



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 46022

**Title:** Intraoperative intraperitoneal chemotherapy increases the incidence of anastomotic leakage after anterior resection of rectal tumor

**Reviewer’s code:** 02569164

**Reviewer’s country:** United Arab Emirates

**Science editor:** Fang-Fang Ji

**Reviewer accepted review:** 2019-03-08 19:04

**Reviewer performed review:** 2019-03-10 13:27

**Review time:** 1 Day and 18 Hours

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

**SPECIFIC COMMENTS TO AUTHORS**

In the manuscript, “Intraoperative intraperitoneal chemotherapy increases the incidence of anastomotic leakage after anterior resection of rectal tumor” by Zhi-Jie Wang et al., the aim of the work was to find out whether intraoperative intraperitoneal



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chemotherapy increases the incidence of Anastomotic leakage (AL) after anterior resection of rectal neoplasms. They reported that Fluorouracil implants exhibited no association with AL. Instead, lobaplatin significantly increased the incidence of AL. They concluded, “Depending on choice of different chemotherapeutic drugs, intraoperative intraperitoneal chemotherapy might increase the possibility of AL after anterior resection of rectal neoplasms”. This might be interesting finding worth of reporting after putting it in its proper context. Major issues: 1- The finding is primitive and limited to one therapeutic agent and not the other one tested in this work. It cannot be generalized. Therefore, it is clear that the title is over and needs to be amended to reflect the limited finding. 2- In their discussion they mention that “However, this correlation was only observed in cases using lobaplatin. Lobaplatin is a type of cytotoxic drug that can inhibit cell proliferation and induce apoptosis by destroying the structure and function of DNA, especially cells with rapid proliferation. Given that rectal anastomotic stoma healing requires rapid proliferation of regenerative cells, we hypothesize that lobaplatin increased the incidence of AL by inhibiting cell proliferation”. First, if this is the case, then the point of the paper should highlight that the finding is limited to a chemotherapy type and possibly the “mode of administration”. Second and more important, chemotherapy typically affect cancer cell with much less effect on normal cells; which needs to be mentioned and clarified in this context. Typically, the author should support their argument by experimental data e.g. (in vivo using animal models) if available. 3- The conclusion does not reflect the contents of the paper. Minor issues: 1- Some statements need to be supported with evidence such as “The reluctance of patients to receive preoperative radiotherapy might be the reason.” 2- The number of typo and grammar is surprising given that professional company checked the document. The authors are advised to double check and clarify the reason for all of these mistakes such as the following (to mention a few): a. “who didn’t



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received preoperative” b. Lobaplatin is a type of cytotoxic drug that can inhibit cell proliferation and induce apoptosis “by destroying the structure and function of DNA”, especially cells with rapid proliferation. Note the inappropriate use of “destroyed” with DNA structure and function c. “a more sufficient impact on anastomotic stoma than fluorouracil implants” sufficient is not clear; do you mean more “efficient”? d. No consistency in the format of “Fluorouracil” /” Fluorouracil” with capital or small “F”?

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- No

##### ***BPG Search:***

- The same title
- Duplicate publication
- Plagiarism
- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 46022

**Title:** Intraoperative intraperitoneal chemotherapy increases the incidence of anastomotic leakage after anterior resection of rectal tumor

**Reviewer's code:** 03270609

**Reviewer's country:** Russia

**Science editor:** Fang-Fang Ji

**Reviewer accepted review:** 2019-03-15 03:57

**Reviewer performed review:** 2019-03-19 06:27

**Review time:** 4 Days and 2 Hours

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

**SPECIFIC COMMENTS TO AUTHORS**

The authors address important issues related to the treatment of locally advanced colon cancer. They analyze the role of intraperitoneal chemotherapy in the development of such a formidable and sometimes fatal complication, such as the anastomotic leakage



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(AL). An analysis of the current state of the problem of AL has been presented, factors affecting the development of AL and the possibility of preventing this complication are noted. The results of study are scientifically based. Using references are up to date. At the same time, a number of shortcomings and inaccuracies in text attract attention.

**Introduction** Explanation of abbreviations should be given when first mentioned not only in the abstract, but in the text of the manuscript: «AL is a severe and common postoperative issue after anterior resection of rectal neoplasms, with a high incidence ranging from 6.1% to 11.9%[1-3].»

**Result** The data presented in the manuscript make it possible to judge the influence of various factors on the frequency of AL. However, the title and purpose of the study is to study the effect of intraperitoneal chemotherapy on the frequency of AL. The main authors' methodological error lies in the fact that they divided patients into groups with and without AL. However, in order to achieve this goal, they need to divide the patients into groups receiving and not receiving intraperitoneal chemotherapy. With this approach, in the group receiving intraperitoneal chemotherapy, AL will develop in 12 of 256 patients (4.7%), and in the group not treated with intraperitoneal chemotherapy - in 8 of 416 patients (2.0%). I think that in this case the differences will be statistically significant. Analysis of other clinical, tumor-related and operation-related factors in these groups is necessary in order to assess how comparable these groups are. Only in this case it will be possible to assert that the increase in the frequency of AL is associated precisely with the presence of intraperitoneal chemotherapy, and not the inequality of groups in other indicators that also affect this complication. I think that the authors can easily fix it.

**Discussion.** Written very well. The authors competently, based on the literature data, justify the association of various factors, including the features of intraperitoneal chemotherapy with the development of AL, note the existing study limitations. However, I think that the first 8 lines of the discussion are related to the results of the study and should be



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placed in the appropriate section. Table 1. There should be no abbreviations in the name of the table. Table 2 - 3. The presented material does not make it possible to understand how the authors calculated the frequency of the case (percentages). The characteristics should be divided into subgroups, within which the sum of cases will give 100% (for example, as in Table 4). In addition, there is a discrepancy in the number of patients who received chemotherapy. According to the text and in the table, there are 250 of them, but the number of patients who received Lobaplatin and Fluorouracil composes 256 (Table 3). Authors should clarify this discrepancy. English The manuscript is written literate in English, but some discrepancies still were noted: There are grammatical errors, for example: This case control study collected information from 672 consecutive patients who received anterior resection of rectal carcinoma with the double stapling technique in our institution from September 2016 to September 2017. Morphological errors (inconsistent proposal), for example: Peritoneal recurrence is common for patients who have received radical resection of rectal carcinoma, which results from the residual tumor cells after primary tumor removal. Stylistic mistakes, for example: «all locally advanced patients»

## **INITIAL REVIEW OF THE MANUSCRIPT**

### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- No

### ***BPG Search:***

- The same title



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Duplicate publication

Plagiarism

No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 46022

**Title:** Intraoperative intraperitoneal chemotherapy increases the incidence of anastomotic leakage after anterior resection of rectal tumor

**Reviewer's code:** 02544757

**Reviewer's country:** Taiwan

**Science editor:** Fang-Fang Ji

**Reviewer accepted review:** 2019-03-14 04:00

**Reviewer performed review:** 2019-03-26 15:27

**Review time:** 12 Days and 11 Hours

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

**SPECIFIC COMMENTS TO AUTHORS**

Considering peritoneal recurrence is a challenge for patients with locally advanced colorectal cancer, recent studies have explored the clinical benefit of the role of intraoperative intraperitoneal chemotherapy in these patients. In the current study, the



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authors assessed the relationship between multiple clinicopathological factors and treatment factors, including intraoperative intraperitoneal chemotherapy and anastomotic leakage (AL) in rectal cancer patients who underwent anterior resection of rectal neoplasms. In their study, the authors revealed that lobaplatin, male sex and synchronous primary malignancy are risk factor for development of AL. The results of this study are interesting; however, there are still some questions to be resolved. Major comments 1. In the page 5 of Introduction section: In the sentences “ Intraoperative intraperitoneal chemotherapy has been gradually adopted to treat rectal carcinoma patients in eastern countries in the past few years and this is not associated with neoadjuvant or adjuvant therapy[19, 20]”, the intraoperative intraperitoneal chemotherapy (from references of 19 and 20) is used for colorectal cancer patients. However, in the locally rectal cancer patients, most patients will undergo neoadjuvant chemoradiotherapy followed by operation for anal preservation. In addition, preoperative chemoradiotherapy provides better local control and disease-free survival than postoperative chemoradiotherapy for rectal cancer patients in randomized trials. The authors should provide more information of aforementioned results in the Introduction section. Furthermore, authors can describe whether the roles of intraoperative intraperitoneal chemotherapy are different in patients with colon cancer and in those with rectal cancer. 2. In the Methods section, the authors should provide more information of grade B or C according to the proposal from the International Study Group of Rectal Cancer in 2010. In addition, the definition of AL is based both on the clinical symptoms and image findings? what is the criteria for AL in image findings? 3. In the multivariate analyses of the “Results” section: Considering the number of patients from each factors are not different (for example, male: 418, lobaplatin only 16), how to calculate and analyze, these issues should be addressed. In addition, how to define synchronous primary malignancy in your study? 4. In the Discussion section: Since the



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number of use of lobaplatin in the intraoperative intraperitoneal chemotherapy is only 16 patients. It is difficult to conclude that the Intraoperative intraperitoneal chemotherapy can increase the incidence of anastomotic leakage after anterior resection of rectal tumor. At least, the title should be revised as Intraoperative intraperitoneal chemotherapy using lobaplatin may increase the risk of incidence of anastomotic leakage after anterior resection of rectal tumor. Along this line, the authors should provide more information of the relationship between complications and intraoperative intraperitoneal lobaplatin in the other subtypes of cancer patients. Minor comments 1. If authors could provide the examples of images of AL in rectal cancer patients who receive intraoperative intraperitoneal chemotherapy with lobaplatin after anterior resection. 2. There are few grammar errors in the whole article. For example, "Further investigation were performed to explore the respective impacts of different agents." It should be revised as "Further investigation is performed....."

#### INITIAL REVIEW OF THE MANUSCRIPT

##### *Google Search:*

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- Duplicate publication
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- No

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- Plagiarism
- No