

I have reviewed your article titled "Clinical features and prognostic factors of neuroendocrine tumours in the ampullary and nonampullary of the duodenum" and I have some suggestions for major revisions. Here are the areas that need attention:

Title: The title could be more precise. Consider revising it to "Clinical Features and Prognostic Factors of Duodenal Neuroendocrine Tumours: A Comparative Study of Ampullary and Nonampullary Regions".

Clinical Features and Prognostic Factors of Duodenal Neuroendocrine Tumours: A Comparative Study of Ampullary and Nonampullary Regions

Abstract: Background: The background section could benefit from more context about why the study of DNETs is important.

Duodenal neuroendocrine tumours (DNETs) are rare neoplasms. However, the incidence of DNETs has been increasing in recent years, especially as an incidental finding during endoscopic studies. Regrettably, there is no consensus regarding the ideal treatment of DNETs. Even there are few studies on the clinical features and survival analysis of DNETs.

Aim: The verb "analysed" should be "analyze". The correct sentence should be "To analyze the clinical characteristics and prognostic factors of patients with duodenal neuroendocrine tumours."

To analyze the clinical characteristics and prognostic factors of patients with duodenal neuroendocrine tumours.

Conclusion: The conclusion could be strengthened by summarizing the key findings more clearly. Also, consider discussing the implications of your findings for future research or clinical practice.

Surgical treatment is a protective factor for prolonging the survival of DNET patients. Compared to DNETs in the ampullary region, patients in the nonampullary region group had a longer survival period. The liver is the organ most susceptible to distant metastasis of nonampullary DNETs.

Keywords: The keyword "Nonampullary region group" could be simplified to "Nonampullary region".

Duodenum; Neuroendocrine; Tumour; Ampullary region; Nonampullary region; Clinical features; Prognostic

Introduction: Paragraph 1: Please provide more references for the statement "The vater ampulla is composed of a common channel of the common bile duct, pancreatic duct, and duodenal papilla, which is the intersection of the intestinal, pancreatic, and biliary epithelium."

The vater ampulla is composed of a common channel of the common bile duct, pancreatic duct, and duodenal papilla, which is the intersection of the intestinal, pancreatic, and biliary epithelium^[3,4].

3. Pea A, Riva G, Bernasconi R, et al. Ampulla of Vater carcinoma: Molecular landscape and clinical implications. *World J Gastrointest Oncol*. 2018 Nov 15;10(11):370-380. doi: 10.4251/wjgo.v10.i11.370.

4. Beger HG, Treitschke F, Gansauge F, et al. Tumor of the ampulla of Vater: experience with local or radical resection in 171 consecutively treated patients. *Arch Surg*. 1999;134(5):526-532. doi:10.1001/archsurg.134.5.526.

Paragraph 2: The sentence "The standard histological classification and grading standards for tumours released by the WHO in 2019[7] classify DNETs into two categories: NETs and NECs." could be rephrased for clarity. Consider "According to the WHO's 2019 histological classification and grading standards for tumours[7], DNETs are classified into two categories: NETs and NECs."

According to the WHO's 2019 histological classification and grading standards for tumours^[8], DNETs are classified into two categories: NETs and NECs.

Paragraph 3: The statement "Ninety percent of DNETs are nonfunctional neuroendocrine tumours, with only a few exhibiting functional DNETs." could use a better reference for the percentage mentioned.

90% of DNETs are nonfunctional neuroendocrine tumours, and only 10% are functional DNETs

Paragraph 4: The sentence "It is recommended to improve imaging examination and fully evaluate risk factors through endoscopic ultrasonography before making a definitive choice[14]." could be more specific. What kind of improvements are suggested?

It is recommended to use endoscopic ultrasound examination to determine the depth of tumor infiltration, local lymph node metastasis, and puncture biopsy before making a definitive choice.

Materials and Methods: Inclusion and Exclusion Criteria: The criteria for inclusion and exclusion are clear. However, it would be helpful to provide more details about the "China Anti-Cancer Association guidelines for the diagnosis and treatment of neuroendocrine neoplasms (2022 Edition)" that you used for diagnosis. Data Collection: The data collection process is well-described. However, it would be beneficial to provide more information about the process of endoscopy and imaging data collection.

Inclusion criteria: According to the "China Anti-Cancer Association guidelines for the diagnosis and treatment of neuroendocrine neoplasms (2022 Edition)" ^[14], **patients diagnosed with neuroendocrine tumors in duodenal tissue pathology are diagnosed with DNETs**. Exclusion criteria: Incomplete clinical and pathological data.

Survival Status Follow-up: The follow-up method is clear. However, it would be beneficial to provide more details about the process and any challenges encountered during the follow-up.

Date of diagnosis was defined as the date the tumor was first diagnosed through tissue pathology. Length of follow-up was calculated from the date of diagnosis to the date of the doctor's last phone contact, or the date of death. Follow up termination event refers to the end of follow-up or death caused by tumor recurrence and metastasis.

Results: Clinical Data Characteristics: The presentation of clinical data characteristics is clear. However, consider providing more context about the significance of these findings. Comparison of Clinical Features: The comparison of clinical features between the ampullary region group and nonampullary region group is well presented. However, it would be helpful to discuss the implications of these differences.

The basic characteristics of tumours are different from those of foreign countries, which may be related to various factors such as disease awareness, geographical environment, and racial differences.

Discussion: Differences between Ampullary and Nonampullary DNETs: The discussion of the differences between ampullary and nonampullary DNETs is clear. However,

consider discussing the implications of these differences for patient care and treatment. Please consider these revisions to improve the clarity and impact of your article. I look forward to seeing the revised manuscript. Best regards, Reviewer

The selection of surgical resection methods for DNETs patients should be based on comprehensive considerations such as tumor differentiation, tumor diameter, tumor location, and tumor staging. DNETs located around the ampulla have a relatively high degree of malignancy when diagnosed. The analysis results of the SEER database show that^[2] compared to nonampullary areas, DNENs tumors around the ampulla are often larger, with high-grade pathology and more distant metastasis. The median survival time is significantly shorter than that of the nonampullary area group, but there is no statistically significant difference in the median overall survival time between the two groups after surgical resection. Therefore, ENETS suggests that curative resection should be the first choice for DNENs around the ampulla. Milanetto et al.^[17] analyzed 18 cases of dNENs around the ampulla, and the research results showed that the surgical local resection group had shorter surgical time and less blood loss. During the follow-up period, only 3 G3/NEC patients who underwent pancreaticoduodenectomy experienced recurrence. Therefore, it is recommended to perform local resection for dNENs around the ampulla with a diameter of <2cm.