1. Pancreatic cancer with isolated PV/SMV invasion
2) pro

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췌장암은 많은 경우 혈관 침범을 동반한다. 특히 많은 경우 PV/SMV를 침범한다. PV/SMV의 침범에 대하여는 AJCC에서도 전에는 stage III로 inpoerable로 정의 했으나 최근 resection을 권유하며 stage II로 올려놓았다. NCCN guideline이나 MD anderson같은 병원도 PV/SMV를 적극적으로 절제하는 것을 권유하고 있다. 하지만 많은 보고는 이에 대한 논쟁이 있는 것이 사실이다. 최근의 한 보고는 혈관 절제시 높은 합병증을 보고 하였으며 본원의 성적도 좋지 않은 실정이다. 하지만 절제하지 않았을 경우 상당한 예에서 진행과 더불어 좋지 않은 예후를 보여 절제를 결정하기가 쉽지 않은 상태이다. 이에 본 발표에서는 이에 대한 장, 단점에 대해 논의하기로 한다.

2. Small neuroendocrine tumor of the pancreas
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Pancreatic neuroendocrine tumors (pNETs), also known as islet cell tumors, are rare neoplasms that arise in the endocrine tissues of the pancreas. Pancreatic NETs are only 1% to 3% of all pancreatic neoplasms [1]. However, these tumors have been gaining more attention recently, with a 2 to 3-fold increase in incidence for the past decades. According to the Surveillance, Epidemiology, and End Results (SEER) in United States, the age-adjusted annual incidence per 100,000 increased from 0.16 and 0.20 in 1973-1975 to 0.20 and 0.38 in 1996-2000 in female and males, respectively [2.3]. More recently, Japanese study in 2005 showed that an annual incidence was 1.01/100,000 that was approximately three times compared with that of the United States [4]. It could be explained that more people have a regular medical checkup and the resolution of diagnostic imaging tools has been highly improved.

Most pancreatic neuroendocrine tumors (pNETs) have been known to display an indolent course with longer survival compared with pancreatic adenocarcinoma [5]. However, theyhave malignant potential in 5-15% of insulinomas and 50-90% of the other pNETs including gastrinoma, glucagnoma, VIPoma, and nonfunctioning pNETs [6]. Although complete resection of the tumors is mandatory in spite of a substantial morbidity and measurable mortality of pancreatectomy, it is still unclear whether incidentally discovered, sporadic nonfunctioning (NF)-pNETs should be removed if they are small-sized tumors, because morbidity of pancreatectomy is still very high even in high-volume facilities. Therefore, when clinicians face the patients who have incidentally found small NF-pNETs, it would be somewhat hard to make a decision to perform resection immediately. Recently, with the wide use of high-quality cross-sectional imaging the incidental detection of small NF-pNETs has been increasing, whereas their natural history is largely unknown. Therefore, small NF-pNETs without symptoms has become a debating issue regarding to the treatment strategies [7]. New concept in this issue is needed to avoid surgery in carefully selective patients in order to evade morbidity and unnecessary surgery. This concept of selective surgery to incidentally found small NF-pNETs is very familiar to management of adrenal incidentaloma.

According to the data from the Massachusetts General Hospital [5], the mean tumor diameter of NF-pNETs decreased in the last decades (1988 to 1999 being 5.6cm and 2000 to 2005 being 4.1cm).

And the mean size of benign neoplasms was significantly smaller than that of malignant neoplasm (3.1cm vs. 5.0cm). Recent several studies also showed that tumor size correlated with malignant portential in NF-pNETs [8-10]. According to the data from Bettini *et al.*, [8] fifty one (29%) of 177 patients had an incidental diagnosis of pNET with a diameter ≤2cm. After resection, 5-year survival rate was 100% although three (6%) of those patients had a well-differentiated carcinoma. Tumors >2cm or nonincidental diagnosis of the tumor were independent risk factors associated with malignancy in NF-pNET. Lee *et al.* [11] reported that there was no disease progression or disease specific mortality in nonoperative patients with a median tumor size of 1.0cm (range 0.3-3.2) of pNET during mean follow-up of 45 months. Contrast to the strategy of selected management based on tumor size and behaviors, Haynes *et al.* [12] reviewed 139 patients who underwent surgery due to incidentally discovered, NF-pNETs. Recurrences ranged from 3.8-38.5% depending on the size and grading of the tumor. Surprisingly, 7.7% of patients with small tumor (<2cm) had late metastasis or recurrence. The authors suggested that all incidentally found pNETs should be resected, regardless of size or tumor growth pattern.

Surgery could remove NF-pNETs before malignancy develops and can guarantee improved survival [13]. Considering high postoperative morbidity (up to 40-45%) and low malignancy potential of small tumor (<2cm), however, conservative approach would apply carefully in a subset of patients with an incidentally discovered, nonfunctioning sporadic pNETs. This concept is supported by recent evidence of good long-term survival (100% at 15 years) of patients with gastrinomas <2cm after conservative treatment [14].

After considering many data up to date, we can reach the followings most of incidentally detected asymptomatic small NF-pNETs are likely benign and a non-operative approach could be advocated in selected cases, especially in elderly patients and presence of comorbidities. This conservative treatment strategy was accepted in ENETS (European Neuroendocrine Tumor Society) 2012 and NCCN (National Comprehensive Cancer Network) 2013 guidelines, although there is a difference regarding the cutoff value of tumor size, which is 2cm in ENETS guideline and 1cm in NCCN guideline [15,16].

Moreover, ENETS recommend an intensive 3-month follow-up for the first year and the 6 months up to 3 years in NF pNETs <2cm and they also emphasized risk and benefit from pancreatic surgical management should be well balanced in small tumors [16].

References

1. Fischer L, Kleeff J, Esposito I, et al. Clinical outcome and long-term survival in 118 consecutive patients with neuroendocrine tumours of the pancreas. The British journal of surgery 2008;95:627-35.
2. Halfdanarson TR, Rabe KG, Rubin J, Petersen GM. Pancreatic neuroendocrine tumors (PNETs): incidence, prognosis and recent trend toward improved survival. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO 2008;19:1727-33.
3. Yao JC, Hassan M, Phan A, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2008;26: 3063-72.
4. Ito T, Sasano H, Tanaka M, et al. Epidemiological study of gastroenteropancreatic neuroendocrine tumors in Japan. Journal of gastroenterology 2010;45:234-43.
5. Vagefi PA, Razo O, Deshpande V, et al. Evolving patterns in the detection and outcomes of pancreatic neuroendocrine neoplasms: the Massachusetts General Hospital experience from 1977 to 2005. Archives of surgery (Chicago, III : 1960) 2007;142:347-54.

6. Metz DC, Jensen RT. Gastrointestinal neuroendocrine tumors: pancreatic endocrine tumors. Gastroenterology 2008;135:1469-92.(http://www.ncbi.nlm.nih. gov/pubmed/18703061.)
7. La Rosa S, Klersy C, Uccella S, et al. Improved histologic and clinicopathologic criteria for prognostic evaluation of pancreatic endocrine tumors. Human pathology 2009;40:30-40.
8. Bettini R, Partelli S, Boninsegna L, et al. Tumor size correlates with malignancy in nonfunctioning pancreatic endocrine tumor. Surgery 2011;150: 75-82.
9. Gullo L, Migliori M, Falconi M, et al. Nonfunctioning pancreatic endocrine tumors: a multicenter clinical study. The American journal of gastroenterology 2003;98:2435-9.
10. Schindl M, Kaczirek K, Kaserer K, Niederle B. Is the new classification of neuroendocrine pancreatic tumors of clinical help? World journal of surgery 2000;24:1312-8.
11. Lee LC, Grant CS, Salomao DR, et al. Small, nonfunctioning, asymptomatic pancreatic neuroendocrine tumors (PNETs): role for nonoperative management. Surgery 2012;152:965-74. (http://www.ncbi.nlm.nih.gov/pubmed/23102679.)
12. Haynes AB, Deshpande V, Ingkakul T, et al. Implications of incidentally discovered, nonfunctioning pancreaticendocrine tumors: short-term and long-term patient outcomes. Archives of surgery (Chicago, Ill : 1960) 2011;146:534-8.
13. Kouvaraki MA, Shapiro SE, Cote GJ, et al. Management of pancreatic endocrine tumors in multiple endocrine neoplasia type 1. World journal of surgery 2006;30:643-53.
14. Norton JA, Alexander HR, Fraker DL, Venzon DJ, Gibril F, Jensen RT. Comparison of surgical results in patients with advanced and limited disease with multiple endocrine neoplasia type 1 and Zollinger-Ellison syndrome. Annals of surgery 2001;234:495-505; discussion -6
15. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology : Neuroendocrine Tumors Version 2.2013 National Comprehensive Cancer Network .(http://www.nccn.org/professionals/physician_gls/ pdf/neuroendocrine.pdf.)
16. Falconi M, Bartsch DK, Eriksson B, et al. ENETS Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms of the digestive system: well-differentiated pancreatic non-functioning tumors. Neuroendocrinology 2012;95:120-34. (http://www.ncbi.nlm.nih.gov/pubmed/22261872.)

2. Small neuroendocrine tumor of the pancreas
2) pro

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Pancreatic neuroendocrine tumors (PNETs) are rare pancreatic neoplasms with an apparently increasing incidence andare most of the time slow-growing neoplasms carrying an overall favorable prognosis. Nevertheless, because of heterogeneous and unpredictable biological behavior, patients with resectable pancreatic NETs typically undergo surgery with curative intent. The choice of surgical procedure depends on tumor size and location. Enucleation may be considered for small localized tumors if the main pancreatic duct can be preserved. Otherwise, a more formal oncologic surgery is usually required. Pancreaticoduodenectomy (Whipple procedure) is typically performed for resection of tumors in the head or uncinate process of the pancreas, whereas distal pancreatectomy is usually performed for tumors in the mid or distal pancreas. For tumors in the neck or proximal body of the pancreas, options include central versus subtotal pancreatectomy: the former preserves endocrine and exocrine function but is associated with increased risk of pancreatic fistula.

With the widespread use of cross-sectional imaging, asymptomatic sporadic well-differentiated NF-PNETs are now more and more frequently diagnosed and their diameter is usually small with a rate of tumor size smaller than 2cm, ranging from 26% to 61% and has been accompanied by an increase in the number of surgical resections. For these patients, despite its increasing safety, surgical resection has recently been challenged because of its lack of proven effect on long-term survival. Indeed, as stated in the ENETS guidelines, no high-level evidence exists showing a positive effect of surgery on overall survival in nonfunctioning PNETs (NF-PNET) smaller than 2cm in size. This poses a significant management challenge: should all NF-PNETs, even the incidentally detected small ones, be removed? Current practice at most institutions is to resect all NF-PNETs. However, whether some can be safely observed is still not well-defined. Recently, for this subgroup of lesions, a "wait and see" policy has been advocated.

Although tumor size has been the most extensively studied variable to identify the need for resection preoperatively, there is some disagreement as to its accuracy in predicting survival. Two well-performed studies support the use of size to identify patients with aggressive tumors that should be removed. Bettini et al., in a retrospective study of 230 patients undergoing resection for NF-PNET, demonstrated a strong correlation between increasing tumor size and higher tumor grade, positive LN status, and worse overall survival. But, they emphasized that although the tumor size correlated with the risk of malignancy, it should be kept in mind that this prognostic model has a limited accuracy because only 60% of tumors <2cm were benign in their series. Lee etal. revealed that there was no evidence of progression or disease specific mortality in a cohort of patients with small PNETs (median, 1.0cm) managed nonoperatively over a mean follow-up of 45months. Conversely, several other studies caution that tumor size may not be an accurate prognostic indicator. Haynes et al.reviewed the outcomes of 139 patients with incidentally discovered NF-PNETs and found that three of 39 patients with tumors ≤2cm developed metastases after resection and eventually died of their disease. Although a small minority of patients with tumors ≤2cm developed metastatic disease, increased tumor size (≥ 2cm) was a significant predictor of disease progression or metastasis in their study. Futhermore, Kuo et al., in population-level analysis of pancreatic neuroendocrine tumors 2cm or less in size demonstrated that the most significant predictors of disease-specific survival are grade and race and Small size, however, does not preclude malignant behavior. Of the factors Bilimoria KY et al. studied, tumor size, presence of nodal disease, and surgical margin status were not independently associated with survival. Their results did not show an independent association between size and survival even when compared tumors ≤1.0cm to those ≥ 4.0cm. Nodal involvement was also not found to be independently predictive of survival. Unlike most solid organ malignancies, large tumor size and/or nodal involvement should not preclude resection of PNETs

In addition to size, tumor grade is another variable associated with survival that can be assessed in the preoperative setting. Previous studies indicatedthat grade and differentiation are indicators of biologic behavior in NFPNETs and are associated with survival. EUS can be combined with fine-needle aspiration (FNA) or core needle biopsy to evaluate tumor pathology preoperatively. EUS with FNA or core biopsy is an additional preoperative test that could be useful, particularly when it remains unclear if resection is appropriate after tumor size and patient risk have been considered.

Asymptomatic sporadic NFPNETs, especially those smaller than 2cm in size, carry excellent long-term survival, despite a 10% risk of nodal metastasis reported in most surgical series. A cut-point of ≥2cm was associated with a sensitivity of 93.8% for the presence of positive LNs. The negative predictive value of tumor size <2cm was 92.6%. Of the 35 patients with tumors <2cm on preoperative imaging, only two had positive LNs.

One of the patients also had a 2-mm liver metastasis at the time of laparotomy. Overall, tumor size was a very sensitive, though not specific, indicator of LN status. For this subgroup of lesions, a "wait and see" policy may be sometimes risky.

Despite this risk, and because of an overall excellent prognosis, a progressive shift toward non-operative management had taken place. Indeed, the risk of a "wait and see" policy needs to be weighed against the operative morbidity and mortality of pancreatic surgery. Despite recent progress of surgical techniques, morbidity remains problematic, such as pancreatic leak, and long-term results are concernedespecially in view of the post-operative prevalence of pancreatic insufficiency in preoperatively asymptomatic patients. Recently, the outcome of surgery in terms of post-operative mortality and morbidity was satisfactory, emphasizing the improvements made in pancreatic surgery in recent years, including laparoscopic pancreatectomy.

Even in patients who should undergo surgical resection, the appropriate extent of resection is debated. It is reasonable to consider parenchyma-sparing resection without LN harvest in tumors <2cm because of the low risk of LN involvement. NF-PNETs are unlikely to benefit from more extensive resections that include LN dissection. NCCN guidelines recommend parenchyma-sparing resection as a treatment option for tumors <2cm and consideration of LN harvest in tumors 1-2cm in size. When PPRs are pursued, it is essential to accomplish complete resection as positive margin was associated with worse survival in our analysis.

One of the main challenges in PNET management, especially with a small nonfunctioning tumor, is accurately assessing the tumor's natural history, to predict the risk of malignancy and outcome. Prognostic factors such as circumstance of diagnosis, tumor size, presence of node or distant metastasis, Ki-67, mitotic index, tumor grade, and genetic origin have been widely studied, but overall PNET natural history remain highly variable and difficult to predict.

Small tumor size, although a predictor of decreased likelihood of disease progression or metastasis, did not guarantee a good outcome because 3 of 39 patients (7.7%) with tumors 2cm or smaller eventually had disease recurrence and died of their disease, including 1 patient with disease initially classified as benign. One patient with a tumor smaller than 1cm was found to have malignant disease. Incidentally detected, nonfunctioning PETs can display aggressive behavior, even when small. Although patients with malignant disease had diminished survival and increased rates of recurrence, benign histologic findings did not eliminate the possibility of progression. Patients with incidentally discovered, nonfunctioning PETs should undergo tumor resection and careful postoperative surveillance, even if surgical pathologic findings suggest benign disease.

In this particular subgroup of patients, a non-operative management could be advocated in selected cases (ie, elderly patients, presence of comorbidities, and incidental diagnosis in an asymptomatic patient). It is remarkable that, if a conservative approach is chosen, a strict follow-up program must be recommended, and if an increasing diameter is detected, patients should be addressed to operative resection promptly.

A randomized trial comparing observation and resection would provide more definitive results but would be difficult to perform given the low incidence of NF-PNETs.

References

1. Bettini R, Partelli S, Boninsegna L, Capelli P, Crippa S, Pederzoli P, et al. Tumor size correlates with malignancy in nonfunctioning pancreatic endocrine tumor. Surgery. 2011;150(1): 75-82.
2. Gaujoux S, Partelli S, Maire F, D'Onofrio M, Larroque B, Tamburrino D, et al. Observational study of natural history of small sporadic non-functioning pancreatic neuroendocrine tumors. J Clin Endocrinol Metab. 2013;20.

3. Haynes AB, Deshpande V, Ingkakul T, Vagefi PA, Szymonifka J, Thayer SP, et al. Implications of incidentally discovered, non-functioning pancreatic endocrine tumors: short-term and long-term patient outcomes. Arch Surg. 2011;146(5):534-8.
4. Lee LC, Grant CS, Salomao DR, Fletcher JG, Takahashi N, Fidler JL, et al. Small, non-functioning, asymptomatic pancreatic neuroendocrine tumors (PNETs): role for non-operative management. Surgery. 2012;152(6): 965-74.
5. Toste PA, Kadera BE, Tatishchev SF, Dawson DW, Clerkin BM, Muthusamy R, et al. Nonfunctional Pancreatic Neuroendocrine Tumors <2cm on Preoperative Imaging are Associated with a Low Incidence of Nodal Metastasis and an Excellent Overall Survival. J Gastrointest Surg. 2013;8.
6. Gaujoux S, Partelli S, Maire F, D'Onofrio M, Larroque B, Tamburrino D, et al. Observational study of natural history of small sporadic non-functioning pancreatic neuroendocrine tumors. J Clin Endocrinol Metab. 2013;20.
7. Kuo EJ, Salem RR. Population-level analysis of pancreatic neuroendocrine tumors 2cm or less in size. Ann Surg Oncol. 2013;20(9):2815-21.
8. Bilimoria KY, Talamonti MS, Tomlinson JS, Stewart AK, Winchester DP, Ko CY, et al. Prognostic score predicting survival after resection of pancreatic neuroendocrine tumors: analysis of 3851 patients. Ann Surg. 2008;247(3): 490-500.
9. Zerbi A, Capitanio V, Boninsegna L, Pasquali C, Rindi G, Delle Fave G, et al. Surgical treatment of pancreatic endocrine tumours in Italy: results of a prospective multicentre study of 262 cases. Langenbecks Arch Surg. 2011;396(3):313-21.

Symposium 4 (Video, How I do it?) Efforts to obtain more safety margin during surgery for Klatskin tumor

1. Conventional resection

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Bile duct excision

All patients underwent a resection of the extrahepatic biliary tree from the level of the upper border of the pancreas or about 1cm into intrapancreatic portion to the confluence of the left and right hepatic ducts. If the tumour extended lower than the intrapancreatic portion of the common bile duct, this was also removed and pancreaticoduodenectomy was considered. At the upper end of the biliary tree, the extent of biliary resection has depended on the extent of hepatic resection required. Routine frozen-section histopathology has also been used to guide the extent of biliary resection. Care is taken to control bile spillage during resection in order to decrease the risk of postoperative tumor seeding. After the distal portion of the bile duct was cut near the edge of the pancreas early during the operation, the stump of the bile duct was meticulously closed to avoid bile spill. Secondly, the proximal, segmental bile ducts were cut in the liver remnant, preferably as the final step in the procedure, after the parenchymal transection has been completely executed, with application of clamp at the tumor-side. Biliary reconstruction in all patients was performed by retrocolic Roux-en-Y hepaticojejunostomy without biliary stents.

Hepatic resection

Hepatic resection was carried out to include all segments of liver involved by tumour or affected