PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39104

Title: Challenges in diagnosis of pancreatic cancer

Reviewer's code: 01430761

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2018-03-30

Date reviewed: 2018-03-30

Review time: 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[Y] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[ ] Advanced
			[ ] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[ ] No

SPECIFIC COMMENTS TO AUTHORS

This is a well written, narrative review of early diagnosis of pancreatic cancer.   1. Although the authors described ERCP has little role in early diagnosis of pancreatic cancer in Page 22, there is an attempt to utilize ERP with pancreatic juice cytology called SPACE (J Gastroenterol. 2015;50:147-54, Clin J Gastroenterol. 2017;10:541-545). This

should be discussed in detail. 2. Pancreatic cystic neoplasms and diabetes are two important keys to early diagnosis of pancreatic cancer. In particular, there are guidelines for IPMN surveillance. These topics should be included in "screening program" paragraph or as a new paragraph. 3. In Table 1, transabdominal ultrasound and ERP should be added. In Figure 1, ERP should be added in "no mass, no metastatic disease" category. 4. In Figure 2, mass, SpA, SpV should be shown using arrows. 5. Please clarify "reaction to chemotherapy" described in "Treatment protocols." In addition, did gastrointestinal reaction and myelosuppresion include all grades toxicities or severe ones? 6. In their conclusion, the study results aid prediction of survival in pancreatic cancer. However, for clinical use, nomogram analysis is more useful (Br J Cancer. 2014;110:1943-9). 7. In Page 11, CT also plays a role in detecting lung metastases and close attention should also be paid to lungs. 8. In Page 26, SPT should be changed to SPN. Neuroendocrine tumors should also be added as one of mimickers. 9. In Page 4, please describe who performed a manual review. All three authors? How did the authors decide which papers should be included when the review list was different from one reviewer to another? 10. In Page 11, please add short comments on neoadjuvant treatment on borderline resectable pancreatic cancer to clarify the importance of this category rather than just resectable vs. unresectable.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39104

Title: Challenges in diagnosis of pancreatic cancer

Reviewer's code: 01518946

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2018-03-30

Date reviewed: 2018-04-03

Review time: 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[Y] Grade A: Excellent	[ ] Grade A: Priority publishing	[Y] Accept (High priority)	Peer-Review:
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Minor revision	[ ] Onymous
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			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[ ] No

SPECIFIC COMMENTS TO AUTHORS

This manuscript is an excellent review for pancreatic cancer in details. However, the authors should amend a few parts as described below before publication.   There are 2 spaces between each word in some parts.   In page 7, sens and specif should be described as sensitivity and specificity respectively.   ERCP should be described as full

spell, when it is described at first. The authors should show a benefit of ERCP for diagnosis of pancreatic cancer. Even though pancreatic mass is not detected by other image diagnosis, changes of pancreatic duct such as stenosis or disruption are detected by ERCP. There are many papers of possible biomarkers for pancreatic cancer. The authors should cite more papers about novel biomarkers with benefit and/or limitation.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39104

Title: Challenges in diagnosis of pancreatic cancer

Reviewer's code: 02544727

Reviewer's country: Greece

Science editor: Ze-Mao Gong

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Date reviewed: 2018-04-04

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
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			[ ] No

SPECIFIC COMMENTS TO AUTHORS

1) The statements "Its high mortality rate is attributed to its difficulty of diagnosis ..." in the Abstarct and "The high mortality rate undoubtedly relates to the difficulty in obtaining an early stage diagnosis, ..." in the Introduction, are not completely correct because the aggressive biological behaviour of pancreatic adenocarcinoma is the major

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

determinant of poor prognosis. Therefore these statements should be modified.   2) The diagnostic algorithm for suspected pancreatic adenocarcinoma shown in Figure 1 is probably better and more sensible to be placed as a sum up after the presentation of the available diagnostic modalities. In this algorithm there are two options that might need an explanatory footnote. In the scenario of a patient with a diagnostic CT or MRI for pancreatic cancer (and resectable tumor) without distant metastases do the authors consider EUS+FNA as a pre-requirement for all patients before their referral to MDT? In the scenario of a patient with clinical suspicion for pancreatic adenocarcinoma but without pancreatic mass or distant metastatic lesions on imaging, the authors suggest EUS±FNA to confirm the absence of pancreatic cancer. The conditions imposing EUS±FNA in this scenario should be better clarified in a footnote.   3) The expression "…. and injection of neutral oral contrast." in the "Computed tomography scanning" paragraph is not accurate. You cannot inject an oral agent.   4) In the "Computed tomography scanning" paragraph the authors state "Discussions regarding general diagnosis of "borderline resectable" disease occurs later." No such section was found in the manuscript.   5) In the "Magnetic resonance imaging" paragraph, the authors state "… on post-contrast T1-weighted images, as seen in Figure 5." This is a skip in figure numbering.   6) Tumor size and nodal status might be more appropriate expressions instead of T1–2 staging, and N staging, respectively.   7) The diagnostic accuracy between MDCT and EUS for nodal staging an resectability has been similar. Showing percentages of diagnostic accuracy might be necessary.   8) "…. minimising the risk of tumour seeding." Tumor seeding during FNA or needle biopsy is a major concern and providing some data or extending a little a bit this issue might be useful.   9) "There was however no difference in diagnostic accuracy, technical failure or complication rates." in the "Fine needle aspiration technique" paragraph. It's good to present some figures or actual comparative data. The same applies to "… and a recent meta-analysis showing no

significant difference in performance or diagnostic yield found between biopsy and aspiration needles" in the "EUS Fine needle aspiration vs. Fine needle biopsy" paragraph.   10) Panel (a) in Figure 5 is a coronal plane view not an axial view.   11) The pancreas is a retroperitoneal organ and hence the sensitivity of transabdominal ultrasound is poor in the "Ultrasound and ERCP"paragraph. Data supporting this statement?   12) " … depending if pre-cancerous lesions (cysts, branch duct IPMN) are included or not" in the "Screening programs" paragraph. Which are these cysts considered as premalignant lesions and what about main duct IPMNs?   13) The use of arrows or other indicators to delineate the lesions, points of interest or the findings presented in the figures might be useful for the readers.   14) Please pay attention to grammatical errors. Some examples include: Discussions regarding general diagnosis of "borderline resectable" disease occurs later. For this reason, while MRI is not widely used Longitudinal studies have also observed a significant increase in diagnostic accuracy over time, likely reflecting increasing operator proficiency The diagnostic accuracy between MDCT and EUS for nodal staging an resectability has been similar compared to the 4 passes needed for when real-time evaluation of specimens A study comparing 22-gauge FNA vs FNB ....   and a recent meta-analysis showing no significant difference enhanced 18FDG-PET have been combined with CT to produce one fusion image, as seen in Figure 5. IgG4 staining of the ampulla biopsy are also suggestive It is also important to not incorrectly diagnoses adenocarcinoma in patients with SPT   15) Please be also consisted with the terminology: See …for indeterminate pancreato-biliary stricture and ….with pancreaticobiliary expertise

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39104

Title: Challenges in diagnosis of pancreatic cancer

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SPECIFIC COMMENTS TO AUTHORS

Good review on a common topic.

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