



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 63503

Title: Impact of surgery for chronic pancreatitis on the risk of pancreatic cancer: untying the Gordian knot

Reviewer's code: 05386976

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor, Surgeon, Surgical Oncologist

Reviewer's Country/Territory: Russia

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Manuscript submission date: 2021-01-28

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-04-01 16:21

Reviewer performed review: 2021-04-20 02:33

Review time: 18 Days and 10 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 Grade E: Do not publish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 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 checked="" type="checkbox"/> Minor revision <input 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



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SPECIFIC COMMENTS TO AUTHORS

The review presented is a weighted point of view at the new strategy of preventive pancreatic surgery addressed to the cases with high risk of pancreatic cancer. The main attention of the authors was paid as to complex interrelations between chronic pancreatitis (CP) and PDAC, so as to correlation between PDAC and surgery for CP. The literature search in PubMed was adequate. Critical consideration of epidemiological studies and their meta-analyses have shown their demerits and potential false escalation of cancer risks in CP. Good work was done in assessment of studies for genetic predisposition for CP with the risks of PDAC, studies have demonstrated indirect correlations between the type of CP-related mutation and cancer risks, studies showing higher cancer risks for PRSS1 mutations, advanced inflammation and external factors. Discussing the known paper, which suggested clustering of outcomes and complications in three groups, authors underlined that fibrosis and ducts blockage with concurrent complications look the most possible cancer risk factors. Authors assessed the impact of different factors on cancer risks, paying attention to the universal approaches for cancer prevention – nutrition modification, BMI normalization, stopping with smoking and alcohol consumption. Especially interesting was the analysis of the two recent retrospective studies, which have shown an increased pancreatic cancer risk with increase of the length of CP and decrease of these risks after mainly resectional surgery for CP. It was underlined that surgery possibly can decrease the risk of PDAC, but not eliminates it. Key factor of cancer prevention can be a timely surgery, i.e. performed shortly after the moment when surgery has become safe because of fibrotic changes of the pancreas. Pancreatic resection with excision of the most part of fibrotic and inflamed tissues can be the most cancer preventive surgical actions, and this ideology can cause the appearance of “risk-decreasing” pancreatic surgery. Authors are quite



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reasonable in evaluating the arguments of different studies, taking into consideration insufficient power, retrospectivity, lack of other risk factors assessment (smoking and alcohol) and other important details. Authors concluded that we need more well organized epidemiological studies, which has to address the point of interest of this work, because today there is no enough data for routine active screening and prophylactic surgery of CP. This strategy can be rational only in persons with confirmed inherited pancreatitis. Our conclusion: the paper "Impact of surgery for chronic pancreatitis on the risk of pancreatic cancer: untying the Gordian knot" can be accepted for publication in the World Journal of Gastroenterology.