who are candidates for resection. Table 5 – please clarify – T4 pancreatic tumors (adenocarcinoma and neuroendocrine) are unresectable. The information on pain and outcomes for adenocarcinoma are very interesting and in itself are important and should be more carefully analyzed. Including these data with the other rare tumor types makes the manuscript unclear and disorganized without a clear message.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7284

Title: Pain sensation in pancreatic diseases is not uniform -- the different facets of pancreatic pain

Reviewer code: 01560081

Science editor: Gou, Su-Xin

Date sent for review: 2013-11-13 13:45

Date reviewed: 2013-11-27 18:35

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 checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	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

Abdominal pain is a major clinical feature in chronic pancreatitis and pancreatic cancer. It is the first study about the pain patterns in all pancreatic tumors and correlate pain with the respective clinicopathological data. This study is well designed and properly performed. The statistical analyses is reasonable. The result is credible. The conclusion is helpful in clinical practice.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7284

Title: Pain sensation in pancreatic diseases is not uniform -- the different facets of pancreatic pain

Reviewer code: 00069137

Science editor: Gou, Su-Xin

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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	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	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

This is the largest study to date with the aim to characterize pain in patients with pancreatic tumors, and provides important information on this common and difficult to treat condition. As such, it is of great interest. It is clearly written. I have some minor comments. There is minor English language editing needed. Why did the authors use that specific pain scale? Where other pain scales (such as the visual analogue scale) performed? Where there differences when considering pain as a continuous variable, instead of a categorical variable? The references on the pathophysiology of "pancreatic pain" are somewhat dated (references 8 and 9). Excellent recent reviews deal exclusively with this subject (Pancreatology. 2012 Mar-Apr;12(2):104-12, Langenbecks Arch Surg. 2011 Feb;396(2):151-60; Gut. 2008 Nov;57(11):1616-27), including some by the authors own research group. The discussion on the mechanisms in the introduction section and the discussion section could be expanded. Besides pain quantification, do the authors have data on pain characteristics? Where all events of "pancreatic pain" of the same quality? (i.e "standard" burning pain vs transflctive pain vs dull pain etc.). If so, does pain characteristics other than intensity predict mortality, outcome or anatomical location of tumor?. There is some evidence that diabetes reduces pain in pancreatic cancer, possibly due to nerve damage (Cancer Med. 2012 Dec;1(3):357-62). The authors data suggests otherwise, this point could be more fully developed as it seems relevant for their ideas. Do the authors speculate regarding the reason for increased mortality in patients with pain other than increased neural invasion? Are there other causes (more hospitalizations, opiate use, comorbidities etc.)?. In tables, p values could be specified by letters (say, for pain II, p=0.2 in PCa vs CP....) to indicate specific differences. Tables 3 and 4 could be collapsed into a single figure table. Table 5 could be eliminated, and the result only mentioned in the text.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7284

Title: Pain sensation in pancreatic diseases is not uniform -- the different facets of pancreatic pain

Reviewer code: 00505438

Science editor: Gou, Su-Xin

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Date reviewed: 2013-12-07 12:25

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" 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	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
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<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

An excellent discussion of pain associated with pancreatic pathology. Some comments: Although there was no obvious difference between tumor stage and pain, was there any correlation between the size of the tumour and pain between head and body/tail. Similarly was there any difference between lymphovascular or neural invasion microscopically between head and body/tail cancers. Similarly if this is the case, then you have confirmed the long standing clinical truism of pain being a surrogate marker of more advanced disease. This should be commented on with some possible comment on whether the presence of pain could be used as an indication for more aggressive regional therapies such as radiotherapy or prolonged adjuvant therapies.