

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 83711

Title: Radiation therapy prior to a pancreaticoduodenectomy for adenocarcinoma is associated with longer operative times and higher blood loss

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03733090

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2023-03-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-31 02:14

Reviewer performed review: 2023-04-12 11:58

Review time: 12 Days and 9 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors reported the association between neoadjuvant radiotherapy and 30-day morbidity and mortality outcomes among patients receiving a pancreaticoduodenectomy for pancreatic adenocarcinoma, compared to surgical resection alone. This study is the first time that such associations have been reported using multivariable analysis with patients receiving only neoadjuvant radiotherapy. It was found a statistically significant increase in total operative time and perioperative transfusion requirements among patients receiving neoadjuvant radiation therapy compared to just surgery alone. Their findings are consistent with those of previous similar studies. Based on the discussion provided, here are some suggestions for further discussion or analysis: 1. The dose of radiotherapy was not mentioned in this study. I speculate that different doses of radiation may affect the outcome of the treatment. 2. Compared with patients undergoing surgery without radiotherapy, patients undergoing neoadjuvant radiotherapy were more likely to be younger, female, non-Hispanic white, diabetic, and of normal body weight, and more likely to have a lower T-stage, a lower N-stage, receive an elective surgery, have a higher wound class,

etc. Further study is warranted to determine whether these factors may affect the occurrence of organ space infection and pancreatic fistula. Therefore, I suggest that multivariable regression analysis should be carried out with organ space infection rate and pancreatic fistula rate as dependent variables, including age, gender, ethnicity, diabetes status and weight status, T stage, N stage, wound grade, pancreatic duct size, and preoperative radiotherapy as independent variables. This analysis is necessary to confirm that direct surgery is an independent risk factor for organ space infection and pancreatic fistula. 3. The term "the two study groups" used in this article can easily be understood as two different research institutions conducting this study, and it is recommended to use "two groups of cases" or other more appropriate names. 4. In Discussion, second paragraph, lines 7-10, "Similarly, a study using NSQIP data from 2014 to 2015 showed that the perioperative transfusion requirement rate among patients receiving neoadjuvant therapy (chemotherapy and/or radiotherapy) was significantly lower than the rate in patients who progressed directly to surgery [21]." Reference [21], Czosnyka et al. (2017) reported "Neoadjuvant treatment was associated with lower rates of pancreatic fistulas (10.2% vs. 13.2%, $P = 0.017$), but higher intra/postoperative transfusion rates (27.4% vs. 20.3%, $P < 0.0001$). <https://doi.org/10.1016/j.hpb.2017.07.001>

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Peer-review model: Single blind

Reviewer's code: 05261202

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-03-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-04-19 01:44

Reviewer performed review: 2023-04-25 15:40

Review time: 6 Days and 13 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors carefully analyzed the data of patients listed in the 2015-2019 NSQIP data set who received a pancreaticoduodenectomy for pancreatic adenocarcinoma. Two groups were formed based off neoadjuvant radiotherapy status. I think the conclusions drawn from this grouping are not in line with the current clinical treatment background. Neoadjuvant chemotherapy has become the treatment of choice for borderline resectable pancreatic cancer and has begun to be used in patients with resectable pancreatic cancer who may have a poor prognosis. I recommend that the control cohort be neoadjuvant chemotherapy patients. In addition to the above mentioned, there are two other questions. 1. The intraoperative difficulty of borderline resectable pancreatic cancer was significantly greater than that of resectable pancreatic cancer. There was no subgroup analysis for this in the two cohorts, and the results would be biased. 2. In "introduction" part, there mentioned "Despite the purported benefits, neoadjuvant therapy is still regarded with caution and its use remains low in the United States[13]". I believe the original article refers to the current status of neoadjuvant therapy in resectable pancreatic cancer.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-03-29

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2023-05-15 00:39

Reviewer performed review: 2023-05-16 07:09

Review time: 1 Day and 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thanks to the authors for answering all my questions.

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Review time: 5 Days and 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The author avoids my serious concerns raised, "comment 2". The response does not address my doubts.