

Surgical Outcomes and Diagnostic Concordance in Patients With Pancreatic Neuroendocrine Tumors Undergoing Pancreatectomy: A Retrospective Cohort Study

ATSUSHI NANASHIMA, MASAHIDE HIYOSHI, NAOYA IMAMURA, YUKI TSUCHIMOCHI,
TAKASHI WADA, TAKEOMI HAMADA, YASUTO SUZUKI and YUUSUKE ARAKI

Division of Hepato-biliary-pancreas Surgery, Department of Surgery,
University of Miyazaki Faculty of Medicine, Miyazaki, Japan

Abstract

Background/Aim: Pancreatic neuroendocrine tumors (PanNETs) are heterogeneous neoplasms for which surgical resection remains the only potentially curative therapy. However, preoperative diagnostic accuracy – particularly tumor grading – often varies, complicating treatment decisions. This study evaluated diagnostic concordance between preoperative assessments and postoperative pathology, as well as surgical outcomes and prognostic factors in patients undergoing pancreatectomy for PanNETs.

Patients and Methods: We retrospectively reviewed the clinical records of 32 patients who underwent surgical resection for PanNETs. Patient demographics, tumor characteristics, surgical procedures, and postoperative outcomes were analyzed. Preoperative imaging and cytology-based diagnoses were compared with final pathological findings to evaluate diagnostic concordance. Prognostic factors were assessed using Kaplan–Meier survival analysis.

Results: Histological grading of resected specimens showed G1 in 53%, G2 in 41%, and G3/NEC in 6%, with a 38% discordance rate from preoperative biopsy. Lymphatic, venous, and perineural invasions were identified in 16%, 44%, and 13% of cases. Lymph node metastasis occurred in 22%. Among 30 patients with follow-up >12 months, eight developed recurrence, most commonly in the liver. The 3-year and 5-year disease-free survival (DFS) rates were 78% and 69%, while overall survival (OS) rates were 96% and 91%. Tumor number >2 and histologic grade G3 were significantly associated with reduced DFS ($p<0.05$). Lymphatic invasion and metachronous liver metastasis were significantly associated with reduced OS ($p<0.01$ and $p<0.05$, respectively). Histological grading mismatch was not associated with survival outcomes.

Conclusion: Pancreatectomy for PanNETs is a safe and effective treatment with favorable long-term outcomes. Histological factors such as tumor grade, lymphatic invasion, and tumor number significantly predict recurrence and survival.

Keywords: Pancreatic neuroendocrine tumor, pancreatectomy, surgical outcomes, diagnostic concordance, prognostic factors.



Atsushi Nanashima, Division of Hepato-biliary-pancreas Surgery, Department of Surgery, University of Miyazaki Faculty of Medicine, 5200 Kiyotake Kihara, Miyazaki 889-1602, Japan. Tel: +81 985852808, Fax: +81 985853780, e-mail: a_nanashima@med.miyazaki-u.ac.jp

Received October 21, 2025 | Revised November 10, 2025 | Accepted November 25, 2025



This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

©2026 The Author(s). Anticancer Research is published by the International Institute of Anticancer Research.

Introduction

Pancreatic neuroendocrine tumors (PanNETs) are relatively rare neoplasms arising from the endocrine cells of the pancreas, accounting for less than 5% of all pancreatic tumors (1). While their clinical behavior ranges from indolent to highly aggressive, surgical resection remains the only potentially curative treatment, especially for localized or resectable disease (2, 3). Despite advances in imaging and cytological diagnostics, preoperative differentiation between functional and non-functional PanNETs and benign and malignant lesions remains challenging. Discrepancies between preoperative assessments and final pathological diagnoses may influence surgical decision-making, postoperative management, and prognostication (4). Therefore, investigating diagnostic concordance and clinical outcomes in patients undergoing pancreatectomy is crucial for optimizing treatment strategies.

Despite improvements in surgical techniques and perioperative care, several challenges remain in managing patients with PanNET undergoing resection. One major issue is tumor biology heterogeneity, making it difficult to predict prognosis solely based on clinical or imaging findings (5). Even in surgically resected cases, recurrence rates vary significantly depending on tumor grade, size, lymph node involvement, and Ki-67 index (6). Moreover, discrepancies between preoperative imaging or cytological diagnosis and final histopathological findings can result in over- or under-treatment (7). The optimal extent of surgery, particularly for small non-functional tumors or tumors incidentally found during imaging, remains controversial (8). These limitations highlight the need to comprehensively evaluate diagnostic accuracy and outcome determinants in surgically treated patients with PanNET. A critical issue in the management of PanNETs is the frequent discordance between preoperative imaging or cytopathological assessments *via* endoscopic procedures and definitive postoperative pathological diagnosis. This misalignment can lead to suboptimal surgical strategies, such as unnecessary

extensive resections or insufficient resection margins in underdiagnosed cases (9). Small biopsies or fine-needle aspiration often fail to provide accurate tumor grading, particularly the Ki-67 proliferation index, which is essential for prognostication and therapeutic planning (10). Furthermore, misclassification between PanNET and other pancreatic neoplasms, such as acinar cell carcinoma or solid pseudopapillary tumors, can result in inappropriate treatment approaches (11). These diagnostic limitations affect operative decision-making and compromise prognostic accuracy and postoperative surveillance strategies. Therefore, understanding the frequency and consequences of diagnostic mismatch is essential for refining preoperative workups and guiding multidisciplinary management. To address the diagnostic and prognostic challenges in PanNETs, we hypothesize that discrepancies between preoperative assessments and postoperative pathological findings significantly influence surgical outcomes and long-term prognosis. Specifically, we propose that diagnostic mismatches are associated with variations in operative strategy, tumor staging, and recurrence risk. By retrospectively analyzing clinical data from surgically resected PanNET cases, we aimed to clarify the extent of diagnostic discordance and clinical impact and identify key factors that can improve preoperative evaluation and individualized surgical planning. To clarify this hypothesis, we retrospectively analyzed 32 patients who underwent surgical resection for PanNET at our academic cancer center. We evaluated clinical, radiologic, cytologic, and histopathologic features to assess the appropriateness of surgical indication and the diagnostic concordance between preoperative and postoperative findings. Furthermore, a survival analysis was performed in 31 cases with complete follow-up data to investigate long-term outcomes, particularly recurrence patterns and prognostic factors in PanNET.

Patients and Methods

Patient background. All thirty-two patients with PanNET, or only those treated by the authors, were examined

consecutively. This study retrospectively collected data at the Department of Surgery, Faculty of Medicine, University of Miyazaki, for ten years from April 2015 to May 2025. The in-hospital data of all patients were retrospectively and consecutively collected from the patient charts. The study design was approved by the Ethics Review Boards of Miyazaki University (approval number: #O-1803, approval date: October 17, 2025). Our institutional ethical policy confirmed patient consent *via* an opt-out procedure through a public announcement at an outpatient clinic and *via* our institutional website for a month. This study adhered to the Declaration of Helsinki on the ethical principles of medical research involving human participants, including research on identifiable human materials and data. Data were retrieved from both the anesthetic and patient electronic charts and institutional databases for the duration of initial hospitalization following radical operations and information at entry into electronic medical records at both institutes. Using this information, patient outcomes were determined based on the data collected by the co-authors.

Comparative measurement of tumor markers and histological findings. Patients' clinicopathological data were retrieved from our institute's archives. Peripheral blood samples were collected from each patient early in the morning before surgery when the patient was stable.

Statistical analysis. Differences in categorical data between groups and prevalence were assessed using the chi-square test, Fisher's exact test, or Dunnett's multiple comparison test. Differences in continuous data between groups were evaluated using Student's *t*-test or the Mann-Whitney test. A two-tailed *p*-value of <0.05 was considered statistically significant. Parameters with a significance of $p < 0.05$, as determined by univariate analysis. The Kaplan-Meier method was used to analyze survival, and the log-rank test was used to compare survival curves. Statistical analyses were performed using SPSS version 23 (Statistical Package for the Social Sciences Inc., Chicago, IL, USA).

Results

Perioperative parameters. The basic data of 32 patients are as follows: female sex was 20 (63%), and the mean age was 65.6 ± 10.7 years at the time of surgery. The disease grade of PanNET by endoscopic ultrasonographic fine needle biopsy (EUS-FNB) was G1 in 16 (50%), G2 in 12 (38%), G3 in two (6%), and pancreatic cancer in two (6%). The mean tumor size of PanNET was 2.68 ± 1.19 cm, and the number of tumors was 1.32 ± 0.83 , including one in 25 patients, two in two, three in one, four in two, and more in two. One patient had multiple NETs in the pancreas and duodenum simultaneously. Eight patients showed other tumors, including gastric adenocarcinoma in two undergoing the simultaneous resection, adenocarcinoma of the duodenal papilla in one, thyroid cancer in two, colonic cancer in one, pancreatic cancer in one, and adrenal gland adenoma in one. One patient had tuberous sclerosis and one had pancreatobiliary maljunction. Concerning pancreatectomy, the subtotal stomach-preserving pancreaticoduodenectomy (PD) was performed in 10 patients, distal pancreatectomy in nine, laparoscopic distal pancreatectomy or partial resection in 12, and staging laparotomy in one. Postoperative pancreatic complications were observed in 17 patients (53%), including grade B or C POPF according to the ISGPC classification (12) in four patients, intra-abdominal abscess in three, delayed gastric emptying in three, and other complications in seven. Re-operation was necessary in one patient during hospitalization, and the mean postoperative hospitalization period was 21 ± 15 days. Mortality was not observed.

Histological findings of the resected specimen, and comparison of pathological findings between pre- and postoperative diagnoses. The histological tumor grade of resected specimens was G1 in 17 patients (53%), G2 in 13 (41%), G3 in one (3%), and neuroendocrine carcinoma in one (3%). Discordance of tumor grade with preoperative biopsy was observed in 12 patients (38%), including upgrading in seven patients and downgrading in five.

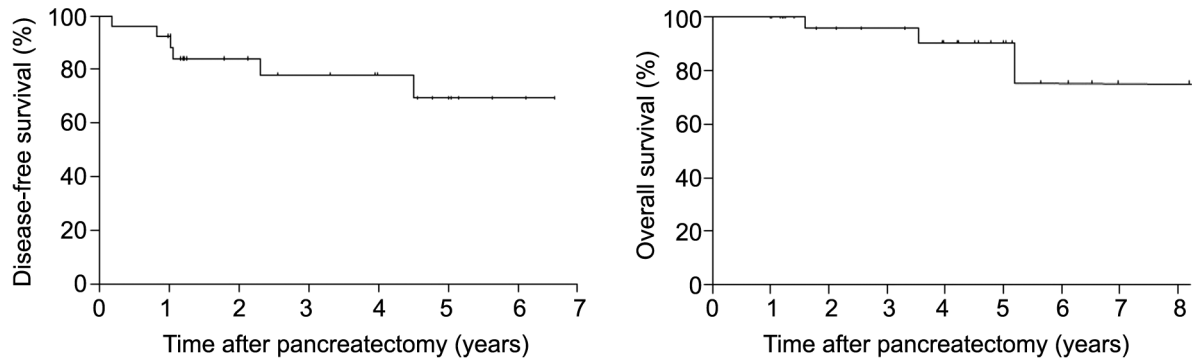


Figure 1. Kaplan–Meier curves for disease-free survival and overall survival in 30 patients with pancreatic neuroendocrine tumors who underwent pancreatectomy.

Lymphatic infiltration was observed in five patients (16%), venous infiltration in 14 (44%), and perineural infiltration in four (13%). Regional lymph node metastasis was observed in seven (22%), including peripancreatic node metastasis in six, but no paraaortic metastasis. Distant organ metastasis was observed in the liver in two patients, and one patient had multiple peritoneal disseminations.

Survival of 30 PanNET patients undergoing radical pancreatic resection. Eight patients (25%) experienced recurrence of PanNET, including five with liver metastases, three with local recurrence, and three with remnant pancreas recurrence. One patient underwent reoperation of remnant distal pancreatectomy with partial liver resection. Cancer death was observed in three patients. Figure 1 shows the disease-free and overall survival in 30 patients with a follow-up period of over 12 months. The 3-year and 5-year disease-free survival (DFS) rates were 78% and 69%, respectively, and the median survival period was 63 months. The 3-year and 5-year overall survival (OS) rates were 96% and 91%, respectively, and the median survival period was 95 months. Table I shows the disease-free and overall survival for each clinicopathological factor. The number of PanNET over 2 showed was significantly associated with lower DFS rates and periods ($p<0.05$), but not with OS. Regarding histologic grading of the resected specimen, the lower grading G3 was significantly associated with lower DFS survival rates and

shorter periods ($p<0.05$), but not with OS. Mismatching of grading with preoperative biopsy specimens was not associated with survival. Histological lymphatic infiltration was significantly associated with lower OS rates and shorter periods ($p<0.01$). Other histological factors, such as lymph node metastasis, were not significantly associated with either survival. Metachronous liver metastasis was significantly associated with lower OS rates and shorter periods ($p<0.05$).

Discussion

Pancreatectomy remains the cornerstone of curative treatment for PanNETs, particularly in patients with localized or regionally confined disease. In our cohort of 32 patients undergoing various forms of pancreatectomy – including pancreaticoduodenectomy, distal pancreatectomy, and minimally invasive resections – the procedures were generally safe and feasible, with no perioperative mortality and an acceptable morbidity profile. Postoperative pancreatic complications occurred in over half of the patients, consistent with prior reports indicating the high incidence of pancreatic fistula and related events in neuroendocrine tumor surgery (12, 13). Notably, the selection of surgical approach, tailored to tumor location and burden, allowed for a high rate of complete resection and long-term disease control. Despite the emergence of non-surgical options for selected cases,

Table I. Relationship between clinicopathological factors and patient survival rate and periods.

	Disease-free survival				Overall survival				
	3-year	5-year	Median survival period (months)	Significance (p-Value)	3-year	5-year	8-year	Median survival period (months)	Significance (p-Value)
Tumor size									
<20 mm (n=8)	88	88	69.8	0.282	100	100	100	79.3	0.241
≥20 mm (n=22)	68	57	58.8		94	86	65	88.2	
Number of tumors									
Solitary (n=24)	81	71	68.6	0.047	95	88	70	78	0.45
Multiple (n=6)	30	30	26.3		100	100	100	108.7	
Histological grading of the tumors									
G1 (n=17)	88	75	71.1	0.012	100	91	91	78.8	0.105
G2 (n=11)	77	77	60.5		100	100	100	108.7	
G3 (n=2)	0	0	6.2		50	50	0	41.3	
Matching with preoperative biopsy									
Match (n=19)	64	53	55.8		93	86	69	89.8	
Unmatch (n=11)	90	90	63	0.106	100	100	100	68.6	0.272
Downgrade (n=4)	100	100	62.7	0.246	100	100	100	62.7	0.546
Upgrade (n=7)	83	83	59.3		100	100	100	68.6	
Lymphatic infiltration									
No (n=25)	78	70	65.9	0.261	95	95	95	104.2	0.0078
Yes (n=5)	0	0	24.5		100	50	0	53.1	
Vessel infiltration									
No (n=16)	71	61	60	0.557	100	92	92	103.7	0.229
Yes (n=14)	74	74	59.7		89	89	44	63.2	
Perineural infiltration									
No (n=26)	78	70	66	0.392	95	89	89	100.1	0.527
Yes (n=4)	38	38	41.6		100	100	50	68.7	
Regional lymph node metastasis									
No (n=23)	81	71	67.9	0.172	94	94	94	103.5	0.123
Yes (n=7)	36	36	38.3		100	75	38	62.3	
Simultaneous distant organ metastasis									
No (n=28)	77	69	65.9	0.241	96	90	72	75.5	0.582
Yes (n=2)	0	0	14.9		100	100	100	108.7	
Pancreatectomy-related complications									
No (n=15)	65	42	59.3	0.215	92	83	55	83.1	0.11
Yes (n=15)	92	92	74.2		100	100	100	79.3	
Tumor recurrence									
No	-	-	-	-	100	100	100	84.7	0.03
Liver	-	-	-	-	75	75	0	52.2	
Local	-	-	-	-	100	67	67	86.8	

these findings underscore the ongoing relevance of surgery as a primary modality in managing PanNET.

Pancreatectomy remains the cornerstone of curative treatment for PanNETs, particularly in patients with localized or regionally confined disease. In our series, various surgical approaches—including PD, distal

pancreatectomy, and laparoscopic resections—were performed based on tumor location and extent. The procedures were conducted with no perioperative mortality and an acceptable morbidity rate, demonstrating the feasibility and relative safety of surgical management. However, postoperative complications such as POPF,

delayed gastric emptying, and intra-abdominal abscesses occurred in over 50% of cases, in line with previous reports emphasizing the technical challenges of pancreatic surgery for soft and highly vascularized neuroendocrine tumors (12, 13). Despite this, our experience suggests that morbidity can be managed with appropriate perioperative care and that reoperation is rarely necessary.

Regarding diagnostic discordance between EUS-FNB and resected specimens, one of the significant clinical findings in our cohort was the discrepancy between tumor grading on preoperative biopsy (EUS-FNB) and postoperative histology, which occurred in 38% of patients. In several cases, underestimation of tumor grade preoperatively led to unexpected upgrading after surgical resection, while others showed downgrading. This diagnostic discordance may reflect tumor heterogeneity and the limitation of small biopsy samples in capturing the full biological behavior of PanNETs. While preoperative biopsy remains essential for treatment planning, our findings suggest clinicians should interpret biopsy results cautiously and be prepared for histological reclassification after surgery (10). However, eventually this mismatch between pre- and postoperative diagnosis was not associated with disease-free or overall survival despite upgrading, and this issue was not a clinically serious problem. In our series, two cases showed pancreatic cancer by the preoperative EUS-FNB; however, in these cases cancer was downgraded. The radical operation was enough for PanNET. In case the pancreatic cancer was diagnosed after pancreatectomy, additional resection or node dissection would be considered.

Regarding histological risk factors and their prognostic impact, our analysis identified several histopathological features that significantly influenced prognosis following pancreatectomy for PanNET. Lymphatic invasion was present in 16% of patients and showed a strong correlation with reduced OS, supporting its role as an independent adverse prognostic factor, in line with prior studies (11-13). Specifically, our finding that lymphatic invasion, but not merely lymph node metastasis, was significantly associated with poorer outcomes ($p < 0.01$) echoes the conclusions of

a recent retrospective cohort of non-functioning PanNETs, where microvascular invasion emerged as a key predictor of recurrence even among tumors smaller than 20 mm and classified as G1–G2 according to the 2022 WHO criteria (14). Similarly, perineural and venous invasions, though less frequent in our series (13% and 44%, respectively), have been linked to increased tumor aggressiveness and risk of recurrence in neuroendocrine neoplasms and other solid cancers (15). This is consistent with our observation that multiple histologic invasions, especially lymphatic and microvascular, negatively affected DFS. These findings suggest that, beyond conventional tumor grade and size, detailed pathological assessment of lympho-vascular and perineural invasion should play a central role in postoperative risk stratification and may inform the need for intensified surveillance or adjunctive treatments in high-risk PanNET patients. Although the relationship with DFS and OS was not always concordant, it was due to the type of recurrence site.

Regarding recurrence patterns and oncologic outcomes, in our cohort, 25% of patients experienced recurrence after radical pancreatectomy, with liver metastasis being the most prevalent (5 of 8 patients), followed by local and remnant pancreas recurrence, echoing the distribution reported in the literature, where distant relapse accounts for the majority of recurrences post-PanNET surgery (16, 17), the 3- and 5-year DFS rates in our study were 78% and 69%, respectively, supporting the favorable oncologic outcomes documented in surgical PanNET series, albeit with a persistent risk of late relapse. The significant association between metachronous liver metastasis and decreased OS in our dataset aligns with findings from systematic reviews indicating that recurrence interval and metastasis site are key prognostic factors in PanNETs (18). The successful reoperation of one patient, who underwent remnant distal pancreatectomy and liver resection, underscores recent evidence supporting repeat surgery or ablation as beneficial in select, isolated recurrences of pancreatic malignancies (19). These observations highlight that while PanNET recurrence predominantly follows a liver-predilected metastatic pattern, long-term survival, especially following

repeat resection, is achievable in well-selected cases. Thus, individualized surveillance and multidisciplinary management strategies remain paramount in the care of post-resection PanNET patients. Since 2022, significant progress has been made in drug therapies and peptide receptor radionuclide therapy (PRRT), enhancing DFS, OS, and symptom management (20, 21). Regarding drug therapy for PanNETs, somatostatin analogs (SSAs), molecular targeted therapies such as Everolimus, Sunitinib, and Surufatinib also showed good efficacy in PanNETs, and the OCLURANDOM trial underscores personalized sequencing of Everolimus *versus* PRRT (22, 23).

Our findings affirm that pancreatectomy continues to be a cornerstone in managing PanNET, yet they also illuminate key considerations for enhancing patient selection and postoperative care. First, the high rate of histological upgrade (38%) from preoperative EUS-FNB emphasizes the limitations of biopsy and underscores the need for improved pre-surgical risk stratification. Emerging data suggest that combining PET/CT with radiomic analysis can more accurately predict tumor grade and guide the intensity of surgical intervention. For instance, a nomogram integrating PET metrics and tumor biology demonstrated promising accuracy in preoperatively distinguishing G1 from G2/G3 PanNETs (24). Moreover, PET-based recurrence risk stratification using uptake values has shown independent prognostic value, suggesting it could inform surgical planning and postoperative follow-up intensity (25). Second, given the significant negative impact of lympho-vascular invasion and metastatic burden on survival, more detailed molecular subclassification of PanNETs, such as MEN1, DAXX/ATRX mutations, or epigenomic subtypes, may further refine prognostication and influence decisions regarding adjuvant therapy (26). Additionally, molecular imaging could be extended intraoperatively to detect occult metastatic disease, aligning with broader concepts of the extent of diseased tissue to guide resection margins (27). Third, our results suggest that patients with multiple tumors or high-grade features may benefit most from early, aggressive surgery. In contrast, those with low-risk features might be candidates for less invasive resection or even active

surveillance. High-risk patients defined by adverse histologic traits or imaging risk scores should perhaps undergo more intensive follow-up or be considered for clinical trials exploring neoadjuvant or adjuvant therapies. As molecular and imaging technologies evolve, interdisciplinary coordination between surgeons, radiologists, pathologists, and medical oncologists will be vital to tailor surgical strategies and follow-up to each patient.

The strengths of the present study are: 1) This study provides a thorough analysis of both perioperative outcomes and detailed histopathological characteristics, including tumor grade concordance, lympho-vascular invasion, and recurrence patterns. 2) Including survival outcomes (disease-free and overall survival at 3 and 5 years) enhances the relevance of the findings for oncologic prognosis and clinical decision-making. 3) The study reflects actual clinical practice, including various types of pancreatectomies (open, laparoscopic, SSPPD, DP), which increases its generalizability to diverse surgical settings. 4) The investigation of grading discordance between EUS-FNB and surgical specimens adds novel insights into the limitations of preoperative diagnostics in PanNET.

Study limitations. 1) The non-randomized, retrospective nature limits the ability to control for confounding variables and introduces potential selection bias. 2) With only 32 patients, the statistical power is limited, particularly for multivariate analysis or subgroup comparisons (*e.g.*, recurrence vs. non-recurrence). 3) The cohort includes a variety of surgical approaches and tumor burdens, including cases with coexisting malignancies, which may introduce variability in outcomes. 4) While pathological features were analyzed, the study did not include molecular profiling or advanced imaging modalities, which are increasingly crucial in PanNET management and could improve risk stratification (24). 5) Although 30 patients had at least 12 months of follow-up, longer-term outcomes beyond 5 years would provide more robust conclusions regarding late recurrence and survival trends.

Our findings clarify several practical points for surgeons managing PanNETs. First, preoperative biopsy

provides valuable information but cannot reliably determine tumor grade; definitive treatment strategies should therefore remain flexible until final pathology is obtained. Second, lymphatic invasion and high-grade histology are the most powerful predictors of poor prognosis and should guide postoperative surveillance intensity. Finally, recurrence, particularly in the liver, remains a persistent risk despite favorable overall survival, underscoring the need for vigilant long-term follow-up and consideration of repeat resection or systemic therapy in appropriately selected patients.

Conclusion

Pancreatectomy for PanNETs remains a safe and effective curative strategy, with favorable long-term survival outcomes. However, recurrence, particularly hepatic metastasis, is not uncommon, underscoring the need for vigilant postoperative surveillance. Our findings highlight the prognostic importance of histological factors such as lymphatic invasion and tumor grade and the diagnostic limitations of preoperative biopsy in accurately reflecting tumor biology. The significant rate of grading discordance between EUS-FNB and surgical specimens suggests that surgical decision-making should not rely solely on biopsy results. Future strategies incorporating molecular profiling and advanced imaging may enhance preoperative risk assessment and personalize surgical and postoperative management. Multidisciplinary approaches remain essential to optimize outcomes for patients with PanNET.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

Concept: AN; Design: AN; Data Collection or Processing: MH, NI, TH, YT, TW, YS, YA; Analysis or Interpretation: AN; Literature Search: AN; Writing: AN.

Funding

The Authors declare that this study received no financial support.

Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

References

- 1 Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, Abdalla EK, Fleming JB, Vauthey J, Rashid A, Evans DB: One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *J Clin Oncol* 26(18): 3063-3072, 2008. DOI: 10.1200/JCO.2007.15.4377
- 2 Falconi M, Eriksson B, Kaltsas G, Bartsch DK, Capdevila J, Caplin M, Kos-Kudla B, Kwekkeboom D, Rindi G, Klöppel G, Reed N, Kianmanesh R, Jensen RT, Vienna Consensus Conference participants: ENETS consensus guidelines update for the management of patients with functional pancreatic neuroendocrine tumors and non-functional pancreatic neuroendocrine tumors. *Neuroendocrinology* 103(2): 153-171, 2016. DOI: 10.1159/000443171
- 3 Norton JA: Surgery for primary pancreatic neuroendocrine tumors. *J Gastrointest Surg* 10(3): 327-331, 2006. DOI: 10.1016/j.gassur.2005.08.023
- 4 Basturk O, Tang L, Hruban RH, Adsay V, Yang Z, Krasinskas AM, Vakiani E, La Rosa S, Jang KT, Frankel WL, Liu X, Zhang L, Giordano TJ, Bellizzi AM, Chen JH, Shi C, Allen P, Reidy DL, Wolfgang CL, Saka B, Rezaee N, Deshpande V, Klimstra DS: Poorly differentiated neuroendocrine carcinomas of the pancreas: a clinicopathologic analysis of 44 cases. *Am J Surg Pathol* 38(4): 437-447, 2014. DOI: 10.1097/PAS.0000000000000169
- 5 Jilesen AP, van Eijck CH, in't Hof KH, van Dieren S, Gouma DJ, van Dijkum EJ: Postoperative complications, in-hospital mortality and 5-year survival after surgical resection for patients with a pancreatic neuroendocrine tumor: a systematic review. *World J Surg* 40(3): 729-748, 2016. DOI: 10.1007/s00268-015-3328-6
- 6 Scarpa A, Mantovani W, Capelli P, Beghelli S, Boninsegna L, Bettini R, Panzuto F, Pederzoli P, delle Fave G, Falconi M: Pancreatic endocrine tumors: improved TNM staging and histopathological grading permit a clinically efficient prognostic stratification of patients. *Mod Pathol* 23(6): 824-833, 2010. DOI: 10.1038/modpathol.2010.58

- 7 Kim JH, Eun HW, Kim YJ, Lee JM, Han JK, Choi BI: Pancreatic neuroendocrine tumour (PNET): Staging accuracy of MDCT and its diagnostic performance for the differentiation of PNET with uncommon CT findings from pancreatic adenocarcinoma. *Eur Radiol* 26(5): 1338-1347, 2016. DOI: 10.1007/s00330-015-3941-7
- 8 Partelli S, Cirocchi R, Crippa S, Cardinali L, Fendrich V, Bartsch DK, Falconi M: Systematic review of active surveillance *versus* surgical management of asymptomatic small non-functioning pancreatic neuroendocrine neoplasms. *Br J Surg* 104(1): 34-41, 2017. DOI: 10.1002/bjs.10312
- 9 Powers BD, Rothermel LD, Fleming JB, Strosberg JR, Anaya DA: A survival analysis of patients with localized, asymptomatic pancreatic neuroendocrine tumors: no surgical survival benefit when examining appropriately selected outcomes. *J Gastrointest Surg* 24(12): 2773-2779, 2020. DOI: 10.1007/s11605-019-04433-4
- 10 Tacelli M, Bina N, Crinò SF, Facciorusso A, Celsa C, Vanni AS, Fantin A, Antonini F, Falconi M, Monica F, Capurso G, Arcidiacono PG, Barresi L, of the Italian Association of Hospital Gastroenterologists and Endoscopists: Reliability of grading preoperative pancreatic neuroendocrine tumors on EUS specimens: a systematic review with meta-analysis of aggregate and individual data. *Gastrointest Endosc* 96(6): 898-908.e23, 2022. DOI: 10.1016/j.gie.2022.07.014
- 11 Hijioka S, Hara K, Mizuno N, Imaoka H, Bhatia V, Mekky MA, Yoshimura K, Yoshida T, Okuno N, Hieda N, Tajika M, Tanaka T, Ishihara M, Yatabe Y, Shimizu Y, Niwa Y, Yamao K: Diagnostic performance and factors influencing the accuracy of EUS-FNA of pancreatic neuroendocrine neoplasms. *J Gastroenterol* 51(9): 923-930, 2016. DOI: 10.1007/s00535-016-1164-6
- 12 Chong E, Ratnayake B, Lee S, French JJ, Wilson C, Roberts KJ, Loveday BP, Manas D, Windsor J, White S, Pandanaboyana S: Systematic review and meta-analysis of risk factors of postoperative pancreatic fistula after distal pancreatectomy in the era of 2016 International Study Group pancreatic fistula definition. *HPB (Oxford)* 23(8): 1139-1151, 2021. DOI: 10.1016/j.hpb.2021.02.015
- 13 Atema JJ, Jilesen AP, Busch OR, van Gulik TM, Gouma DJ, Nieveen van Dijkum EJ: Pancreatic fistulae after pancreatic resections for neuroendocrine tumours compared with resections for other lesions. *HPB (Oxford)* 17(1): 38-45, 2015. DOI: 10.1111/hpb.12319
- 14 Izumo W, Kawaida H, Saito R, Nakata Y, Amemiya H, Maruyama S, Takiguchi K, Shoda K, Shiraishi K, Furuya S, Kawaguchi Y, Mochizuki K, Kondo T, Ichikawa D: Evaluation of the details and importance of lymphatic, microvascular, and perineural invasion in patients with non-functioning pancreatic neuroendocrine neoplasms based on tumor size and the 2022 World Health Organization classification: a 23-year retrospective analysis. *World J Surg Oncol* 23(1): 79, 2025. DOI: 10.1186/s12957-025-03734-0
- 15 Izumo W, Higuchi R, Furukawa T, Shiihara M, Uemura S, Yazawa T, Yamamoto M, Honda G: The importance of microvascular invasion in patients with non-functioning pancreatic neuroendocrine neoplasm. *Langenbecks Arch Surg* 410(1): 8, 2024. DOI: 10.1007/s00423-024-03563-x
- 16 Xiang JX, Zhang XF, Beal EW, Weiss M, Aldrighetti L, Poultsides GA, Bauer TW, Fields RC, Maithel SK, Marques HP, Pawlik TM: Hepatic resection for non-functional neuroendocrine liver metastasis: does the presence of unresected primary tumor or extrahepatic metastatic disease matter? *Ann Surg Oncol* 25(13): 3928-3935, 2018. DOI: 10.1245/s10434-018-6751-8
- 17 Lim S, Chong L, Peeroo S, Onasanya O, He E, Banting S, Croagh D: Recurrence and outcomes of non-functional pancreatic neuroendocrine tumours post-resection: an Australian retrospective, multicentre cohort study. *ANZ J Surg* 93(1-2): 160-165, 2023. DOI: 10.1111/ans.18204
- 18 Liu B, Kudo A, Kinowaki Y, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Tanaka S, Akashi T, Tanabe M: A simple and practical index predicting the prognoses of the patients with well-differentiated pancreatic neuroendocrine neoplasms. *J Gastroenterol* 54(9): 819-828, 2019. DOI: 10.1007/s00535-019-01570-0
- 19 Choi M, Kim NW, Hwang HK, Lee WJ, Kang CM: Repeated pancreatectomy for isolated local recurrence in the remnant pancreas following radical pancreatectomy for pancreatic ductal adenocarcinoma: a pooled analysis. *J Clin Med* 9(12): 3945, 2020. DOI: 10.3390/jcm9123945
- 20 Li YL, Cheng ZX, Yu FH, Tian C, Tan HY: Advances in medical treatment for pancreatic neuroendocrine neoplasms. *World J Gastroenterol* 28(20): 2163-2175, 2022. DOI: 10.3748/wjg.v28.i20.2163
- 21 Hindié E, Baudin E, Hicks RJ, Taïeb D: The latest advances in peptide receptor radionuclide therapy for gastroenteropancreatic neuroendocrine tumors. *J Nucl Med* 64(4): 522-524, 2023. DOI: 10.2967/jnumed.122.264422
- 22 Chan MY, Ma KW, Chan A: Surgical management of neuroendocrine tumor-associated liver metastases: a review. *Gland Surg* 7(1): 28-35, 2018. DOI: 10.21037/gs.2017.11.16
- 23 Hijioka S, Morizane C, Ikeda M, Ishii H, Okusaka T, Furuse J: Current status of medical treatment for gastroenteropancreatic neuroendocrine neoplasms and future perspectives. *Jpn J Clin Oncol* 51(8): 1185-1196, 2021. DOI: 10.1093/jjco/hyab076
- 24 Kostianen I, Majala S, Schildt J, Parviainen H, Kauhanen S, Seppänen H, Miettinen PJ, Matikainen N, Ryhänen EM, Schalin-Jäntti C: Pancreatic imaging in MEN1—comparison of conventional and somatostatin receptor positron emission tomography/computed tomography imaging in real-life setting. *Eur J Endocrinol* 188(5): 421-429, 2023. DOI: 10.1093/ajendo/lvad035
- 25 Ezziddin S, Adler L, Sabet A, Pöppel TD, Grabellus F, Yüce A, Fischer HP, Simon B, Höller T, Biersack HJ, Nagarajah J: Prognostic stratification of metastatic gastroenteropancreatic

- neuroendocrine neoplasms by 18F-FDG PET: feasibility of a metabolic grading system. *J Nucl Med* 55(8): 1260-1266, 2014. DOI: 10.2967/jnumed.114.137166
- 26 Giri S, Sahoo J: Advancements in medical treatment for pancreatic neuroendocrine tumors: A beacon of hope. *World J Gastroenterol* 30(12): 1670-1675, 2024. DOI: 10.3748/wjg.v30.i12.1670
- 27 Norlén O, Montan H, Hellman P, Stålberg P, Sundin A: Preoperative (68)Ga-DOTA-somatostatin analog-PET/CT hybrid imaging increases detection rate of intra-abdominal small intestinal neuroendocrine tumor lesions. *World J Surg* 42(2): 498-505, 2018. DOI: 10.1007/s00268-017-4364-1