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851 resected cystic tumors of the pancreas: A 33-year experience at the Massachusetts General Hospital

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Abstract

Background—The objective of this study was to identify trends in the diagnosis and treatment of cystic neoplasms of the pancreas using a retrospective review of patients from a surgical database at an academic referral center during a 33-year period.

Methods—Patient characteristics, including demographics, pathology, and survival, were analyzed over 5 time periods between 1978 and 2011.

Results—A total of 851 consecutive patients underwent resection for a cystic neoplasm of the pancreas during a 33-year period. Sixty-five percent of patients were female, and mean age was 60 years. The most common pathologic diagnoses were intraductal papillary mucinous neoplasm (38%), mucinous cystic neoplasm (23%), serous cystadenoma (16%), and cystic neuroendocrine neoplasm (7%). There was a stepwise increase in the number of resections across time periods (67 between 1978 and 1989; 376 between 2005 and 2011), with a parallel increase in the proportion of incidentally discovered lesions (22% to 50%). Diagnosis of intraductal papillary mucinous neoplasm was very uncommon in the first 2 time periods (before the first recognition of intraductal papillary mucinous neoplasm as a distinct entity) but predominated in the last 2 (41% and 49%), and cystic neuroendocrine neoplasms, which constituted 3% of the cystic neoplasms in the first time-period, now comprise more than 8% of pancreatic cystic neoplasms. The proportion of malignant neoplasms decreased over time (41% between 1978 and 1989; 12% between 2005 and 2011), reflecting probably the earlier diagnosis and treatment of premalignant neoplasms. Although operative mortality was minimal (4/849, 0.5%), the postoperative complication rate was 38%. Overall 5-year survival for all mucinous lesions was 87%.

Conclusion—Cystic neoplasms of the pancreas are being diagnosed and treated with increasing frequency. At present, most are incidentally discovered intraductal papillary mucinous neoplasms. (*Surgery* 2012;152:S4–12.)

After the seminal papers of Compagno and Oertel that distinguished mucinous from serous cystic neoplasms of the pancreas in the late 1970s,^{1,2} there was an increased interest and awareness of the differential diagnosis of all cystic lesions of the pancreas and of the malignant potential and curability of mucin-producing cysts. In 1990, Warshaw et al³ reported on what was then the largest single-institutional series on pancreatic cystic neoplasms, describing the clinical and pathologic characteristics of 67 cystic neoplasms.

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Since then, our understanding of pancreatic cystic neoplasms and their optimal diagnostic and therapeutic approach has improved considerably, and the number of cases identified incidentally by cross-sectional imaging has increased markedly.

The objective of this study was to update the published experience of a large academic center with resected pancreatic cystic lesions. Herein, we describe the clinicopathologic features, operative management, and short- and long-term outcomes of 851 patients who underwent an operation for a cystic neoplasm of the pancreas at the Massachusetts General Hospital during the last 33 years and examine trends in their diagnosis and treatment.

METHODS

Patients and data collection

A retrospective review of medical records was performed for all patients ($n = 851$) who underwent resection for a cystic neoplasm of the pancreas at the Massachusetts General Hospital between 1978 and 2011. Demographic information, diagnosis, dates of contact, and complications for a majority of these patients was derived from our prospective database. Subsequently, a retrospective review of electronic medical records, including physician notes, pathology reports, and discharge summaries, was made for the remaining patients. For all patients, we collected data regarding (1) incidental diagnosis, (2) presenting symptoms, (3) diagnostic tests, (4) tumor size, (5) sites of involvement, (6) surgical procedure performed, (7) margin status, (8) histologic diagnosis, (9) lymph nodes examined and positive, (10) duration of stay, and (11) complications. Patients were said to have an incidental diagnosis in the presence of vague abdominal symptoms or a complete absence of symptoms; for these patients, the reasons for the diagnostic test also were noted. Alternatively, asymptomatic increases of liver enzymes were interpreted as a symptomatic diagnosis. Symptoms such as abdominal pain, pancreatitis, jaundice, weight loss, malabsorption, nausea, vomiting, satiety, and the presence of a palpable abdominal mass were recorded. Cysts were labeled as malignant on the basis of (1) spread to lymph nodes or (2) the presence of micro- or macroscopic invasion.

Complications

Operative mortality was defined as death within 30 days after the operation or during the hospital stay. Patients were considered to have pancreatic fistula if there was presence of 30 mL or greater of amylase-rich fluid ($3 \times$ greater than a normal serum value) from surgical drains after the 7th postoperative day. Delayed gastric emptying was said to be present if the nasogastric tube was in place for more than 3 days, if it was reinserted after postoperative day 3 for persistent vomiting, or if the patient was unable to tolerate a solid diet after postoperative day 7. Other major complications noted were defined as described previously.⁴

Survival analysis

The MGH research patient data registry (RPDR) was queried for survival information on the patients that we had identified. The RPDR generated survival information on the basis of institutional follow-up dates and the Social Security Death Master Index. Using the *vital status* and *date of last follow-up* from RPDR, we calculated survival and updated the result to the core database. Statistical analyses were performed in SPSS version 15, Chicago, IL. Survival analysis was performed with the Kaplan-Meier method. Comparisons between Kaplan-Meier curves were made with the log-rank test.

Statistical analysis

Variables in the dataset were identified as either continuous or categorical. Continuous variables, such as tumor size, age at diagnosis, lymph nodes examined, and lymph nodes positive, were compared between 2 groups by use of the independent samples *t* test. When more than 2 groups were used for comparison, we used analysis of variance, and one-on-one group comparisons were made using the post hoc Tukey test. Categorical variables were compared using the Fisher exact test or χ^2 test as appropriate. The *year of diagnosis* variable was binned into 5 time periods, and the cut-points for these time periods were 1990, 1995, 2000, and 2005. Clinical and pathologic variables were compared and trended across these time periods. The alpha for all tests was set at 0.05, with $P < .05$ required for significance. This study was approved by the institutional review board of the Massachusetts General Hospital.

RESULTS

Demographic characteristics

Between 1978 and 2011, 851 patients underwent resection of a cystic neoplasm of the pancreas (Fig 1). Mucin-producing neoplasms, the most common, represented 62% of the patient population. By diagnosis, the most frequent was intraductal papillary mucinous neoplasm (IPMN), comprising 38% of the patients, followed by mucinous cystic neoplasm (MCN), 23%; serous cystadenoma (SCA), 16%; and cystic neuroendocrine neoplasms (CNEN), 7%. The various diagnoses were characterized by differences in age and sex of the patients affected, site of involvement within the pancreas, and tumor size (Table I). In mucin-producing neoplasms, patients with IPMN were older than those with MCN (mean age, 69 years vs 51 years, $P < .05$). Within the IPMNs, main-duct IPMN (MD-IPMN) affected male and female patients equally, whereas branch duct IPMN (BD-IPMN) had a predilection for female patients. With MCN, 84% were females. IPMNs were smaller compared with other cystic neoplasms with a diameter ($X \pm SD$) of 28.8 ± 16.6 mm for MD-IPMN, and 29.1 ± 17.1 mm for BD-IPMN, and both were significantly smaller than MCNs, which had a diameter of 44.1 ± 30.4 mm. IPMNs were far more likely to involve the head, uncinate process, and neck of pancreas, whereas MCNs were more likely to involve the body and tail.

More than two-thirds of patients with SCA were female, and the age at diagnosis was 61 years. These neoplasms were distributed equally across the pancreas with 53% involving the body and tail. SCA tumors were the largest in this series, with a diameter of 46.1 ± 32.5 mm. CNEN and solid pseudopapillary neoplasm (SPN) constituted 7.4% and 3.7% of the cases, respectively. SPNs were the youngest patient population with a mean age of 33 years (range, 14–60). Women comprised the majority of SPNs (88%), which involved primarily the body and tail (69%) of the pancreas. CNENs had no predilection for either sex, occurred at an age of 59 years, and 69% involved the body and tail of the pancreas.

Surgical procedures and complications

The surgical procedures performed included pancreatoduodenectomy, distal pancreatectomy performed either with or without splenic preservation, middle pancreatectomy, total pancreatectomy, and tumor enucleation. A small number of patients ($n = 22$; 2.5%) underwent a laparoscopic distal pancreatectomy (Table II). There were 4 postoperative deaths resulting in an operative mortality of 0.5%. Overall, roughly the same numbers of patients underwent pancreatoduodenectomy (368, 43.2%) and distal pancreatectomy (373, 43.8%); middle pancreatectomy was performed in 7.4% and 5.5% of patients underwent other procedures.

For patients who underwent a pancreatoduodenectomy, the most common indication was IPMN, whereas distal pancreatectomy was indicated most commonly for MCN and SCA (Table II). Those patients who underwent a middle pancreatectomy had smallest neoplasms; the most common diagnoses were SCA and BD-IPMN. Total pancreatectomy was indicated primarily for multicentric IPMN. On final histology, 37% of the neoplasms after a total pancreatectomy and 23.5% after a pancreatoduodenectomy were malignant; 8.8% of all distal pancreatectomies and 4 cysts (6.3%) after a middle pancreatectomy were malignant. Of the latter 4 cysts, 3 were BD-IPMNs (one of which was associated with a retention cyst), and the fourth was a MD-IPMN.

Between 30% and 50% of patients experienced postoperative complications depending on the type of surgical procedure performed. Middle pancreatectomy was associated with the greatest complication rate (49.2%). Among these complications, pancreatic fistula was seen in 35.5%. In comparison, the pancreatic fistula rate for other procedures was significantly less. Distal pancreatectomies and pancreatoduodenectomies had fistula rates of 18.2% ($P_{\text{middle versus distal}} = .002$) and 12.5% ($P_{\text{middle versus whipple}} < .001$), respectively.

Approximately 12% of the patients experienced other major complications regardless of the type of operation performed, including abdominal fluid collections, wound infection, pneumonia, acute renal failure, and gastrointestinal bleeding. The median duration of hospital stay was 8.5 days after a pancreatoduodenectomy and 8 days after total pancreatectomy, whereas median stay was 6 days for both middle and distal pancreatectomy. As shown in Fig 2, the duration of stay for each type of surgical procedure decreased significantly over the time of the study.

Change in spectrum of cystic neoplasms

There was a significant and step-wise increase in the number of patients who underwent pancreatic resection for a cystic neoplasm (Table III). The number of patients operated in the first time period (1978–1989) was 67; this number increased to 376 patients after 2005. There was a 2-fold increase in incidentally diagnosed cystic neoplasms during the last 3 time periods, and currently, nearly one-half of resected cystic neoplasms are diagnosed this way. Within the subset of symptomatic patients, the presenting complaints did not change across the time periods.

The diagnostic workup of cystic neoplasms usually included an abdominal computed tomography (CT, 95%). Among the asymptomatic patients, the most common indications for a CT were hematuria or symptoms suggestive of renal stones, diverticular disease, suspected gallstone disease, or workup for another malignancy. Other tests were also used such as magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRI/magnetic resonance cholangiopancreatography), endoscopic ultrasonography/fine-needle aspiration (EUS/FNA), and endoscopic retrograde cholangiopancreatography (ERCP). Over time, the use of noninvasive diagnostic modalities increased, whereas invasive techniques such as ERCP were used less frequently. MRI/magnetic resonance cholangiopancreatography showed a steady increase in use from 1.7% between 1990 and 1994 to 30.6% of the patients after 2005. Before 1989, ERCP was used routinely in the diagnostic workup and was used in 59% of the patients; however, it was used only in 12% of the patient population after 2005. In addition, there was a marked increase in the proportion of patients who underwent EUS, from 6.8% in 1990 to 1994 to 55.3% in the present time. In the last time period, cytologic examination was used as part of the diagnostic workup in 35.9% of patients, whereas it had been used only in 8.9% of the patients before 1989.

There was also a marked shift in the pathologic diagnoses of tumors seen over time. MCN and SCA represented the dominant pancreatic cystic neoplasm between 1978 and 1989, whereas recently IPMN is the most common type resected. Among the pathologic

diagnoses, MCNs comprised 63% of the resections in the first time period, decreasing to 16% of the resections period; a similar trend occur with SCA, from 27% to 12%. Conversely IPMN, which was an exceptional diagnosis before 1990 (only 3% of the patients), is now the most common diagnosis, accounting for nearly one-half of the resected cystic neoplasms in the last 5 years. There has also been a steady increase in the proportion of CNENs resected from 3% in the 1980s to 9% between 2005 and 2011. There has been a downward trend in the proportion of patients that were found to harbor malignant cystic neoplasms, likely a reflection of earlier diagnosis and treatment. Malignant neoplasms comprised 41% of cystic neoplasms in the first time period but only 11.7% in the last.

Survival analysis

The median follow-up time for all patients was 62 months (range, 1–242). The overall 5- and 10-year survivals (Fig 3) were worse for MD-IPMN (83%, 78%) and BD-IPMN (88%, 80%) when compared with SPN (100%, 100%) and SCA (97%, 90%). The worst survival was that of the few patients with typical ductal adenocarcinoma with cystic changes mimicking a primary pancreatic cystic neoplasm (median survival, 6 months, 5-year survival, 0%). The survival analysis showed that there was no significant difference between patients who were *diagnosed incidentally* and those who were *symptomatic* (data not shown).

DISCUSSION

This series, which to our knowledge represents the largest single-institution cohort of resected cystic neoplasms of the pancreas, shows that during the last 3 decades, the landscape of these lesions has changed. Cystic pancreatic neoplasms are now being diagnosed in far greater numbers compared with earlier time-periods, and the majority of the diagnoses are made incidentally at the time of evaluation for unrelated symptoms. This trend has been associated with a marked decrease in patients found to have invasive cancer. Diagnoses like IPMN and CNEN were very rare 20 years ago but are seen in greater numbers more recently. The approach and management of patients with pancreatic cysts has also changed over time, with an increase in the use of MRI, EUS, and FNA as seen in our results, and a parallel decrease in the use of ERCP. Operative resection was associated with very low operative mortality (0.5%) but the complication rate remained high. For patients with cystic neoplasms of the pancreas, long-term survival after resection is usually the case; >85% of patients were alive 5 years after resection.

Review of other published series^{5–11} of resected cystic neoplasms of the pancreas indicates that large, academic referral centers have similar experiences with regard to patient presentation, management, and postoperative outcomes. Gaujoux et al¹¹ published recently an updated experience with pancreatic cystic neoplasms at the Memorial Sloan-Kettering Cancer Center. They showed that during a 15-year period, the use of MRI and EUS/FNA increased markedly and that there was a concomitant decrease in the percentage of patients who presented with symptoms. In addition, among the 422 pancreatic resections for cystic neoplasms in their report, operative mortality was low (0.7%) but morbidity (grade III) was still 36%. These results echo our 20-year trend.

When compared with series that included fewer patients, we observed small differences with respect to the relative proportions of different pathologic diagnoses. In a study that included 125 resections from the Cleveland Clinic, Walsh et al¹² noted that IPMN and MCN constituted 21% and 36% of their patient populations, respectively whereas in the series by Spinelli et al,¹³ only 22% of the patients were diagnosed with an IPMN. By contrast, IPMN was the diagnosis in almost 40% of our series and constituted nearly one-half of the resections in the last 5-year time period. A lesser prevalence of IPMN has also been reported

in other series outside of the United States. In a study that comprised patients at the Singapore General Hospital, Goh et al⁷ examined 220 resected cystic neoplasms, of which 21% were IPMN, 14% were MCN, 21% were SCA, and 4% were CNEN. Comparable with data from our study, approximately 40% of the patients were diagnosed incidentally, and postoperative mortality and morbidity were low. All these studies confirm that at large academic centers, the diagnoses of pancreatic cystic neoplasms are being made incidentally in increasing numbers, undoubtedly the result of our advanced techniques of cross-sectional imaging.

One of the more interesting findings of our study is the notable increase in the relative proportion of IPMN during the last 3 decades. IPMN accounted for 2% of cases before 1991, whereas they are currently the diagnosis in 49% of patients with a resected cystic neoplasm. There has been considerable debate over the perceived increase in the incidence of IPMN and whether this represents a true increase in incidence as the result of unknown environmental factors or whether the increased rate of detection is simply a reflection of larger numbers of incidentally discovered neoplasms attributed to better imaging and different pathologic classification of mucin-producing neoplasms.

Some authors have performed a review of archived histologic slides in an attempt to reclassify and correctly identify IPMNs. In a study of resected IPMN, Niedergethmann et al⁵ reevaluated pathology slides from previous reports, and among 207 cases, they reclassified 54 as IPMN that were diagnosed incorrectly in the original pathology report. These cases represented a more than 125% increase because there were only 43 patients who had been diagnosed primarily as IPMN among the original cases. Their results also showed that patients were more likely to be diagnosed incorrectly in the earlier time-period (1996–2001) of their study.

Supportive of the aforementioned results is a study from the Mayo Clinic by Tollefson et al.¹⁴ In this study, pathology reports for all patients diagnosed with unusual variants of pancreatic cancer between 1960 and 1980 were reevaluated and, histologic slides re-reviewed in those cases where the descriptors “mucinous”, “cystic” or “papillary” were present in the report. Among the 84 cases that were re-reviewed, 21 cases of IPMN were diagnosed incorrectly initially, indicating that IPMNs *did* exist before the first report of IPMN by Ohashi and Murakami¹⁵ in 1982. The authors concluded that these neoplasms have been confused with unusual forms of chronic pancreatitis or adenocarcinoma of the pancreas. Although an increase in incidental detection of IPMN certainly plays a role in the greater proportion of this diagnosis amongst resected cystic neoplasms in our series, analysis of our results also supports the notion that improved pathologic classification is an important factor, because overall, the percentage contribution of mucinous neoplasms (IPMN, MCN) has remained stable between 50% and 70% throughout the time periods.

In the 1991 report by Warshaw et al,³ 62% of the patients were classified as MCN, whereas this diagnosis currently comprises only 16%. We believe it is quite likely that many (perhaps even the majority) of those MCNs would currently be classified as IPMNs, because many were in elderly or male patients or the tumor located in the head of the pancreas. Compliance with the currently accepted pathologic criteria that require the presence of ovarian-like stroma to diagnose an MCN indicate that >95% of cases occur in women with a mean age of 53 years and are located in the body and tail of the pancreas.¹⁶ A definitive answer to the question of erroneous classification of MCN and IPMN before 1991 would require comprehensive pathologic review of the archival material that unfortunately is incomplete.

Another change over time has been the 3-fold increase in pancreatic CNENs. Currently, 1 of every 12 resected pancreatic cystic neoplasms is a CNEN, and most of these are either incidentally discovered or detected because of surveillance of patients with MEN-1. We have described previously that MEN-1 was three and half times more likely to be present in a patient with a pancreatic CNEN relative to a solid neuroendocrine neoplasm.¹⁷ Of the 62 CNENs in this series, 84% were nonfunctional and 12% were part of the MEN-1 complex reflecting our referral practice.

Our data indicate that between 46% and 50% of patients who underwent resection for a cystic neoplasm of the pancreas in the time-periods of 2000 to 2004, and 2005 to 2010 were incidentally diagnosed. This trend represents a 20% increase relative to the prior time period (1995–1999) and is related likely to the increased availability and use of both CT and MRI.^{18,19} This trend is opposite to the prevalence of malignancy in the resected specimens, which has been 12% since 2000, but was 28% between 1995 and 1999. Because we are resecting many more pancreatic cystic lesions, it could be argued that we are perhaps doing unnecessary resections in many patients. This question cannot be answered with the data we have, although it is clear that we are operating only on a small fraction of all the newly discovered asymptomatic pancreatic cysts.

Recent studies have shown that up to 13.5% of patients with no pancreatic history will have a pancreatic cystic area recognized by MRI²⁰ and 2.6% by CT.²¹ Most of these “cysts” are thought to represent BD–IPMN, and current guidelines²² recommend resection for only a minority of them (lesions >3 cm, or for smaller ones that have mural nodules, symptoms, or concomitant dilation of the pancreatic duct). Although it is true that the majority of cystic neoplasms that meet criteria for resection are not malignant, it is important to underscore that the goal is not only to remove lesions that have invasive cancer but also those with high-grade, and perhaps moderate, dysplasia. Of the 326 IPMNs of this series, 23% had invasive cancer, 15% had high-grade dysplasia (formerly carcinoma in situ), 21% had moderate dysplasia (formerly borderline neoplasms), and only 41% were adenomas with low-grade dysplasia. Ideally, we would like to remove all lesions *before* they become invasive cancer and at the same time spare resection for lesions that have no or very little risk of progressing to moderate or high-grade dysplasia.

Multiple efforts in cyst imaging and analysis of the cystic fluid are underway to try to refine this differential diagnosis.^{23–25} Our data show that the overall 5-year survival after resection is 87% for all cystic lesions and 62% for those with malignancy. Furthermore, these operations, although still fraught with complications in approximately one-third of patients, have an operative mortality of less than 1%. In the future, studies addressing the risk/benefit of resection of incidentally discovered pancreatic cysts need to address not only the risk of malignancy or dysplasia in the lesions and the risk of dying or having a serious complication from the operation, but also long term sequelae from the resection including, the development of diabetes and pancreatic exocrine insufficiency, as well as effects on quality of life.

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References

1. Compagno J, Oertel JE. Microcystic adenomas of the pancreas (glycogen-rich cystadenomas): a clinicopathologic study of 34 cases. *Am J Clin Pathol*. 1978; 69:289–98. [PubMed: 637043]

2. Compagno J, Oertel JE. Mucinous cystic neoplasms of the pancreas with overt and latent malignancy (cystadenocarcinoma and cystadenoma). A clinicopathologic study of 41 cases. *Am J Clin Pathol.* 1978; 69:573–80. [PubMed: 665578]
3. Warshaw A, Compton C, Lewandrowski K, Cardenosa G, Mueller P. Cystic tumors of the pancreas. New clinical, radiologic, and pathologic observations in 67 patients. *Ann Surg.* 1990; 212:432–43. [PubMed: 2171441]
4. Balcom JH, Rattner DW, Warshaw AL, Chang Y, Fernandez-del Castillo C. Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. *Arch Surg.* 2001; 136:391–8. [PubMed: 11296108]
5. Niedergethmann M, Grützmann R, Hildenbrand R, Dittert D, Aramin N, Franz M, et al. Outcome of invasive and non-invasive intraductal papillary-mucinous neoplasms of the pancreas (IPMN): a 10-year experience. *World J Surg.* 2008; 32:2253–60. [PubMed: 18668283]
6. Schnelldorfer T, Sarr MG, Nagorney DM, Zhang L, Smyrk TC, Qin R, et al. Experience with 208 resections for intra-ductal papillary mucinous neoplasm of the pancreas. *Arch Surg.* 2008; 143:639–46. [PubMed: 18645105]
7. Goh BKP, Tan Y-M, Thng C-H, Cheow P-C, Chung Y-FA, Chow PKH, et al. How useful are clinical, biochemical, and cross-sectional imaging features in predicting potentially malignant or malignant cystic lesions of the pancreas? Results from a single institution experience with 220 surgically treated patients. *J Am Coll Surg.* 2008; 206:17–27. [PubMed: 18155564]
8. Galanis C, Zamani A, Cameron JL, Campbell KA, Lillemoe KD, Caparelli D, et al. Resected serous cystic neoplasms of the pancreas: a review of 158 patients with recommendations for treatment. *J Gastrointest Surg.* 2007; 11:820–6. [PubMed: 17440789]
9. Allen PJ, D'Angelica M, Gonen M, Jaques DP, Coit DG, Jar-nagin WR, et al. A selective approach to the resection of cystic lesions of the pancreas: results from 539 consecutive patients. *Ann Surg.* 2006; 244:572–82. [PubMed: 16998366]
10. Ferrone CR, Konstantinidis IT, Sahani DV, Wargo JA, Fernandez-del Castillo C, Warshaw AL. Twenty-three years of the Warshaw operation for distal pancreatectomy with preservation of the spleen. *Ann Surg.* 2011; 253:1136–9. [PubMed: 21394008]
11. 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; 212:590–600. [PubMed: 21463795]
12. Walsh RM, Vogt DP, Henderson JM, Hirose K, Mason T, Bencsath K, et al. Management of suspected pancreatic cystic neoplasms based on cyst size. *Surgery.* 2008; 144:677–84. [PubMed: 18847654]
13. Spinelli KS, Fromwiller TE, Daniel RA, Kiely JM, Nakeeb A, Komorowski RA, et al. Cystic pancreatic neoplasms: observe or operate. *Ann Surg.* 2004; 239:651–7. [PubMed: 15082969]
14. Tollefson MK, Libsch KD, Sarr MG, Chari ST, DiMaggio EP, Urrutia R, et al. Intraductal papillary mucinous neoplasm: did it exist prior to 1980? *Pancreas.* 2003; 26:e55–8. [PubMed: 12657965]
15. Ohashi K, Murakami Y. Four cases of “mucin-producing” cancer of the pancreas (Japanese). *Prog Digest Endosc.* 1982; 20:348–51.
16. Sakorafas GH, Sarr MG. Cystic neoplasms of the pancreas; what a clinician should know. *Cancer Treat Rev.* 2005; 31:507–35. [PubMed: 16257126]
17. Bordeianou L, Vagefi PA, Sahani D, Deshpande V, Rakhlin E, Warshaw AL, et al. Cystic pancreatic endocrine neoplasms: a distinct tumor type? *J Am Coll Surg.* 2008; 206:1154–8. [PubMed: 18501813]
18. Megibow AJ, Baker ME, Gore RM, Taylor A. The incidental pancreatic cyst. *Radiol Clin North Am.* 2011; 49:349–59. [PubMed: 21333781]
19. Parra-Herran CE, Garcia MT, Herrera L, Bejarano PA. Cystic lesions of the pancreas: clinical and pathologic review of cases in a five year period. *JOP.* 2010; 11:358–64. [PubMed: 20601810]
20. Lee KS, Sekhar A, Rofsky NM, Pedrosa I. Prevalence of incidental pancreatic cysts in the adult population on MR imaging. *Am J Gastroenterol.* 2010; 105:2079–84. [PubMed: 20354507]
21. 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; 191:802–7. [PubMed: 18716113]

22. Tanaka M, Chari S, Adsay V, Fernandez-del Castillo C, Fal-coni M, Shimizu M, et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. *Pancreatology*. 2006; 6:17–32. [PubMed: 16327281]
23. Shen J, Brugge WR, Dimaio CJ, Pitman MB. Molecular analysis of pancreatic cyst fluid: a comparative analysis with current practice of diagnosis. *Cancer*. 2009; 117:217–27. [PubMed: 19415731]
24. Ryu JK, Matthaei H, Dal Molin M, Hong S-M, Canto MI, Schulick RD, et al. Elevated microRNA miR-21 levels in pancreatic cyst fluid are predictive of mucinous precursor lesions of ductal adenocarcinoma. *Pancreatology*. 2011; 11:343–50. [PubMed: 21757972]
25. Bhutani MS, Gupta V, Guha S, Gheonea DI, Saftoiu A. Pancreatic cyst fluid analysis---a review. *J Gastrointest Liver Dis*. 2011; 20:175–80.

Fig 1. Distribution of pathologic diagnoses in 851 resected cystic neoplasms of the pancreas. Lesions classified as “other” included pseudocysts, 25; benign epithelial cysts, 11; acinar cell cystadenomas and cystad-enocarcinomas, 3; lymphoepithelial cysts, 5; choledochal cysts, 4; lymphangiomas, 4; hemangiomas, 2; and other unclassified epithelial cysts.

Fig 2.
Changing trends in the duration of stay by the type of operative procedure.

Fig 3.
Kaplan-Meier survival curve for overall survival by pathologic diagnoses.

Table I

Clinical and pathologic variables for cysts

	SCA	SPN	MCN	MD-IPMN	BD-IPMN	CNEN
<i>n</i>	137	29	199	180	146	62
Age (95% confidence interval)	61 (59–63)	33 (28–35)	51 (48–54)	69 (67–72)	68 (65–69)	54 (49–57)
Sex (female, %)	68	88	84	50	57	47
Site involved, <i>n</i> , %						
Head, uncinate, neck	58, 42.3%	9, 31%	52, 26.1%	129, 71.7%	86, 58.9%	14, 22.6%
Body or tail	73, 53.3%	20, 69%	134, 67.3%	55, 30.6%	54, 37.0%	43, 69.4%
Mean size $\pm$ SD, mm	46.1 $\pm$ 32.5	40.6 $\pm$ 30.1	44.1 $\pm$ 30.4	28.8 $\pm$ 16.6	29.1 $\pm$ 17.1	37.6 $\pm$ 30.2
Surgical procedures, <i>n</i> , %						
Pancreatoduodenectomy	48, 35%	8, 27.6%	49, 24.6%	132, 73.3%	81, 55.5%	13, 21.0%
Middle pancreatectomy	21, 15.3%	6, 20.7%	7, 3.5%	3, 1.7%	19, 13.0%	2, 3.2%
Distal pancreatectomy	66, 48.2%	15, 51.7%	127, 63.8%	30, 16.7%	43, 29.5%	44, 71.0%
Other	2, 1.5%	0	16, 8%	15, 8.3%	3, 8.3%	3, 4.8%
Malignant, %	0	0	10.3%	33.7%	13.7%	10.7%
Overall survival						
3-year survival (%)	97%	100%	94%	83%	88%	98%
5-year survival (%)	90%	100%	90%	78%	80%	98%

BD-IPMN, Branch duct intraductal papillary mucinous neoplasm; *CNEN*, cystic neuroendocrine neoplasm; *MCN*, mucinous cystic neoplasm; *MD-IPMN*, main-duct intraductal papillary mucinous neoplasm; *SCA*, serous cystadenoma; *SPN*, solid pseudopapillary neoplasm.

Table II

Resections and complications

	Pancreatoduodenectomy	Middle pancreatectomy	Distal pancreatectomy	Other
Frequency, <i>n</i> (%)	368 (43.2%)	63 (7.4%)	373 (43.8%)	47 (5.5%)
Mean tumor diameter, mm	32.5	28.8	41.2	47.7
Operative mortality, <i>n</i>	2	0	1	1
SPN	8, 2.2%	6, 9.5%	15, 4.0%	0%
PDAC	4, 1.1%	0%	2, 0.5%	1, 2.1%
MD-IPMN	132, 35.9%	3, 4.8%	30, 8.0%	15, 31.9%
BD-IPMN	81, 22.0%	19, 30.2%	43, 11.5%	3, 6.4%
MCN	49, 13.3%	7, 11.1%	127, 34.0%	16, 34%
SCA	48, 13.0%	21, 33.3%	66, 17.7%	2, 4.3%
CNEN	13, 3.5%	2, 3.2%	44, 11.8%	3, 6.4%
Other	33, 9.0%	5, 7.9%	46, 12.3%	7, 14.9%
Complications, %	40%	49.2%	36.4%	32.4%
Pancreatic fistula	12.5%	35.5%	18.2%	8.8%
Delayed gastric emptying	6.5%	0%	0.3%	0%
Other major complication	12.9%	12.7%	12.6%	11.8%
Final histology, % malignant	23.4%	6.3%	8.8%	42.6%
Median duration of stay	8 days	6 days	6 days	8 days

BD-IPMN, Branch duct intraductal papillary mucinous neoplasm; *CNEN*, cystic neuroendocrine neoplasm; *MCN*, mucinous cystic neoplasm; *MD-IPMN*, main-duct intraductal papillary mucinous neoplasm; *PDAC*, pancreatic ductal adenocarcinoma; *SCA*, serous cystadenoma; *SPN*, solid pseudopapillary neoplasm.

Table III

Trends in cystic neoplasms during a 33-year time period

Factor	1978–1989	1990–1994	1995–1999	2000–2004	2005 to present
<i>n</i>	67	58	120	230	376
Incidental diagnosis, %	22	6.8	28.3	45.7	49.7
Abdominal pain, %	—	35.6	50.8	37.4	36.5
Jaundice, %	10.4	11.9	10.8	6.5	5.3
Weight loss, %	—	8.5	25.8	12.6	10.4
Pancreatitis, %	—	16.9	20	7.8	14.9
Diagnostic tests, %					
MR	0	1.7	4.2	18.3	30.6
ERCP	59	25.4	35.8	17.4	12
EUS	0	6.8	28.3	47.4	55.3
Cytology	8.9	15.3	17.5	35.2	35.9
Pathological diagnoses, n, %					
SPN	0%	0%	4, 3.3%	7, 3.0%	18, 4.8%
PDAC	0%	0%	0%	3, 1.3%	4, 1.1%
MD–IPMN	2, 3.0%	5, 8.6%	30, 25.0%	43, 18.7%	100, 26.6%
BD–IPMN	0%	0%	10, 8.3%	52, 22.6%	84, 22.3%
MCN	42, 62.7%	15, 25.9%	34, 28.3%	48, 20.9%	60, 16.0%
SCA	18, 26.9%	17, 29.3%	24, 20.0%	34, 14.8%	44, 11.7%
CNEN	2, 3.0%	1, 1.7%	7, 5.8%	20, 8.7%	32, 8.5%
Other	3, 4.4%	20, 34.5%	11, 9.2%	23, 10%	34, 9.0%
Malignant, %	41	15.5	27.5	12.2	11.7
Procedures performed, n, %					
Pancreatoduodenectomy	29, 43.3%	24, 41.4%	54, 45.0%	113, 49.1%	148, 39.4%
Middle pancreatectomy	0%	3, 5.1%	8, 6.7%	18, 7.8%	34, 9.0%
Distal pancreatectomy	25, 37.3%	26, 44.9%	52, 43.3%	86, 37.4%	184, 48.9%
Other	13, 19.4%	5, 8.6%	6, 5.0%	13, 5.7%	10, 2.7%

BD–IPMN, Branch duct intraductal papillary mucinous neoplasm; *CNEN*, cystic neuroendocrine neoplasm; *ERCP*, endoscopic retrograde cholangiopancreatography; *EUS*, endoscopic ultrasound; *MCN*, mucinous cystic neoplasm; *MD–IPMN*, main-duct intraductal papillary mucinous neoplasm; *MR*, magnetic resonance; *PDAC*, pancreatic ductal adenocarcinoma; *SCA*, serous cystadenoma; *SPN*, solid pseudopapillary neoplasm.