Dear editors and reviewers

Thank you for giving us the opportunity to revise our manuscript. We have modified our manuscript as per the reviewers' suggestions and have outlined all changes made in the responses below.

Reviewer#1

Thank you for inviting me to review this manuscript. The authors reviewed the patients who underwent definitive surgery from 2 centers with 20 years experience. Nevertheless, I have some questions and suggestions

Answer: We appreciate the time taken to review our manuscript. We have responded to each of your questions accordingly and revised the manuscript, tables, and figures.

1. The authors included only resectable patients of DC-II and AC, which are only a minority of total patients with these diseases. I'd rather suggest the authors to change the title to be more representative of the study population. I was mislead by the title and expected to see the data of all staging of those patients.

Answer: Thank you for your suggestion. We have now changed the title from "Comparison of clinicopathological characteristics between ampullary carcinoma and carcinoma of the second portion of the duodenenum" to *"Comparison of clinicopathological characteristics between resected ampullary carcinoma and carcinoma of the second portion of the duodenenum*."

2. As these 2 primary tumors usually have overlapping lesion and presentation symptoms and signs, how could you ascertain the diagnosis of AC and DC-II separately? –

Answer: That is a pertinent query. We confirmed the site of tumor origin pathologically, and we subsequently diagnosed AC when the tumor originated from the papilla of the duodenum. In contrast, DC-II was diagnosed in cases where the tumor originated from the second portion of the duodenum.

3. Table 1 should be a part of results (baseline characteristics of the enrolled patients), not in the method part. –

Answer: Thank you for your kind comments. We have now deleted "Table 1" from the "Patients and methods" section and combined it with Table 2.

4. In determining overall survival and recurrence free survival, how did the authors obtain the date of death data? And how did the authors define recurrence? These should be mentioned in the method part.

Answer: We appreciate your valuable feedback.

Firstly, we performed a follow-up survey, and the median follow-up period was 36.5 months. Recurrence was defined when the tumor was detected again using imaging modalities, such as enhanced CT. Therefore, we added the following sentence on page 6 (lines 2–4) in the “Patients and methods” section:

“Recurrence was defined when the tumor was detected again using imaging modalities, such as enhanced CT.”

5. For statistical analysis, the authors stated only categorical variables comparisons, how about continuous variables? –

Answer: Thank you for your kind comments. Continuous variables were compared using Mann–Whitney U tests. Consequently, we have now added the following sentence on page 7, (line 9) in our statistical analysis: “Continuous variables were compared using Mann–Whitney U tests.”

6. What is actuarial survival? Should it be actual survival instead? –

Answer: We appreciate your helpful comment. We have now removed “actuarial” and replaced it with “actual” which is the correct term.

7. The term 'Digestive Symptoms' is very vague, more details of symptoms e.g., pain, GI bleeding, bloating, dyspepsia, etc. will be more useful for readers in understanding the presentation of both tumors. –

Answer: Thank you for your valuable comment. Among the preoperative symptoms, we examined digestive symptoms, such as nausea, vomiting, and abdominal pain and also symptoms of anemia, such as anemia and tarry stool. Therefore, we have now changed “digestive symptoms” into “*digestive symptoms i.e., vomiting, nausea, or abdominal pain”* on page 7, lines 26–27.

8. When the authors mentioned how many patients had disease recurrence, the recurrent rate developed in what timeframe? 5-years? 10-years? or 1-year?

Answer: Thank you for your question. The median follow-up period was 36.5 months.

9. In the tables: Table 1 and 2 are almost the entirely the same, they could be wrapped

up into only 1 table.

Answer: Thank you for your kind comment. We have now combined Table 1 and Table 2.

Reviewer#2

1. This study on the comparison between duodenal and AoV cancer is valuable in that there are few studies reported so far. And your comment on lymph node metastasis in Discussion was plausible. I really enjoyed reading this manuscript with great interest. I would like to ask you a few questionable points.

   Answer: We appreciate the time taken to review our manuscript. We have carefully answered each of your questions and made the appropriate changes in our manuscript.

2. “both tumors arise from anatomically similar locations”… I think both tumors arise from anatomically close locations, not similar locations.

Answer: Thank you for pinpointing this. We have now revised “anatomically similar locations” to “anatomically close locations” on page 3, line 5 in the “Abstract” section.

3. What did the ‘standard pancreatoduodenectomy’ in Method mean? How much stomach was resected in this ‘standard’ PD? I think you need to clarify it.

Answer: Thank you for pointing this out. “Standard pancreatoduodenectomy” represents classical pancreatodudonectomy or Whipple procedure. We have therefore replaced “standard pancreatoduodenectomy” with “classical pancreatoduodenectomy (Whipple procedure)” in the “Materials and methods” section.

4. You classified regional lymph nodes into superior pancreaticoduodenal lymph nodes (N SP), inferior pancreaticoduodenal lymph nodes (N IP), pyloric lymph nodes (N Py), hepatic lymph nodes (N He) and superior mesenteric lymph nodes (N SM). My questions are 1) with what criteria did you divide PD nodes into superior and inferior? 2) why didn’t you divide PD nodes into posterior and anterior as you cited that lymphatic spread from ampullary carcinoma mainly extended from the posterior pancreaticoduodenal region to the superior mesenteric lymph nodes in Discussion sector? and 3) In figure 3, N-SM resided in the left of the SMA. Did you intend to describe N-SM as depicted in figure 3? If so, there seems to be much differences from other authors in the perception of number 14 superior mesenteric lymph nodes.

Answer: 1) and 2) We appreciate your accurate indications and suggestions. In this

study, we divided pancreaticoduodenal lymph nodes into superior and inferior nodes in accordance with the regional lymph nodes of the duodenum in AJCC Cancer Staging 7th edition. We also referred to a previous research study “Prognostic Factors and Lymph Node Metastasis Patterns of Primary Duodenal Cancer” (World J Surg.2022 Jan;46 (1): 163-171).

3) We would like to apologize for the misleading figure. N-SM did not represent mean lymph node on the left side of the SMA. We have now revised the position of N-SM in Figure 3.

5. In Table 1 and 2, there are some numerical errors. The numerical values of AGE, mGPS are written differently. Age: Table 1_DC-II..64(37-84); AC..69(41-85) Table 2_ DC-II..69(41-85);AC.. 64(37-84) mGPS: Table 1_DC-II.. mGPS 0 =16 Table 2_mGPS 0=17

Answer: Thank you for your kind comments. We have now revised Table 1 accordingly.

6. Table 1 and 2 are listed with almost the same contents, so it would be better to make them as one table. If not, p-values should be added to compare the basic characteristics between the two groups in Table 1.

Answer: Thank you for your kind comment. We have now merged Tables 1 and 2 into Table 2.