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Review Article

Small Pancreas Neuroendocrine Tumors: How Small is Small?

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Abstract

Objective: The current study aimed to investigate the issues in contemporary management strategies that focus on small pancreatic neuroendocrine tumors (PNETs). **Data Sources and Study Selection:** We searched various scientific databases using specific keywords. **Results:** Surveillance-only strategies were considered for selected patients. The exact cut-off value of small neuroendocrine tumors for surveillance-only strategies needs to be verified with additional high-level evidence. **Conclusion:** There is no consensus on the size and treatment strategy for small PNETs currently. Patients with small nonfunctioning PNETs require individualized recommendations for surgery versus active surveillance based on tumor size, radiographic characteristics, and patient characteristics, such as age and comorbidities and also patient references.

Keywords: Pancreatic neuroendocrine tumors, small, treatment

Introduction

Pancreatic neuroendocrine tumors (PNETs) are a rare heterogeneous group of endocrine neoplasms originating from the pancreas. They comprise approximately 3% of all pancreatic tumors and represent 7% of neuroendocrine tumors.[1-4] Incidences of PNETs in Taiwan have increased over the previous two decades, rising from 0.017/100,000 in 1996 to 0.446/100,000 in 2015.[5] The widespread use of endoscopy and cross-sectional imaging for cancer screening, as well as heightened awareness among clinicians and pathologists, has increased the incidental discovery of small asymptomatic PNETs over the past decade.[4-7] However, the clinical heterogeneity of PNETs poses several challenges for

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optimal management.[4] The current review highlights issues presented by contemporary management strategies with a focus on small PNETs.

Data Sources and Study Selection

We searched Medline, PubMed, and Google Scholar electronic databases using a set group of keywords to identify relevant articles: PNET, pancreatic neuroendocrine neoplasm, size, prognosis, and/or survival. Only articles published in English were selected. Due to the heterogeneity of the currently available data, we systematized the current review using specific topics: (1) the role of surgical intervention on small PNETs, (2) the size criteria of small PNETs, and (3) the evolving consensus on small PNETs that has occurred over the previous decade.

Results

The role of surgical intervention in small pancreatic neuroendocrine tumor

Surgical resection is the only curative management for patients with localized PNETs, as it can increase overall survival (OS) even in the presence of distant metastases.[7,8] The National Comprehensive Cancer Network (NCCN) guidelines recommend standard oncologic surgery (distal pancreatectomy, splenectomy, or pancreaticoduodenectomy) as appropriate for most resectable, nonmetastatic PNETs.[9] The pancreas 2000 research group recommends a standard pancreatectomy (pancreaticoduodenectomy or distal pancreatectomy) with regional lymphadenectomy for functional PNETs, PNETs >2 cm, symptomatic nonfunctioning PNETs (NF-PNETs), and in patients with biliary or pancreatic duct dilatation on preoperative computed tomography (CT).[7,9,10]

Surgical issues for small nonfunctioning-pancreatic neuroendocrine tumor

Optimizing the quality of life by preserving pancreatic function following surgical intervention is important in patients with small or low-grade PNETs, considering their excellent long-term survival. Pancreas-sparing resections, such as enucleation and central pancreatectomy, can maintain pancreatic endocrine and exocrine functions and have been proposed for use in patients with small NF-PNETs; however, enucleation is associated with a high complication rate and is mostly related with postoperative pancreatic fistula (POPFs). The globally reported incidence of POPFs after enucleation is higher than that of major pancreatic resections, especially when lesions are located in the pancreatic head (18%–50% vs. 12%).[11] The incidence of POPFs after central pancreatectomy can be as high as 66%. Therefore, the benefits of pancreas-sparing resection must be balanced with higher overall morbidity rates and risks of POPFS.[10]

During distal pancreatectomy, splenic preservation helps maintain innate immune functions; however, the procedure is technically challenging, carries risks of hemorrhage or infarction, and may also limit nodal retrieval. There is conflicting evidence on the benefits of splenic preservation, with some studies suggesting that it may not be advisable when PNETs are large or when they have invaded the splenic vein and/or surrounding structures.[10] The NCCN guidelines recommend generally including splenectomy with the caveat that one should consider spleen preservation with benign insulinoma.[9]

Although surgical resection is recognized as the only potential cure for pancreatic tumors, there are significant differences in survival outcomes between patients with PNETs and those with pancreatic carcinoma. The natural evolution of tumors smaller than 2 cm remains unknown. Considering the potential risks from surgery, the necessity to resect all small PNET has recently been challenged [Table 1].

Literature pros for immediate surgery of small nonfunctioning-pancreatic neuroendocrine tumor

The NCCN guidelines recommend lymphadenectomy in the presence of small (1–2 cm) tumors owing to the risk of lymph node metastasis (LNM).[9] Studies have reported the potential for lymphatic spread with small PNETs, estimating the rate of LNM to be 12%–25%.[8,12] Risk stratification and prognostic significance of LNM in PNETs were investigated by a recent meta-analysis which included 13,374 patients undergoing resection for PNETs. PNETs that were larger, of a higher histological grade, located in the pancreatic head, or solid tumors showed higher rates of LNM. Among the different subtypes, the weighted median rate of LNM was lowest for insulinoma (5.2%) and slightly higher for small (≤2 cm) NF-PNETs at 11.2%. The occurrence of LNM was seen in 10.3% of patients with G1 PNETs. LNM rates of NF-PNETs were significantly associated with poor recurrence-free survival (hazard ratio [HR] 6.06, 95% confidence interval [CI] 4.22–8.69; $P < 0.001$) and OS (HR 4.98, 95% CI 2.18–8.83; $P < 0.001$). LNM may be prevalent even in small or low-grade NF-PNETs and is associated with a worsening prognosis. The authors recommended reappraising the watch-and-wait strategy for small NF-PNETs.[13]

A European multi-institutional study evaluated 210 resected sporadic nonmetastatic small NF-PNETs (<2 cm) and found that the presence of biliary or pancreatic duct dilatation on preoperative CT and WHO grade 2–3 were risk factors for aggressive tumor biology. Therefore, the authors advocated that these patients should undergo surgery regardless of the tumor size.[7]

Literature pros for active surveillance of small nonfunctioning-pancreatic neuroendocrine tumor

A matched case–control study conducted by Sadot *et al*. at the Memorial Sloan Kettering Cancer Center evaluated 464 patients with NF-PNETs <3 cm and found an increased incidence of small PNETs during the study period (1993–2013) and favorable survival outcomes in both the observation and

Table 1: Summary of the studies reporting outcomes of patients with pancreatic neuroendocrine tumors

Study	Methods	Results
Pros for immediate surgery of small PNETs		
Ausania *et al*.[8]	43 studies (systemic review up to 2017)	12%-14% of LNM for tumors ≤1 cm, up to 25% for those≤2 cm. 7.5%-23.1% of LNM in G1 tumors
Fischer *et al*.[12]	*n*=310 undergoing resections for PNETs (2001–2012) Median FU=31 months	In 61 patients with asymptomatic small PNET (≤2 cm), 8 of the 61 had PNET G2 or PNEC G3 and 6 of 51 patients with excised LNs had LNM
Tanaka *et al*.[13]	*n*=13,374 (systemic review) undergoing resection for PNETs	LNM occurred in 11.2% of patients with small PNETs and 10.3% of patients with G1 PNETs
Hill *et al*.[14]	*n*=728 PNET, (SEER database, 1988–2002) Median FU=26 months	Patients who underwent resection had a survival advantage compared with recommended Not resected patients (HR of 0.48; 95% CI, 0.35-0.66)
Cherenfant *et al*.[15]	*n*=128 undergoing pancreatectomies for NF-PNETs (1998–2011) Median FU=33 months	Tumor size (<2 cm) was not a predictive factor for death; LN and liver metastasis, high-grade (G3) pathology, and death still occurred in patients with small NF-PNET
Kuo and Salem[16]	*n*=1,371 NF-PNETs (SEER database; 1988–2009) Median FU=4.2 years	Patients with small NF-PNETs developed distant metastases (9.1%) and LN metastases (27.3%)
Pros for surveillance of small PNET		
Sadot *et al*.[17]	*n*=464 incidentally discovered, sporadic, small (<3 cm), stage III PanNET (1993 and 2013) Median FU=44 months	No differences in survival data between the observation and resection groups
Sallinen *et al*.[18]	*n*=344 sporadic NF-PNETs (systemic review) Median FU of 34 months	Sporadic small (≤2 cm) asymptomatic tumors displayed low rate of growth (22%), need for secondary surgical resection (12%), and disseminated disease in FU (0%)
Rosenberg *et al*.[19]	*n*=34 incidentally discovered NF-PNETs (based on CT and MRI) Median FU=30 months	No increases in progression, metastasis, or mortality for patients with small NF-PNETs (<2 cm) regardless of whether they were treated operatively or nonoperatively

LN: Lymph node, FU: Follow-up, LNM: LN metastasis, PNET: Pancreatic neuroendocrine tumors, PNEC: Pancreatic neuroendocrine carcinoma, SEER: Surveillance epidemiology and end results, HR: Hazard ratio, NF-PNETs: Nonfunctioning PNETs, CT: Computed tomography, MRI: Magnetic resonance imaging, CI: Confidence interval

surgical resection groups of patients with small NF-PNET. These outcomes were attributed to the rigorous selection process of "low-risk" tumors in both groups. The authors concluded that not all sporadic PNETs require resection, and it was reasonable and safe to initiate an initial observational approach with selected patients diagnosed with small (<3 cm), stable, incidentally discovered PNETs, as this subset of patients may not benefit from resections, which could increase the risk of operative morbidity and mortality.[17]

The meta-analysis conducted by Sallinen *et al*. showed a low tumor growth rate (yearly growth of 0.12 mm at a median follow-up of 34 months) and zero metastases of small asymptomatic NF-PNET.[18] However, these results were subject to inherited biases due to attributes like the retrospective nature of the study, using only data on resected patients, and a potentially insufficient length of follow-up. Another retrospective study of 35 patients with incidentally discovered NF-PNETs found no increase in progression, metastasis, or mortality in patients with small NF-PNETs (<2 cm), regardless of whether they were treated operatively or nonoperatively over a 28-month follow-up period. In contrast, patients with tumors ≥2 cm who were managed nonoperatively showed higher rates of metastases than those who underwent surgery. However, the morbidity in the operative group was 35%, with pancreatic pseudocysts being the most common complication. Therefore, a passive approach may be adopted for patients with incidentally discovered NF-PNETs <2 cm, and NF-PNETs measuring ≥2 cm at the initial diagnosis, only considering resection of tumors that increase in size during the follow-up.[19]

A similar observation was demonstrated in a European multi-institutional study that included 210 patients with resected sporadic nonmetastatic small NF-PNETs (<2 cm). The study revealed that although a small percentage (7%) of tumors presented with nodal metastasis at the time of resection, postoperative and long-term outcomes in small NF-PNET are excellent for the majority of patients (approximately 94% 5-year disease-free survival), and all patients with tumors smaller than 1 cm were disease-free at the last follow-up. Therefore, a watch-and-wait policy could be adopted for patients with a low risk of recurrence.[7]

How small is small?

Tumor size is one of the most commonly available predictive factors of malignancy.[20] Current evidence-based international guidelines drafted by the European Neuroendocrine Tumor Society (ENETS) and the NCCN recommend a watch-and-wait strategy for patients with PNETs <2 cm;[9,21] The tumor size can be defined either by CT or endoscopic ultrasonography. However, controversy regarding the 2-cm cutoff value for small nonfunctioning PNETs is persistent [Table 2].

Two centimeters is enough

Several retrospective studies have demonstrated an indolent course of small PNETs. In an early (1999–2010) retrospective study including 143 nonmetastatic PNETs, four patients with incidentally detected Stage I tumors pathologically confirmed by endoscopic ultrasound-guided fine-needle aspiration were selected to undergo surveillance instead of surgical resection. Their tumor's sizes were 0.7–2.3 cm at initial diagnosis, and none of the patients

Table 2: Summary of the studies analyzing the association between outcome and tumor size in pancreatic neuroendocrine tumors

Study	Methods	Results
2 cm is sufficient for the surveillance strategy of small PNETs		
Cheema *et al*.[22]	*n*=143 nonmetastatic PNETs (1999–2010). Median FU=2 years for those who underwent surveillance	4 patients with early-stage incidental tumors underwent surveillance strategy. None of them experienced tumor growth
Crippa *et al*.[23]	*n*=355 proven NF-PNET (1990–2009) Median FU=36 months for those who underwent surveillance	12 patients underwent nonoperative management of NF-PNET without malignant features. None of them developed tumor progression or had tumor growth
Gaujoux *et al*.[24]	*n*=46 sporadic small (≤2 cm) evaluated by CT or MRI Median FU=34 months	No distant or nodal metastases and only 13% (6/46) of patients displayed tumor growth greater than 20%
Sadot *et al*.[17]	*n*=464 incidentally discovered, sporadic, small (<3 cm), stage III PanNET (1993 and 2013) Median FU=44 months	No differences in survival data between the observation and resection groups
Rosenberg *et al*.[19]	*n*=34 incidentally discovered NF-PNETs (based on CT and MRI) Median FU=30 months	No increases in progression, metastasis or mortality for patients with small NF-PNETs (<2 cm), regardless of whether they were treated operatively or nonoperatively
Sallinen *et al*.[18]	*n*=344 sporadic NF-PNETs (systemic review) Median FU=34 months	Sporadic small (≤2 cm) asymptomatic tumors displayed low rate of growth (22%), need for secondary surgical resection (12%), and disseminated disease in FU (0%)
2 cm is not perfect for surveillance strategy of small PNETs		
Hill *et al*.[14]	*n*=728 PNET, (SEER database, 1988–2002) Median FU=26 months	Patients who underwent resection had a survival advantage compared with recommended Not resected patients (HR of 0.48; 95% CI, 0.35–0.66)
Kuo and Salem[16]	*n*=1371 NF-PNETs (SEER database; 1988–2009) Median FU=4.2 years	Patients with small NF-PNETs developed distant metastases (9.1%) and LN metastases (27.3%)
Cherenfant *et al*.[15]	*n*=128 undergoing pancreatectomies for NF-PNETs (1998–2011) Median FU=33 months	Tumor size (<2 cm) was not a predictive factor for death; LN and liver metastasis, high grade (G3) pathology, and death still occurred in patients with small NF-PNET
Sallinen *et al*.[25]	*n*=58 undergoing resection for PNETs (2001–2013) Median FU=24 months	7 of 16 with symptomatic small PNETs (≤2 cm) had signs of malignant behavior
Tanaka *et al*.[13]	*n*=13,374 (systemic review) undergoing resection for PNETs	LNM occurred in 11.2% of patients with small PNETs and 10.3% of patients with G1 PNETs

FU: Follow-up, G1: Grade 1, G3: Grade 3, LNM: LN metastasis, PNET: Pancreatic neuroendocrine tumors, SEER: Surveillance epidemiology and end results, HR: Hazard ratio, NF-PNETs: Nonfunctioning PNETs, CT: Computed tomography, MRI: Magnetic resonance imaging, CI: Confidence interval

experienced tumor growth after a median follow-up of 2 years.[22] Another Italian study that included 355 patients with NF-PNETs found tumor size >3.5 cm to be an independent multivariate factor for progression-free survival. They used high-resolution imaging techniques, including CT and/or magnetic resonance imaging (MRI), and contrast-enhanced ultrasonography to evaluate tumor size. Diagnostic workup also included functional imaging, such as somatostatin receptor imaging (since 1998) and gallium-PET (after 2007).[23] An observational study that included 46 patients with sporadic NF-PNETs smaller than 2 cm (evaluated by CT or MRI) demonstrated no distant or nodal metastases after a median of 34 months of observation, and only 13% (6/46) of the patients displayed tumor growth >20%.[24] The aforementioned study conducted by Sadot *et al*. found observation to be a reasonable strategy for stable, small, incidentally discovered PNETs (details of work-up not stated) based on their results showing no differences in survival data between the observation and resection groups.[17] Similarly, another study by Rosenberg *et al*. found that patients with NF-PNETs <2 cm (based on CT and MRI) showed no evidence of tumor progression or metastasis, regardless of whether they were in the operative or nonoperative group.[19] A recent systematic review of nine articles including a total of 344 patients with sporadic NF-PNETs found that sporadic small (≤2 cm) asymptomatic tumors displayed a low rate of growth (22%), low need for secondary surgical resection (12%), and no occurrences of disseminated disease at follow-up (0%). The authors concluded that expectant management of small asymptomatic sporadic NF-PNETs could be a reasonable option in a selective group of patients.[18]

Two centimeters is not ideal

However, some small PNETs manifest more aggressively, and the potential for regional or metastatic spread has been reported in several studies.[26] The analysis of 1371 NF-PNETs taken from the Surveillance, Epidemiology, and End Results (SEER) database (1988–2009) revealed that long-term survival was higher in patients with NF-PNETs <2 cm, but many patients with small NF-PNETs also developed distant metastases (9.1%) and LNM (27.3%).[16] A study of 128 patients undergoing pancreatectomy for NF-PNETs found that tumor size (<2 cm)

was not a predictive factor for death; lymph node (LN) and liver metastasis, high-grade (G3) pathology, and death still occurred in patients with small NF-PNETs.[15] Another study found that all patients with small NF-PNETs who developed liver metastasis, LNM, or died were symptomatic.[25] A recent systematic review of 13,374 patients undergoing resection for PNETs found that LNM occurred in 11.2% of patients with small PNETs and 10.3% of patients with G1 PNETs, and recommended that the watch-and-wait strategy for small NF-PNETs should be reappraised.[13]

Does size matter?

Many investigators have observed a clear relationship between the tumor diameter and the risks of malignancy and systemic progression. A study of 50 patients undergoing endoscopic ultrasonography found that a cutoff point of 18 mm showed higher sensitivity (95% vs. 85%) but lower specificity than 20 mm (40% vs. 46.7%) for the prediction of metastasis.[27] A French multicenter study found that tumor size had a significant impact on NF-PNET malignancy, and the tumor size cutoff value found on the receiver operating characteristic curve was 1.7 cm with a sensitivity of 92% and a specificity of 75% for predicting malignancy.[20] Another study tracked 90 patients with NF-PNET for 19–162 months and found that the risks of metastasis and recurrence increased significantly once tumor sizes exceed 1.5 cm.[1] A European multicenter study also confirmed that tumor size <1 cm was an independent prognostic factor.[7] The Chinese Study Group for Neuroendocrine Tumors recommends surveillance only for patients with NF-PNETs <1 cm.[28] Similarly, the latest guidelines from the North American Neuroendocrine Tumor Society recommend observation for asymptomatic NF-PNETs <1 cm in size and suggest that the choice of resection versus observation for PNETs 1–2 cm should be individualized based on patient age, comorbidities, tumor growth over time, estimated risk of symptom development, imaging details, tumor grade, extent of surgical resection required, patient preference, and access to long-term follow-up.[10]

Lymph node status in pancreatic neuroendocrine tumors-preoperative factors that predict lymph node metastasis

The association between LNM and poor outcomes of PNETs has been demonstrated in previous studies; however, predicting factors for LNM are still being investigated. A multi-institutional study from the US Neuroendocrine Tumor Study Group (US-NETSG) evaluated a total of 695 patients with NF-PNETs undergoing curative-intent resections, and found that preoperative factors that predict LNMs positivity include tumor size ≥2 cm (odds ratio [OR] 4.9, 95% CI 2.7–8.8, $P < 0.001$), proximal location (OR 1.9, 95% CI 1.2–3.2, $P = 0.008$), moderate differentiation (OR 2.1, 95% CI 1.2–3.7, $P = 0.006$), and Ki-67 ≥3% (3%–20%, OR 2.2, 95% CI 1.3–3.7, $P = 0.004$). In addition, for patients who underwent distal pancreatectomy, removal of less than seven LNs did not result in significant differences in 5-year recurrent free survival between LN-positive and LN-negative patients, while pancreatoduodenectomy inherently includes sufficient LN removal. The authors recommended the removal of at least seven nodes to enable accurate nodal staging.[29] Another study using data compiled from the US-NETSG and SEER databases between 2006 and 2016 confirmed that the number of LNs examined during surgery for PNETs nearly quadrupled over the last decade in clinical practice.[30]

The evolving consensus on small pancreatic neuroendocrine tumors over the previous decade

The treatment strategy for PNETs has undergone a paradigm shift over the previous decade.[31] Previously, surgery was the primary treatment for any localized pancreatic neoplasm as it was associated with significant survival benefits.[14,32,33] In 2011, Klöppel from the Armed Forces Institute of Pathology advocated surgical excision for all PNETs regardless of size, while also noting that tumor size (>2 cm), gross infiltrative growth, metastasis, angioinvasion, and proliferative activity determine the prognosis and metastatic potential.[34] In 2016, the ENETS updated their management guidelines for PNETs and added surveillance as a treatment option for NF-PNETs smaller than 2 cm; however, surgical resection has been advocated as the optimal treatment for all functioning, sporadic PNETs, regardless of tumor size.[21] In line with ENETS, the latest Clinical Practice Guidelines for Neuroendocrine Tumors of the NCCN also suggest a surveillance strategy for the management of NF-PNETs (using 2 cm as a cutoff value), but not for functional PNETs.[9] In addition, level 1 evidence is currently difficult to obtain, as there are no tools to predict the natural evolution of these small lesions. Further investigation of the disease dynamics is required for further optimization of management strategies a comparison of the current guidelines from different societies is summarized in Table 3.

Systemic therapy in small pancreatic neuroendocrine tumors

Currently, there are limited data on the role of systemic therapy in PNETs as either a neoadjuvant or adjuvant treatment.[4,9] Somatostatin analogs are the mainstay for the management of hormone-related symptoms and complications (including carcinoid syndrome) and can provide significant symptomatic relief in up to 80% of patients. The current NCCN guidelines recommend octreotide and lanreotide for symptom and/or tumor control in gastrinoma, glucagonoma, and insulinoma.[9,35]

How is the consensus or recommendation of guidelines followed in daily practice?

Currently, most guidelines adopt a conservative approach, where annual surveillance through high-quality imaging is recommended for incidentally discovered NF-PNETs ≤2 cm in size.[9,10,21] Nevertheless, clinical practice patterns vary widely. A recent study using data taken from the American National Cancer Database evaluated 3243 patients with small PNETs diagnosed between 2000 and 2014, most of whom (78.9%, or 2552 out of 3243) with tumors ≤2 cm underwent primary site resection, which is contrary to current recommendations.

Table 3: Comparison of the current international recommendations for the management of nonfunctioning pancreatic neuroendocrine tumors

Guidelines	Upper limits of small PENTs (cm)	Recommended strategy for small PNETs
ENETS (2016)[9]	2	Option 1. Surveillance for NF-PNET Option 2. Surgery: G2, symptoms, patient wishes
CSNET (2017)[16]	1	Surveillance only for patients with NF-PNETs<1 cm Surgery if progression (≥1 cm or >20% of original size)
NANSETS (2020)[15]	1	Initial observation period of asymptomatic patients with small PNET The decision to observe or resect an asymptomatic 1-2 cm PNET should be evaluated on a case-by-case basis
NCCN version 1 (2022)[10]	2	Decision on surgery versus active surveillance is made on a case-by-case basis for small low-grade NETs

G2: Grade 2, PNETs: Pancreatic neuroendocrine tumors, NF-PNET: Nonfunctioning PNETs, ENETS: European Neuroendocrine Tumor Society, CSNET: Chinese Study Group for Neuroendocrine Tumors, NANSETS: North American Neuroendocrine Tumor Society, NCCN: National Comprehensive Cancer Network, NETs: Neuroendocrine tumors

Patients with PNETs were more likely to undergo resection if they had positive nodes or a moderately or well-differentiated morphology on histopathology, if their tumor was in the pancreatic body or tail, or if they underwent treatment at an academic medical center. Patients with PNETs ranging between 1 and 2 cm in size who underwent primary site resection had significant survival benefits compared to those who did not, regardless of node status.[36] Among patients with tumor sizes between 1 and 2 cm, the median survival time for those who did not undergo primary site resection was more than 7 years, and longer survival (median survival time not reached) was observed in those who underwent resection.[36] Considering that the average life expectancy in Taiwan was 81.32 years (male 78.11, female 84.75) in 2020, the decision of surgery versus surveillance needs to be carefully weighed according to patient age and impact of surgery on quality of life.[37]

Conclusion

The management of small PNETs is complex and challenging; surgery is the cornerstone and only curative treatment for patients with PNETs which should be considered in patients with functional PNETs, large or growing NF-PNETs, and when presented with any other indications for surgery. As one size cannot fit all patients, patients with small NF-PNETs require individualized recommendations for surgery versus active surveillance based on tumor size, radiographic characteristics, and patient characteristics such as age and comorbidities [Figure 1]. The exact cutoff value of small NETs for surveillance-only strategies needs to be verified with more high-level evidence. In addition, patient preferences should also be considered. For patients who adapt surveillance strategies, fine-needle biopsy to confirm the diagnosis and grading is suggested if technically feasible. High-quality imaging at the 6–12 months' follow-up may be sufficient for monitoring small NF-NETs owing to their slow growth. Multidisciplinary teams containing radiologists can provide better tumor monitoring during follow-up and offer additional benefits for patient care.

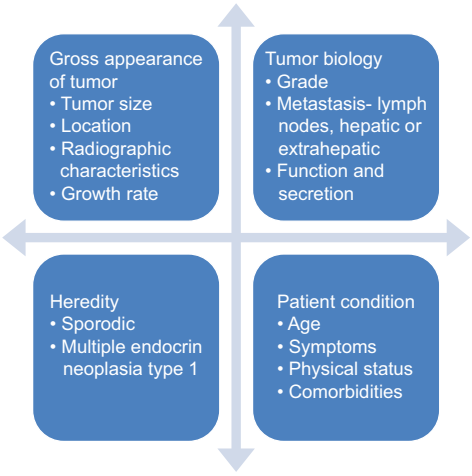

Figure 1: Depiction of the various factors that should be considered in the management of small PNETs. PNETs: Pancreatic neuroendocrine tumors

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Conflicts of interest

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