Reviewer 1

This is an interesting manuscript which attempts to cover a knowledge gap. The paper can be accepted as long as the authors are willing to address the following recommendations:

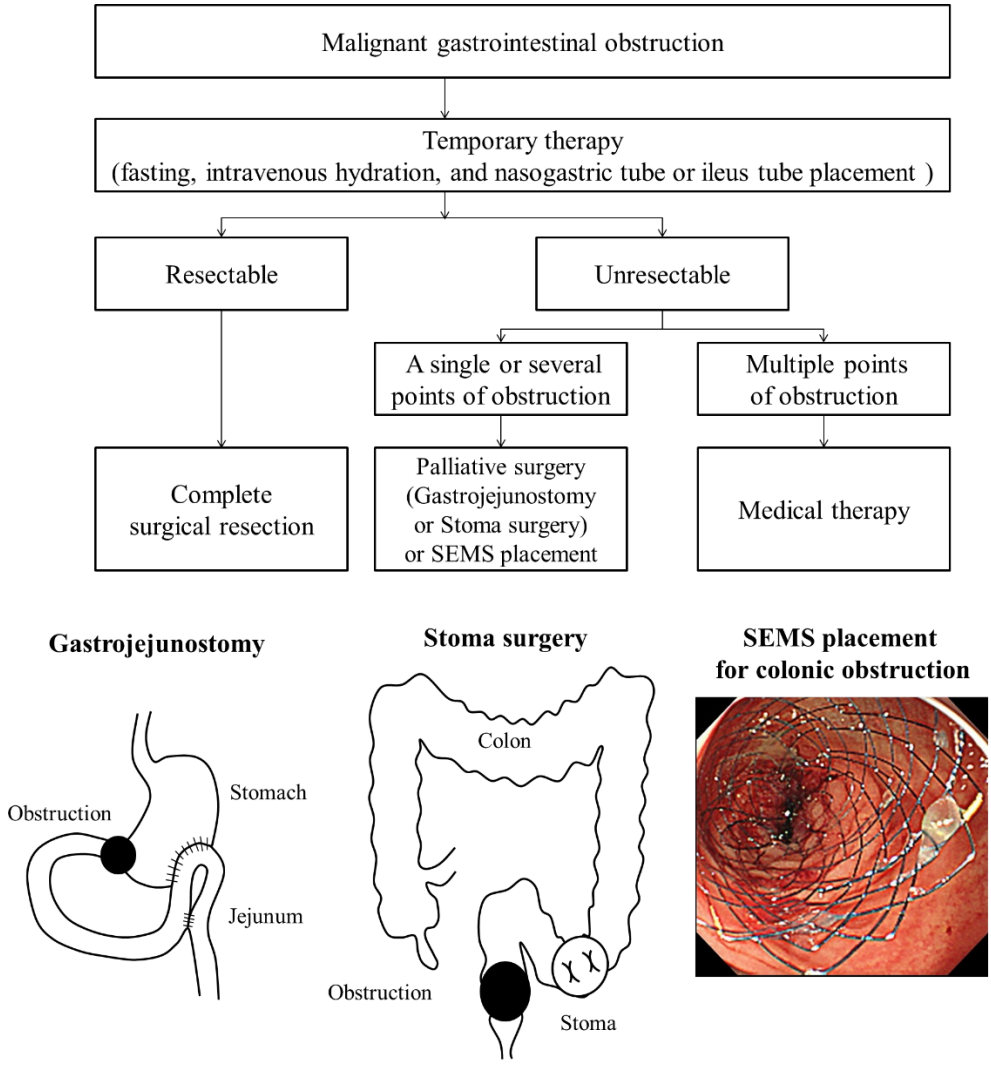
#1. Provide more context about the current management algorithms/guidelines for gastrointestinal cancers leading to gastrointestinal objection in the introduction. Probably a figure could illustrate so, but I would leave this to the judgement of the authors.

Response: We have added context and a figure to the Introduction section to explain the current management algorithms for gastrointestinal cancers leading to gastrointestinal obstruction, as follows:

"Gastrointestinal obstruction causes oral intake impairment, nausea, vomiting, and abdominal pain, and increase a risk of gastrointestinal perforation. Primary therapy involves fasting, intravenous hydration, and nasogastric tube or ileus tube placement for bowel rest and decompression [Int J Clin Oncol. 25:1-42:2020; Endoscopy 2020; 52(5):389-407]. In secondary therapy, complete surgical resection is performed for resectable malignant gastrointestinal obstruction; palliative surgery, including bypass and stoma surgery or self-expandable metal stent (SEMS) placement, is performed at one or more points of unresectable malignant gastrointestinal obstruction (Figure. 1).

Chemotherapy after palliative surgery or SEMS placement is a particularly challenging clinical issue. Although it can improve overall survival [4-6], little is known regarding the difference in overall survival between patients undergoing chemotherapy treatment and those receiving best supportive care (BSC). In addition, the risk of gastrointestinal perforation is a concern for treatment involving chemotherapy combined with SEMS [7, 8]." (Page 4, Lines 3–15)

Figure 1. Our management of malignant gastrointestinal obstruction



#2. Elaborate on the limitations of their study (e.g. inclusion of patients with different types of cancer, the different number of participants in the study groups).

Response: We have added information regarding the study limitations, as follows:

"First, it was a retrospective study. Although we used multivariate cox proportional hazard models to reduce the effects of confounding factors, some bias may remain because the decision to undergo chemotherapy depends on so many factors

including unmeasured confounders. It is difficult to evaluate the effect of chemotherapy more accurately in our setting. Second, our study included patients with different types of cancer and there were different numbers of patients among the cancer groups. Third, the DPC database lacked information on potential prognostic factors such as radiotherapy history and pathological findings.” (Page 10, Lines 26–32)

#3. Recommend future research based on their findings and limitations. In this context the authors can consider briefly discussing precision medicine approaches (such as liquid biopsies, tumor genetic profiling or microbiome analysis - the latter have been stressed in some recent review studies regarding gastrointestinal malignancies - either resectable or not. https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC6960076/ https://pubmed.ncbi.nlm.nih.gov/34298740/ - these references serve as an example, the authors can select studies that support their arguments on the matter)

Response: Thanks for thoughtful suggestions. We have added sentences to the Discussion section about future studies and advances in precision medicine as follows:

“The effectiveness of chemotherapy after the intervention was similar among the cancer types and obstruction sites. Especially in cases of pancreatic cancer and gastroduodenal obstruction, chemotherapy may be more beneficial. These findings will help guide future research on treatment approaches and precision medicine. Currently, overall survival and recurrence risk are predicted based on limited data such as pathological findings. However, recent biological research has suggested potential biomarkers, including circulating tumor DNA and micro-RNA, as well as microbiome profiling, to predict overall survival and recurrence [13-15]. In the near future, these precision medicine methods are expected to contribute to cancer therapies including molecular targeted anti-cancer drugs, monoclonal antibody therapy, and antibiotic therapies.” (Page 10, Lines 12–22)

Reviewer 2

Thank you for this important paper. This is useful to inform patients about the ability to have cases of longer survival after intervention for malignant obstruction. There are a few concerns with the paper that should be addressed.

#1. "multiple obstructions" - does this mean multiple occurrences of obstruction, or multifocal obstruction- should be clarified

Response: "Multifocal obstruction" is our intended meaning. We have clarified the term in the revised manuscript (Page 6, line 9 and page 7, line 29).

#2. This type of literature is extremely biased, because receipt of chemotherapy depends on so many factors beyond BI and age, and the extent of disease is difficult to capture and quantify. This limitation needs to be addressed.

Response: We have added this as a limitation, as follows:

"First, it was a retrospective study. Although we used multivariate cox proportional hazard models to reduce the effects of confounding factors, some bias may remain because the decision to undergo chemotherapy depends on so many factors including unmeasured confounders. It is difficult to evaluate the effect of chemotherapy more accurately in our setting." (Page 10, line 27)

#3. I question whether the primary outcome should be overall survival, rather than patency. We know that systemic chemotherapy increases survival, and those that are able to obtain chemotherapy are going to live longer. Patency, however, is something that we value and it is novel in understanding the role of chemotherapy in maintaining GI tract patency. Please address why you chose this outcome. I do commend you on trying to inform this complex patient population.

Response: We thank the reviewer for this positive comment. We chose patency as a secondary outcome because all eligible patients exhibited gastrointestinal obstructions. Patency is commonly used to evaluate the therapeutic effects of palliative surgeries and self-expandable metal stent (SEMS) placement for patients with malignant obstructions [Dig Dis Sci 2010; 55: 668-674; Surg Endosc 2016; 30: 4765-4775; Langenbecks Arch Surg 2020; 405]. Thus, we included that outcome in

our study. We emphasize that chemotherapy improves patency outcomes; this is a strength of our study.

In addition, our finding showed that chemotherapy was associated with prolongs gastrointestinal patency. (Page 10, line 25)

Reviewer 3

This manuscript, result of a multicentre study, obviously has great merits. Results are supported by tables, supplementary tables and figures. I have listed some suggestions for consideration below:

#1. Key words: The authors may consider inserting here also “palliative surgery”. The importance of Key words is to improve indexing. Also, it increases the chances for the manuscript to be found by readers, during their searches.

Response: We have added the suggested key words.

#2. Core Tip: Here, the authors should briefly insert their findings, not only the controversies in the literature and the lack of multicentre experience. Their findings contribute to fill this gap and they are important. There are enough words left for the length of the Core Tip.

Response: We have revised the Core Tip to read:

“Core tip: The impacts of chemotherapy on patients with malignant gastrointestinal obstructions remain unclear and multicenter evidence is lacking. Does chemotherapy improve the duration of gastrointestinal patency (and thus overall survival) in such patients? This multicenter observational study revealed that the median patency duration in the chemotherapy group was longer than that in the best supportive care (BSC) group (9.7 vs. 2.5 months). Similarly, the median overall survival was longer in the chemotherapy than the BSC group (19.3 vs. 5.4 months, log-rank test, $P < 0.01$).”

#3. Introduction: As the following sentence represents a result, not an aim, please reformulate it: “In addition, we identified the optimal population for chemotherapy after palliative surgery or SEMS placement.” Instead of “we identified” you could use “we aimed to identify…”.

Response: We have corrected the text.

#4. Material and methods: a. page 4: Since Figure 1 does not show any comparison between the two groups, I suggest to replace the verb “compared” with “selected” (or another verb chosen by the authors) and adjust the sentence accordingly [in the sentence “We compared the chemotherapy group (patients who received any chemotherapy drugs after the intervention) with the BSC group (patients who did not receive chemotherapy

drugs after the intervention) (Figure 1)].” Same mention for the sentence in Results (Patient characteristics). b. Page 4: please rewrite the sentence “Gastrointestinal bleeding was defined as endoscopic hemostasis”, maybe “was defined as any GI bleeding requiring endoscopic hemostasis.”

Response: We have corrected the text.

#5. Results: Table 1 shows multiple significant differences between the two groups. Please develop on this in Discussion. The authors used a lot of statistics in the Tables (correct, otherwise), but many results have to be interpret with caution and they have to be discussed in detail in “Discussion”.

Response: Thank you. Indeed, a retrospective observational study may be affected by unmeasured confounders. Younger patients of better performance status may have been preferred for chemotherapy. We emphasize this in the Discussion, as follows:

“Second, bias in terms of patient characteristics may have influenced the results. The chemotherapy group included younger patients, those of higher BI, and more NSAID users. This suggests that the chemotherapy group may have previously been treated for other diseases. In turn, this may have increased palliative surgery performance, and improved the patency and survival durations.” (Page 9, line 29)

#6. Discussion paragraph should include more limitations.

Response: First, it was a retrospective study. Although we used multivariate cox proportional hazard models to reduce the effects of confounding factors, some bias may remain because the decision to undergo chemotherapy depends on so many factors including unmeasured confounders. It is difficult to evaluate the effect of chemotherapy more accurately in our setting. Second, our study included patients with different types of cancer and there were different numbers of patients among the cancer groups. Third, the DPC database lacked information on potential prognostic factors such as radiotherapy history and pathological findings.” (Page 10, lines 27–32)

#7. Please insert also a paragraph indicating concrete directions for prospective research.

Response: Thank you. Chemotherapy may be particularly beneficial for patients with pancreatic cancer accompanied by gastroduodenal obstruction. Our findings suggest that such patients may be candidates for precision medicine. Currently,

overall survival and the recurrence risk are predicted on the basis of limited data such as pathological metastatic findings. However, recent research has suggested that circulating tumor DNA and micro-RNA levels, and the microbiome profile, may predict overall survival and recurrence. In future, such precision medicine approaches may translate to specific cancer therapies including molecularly targeted anti-cancer drugs, monoclonal antibodies, and antibiotics. We have added text to the Discussion. (Page 22, Lines 15–22)

#8. Reference 7 – Please correct the first author' name to "Brierley" and remove the repeated word "ed".

Response: We have made the correction.

#9. Please also insert ORCID for the Authors, according to the requirements of the journal.

Response: We have added the ORCID data.

#10. Also, there are no « Conflict-of-Interest Disclosure Form » and « Copyright License Agreement ». Please insert.

Response: We attach these documents to the revision.