

Characteristics and long-term survival of resected pancreatic cystic neoplasms in Finland. The first nationwide study.

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Funding

This work was supported by the State Research Funding (VTR), Finland, and the Sigrid Juselius Foundation, Finland. No involvement in the study design, data collection, data analysis, manuscript preparation or publication decisions.

Original article

Abstract

Background

Pancreatic cystic neoplasms (PCN) are being found increasingly in imaging studies. Even though the characteristics of PCN lesions have been studied extensively in single and multicentre settings, nationwide data is lacking. The aim of this study was to determine the nationwide epidemiologic characteristics and long-term survival of all resected PCNs.

Methods

All PCNs operated on in Finland during the period 2000-2008 were identified. Data was collected from all patients: on demographics, comorbidities, symptoms, radiological findings, surgical procedures, complications, histopathological diagnoses and survival. Incomplete pathology reports and any uncertain diagnoses were re-assessed. Survival data was collected after a five-year follow-up period.

Results

The final database included 225 patients with operated PCN. After reviewing the incomplete pathology reports, in 44 cases the original diagnosis was changed, mostly from MCN to IPMN. The most common histopathological diagnoses were IPMN (90/225; 50/225 MD-IPMN, 30/225 MX-IPMN and 14/225 BD-IPMN), SCN (41/225) and MCN (40/225). Overall, 53/225 (23.6%) of the tumours were malignant. Malignancy was detected in MD-IPMN 29/50 (58%), MX-IPMN 10/30 (33.3%), MCN 12/40 (30%), BD-IPMN 2/14 (14.3%) patients. Median 5-year survival for all patients was 77%: 87% in patients without malignancy, 77% with HGD and 27% in patients with a malignant resected PCN.

Conclusion

One fourth of the PCNs operated on nationwide were malignant, with a five-year survival of 27%, compared to overall survival of 87% in patients with non-malignant disease and 77% in those with HGD. Detecting – and operating on - a PCN before the malignant transfer remains a great challenge.

Introduction

Pancreatic cystic lesions (PCN) are being found increasingly in imaging studies, mainly due to ageing, increased imaging and improved radiological techniques¹⁻². The prevalence of resected intraductal papillary mucinous neoplasms (IPMN) has been reported to be on the increase, while the prevalence of mucinous cystadenoma (MCN) seems stable or is decreasing¹⁻³. The reasons for this change remain unknown, but it has been suggested that some IPMNs have earlier been misdiagnosed as MCNs⁴. The malignant potential of PCNs varies from completely benign tumours, such as serous cystadenoma (SCN) and epithelial non-neoplastic tumours (EPIT), to tumours with a low malignant potential, such as branch duct (BD) IPMN, and to tumours with high malignant potential, such as main duct (MD) and mixed type (MX) IPMNs and solid pseudopapillary neoplasms (SPN)⁵⁻⁶. In earlier reports the majority of resected PCNs have been benign. To avoid unnecessary operations, good-quality preoperative assignment is crucial⁷.

Even though the characteristics of resected PCNs have been studied extensively in single and multicentre settings, nationwide epidemiologic data is lacking.

The aim of this study was to determine the nationwide epidemiologic characteristics and long-term survival of all resected PCNs.

Methods

All pancreatic lesions operated on in Finland during the period 2000-2008 were identified by combining data from the national operations register and patient archives. After this, patients' medical records, including pre and postoperative data, were reviewed to identify patients likely to have undergone resection of a PCN. Conditions other than PCNs (mostly pseudocysts and pancreatic ductal adenocarcinomas) were excluded. The patients with resected PCN formed the final study population.

For the final study population, data was collected on demographics, comorbidities, symptoms, radiological findings, surgical procedures, complications, final histopathological diagnoses and survival. Due to incomplete patient records, preoperative data, including radiological findings, were partially missing for some patients. Variables with incomplete data sets were displayed with available data. A patient was deemed "symptomatic" if pancreas-related symptoms such as upper abdominal pain, jaundice, pancreatitis or weight loss were recorded at the time of PCN resection.

Radiological pancreatic findings such as size, location and number of cysts were gathered from the radiology reports. Postoperative complications were registered from the each hospital's medical records and graded according to the Clavien-Dindo Classification of Surgical Complications⁸.

Pathology reports were reviewed. Incomplete reports and any uncertain diagnoses were re-assessed and, whenever necessary, the histopathological slides re-reviewed by an experienced pancreatic pathologist. These typically included any cases where a PCN had been classified as an MCN without mentioning the content of an ovarian type stroma.

Short and long-term mortality data was gathered from the Finnish registry office 31/3/2016. Follow-up time for all patients was five years.

Statistical analyses were performed using SPSS 22.0 for Windows (IBM Inc., Somers, USA). Unless otherwise specified descriptive statistics are reported using count, percentage, median and range. Chi-square test was used in univariate analyses and logistic regression analysis for multivariate analyses. $P < 0.05$ was considered statistically significant. Kaplan-Mayer analysis was used to analyze long-term survival.

Permission to review patient files and histological slides was obtained from the National Supervisory Authority for Welfare and Health (Valvira) (permission 10263/06.01.03.01/2012) and from National institute for health and welfare (THL) (permission 1854/5.05.00/2012).

Results

During the period 2000-2008 pancreatic resections were performed in 22 hospitals in Finland; most of these were regarded as low volume centres. During the study period a total of 2,024 patients underwent pancreatic surgery. Of these, 503 were identified as having presumably undergone resection of PCN. After carefully reviewing the patient records including preoperative radiological reports and postoperative histological reports, 147 patients without a real PCN and 61 patients with a pseudocyst were excluded. A further 70 cases for whom the patient records were not available were excluded. Thus 225 patients were included in the final study cohort (Figure 1).

Frequency of pancreatic resections for PCN per year doubled during the study period 2000-2008. The population of Finland was 5.18 million in 2000 and 5.31 million in 2008. During the period 2000-2002 a resection for PCN was performed on 0.3/100 000, and during 2006-2008 on 0.6/100 000 people.

Preoperative findings

Median age was 61.0 (14-87) years, and 143 (63.3%) patients were female. At the time of operation, 25/154 (16.2%) patients had type 2 and 4/154 (2.6%) type 1 diabetes. Smokers amounted to 11/121 (9.1%) and 146/210 (69.5%) patients had symptoms related to PCN, the most common being pain 98/201 (46.7%), jaundice 21/201 (10.0%) and pancreatitis 20/210 (9.5%) weight loss 19/210 (9.0%), (Table 1).

In the preoperative imaging, computed tomography (CT) was performed in 191/198 (96.5%), magnetic resonance imaging (MRI) in 56/198 (28.2%) and endoscopic ultrasound (EUS) in 13/198 (6.6%) of the patients. In imaging the median tumour diameter was 40.0 (range 4-220) mm, 104/119 (87.4%) of the cysts were solitary lesions, and 125/188 (66.5%) of tumours were located left of the portal vein; the location was in the tail in 82/188 (43.6%), in the body in 43/188 (22.9%), in the head 58/188 (30.9%) and in the uncinatus area in 5/188 (2.7%) of the patients. Main pancreatic duct dilatation over 6mm, calcifications of cysts or mural nodules were observed in 19/188 (21.5%) of the patients (Table 1, 2, Figure 2a).

Surgery and complications

Distal pancreatic resection (DR) (tail resection or body and tail resection) was performed on 134/225 (59.6 %), pancreaticoduodenectomy (PD) on 73/225 (32.4%), total pancreatectomy 12/225 (5.3%) and enucleation on 6/225 (2.7%) patients (Table 3).

Overall morbidity according to the Clavien-Dindo Classification was 111/225 (49.3%). Of the complications 68/225 (30.2%) were classified as minor (Clavien-Dindo 1-2) and 40/225 (17.8%) as major (Clavien-Dindo 3-4). In-hospital mortality (Clavien-Dingo 5) was 3/225 (1.3%). Overall 30-day mortality was 5/225 (2.2%). Out of these five patients, four underwent PD and one patient DP. Four out of five patients had a malignant tumour. Ninety-day mortality was 7/225 (3.1%). After PD overall major complications (Clavien-Dindo 3-5) were more than after DP (21 (28.7%) vs. 15 (11.2%) , $p < 0.001$) (Tables 3a, 3b).

Histopathological results

In the histopathological analyses median tumour size was 35mm (range 2-180). Malignant tumours were seen in 53/225 (23.5%) of the patients and high-grade dysplasia (HGD) was present in 15/225 (6.6%) of the specimens (Table 4).

The most common histopathological diagnosis was IPMN, 94/225 (41.7%); 50/225 (22.1%) MD-IPMN, 30/225 13.3% MX-IPMN and 14/225 (6.2%) BD-IPMN. Other common diagnoses were SCN in 41/225 (18.1%), MCN in 40/225 (17.7%), EPIT in 22/225 (9.7%), and SPN in 8/225 (3.5%). Other, more rare tumours, such as cystic neuroendocrine tumours, myofibroclastic tumours, lymphangioma and acinar cell neoplasms accounted for a total of 20/225 (8.8%) of the cases (Table 4, Figure 2b).

IPMNs were evenly distributed for gender, whereas 7/8 of SPNs and 40/40 of MCNs were seen in females. IPMNs were located equally in the right and left side of portal vein, 30/40 (75%) of MCNs were located in the body or tail (Table 4).

Overall, 53/225 (23.6%) of the tumours were malignant and 15/225 (6.7%) had HDG. Malignancy was detected in MD-IPMN 29/50 (58%), MX-IPMN 10/30 (33.3%), MCN 12/40 (30%), BD-IPMN 2/14 (14.3%), SPN 0/8 (0%), SCN 0/41 (0%) and others 0/20 (0%). Quantities of HGD tumours were: MD-IPMN 6/50 (12%), MX-IPMN 3/30 (10%), MCN 2/40 (5%), BD-IPMN 0/14 (0%), SPN 2/8 (25%), SCN 0/40 (0%) and others 2/20 10%. Of the PDs

33/73 (45.2%) and of the DPs 16/134 (11.9%) were performed for malignant tumours (Table 6.).

Risk factors for malignancy in univariate analyses were age over 60 years ($p < 0.01$), symptoms ($p = 0.03$) and tumour location in the pancreatic head or uncinatus area ($p < 0.01$). The same risk factors for malignancy lasted in multivariate analyses: age over 60 years ($p < 0.003$, odds ratio 3.486), symptoms ($p < 0.016$, odds ratio 3.259), and tumour location in the pancreatic head or uncinatus area ($p < 0.016$, odds ratio 2.624). Equal numbers of malignant tumours were seen in patients with and without potential risk factors, including smoking, diabetes or cyst size > 3 cm. PCNs with and without worrisome features in preoperative imaging (main pancreatic duct dilatation over 6 mm, calcification of cysts, mural nodules) also had similar frequency of malignancy^{7,11} (Table 5a, 5b).

In 67/225 (29.8%) of the patients the original pathological reports were inconclusive. In 25 cases re-evaluation was made by experienced pancreatic pathologist based on original pathological reports and 42 cases histopathological slides needed to be re-reviewed. In most of these cases, the tumours were classified as MCNs in the original pathologic report but did not fulfill the criteria regarding the presence of ovarian type-stroma⁶. Original MCN diagnoses were confirmed in 23 cases, and in 44 cases the diagnoses changed. Changed diagnoses included 27 MD-IPMN, 9 MX-IPMN, 2 BD-IPMN, 3 SCN, 2 acinar cell neoplasms and 1 ductal adenocarcinoma.

Long-term survival

Of the patients 220/225 (97.8%) survived over 30 days after the operation. Median 5-year survival for all patients with resected PCN was 76.7%: 86.9% for patients without malignancy, 76.6% for patients with HGD and 27.3% for patients with malignant resected PCN. In 46/53 (86.8%) of the patients with a malignant tumour death was related to pancreatic cancer (Table 6, Figure 3b).

Out of the total 94 IPMNs, 53 were benign. Three (5.7%) of these patients (BD-IPMN with LGD, MX-IPMN with LGD and MD-IPMN with HGD) died of pancreatic cancer during the follow-up period, 49-79 months after the operation.

Discussion

PCNs are a heterogeneous group of tumours with a varying malignancy potential. The nationwide epidemiologic characteristics of resected PCNs are largely unknown. Our aim was to study the nationwide characteristics and long-term prognosis of resected PCNs in Finland.

This paper described the preoperative characteristics, surgical details, distribution of diagnoses and long-term survival of all resected PCNs in Finland between 2000 and 2008. By

having an experienced pancreatic pathologist re-review the histopathological analyses whenever necessary we were able to set the correct diagnoses of the tumours. To the best of our knowledge this is the first nationwide study on resected PCNs. There are larger published series of resected PCNs from high-volume academic centres and of multicentre origin, which may contain selection bias, which should not be present in this nationwide study ^{4,7}.

According to the literature, the number of incidentally found, resected PCNs is rising ⁵. PCNs are detected more often mostly due to improvements in and increased usage of imaging techniques. Moreover incidental PCNs have been monitored more closely since European ⁹ and international ¹⁰ guidelines were published in 2013 and 2012. The size of resected PCNs has decreased in recent decades ⁷. In this study the resected PCNs were mostly symptomatic 146/210 (69.5) and the median size of the tumour was also larger than reported in the recent literature. Tumour size and high proportion of symptomatic patients can be explained by changes in the criteria concerning operating on PCNs and by better imaging techniques. In the early 2000s the availability of MRI and EUS was inferior compared to today, which explains the fairly frequent use of CT and low use of MRI and EUS ¹¹.

The rate of morbidity - and even mortality - after pancreatic surgery was high, but around the same level as described in the literature (Table 3). A patient who is fit for surgery and with a strong indication renders it advisable to proceed to operation. If, on the other hand, the patient is borderline operable and/or the indication is relative, the decision whether to operate becomes less clear-cut. As described by Del Chiaro, patients unfit for surgery had relatively high IPMN-specific survival ¹². In any case, optimal results for patients with PCN demand high quality preoperative workup, correct patient selection as well as proper follow-up.

Since IPMN tumours were first described by Ohashi in 1982 ¹³, the incidence of IPMN has been increasing in large retrospective series ^{3,5}. During the same period of time, the proportional incidence of resected MCNs has decreased significantly. There is an ongoing discussion - as Valsangkar et al. ⁴ point out - whether the actual incidence is increasing, or whether the reported increase is more related to the change in the histopathological classification of tumours. Niedergethmann et al. ¹⁴ reviewed histological specimens of 207 cystic or small solid tumours out of 1,424 pancreatic specimens. Fifty-four of these specimens revealed an IPMN tumour. Our results were similar: a significant proportion of the original diagnoses changed to IPMN after reviewing. Most of these had previously been diagnosed as MCN or unclassified cystic tumour of the pancreas. These findings support the hypothesis that the real incidence of IPMN-tumours may not be increasing, at least not as dramatically as suggested. Thus the reason for the increase in the incidence of IPMN may be related to changes in pathological criteria, improvement in the quality of pathology, improved imaging techniques and an increase in the frequency of cross-sectional imaging.

The relevance of making an accurate distinction between IPMN and MCN tumours is related to the different recurrence pattern of IPMN and MCN. Even after resection IPMN tumours require life-long surveillance (total pancreatectomy patients excluded) since there is a substantial risk

of recurrence even if the resection margins were negative ^{4,9,15}. Benign MCNs, on the contrary, have a recurrence level close to zero so follow-up is not recommended ^{4,16}.

In our material the proportion of IPMN tumours was 94/225 (42%), SCN 41/225 (18%) and MCN 40/225(18%). Distribution of diagnoses is similar to that reported for large series of resected PCNs ^{4,5,7,13}. The number of IPMN tumours is slightly higher, which can be partially explained by the revised diagnoses after re-reviewing the histopathology. SCN tumours should only be resected when symptomatic, in case of rapid growth, if the diagnosis is uncertain or if there is concern about malignancy ^{17,18,19}. However, imaging diagnostics of SCN is not always easy. Making a radiologic distinction between SCNs and MCNs can be especially difficult ²⁰. Availability of MRI and EUS was moreover limited during the study period, which impaired the quality of the preoperative assessment and likely resulted in unnecessary operations. In our material, 24/41 (59%) of the patients with resected SCNs had pancreas related symptoms as expected, even though none of the patients had any signs of malignancy or HGD in histopathological analyses (Table 1a, 4).

The European and international guidelines for IPMN and MCN have gathered risk factors related to the risk of tumours transforming from benign to malign ^{9,10}. From radiology reports we were able to obtain data on main pancreatic duct dilatation over 6mm, calcification of cysts and mural nodules. In our analyses none of these factors were significant risk factors for malignant tumours. Main pancreatic duct dilatation is diagnosed reliably by MRI examination. In this population only 56/198 (28.2%) of patients were examined by MRI. A lack of MRI studies can partially explain why main pancreatic duct dilatation is not a risk factor for malignancy, or even for HGD, in this study. In this material the risk factors for malignant tumours were age over 60 years ($p<0.01$), symptomatic patient ($p=0.03$) and tumour location in the caput or uncinatus of the pancreas ($p<0.01$). These factors were also independent risk factors in the multivariate logistic regression analyses. It is known that symptomatic tumours carry more risk of malignancy and that age increases the cumulative risk of having a malignant tumour. Patient age and/or poor general condition may lead to more pressing indications for surgery, which causes fewer tumours to be operated on before they become malignant. It has been reported that IPMN tumours to the right of the porta carry an increased risk of progression compared to those on the left side of the porta ¹². Also, the majority of zero or low malignancy potential tumours such as SCN and EPIT were located on the left side of the vena portae (Table 4., Table 6.).

Most patients with resected PCNs were females (143/225). The literature reports no gender difference in the prevalence of PCNs ^{1,21}. In our material, however, a large proportion of tumours were diagnosed as MCNs or SCNs, which are predominantly diagnosed in women, explaining the difference in gender distribution (Table 4.).

Out of the 94 IPMNs 44 showed no signs of malignancy or HGD in the histopathological analyses. During long-term follow-up three of these 44 patients (6.8%) still died of pancreatic cancer. This strongly supports the guidelines recommending follow-up of resected IPMNs.

Patients with benign tumours had 87% 5-year survival. Even with HGD tumours the 5-year survival was 76.6%, whereas in malignant tumours it was only 27%. These numbers serve to confirm that detecting – and operating on - a PCN before malignant transfer is essential for long-term survival. In spite of the significant morbidity involved in pancreatic resections, in benign cases it does not affect patients' 5-year survival compared to that of general population ²².

We conclude that in this first nationwide study of resected PCNs, one fourth of the tumours were malignant, with a five-year survival of 27%, compared to overall 87% in patients with non-malignant disease and 77% with HGD. A surprisingly large number of diagnoses were revised after re-review of the specimens by an experienced pancreatic pathologist. A correct histopathological diagnosis affects the optimal follow up plan for each patient. As the number of detected PCNs is increasing, all efforts should be invested in optimal pre- and postoperative workup of these patients. Operating a PCN before the malignant transfer as well as prompt recognition of entirely benign lesions, to spare patients from the morbidity inevitably related to pancreatic surgery, remain a great challenge.

References

1. Laffan TA, Horton KM, Klein AP, Berlanstein B, Siegelman SS, Kawamoto S, et al. Prevalence of unsuspected pancreatic cysts on MDCT. *AJR Am J Roentgenol* 2008 Sep;191(3):802-807.
2. Zhang X, Mitchell DG, Dohke M, Holland GA, Parker L. Pancreatic cysts: depiction on single-shot fast spin-echo MR images. *Radiology* 2002 May;223(2):547-553.
3. Klibansky, David A.|Reid-Lombardo, Kaye M.|Gordon, Stuart R.|Gardner, Timothy B. The Clinical Relevance of the Increasing Incidence of Intraductal Papillary Mucinous Neoplasm. *Clinical Gastroenterology and Hepatology* 2012;10(5):555-558.
4. Valsangkar, Nakul P., MD|Moraes-Oyarvide, Vicente, MD|Thayer, Sarah P., MD, PhD|Ferrone, Cristina R., MD|Wargo, Jennifer A., MD|Warshaw, Andrew L., MD|Fernández-del Castillo, Carlos, MD. 851 resected cystic tumors of the pancreas: A 33-year experience at the Massachusetts General Hospital. *Surgery: Official Journal of the Society of University Surgeons, Central Surgical Association, and the American Association of Endocrine Surgeons* 2012;152(3):S12.
5. Postlewait LM, Ethun CG, McInnis MR, Merchant N, Parikh A, Idrees K, et al. Association of Preoperative Risk Factors With Malignancy in Pancreatic Mucinous Cystic Neoplasms: A Multicenter Study. *JAMA Surg* 2017 Jan 01;152(1):19-25.
6. Basturk O, Coban I, Adsay NV. Pancreatic cysts: pathologic classification, differential diagnosis, and clinical implications. *Arch Pathol Lab Med* 2009 Mar;133(3):423-438
7. Gaujoux S, Brennan MF, Gonen M, D'Angelica MI, DeMatteo R, Fong Y, et al. Cystic lesions of the pancreas: changes in the presentation and management of 1,424 patients at a single institution over a 15-year time period. *J Am Coll Surg* 2011 Apr;212(4):603.
8. Dindo D, Demartines N, Clavien P. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004 Aug;240(2):205-213.
9. European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. *Gut* 2018 May;67(5):789-804.
10. Tanaka M, Fernández-del Castillo C, Adsay V, Chari S, Falconi M, Jang J, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. *Pancreatology* 2012 May-Jun;12(3):183-197.
11. Healthcare resource statistics - technical resources and medical technology Eurostat.

12. Del Chiaro M, Ateeb Z, Hansson MR, Rangelova E, Segersvärd R, Kartalis N, et al. Survival Analysis and Risk for Progression of Intraductal Papillary Mucinous Neoplasia of the Pancreas (IPMN) Under Surveillance: A Single-Institution Experience. *Ann Surg Oncol* 2017 Apr;24(4):1120-1126.
13. Ohashi K, Murakami Y, Takeoshi T, Ohta H, Ohashi I. Four cases of mucin producing cancer of the pancreas on specific findings of the papilla of Vater (Japanese) *Prog Dig Endosc*. 1982;20:348-351.
14. Niedergethmann M, Grützmann R, Hildenbrand R, Dittert D, Aramin N, Franz M, et al. Outcome of invasive and noninvasive intraductal papillary-mucinous neoplasms of the pancreas (IPMN): a 10-year experience. *World J Surg* 2008 Oct;32(10):2253-2260.
15. Schnelldorfer T, Sarr MG, Nagorney DM, Zhang L, Smyrk TC, Qin R, et al. Experience with 208 resections for intraductal papillary mucinous neoplasm of the pancreas. *Arch Surg* 2008 Jul;143(7):646; discussion 646.
16. Crippa S, Salvia R, Warshaw AL, Domínguez I, Bassi C, Falconi M, et al. Mucinous cystic neoplasm of the pancreas is not an aggressive entity: lessons from 163 resected patients. *Ann Surg* 2008 Apr;247(4):571-579.
17. (1) Allen PJ, D'Angelica M, Gonen M, Jaques DP, Coit DG, Jarnagin WR, et al. A selective approach to the resection of cystic lesions of the pancreas: results from 539 consecutive patients. *Ann Surg* 2006 Oct;244(4):572-582.
18. Jais B, Rebours V, Malleo G, Salvia R, Fontana M, Maggino L, et al. Serous cystic neoplasm of the pancreas: a multinational study of 2622 patients under the auspices of the International Association of Pancreatology and European Pancreatic Club (European Study Group on Cystic Tumors of the Pancreas). *Gut* 2016 Feb;65(2):305-312.
19. Huh J, Byun JH, Hong S, Kim KW, Kim JH, Lee SS, et al. Malignant pancreatic serous cystic neoplasms: systematic review with a new case. *BMC Gastroenterol* 2016 Aug 22;16(1):97.
20. Goh BKP, Tan Y, Yap W, Cheow P, Chow PKH, Chung YA, et al. Pancreatic serous oligocystic adenomas: clinicopathologic features and a comparison with serous microcystic adenomas and mucinous cystic neoplasms. *World J Surg* 2006 Aug;30(8):1553-1559.
21. Lee KS, Sekhar A, Rofsky NM, Pedrosa I. Prevalence of incidental pancreatic cysts in the adult population on MR imaging. *Am J Gastroenterol* 2010 Sep;105(9):2079-2084.
22. Statistics Finland: Survival by age in general population in Finland 2000-2007 (Kuolleisuus- ja eloonjäämislukuja 2000-2007)

Figure 1. Flow-chart of the resected pancreatic tumors in Finland 2000-2008

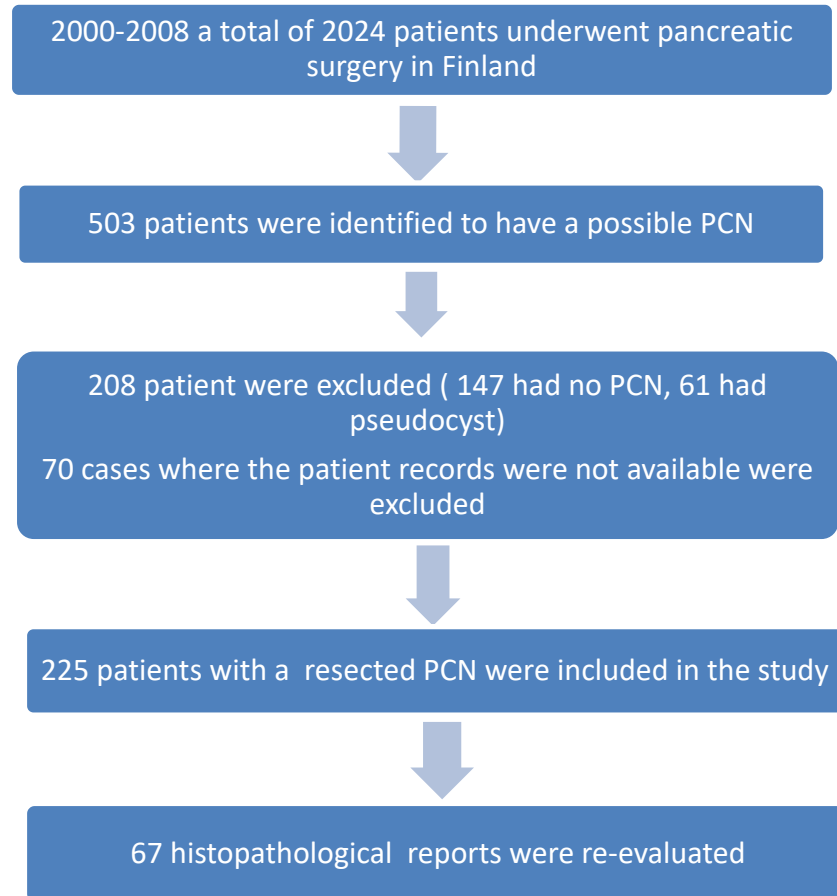


Figure 2a. Kaplan-Meier survival curves for each diagnoses of resected PCN:s

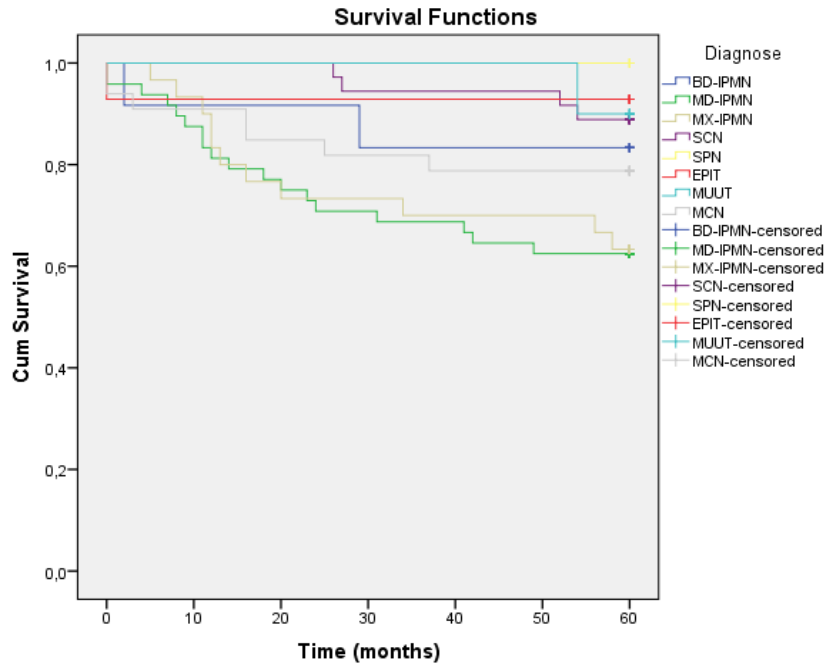


Figure 2b. Kaplan-Meier survival curves for benign, HGD and malignant tumors

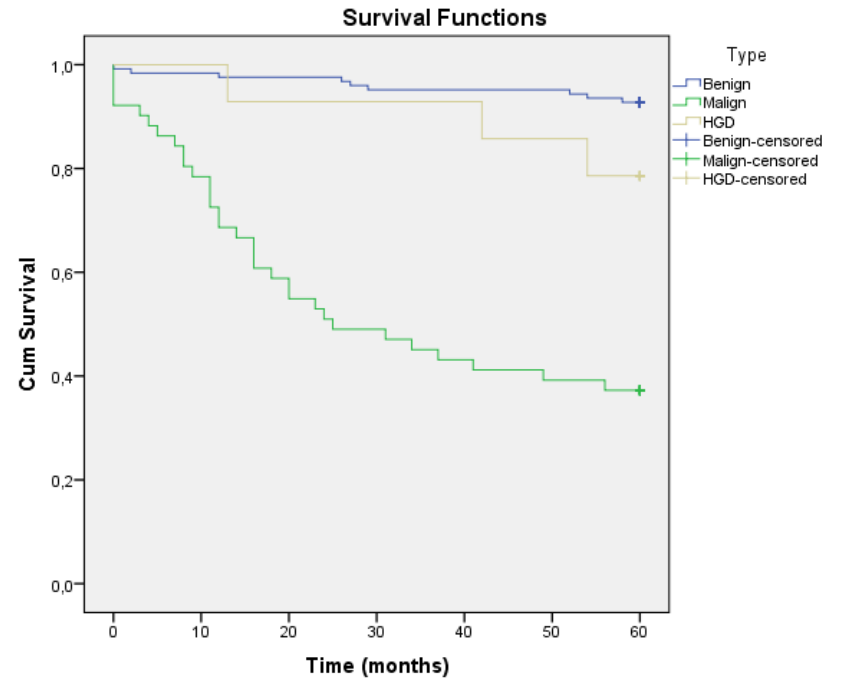


Table 1. Baseline characteristics and preoperative findings of patient's with resected PCN:n 2000-2008 in Finland

Baseline characteristics	
Median age years, range	61.0 (14-87)
Gender, female/male, n (%)	143/82 (63.3/37.7)
Smoking, n (%)	11/121 (9.1)
Diabetes, n (%)	29/154 (18.8)
Symptoms	
Symptomatic, n (%)	146/210 (69.5)
Pain, n (%)	98 (46.7)
Jaundice, n (%)	21(10.0)
Pancreatitis, n (%)	20 (9.5)
Weight loss, n (%)	19(9.0)
Examinations	
CT, n (%)	191/198 (96.5)
MRI, n (%)	56/193 (29.0)
EUS, n (%)	13/192 (6.8)

Table 2. Radiological findings of patient's with resected PCN:n 2000-2008 in Finland

Size of tumor	
Median diameter of cyst, (range)mm	40.0 (4-220)
Location of cysts	
Head	58 (30.9)
Uncinatus	5 (2.7)
Body	43 (22.9)
Tail	82 (43.6)
Number of cysts	
1	87.4
2	4.2
3	0.9
>3	3.5
Worrisome features	
Any features, n (%)	19/88 (21.5)
MPD over 6mm, n (%)	9/88 (10.2)
Calcification of cysts, n (%)	8/88 (9.1)
Mural nodules, n (%)	8/88 (9.1)

Table 3a. Type of surgery, rate of complications by Clavien-Dindo score , 30 and 90 day mortality of resected PCN:s,

Type of surgery	
¹ DP, n (%)	134, (59.6)
² PD, n (%)	73, (32.4)
Total pancreatectomy, n (%)	12 (5.3)
Enucleation, n (%)	6 (2.7)
Complications	
Operation related morbidity and mortality	111 (48.4)
Clavien-Dindo 1-2, n (%)	68 (30.2)
Clavien-Dindo 3-4, n (%)	40 (17.8)
Clavien Dindo 5, n (%)	3 (1,3)
30 day mortality, n (%)	5 ³ (2.2)
90 day mortality, n (%)	7 (3,1)

Table 3b. Clavien-Dindo score for each type of surgery

	Clavien-Dindo 0	Clavien-Dindo 1-2	Clavien-Dindo 3-4	Clavien-Dindo 5
² PD, n (%)	27 (37,0)	24 (32,8)	21 (28,7)	3 (1,3)
¹ DP, n (%)	78 (58,2)	41 (30,6)	15 (11,2)	0 (0)
Enucleation, n (%)	5 (83,3)	1 (16,7)	0 (0)	0 (0)
Total Pancreatectomy, n (%)	6 (50,0)	2 (16,7)	4 (33,3)	0 (0)

¹DP= Distal pancreatic resection, ²PD= Pancreaticodudenectomy, ³ 2 patients died after discharging from hospital

Table 4. Characteristics of resected PCN:s

Variable	MD- IPMN	MX- IPMN	BD- IPMN	MCN	SCN	SPN	EPIT	Other	All
N	50	30	14	40	41	8	22	20	225
Age years, median (range)	70.5 (44-87)	67.0 (40-81)	63.5 (53-72)	51.0 (27- 82)	64.0 (33- 79)	21.0 (14-47)	56 (24-75)	47.0 (24-75)	61.0 (14-87)
Sex Female %	50	56,6	42,9	100,0	82,9	87,5	27,3	40,0	63,6
N, %	50 (22,1)	30 (13,3)	14 (6,2)	40 (17,7)	41 (18,1)	8 (3,5)	22 (9,7)	20 (8,8)	225
Tumor size, median (range) mm	33 (3-120)	40 (10-95)	30 (10-50)	50 (2-180)	40 (8-120)	65 (13-130)	25 (6-80)	25 (12-100)	35 (2-180)
Location, n (%)									
1Head	19 (48,7)	10 (41,7)	7 (50)	4 (11,4)	9 (25,7)	2 (25,0)	4 (28,6)	3 (15,0)	58 (30,9)
2 Uncinatus	1 (2,6)	0 (0,0)	1 (7,1)	1 (2,9)	1 (2,95)	0 (0,0)	0 (0,0)	1 (5,0)	5 (2,7)
3 Body	6 (15,4)	7 (29,2)	3 (21,4)	10 (28,6)	7 (20,0)	3 (37,5)	4 (28,6)	3 (15)	43 (22,9)
4 Tail	13 (33,3)	7 (29,2)	3 (21,4)	20 (57,1)	18 (51,4)	3 (37,5)	6 (42,9)	13 (65)	82(43,6)
Operation, n (%)									
1 PD	25 (50)	14 (46,7)	8 (57,1)	6 (15)	10(24,4)	2 (25,0)	6 (27,3)	2 (10,0)	73(32,3)
2 DP	19 (38)	13(43,3)	3 (21,4)	33(82,5)	29(70,7)	68 (75,0)	16 (72,7)	15 (75,0)	134 (59,3)
3 Enucleation	0 (0,0)	1 (3,3)	0 (0,0)	1 (2,5)	1 (2,4)	0 (0,0)	0 (0,0)	3 (15,0)	6 (5,3)
4 total	6 (12)	2 (6,7)	3 (21,4)	0 (0)	1 (2,4)	0 (0,0)	0 (0,0)	0 (0,0)	12 (5,3)
Symptomatic, n (%)	38 (84,4)	21 (75,0)	6 (42,9)	27 (77,1)	23 (59)	6 (75)	13 (59,1)	12 (63,2)	146 (69,5)

Table 5a. Risk factors for malignancy in resected PCN:s

Variable	No carcinoma n=172	Carcinoma n=53	p-value
Age 60 years or more / age less than 60 years	65.6%/89.3%	34.4%/10.7%	<0.001
Tumor location ¹	65.1%/86.4%	34.9%/13.6%	<0.001
Symptomatic/asymptomatic	72.2%/89.4%	27.8%/10.6%	0.0030
Gender female/male	77.6%/74.4%	22.4%/25.6%	0.737
Diabetes	75.9%/76.0%	24.1%/24.0%	0.988
Cyst size 3cm or more	76.3%/88.9%	23.7%/11.1%	0.055

¹ 1: caput or uncinatus; 2: body or tail

Table 5b. Multivariate logistic regression analyze for risk of malignancy

Variable	p-value	Odds ratio	95% Confidence interval
Age over 60 years	0.003	3.486	1.523-7.984
Tumor location	0.016	2.624	1.193-5.772
Symptomatic	0.028	3.259	1.136-9.344

