

Pancreatic Cystic Neoplasms: Predictors of Malignant Behavior and Management

Ehab Atef, Ayman El Nakeeb, Ehab El Hanafy, Mohamed El Hemaly, Emad Hamdy, Ahmed El-Geidie

Gastroenterology Surgical Center, Mansoura University, Egypt

Address for correspondence:
Prof. Ayman El Nakeeb,
Gastroenterology Surgical Center, Mansoura University, Egypt.
E-mail: elnakeebayman@yahoo.com

ABSTRACT

Background/Aim: Pancreatic cystic neoplasms are being increasingly identified with the widespread use of advanced imaging techniques. In the absence of a good radiologic or pathologic test to preoperatively determine the diagnosis, clinical characteristics might be helpful. The objectives of this analysis were to define the incidence and predictors of malignancy in pancreatic cysts. **Patients and Methods:** Patients with true pancreatic cysts who were treated at our institution were included. Patients with documented pseudocysts were excluded. Demographic data, clinical manifestations, radiological, surgical, and pathological records of those patients were reviewed. **Results:** Eighty-one patients had true pancreatic cyst. The mean age was 47 ± 15.5 years. There were 28.4% serous cystadenoma, 21% mucinous cystadenoma, 6.2% intraductal papillary tumors, 8.6% solid pseudopapillary tumors, 1.2% neuroendocrinal tumor, 3.7% ductal adenocarcinoma, and 30.9% mucinous cystadenocarcinoma. Malignancy was significantly associated with men ($P = 0.04$), older age (0.0001), cysts larger than 3 cm in diameter ($P = 0.001$), presence of solid component ($P = 0.0001$), and cyst wall thickening ($P = 0.0001$). The majority of patients with malignancy were symptomatic (26/28, 92.9%). The symptoms that correlated with malignancy included abdominal pain ($P = 0.04$) and weight loss ($P = 0.0001$). Surgical procedures were based on the location and extension of the lesion. **Conclusion:** The most common pancreatic cysts were serous and mucinous cysts. These tumors were more common in females. Old age, male gender, large tumor, presence of solid component, wall thickness, and presence of symptoms may predict malignancy in the cyst.

Key Words: Cystadenocarcinoma, cystadenoma, enucleation, pancreatic cyst, pseudocyst

Received: 09.05.2012, Accepted: 08.07.2012

How to cite this article: Atef E, El Nakeeb A, El Hanafy E, El Hemaly M, Hamdy E, El-Geidie A. Pancreatic Cystic neoplasms: Predictors of malignant behavior and management. Saudi J Gastroenterol 2013;19:45-53.

True pancreatic cystic lesions account for only 10 to 15% of all pancreatic cystic lesions and less than 1% of pancreatic tumors.^[1-3] Pancreatic cystic lesions are being increasingly identified with the widespread use of advanced radiological techniques.^[4] The incidence of pancreatic cysts (PC) has been estimated to be between 1% and 2% in patients who had a computed tomography (CT)/magnetic resonance (MRI) imaging performed.^[5,6]

Pancreatic cystic neoplasms (PCN) comprise a different

group of histopathologic entities. True pancreatic cystic tumors fall into one of the following types; serous tumors (including serous cystadenoma (SCA) and cystadenocarcinoma), mucinous tumors (including mucinous cystadenomas (MCN), mucinous cystadenocarcinomas, intraductal papillary adenomas, and intraductal papillary adenocarcinoma) and solid pseudopapillary tumors (SPT).^[2,3,7] The majority of cystic tumors of the pancreas are slow-growing and asymptomatic. When symptoms do occur, they are usually secondary to a mass effect and tend to be vague and poorly localized in nature.^[4,6,7]

Several studies reported that no imaging modalities are sufficiently accurate to differentiate among the benign, premalignant, and malignant lesions that are visualized by ultrasound (US), CT, or MRI scans.^[8-10] Percutaneous or endoscopic aspiration has the potential to spill malignant cells with the possibility of reducing survival. For this reason,

Access this article online	
Quick Response Code: 	Website: www.saudijgastro.com
	DOI: 10.4103/1319-3767.105927

it is not routinely recommended to use these invasive and expensive diagnostic modalities. In the absence of a good radiologic or pathologic test to preoperatively determine the diagnosis, clinical characteristics such as age, gender, the presence of symptoms, cyst size, or location might be helpful.^[6,8,10]

The ideal management of PCN remains controversial for a number of reasons including the difficulty in achieving an accurate preoperative diagnosis, the increasing detection of incidental lesions, the wide variability in malignant potential, and the poorly understood natural history of these lesions.^[10-12]

The aim of this study was to show the incidence and predictors of malignancy in true PC, and also to determine patients who can safely be observed and followed up and those who should undergo resection.

PATIENTS AND METHODS

A retrospective study was carried out including all patients who underwent surgery for PCN in the period between April 2001 and February 2012 at the Gastroenterology Surgical Center, Mansoura University, Egypt. The Institutional Review Board granted approval for the protocol. Patients with documented pseudocysts were excluded. Demographic data, clinical manifestations, radiological, surgical, and pathological records were reviewed for these patients. The hospital medical records were searched to determine the patient's age, gender, presenting symptoms, and any history of pancreatitis, or diabetes mellitus. These data were collected manually from our hospital medical records by all authors.

Clinical presentation included abdominal pain, vomiting,

jaundice, loss of weight, or abdominal mass; however, some cases were asymptomatic. Routine blood investigations were performed including hepatic and renal function tests. Cardiopulmonary assessments were done for all patients. Serum amylase and tumor markers (CEA and CA19-9) were done in some patients preoperatively. Magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) were done for patients presenting with obstructive jaundice to relieve the obstruction preoperatively. However, we did not do routine pancreatic duct cannulation and pancreaticogram for those patients for fear of inducing pancreatitis [Figure 1].

The morphology of the PC was recorded from the CT finding and the procedure report. CT was performed for all patients to show size of the cyst, site, loculations, calcification, central scar, wall thickness, and solid component. For oval-shaped cysts, the largest diameter was used [Figures 2-4]. Cyst fluid was collected by intraoperative needle aspiration or, when complete resection was planned, by needle aspiration immediately after surgical removal of the cyst. It was assessed for its viscosity and nature (serous, mucous, hemorrhagic, or hemorrhagic and necrotic).

Surgical treatment depends on the location and extension of the cyst. Distal pancreatectomy was performed for cyst located in the body. Small lesions of the body and neck of the pancreas were treated by median pancreatectomy or enucleation, with closing of proximal pancreatic segment and drainage of the distal segment with a Roux en Y pancreaticojejunostomy [Figure 5]. Tumors of the head and/or uncinate process were treated by pancreatoduodenectomy (PD), with or without pylorus preservation, with pancreaticogastrostomy (PG) or pancreaticojejunostomy (PJ) based on surgeon's preference. Advanced tumors underwent bypass if obstructing the

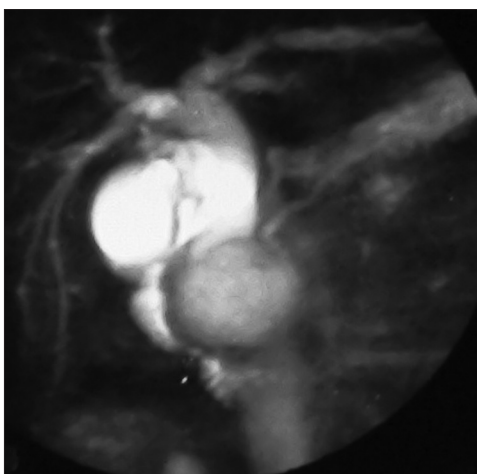


Figure 1: MRCP for pancreatic cystic lesion in the head of pancreas in a female patient aged 15 years; histopathology revealed solid pseudopapillary tumor



Figure 2: Pancreatic cystic lesion in the head of pancreas in a female patient aged 24 years; histopathology revealed mucinous cystadenoma

common bile duct and/or stomach. In the enucleation group, intraoperative US imaging was used routinely to assess the relationship between the pancreatic duct and the cystic lesion. In addition, the pancreatic defect after enucleation was closed. Frozen section of the surgical margins had an important role in the intraoperative management of cysts in some patients to determine free safety margin. Closure was usually performed with 3-0 absorbable sutures, taking care not to injure the pancreatic duct. Sandostatin was given for all patients postoperatively. Operative time, morbidity, and hospital stay were collected from medical records. Follow-up data including recurrence, morbidity, and survival information were collected.

All pathologic specimens were reviewed and tumors were classified as benign (including SCA, SPT, MCN, intraductal papillary mucinous neoplasm (IPMN), and cystic neuroendocrine tumors) and malignant as cystadenocarcinoma, and ductal adenocarcinoma with degeneration.^[2,3,6]

Statistical analysis of the data in this study was performed

using SPSS software, version 17 (Chicago, IL). For continuous variables, descriptive statistics were calculated and were reported as mean \pm standard deviation (SD) or as median with range. Categorical variables were described using frequency distributions. Independent sample *t*-test was used to detect differences in the means of continuous variables and Chi-square test was used in cases with low expected frequencies. One-way ANOVA test was used to detect differences between three groups. *P* values $<$ 0.05 were considered significant.

RESULTS

Eighty-one patients (34 men) with median age 45 years (range, 15-72 years), had undergone surgery for cystic pancreatic neoplasms at the Gastroenterology Surgical Center, Mansoura University, Egypt, in the period between April 2001 and February 2012. Of the 81 patients, 53 patients had benign cysts and 28 patients had malignant cysts (25 mucinous cystadenocarcinoma and three ductal adenocarcinomas) based on pathological results [Table 1].



Figure 3: Pancreatic cystic lesion in the body of pancreas in a female patient aged 35 years; histopathology revealed serous cystadenoma (mid-pancreatectomy)

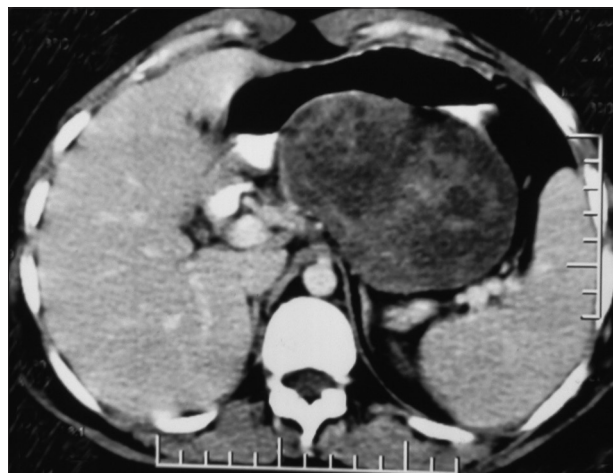


Figure 4: Pancreatic cystic lesion in the tail of pancreas in a male patient aged 52 years with solid areas inside; histopathology revealed mucinous cystadenocarcinoma

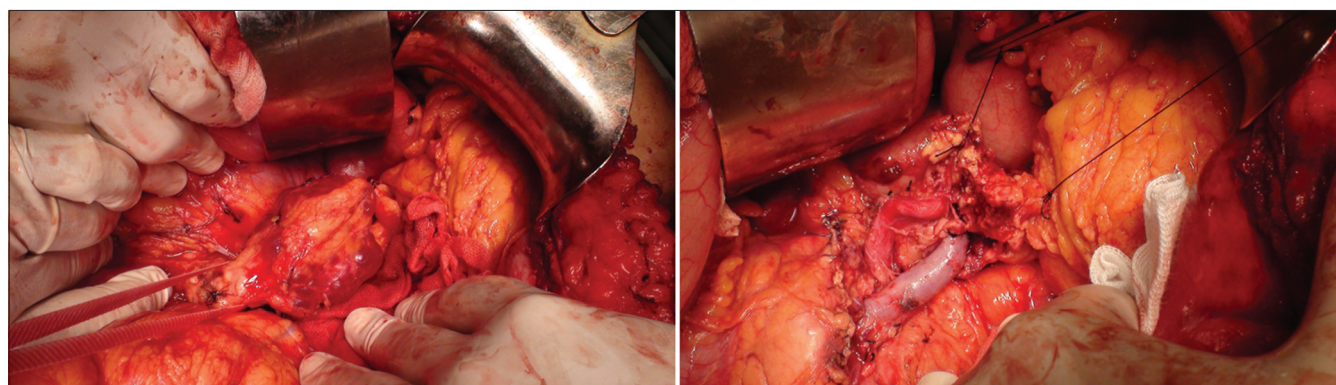


Figure 5: Mid-pancreatectomy for serous cystadenoma in mid body of pancreas in a female patient aged 49 years

Clinical manifestations varied according to the size and location of the cyst. Sixty patients had one or more symptoms including abdominal pain, jaundice, weight loss, nausea, vomiting, and mass. However, 21 (25.9%) patients were asymptomatic as seen in Table 1. Abdominal pain on presentation was recorded more often in malignant group (16/28; 57.12%) than in benign group (18/53; 34%); $P = 0.04$. Weight loss occurred more often in the malignant group (18/28, 64.3%) than in benign group (13/53, 24.5%); $P = 0.0001$. Nausea, vomiting, jaundice, and palpable abdominal mass were not helpful in predicting malignancy. Asymptomatic patients were more in benign group than in malignant group (35.8% vs 7.1%, respectively); $P = 0.005$ [Table 2].

ERCP was performed for 17 patients presenting with obstructive jaundice revealing stricture in lower third common bile duct with stent insertion to relieve jaundice preoperatively.

Older age was significantly associated with malignancy in patients with benign cyst, (40 years vs. 64 years; $P = 0.0001$) [Table 2]. Regardless of the type of tumor, there was a greater prevalence of PC in female (47, 58%). The overall incidence of malignancy was higher in men ($P = 0.004$) [Table 2]. The majority of patients with mucinous cystadenoma were female (13/17, 76.4%), 65.2% (15/23) in SCA, 100% (7/7) in SPT, and 42.9% (12/28) in malignant cyst [Table 3].

The mean transverse diameter of the PC was 4.7 ± 2.3 cm. The maximum cyst diameter was significantly greater in the malignant cysts (6.5 ± 2.5) as compared with benign cysts (3.7 ± 1.4) ($P = 0.008$). Five of 34 (14.7%) patients with cystic pancreatic lesions < 3 cm had malignant tumors [Table 2].

The majority of PC located in the tail (49.4%), 35.8% in the head, and 14.8% in the body of the pancreas [Table 1]. Location of cystic lesion did not predict malignant pathology [Table 2]. The majority of serous and mucinous tumors located in the tail (14/23; 60.8% and 12/17; 70.6%, respectively). All of intraductal papillary mucinous tumors were found in the head and 85.7% of the SPT located in the head [Table 3].

Solid component inside the cyst was recorded in 20 patients (24.7%). Of the 20 patients, 4 cysts were benign and 16 cysts were malignant; $P = 0.0001$. Calcification was found in 20 patients (24.7%), of which, 13 were in benign cysts; $P = 0.96$. Wall thickening was recorded in 29 cases (35.8%), of which, 18 were malignant; $P = 0.0001$ [Tables 1 and 2].

Serum CA19-9, CEA, and serum amylase were measured in

Table 1: Demographic data of the 81 patients

Variables	All cases
The median age (years)	45 (15-72)
Sex	
Male	34 (42%)
Female	47 (58%)
Site	
Head	29 (35.8%)
Body	12 (14.8%)
Tail	40 (49.4%)
Size (cm)	4.7 ± 2.3 (2-10)
Clinical picture	
Asymptomatic	21 (25.9%)
Pain	34 (42%)
Mass	13 (16%)
Jaundice	22 (27.2%)
Weight loss	31 (38%)
Vomiting	14 (17.3%)
CT finding	
Wall thickness	
Thick wall	29 (35.8%)
Thin wall	52 (64.2%)
Solid part	20 (24.7%)
Calcification	20 (24.7%)
Pathological diagnosis	
Serous cystadenoma	23 (28.4%)
Mucinous cystadenoma	17 (21%)
Intra ductal papillary tumor	5 (6.2%)
Solid pseudopapillary tumor	7 (8.6%)
Mucinous cystadenocarcinoma	25 (30.9%)
Ductal adenocarcinoma with cystic degeneration	3 (3.7%)
Neuroendocrinal tumor	1 (1.2%)
Surgery	
Pancreatoduodenectomy	25 (30.9%)
Distal pancreatectomy	36 (44.4%)
Median pancreatectomy	7 (8.6%)
Exploration	7 (8.6%)
Bypass	3 (3.7%)
Enucleation	3 (3.7%)

66/81 cysts. They were not helpful in differentiating benign from malignant pathology.

All surgeries were performed with a curative intent, 25 patients (30.9%) underwent PD operation with PG (in 19 patients) or PJ (in 6 patients), and 7 patients underwent pylorus preserving PD and 18 patients underwent classic PD, 36 patients (44.4%) underwent distal pancreatectomy, 7 patients (8.6%) underwent median pancreatectomy, 3 patients (3.7%) underwent enucleation, and 10 patients (12.4%) had advanced tumor (underwent bypass in 3 patients and nothing was done in 7 patients). The mean postoperative stay was 7.5 ± 2.5 days (4-21 days) for the

Table 2: Comparison between patients with benign and malignant tumors

Variables	Benign (53)	Malignant (28)	P value
The median age (years)	40 (16-70)	64 (15-72)	0.0001
Sex			0.04
Male	18 (34%)	16 (57.1%)	
Female	35 (66%)	12 (42.9%)	
Clinical picture			
Asymptomatic	19 (35.8%)	2 (7.1%)	0.005
Pain	18 (34%)	16 (57.1%)	0.04
Nausea and vomiting	9 (17%)	5 (17.9%)	0.91
Loss of weight	13 (24.5%)	18 (64.3%)	0.0001
Jaundice	14 (26.4%)	8 (28.6%)	0.83
Mass	8 (15.1%)	5 (17.9%)	0.74
Cyst size (cm)	3.7±1.4	6.5±2.5	0.008
Cyst <3 cm (34 patients)	29 (54.7%)	5 (17.9%)	
Cyst >3 cm (47 patients)	24 (45.3%)	23 (82.1)	0.001
CT finding			
Solid part	4 (7.5%)	16 (57.1%)	0.0001
Calcification	13 (24.5%)	7 (25%)	0.96
Cyst location			0.99
Head	19 (35.8%)	10 (35.7%)	
Body	8 (15.1%)	4 (14.3%)	
Tail	26 (49.1%)	14 (50%)	
Pancreatic duct (mm)	1.9±0.6	4.2±2.1	0.0001
Appearance			
Unilocular	44 (83%)	13 (46.4%)	0.001
Multilocular	9 (17%)	15 (53.6%)	
Wall thickness			
Thick wall	11 (20.8%)	18 (64.3%)	0.0001
Thin wall	42 (79.2%)	10 (35.7%)	
Cyst fluid			
Viscosity			0.58
Low	33 (62.3%)	18 (64.3%)	
High	20 (37.7%)	10 (35.6%)	
Nature			
Serous	23 (43.4%)	3 (10.7)	
Mucous	20 (37.7%)	17 (60.7%)	0.01
Haemorrhage	4 (7.5%)	5 (17.9%)	
Haemorrhage and necrosis	6 (11.3%)	3 (10.7%)	
Operative time (minutes)	209.7±69.5	189.6±85.7	0.25
Hospital stay (days)	6.5±2.5	8.3 ±± 8.2	0.13
Serum			
CA19-9	36.1±42.9	25.1±25.5	0.27
CEA	9.6±21.8	4±9.7	0.26
Amylase	174.6±152.6	173.4±128.9	0.97
Surgery			0.0001
Pancreatoduodenectomy	19 (38%)	6 (21.4%)	
Distal pancreatectomy	26 (49.1%)	10 (35.7%)	
Median pancreatectomy	5 (9.4%)	2 (7.1%)	
Enucleation	3 (5.7%)	0	
Bypass	0	3 (10.7%)	
Exploration	0	7 (25%)	

benign cyst and 8.3 ± 8.2 days (2-36 days) for the malignant group.

Univariate analysis showed 10 variables to be significantly predictive of malignancy in cyst: male gender, abdominal pain, loss of weight, tumor size, presence of solid part, pancreatic duct dilatation, wall thickness, content of the cyst, loculation of the cyst, and cyst amylase. These 10 predictive factors of malignancy in PC identified in univariate analysis were further analyzed in multivariate analysis. The *P* values for only 3 factors (tumor size, presence of solid part, and wall thickness) in the multivariate analysis were < 0.05 [Table 4].

DISCUSSION

Due to widespread use of radiological studies, cystic pancreatic tumor cases are increasing. The diagnosis of malignancy in cystic pancreatic tumor cases requires pancreatic resection. Little information is presently available on the incidence and behavior of PC. Clinical and laboratory features of cystic pancreatic lesions may predict underlying malignancy.^[6,13]

Many studies reported that SCAs occurred in patients with a median age around 50 years.^[9,10,12-16] Solid and cystic papillary tumors as well as simple cysts have generally been reported in younger patients.^[6,8,13,17,18] Benign mucinous cystic neoplasm have a median age around 50 to 55 years, whereas mucinous cystadenocarcinoma generally have a median age of 60 to 65 years.^[8,13,15,19] In our study, patients with malignant cysts were older than patients with benign cysts with statistical significance (the median age was 40 years in patients with benign cysts, compared with 64 years in patients with malignant cyst, $P = 0.0001$); thus, older patients are more likely to have premalignant or malignant cystic pancreatic neoplasms.

The majority of cystic neoplasms in our study occurred in women. The overall incidence of malignancy was higher in men (18/53; 34% in benign group vs 16/28; 57.1% in malignant group; $P = 0.004$). The majority of patients with mucinous cystadenoma were females, 65.2% in SCA, 100% in SPT, and 42.9% in malignant cyst. Prevalence of cystic neoplasms in female patients has been observed in other studies as well.^[8,10,13-16,19-21] Lee *et al.*^[22] reported that the overall incidence of malignancy was significantly higher in men, 14 of 67 (28%), compared to women, 12 of 99 (12%) ($P < 0.02$). Thus, male gender may suggest malignant behavior of PC.

In this study, 60 patients had one or more symptoms including abdominal pain, jaundice, weight loss, nausea, vomiting, and mass. However, 21 patients were

Table 3: Histopathological type of cystic pancreatic tumors

Variables	Serous cystadenoma (23) 39 (19-58)	Mucinous cystadenoma (17) 42 (24-65)	Solid pseudopapillary (7) 28 (16-64)	Intra ductal papillary tumor (5) 65 (57-70)	Mucinous cystadenocarcinoma (25) 64 (15-75)	Adenocarcinomawithcystic degeneration (3) 61 (59-65)	P value
The median age (years)							0.0001
Sex							0.004
Male	8	4	0	5	14	2	
Female	15	13	7	0	11	1	
Cyst size (cm)	3.4±1 (2-6)	4.5±1.8 (2-8)	3.5±0.8 (2.8-5)	2.5±0.4 (2-3)	6.4±2.5 (2.8-10)	7.3±3.7 (3-10)	0.0001
CT finding							
Solid part	1	2	1	0	12	3	0.0001
Calcification	9	1	2	1	6	1	0.38
Cyst location							
Head	4	3	6	5	9	1	
Body	5	2	1	0	4	0	0.009
Tail	14	12	0	0	12	2	
Appearance							
Unilocular	20	14	5	4	12	1	0.04
Multilocular	3	3	2	1	13	2	
Wall thickness							
Thick wall	1	5	3	1	16	2	
Thin wall	22	12	4	4	9	1	0.001
Cyst fluid							
Viscosity							
Low	20	5	5	2	15	3	0.007
High	3	12	2	3	10	0	
Nature							
Serous	19	1	1	2	2	1	
Mucous	2	14	0	3	17	0	0.0001
Haemorrhage	2	2	0	0	4	1	
Haemorrhage and necrosis	0	0	6	0	2	1	
Serum							
CA19-9	47.3±59	29.3±18.2	22.8±22.8	40.7±46.2	26.3±27.2	17.5±9.8	0.55
CEA	8.3±5.1	2.9±3.9	9.8±16.7	33.7±61	4.3±10.5	2.11±0.4	0.06
Amylase	145.7±148.9	216.6±148.9	209.1±168.2	137±66.4	178.6±138.8	142.7±27.6	0.75
Surgery							
Pancreatoduodenectomy	4	3	6	5	6	0	
Distal pancreatectomy	14	12	0	0	10	0	
Median pancreatectomy	2	2	1	0	2	0	0.0001
Enucleation	3	0	0	0	0	0	
Bypass	0	0	0	0	2	1	
Exploration	0	0	0	0	5	2	

Table 4: Multivariate analysis of significant factors associated with malignancy

Variables	OR	95% CI	P value
Age	1.123	0.992-1.272	0.067
Male gender	0.107	0.002-4.816	0.250
Abdominal pain	4.210	0.634-27.960	0.137
Loss of weigh	1.676	0.217-12.937	0.620
Cyst size (cm)	2.906	1.078-7.834	0.035
Presence of solid component	37.390	1.611-867.530	0.024
Wall thickness	0.038	0.003-0.445	0.009
Content of the cyst	0.555	0.101-3.043	0.498
Loculation	0.655	0.055-7.794	0.738
Viscosity of fluid	0.225	0.028-1.826	0.162

OR: Odds ratio, CI: Confidence interval

asymptomatic. Asymptomatic patients were more in the benign group than in the malignant group (35.8% vs 7.1%, respectively; $P = 0.005$). Symptoms of abdominal pain and weight loss had a significant association with malignant tumors. Fernandez-del Castillo *et al.*^[10] found that 134 of their 212 patients (63%) with PC were symptomatic. Malignant lesions were found in 40% of their symptomatic patients compared with only 17% of their asymptomatic patients ($P = 0.001$). Lee *et al.*^[22] reported that the presence of one or more symptoms was a significant predictor of malignant pathology. Symptoms of jaundice, weight loss, and anorexia had associations with malignant tumors. Moesinger *et al.*^[13] found that less than half of their patients with SCAs and benign mucinous cystic tumors had symptoms, whereas 80% to 85% of their patients with mucinous cystadenocarcinoma were symptomatic. Spinelli *et al.*^[6] reported that the presence of symptoms predicted premalignant or malignant pathology. Javle *et al.*^[23] found that palpable abdominal mass on presentation was significantly more in the malignant group (4/17 patients) than in the benign group (0/18 patients). Weight loss occurred more in the malignant group (7/17 patients) than in the benign group (2/18 patients) with statistical significance.

Several studies correlating size and malignancy risk have revealed that smaller cystic neoplasms are less likely to be malignant.^[6,22] In our study, the maximum cyst diameter was significantly greater ($P = 0.008$) in the malignant cysts (6.5 ± 2.5 cm) as compared with the benign group (3.7 ± 1.4 cm). Five of 34 (14.7%) patients with cystic pancreatic lesions < 3 cm had malignant tumor. Spinelli *et al.*^[6] reported that cyst size did not correlate with final pathology. Sarr *et al.* found no difference in the mean size of benign mucinous cystadenoma and mucinous cystadenocarcinoma.^[15] On the other hand, Chari *et al.* found that their 73 noninvasive IPMN was 5.2 cm in diameter, whereas their 40 invasive IPMN was 6.6 cm.^[21] Lee *et al.*^[22] reported that 31 of 166 (19%) patients with

cystic pancreatic tumors < 3 cm had malignancy, which is in accordance with the results of other series that report malignancy rates ranging between 13 and 20% in small lesions.^[23-26] Thus, cysts of small size do not exclude its malignant potential but malignancy is more with larger cyst size.

In our study, cyst location did not predict malignant behavior of the cyst. In some studies, the mucinous types of PC arise from the duct epithelium, are often large (sometimes >10 cm), and usually located in pancreatic body or tail; SCAs are smaller (<2 cm), and often seen on head of the pancreas^[8,16,19,23] and conversely, mucinous cystadenocarcinoma have a tendency to occur more often in the head of the pancreas.^[6,13,15,21]

Many studies have reported the presence of solid component inside the cyst to be a significant predictor of malignancy.^[22-26] In our study, the most significant radiological findings associated with malignancy were the presence of a solid component ($P = 0.0001$), loculation ($P = 0.001$), and wall thickening (0.0001). Both the presence of solid component and wall thickening were found to be independent predictors when considered in a multivariate analysis.

Endoscopic US with fine needle aspiration has been suggested as a diagnostic tool to differentiate between benign and malignant cysts. However, aspiration by the needle has the potential to spill malignant cells with possibility of reducing survival.^[6,8-10] For this risk, as well as the accuracy of fluid analysis, several studies^[6,8,9] and as also in our study, did routinely use endoscopic US which is expensive, invasive, and needs experience. Recently, positron emission tomography has been found to be accurate in detecting small pancreatic cancers, but it is very expensive.^[27]

The management of pancreatic cystic lesions remains controversial. Although an aggressive resectional approach is advocated by some,^[28] an increasing number of clinicians are now questioning the practicality of this strategy with the marked increase in the incidence of PC detected incidentally on radiologic imaging.^[26,29]

In the absence of randomized controlled data to guide treatment recommendation, the International Association of Pancreatology identified several factors as indication for resection of PC IPMNs. These include diameter > 3 cm, any solid component, and the presence of symptoms attributable to the cyst.^[30,31] However, any lesion thought to be MCN should be resected. SCA should be resected only if symptomatic, or if the diagnosis remains doubtful.^[32] Malignant SPT can be cured when completely excised,

and prolonged survival can be seen even in the presence of metastatic disease. Management of PCN is based upon a balance of malignant potential and risk of surgical resection.^[32]

In our study, major pancreatic resection was recommended for symptomatic cysts, large lesions and for cysts that have potential malignancy or are malignant. Spinelli *et al.*^[6] reported that majority of benign lesions are SCAs as well as solid and cystic papillary tumors. These benign tumors frequently can become large and symptomatic; eventually need a major pancreatectomy, whereas early management might allow limited resection. Similarly, early surgery in patients with mucinous cystadenoma, cystic neuroendocrine tumor, and benign IPMN will prevent malignant transformation and is likely to be more cost-effective than observation. James M. Kiely *et al.*^[33] reported that for small cystic tumors in the uncinata, head, neck, and body of the pancreas, enucleation has advantages over pancreatic resection as regards to operative time, blood loss, and preservation of pancreatic parenchyma. Because the pancreas is otherwise normal in these patients, the risk of pancreatic leakage is high.

Allen *et al.*^[26] have recommended follow up by high-quality CT or MRCP every year for asymptomatic cysts smaller than 2.5 cm. Also, Fernandez-del Castillo and Warshaw^[21] have recommended periodic imaging for small, asymptomatic PC. They recommend resection for larger cysts in young and middle-aged patients and cyst fluid aspiration for analysis for older patients.

CONCLUSION

In conclusion, this study demonstrated that preoperative clinical characteristic such as patients' age, male gender, tumor size, and presence of symptoms can predict malignancy in the cyst. CT scan is not sufficiently accurate to differentiate among the benign and malignant pancreatic cystic lesions. Surgical treatment depends on the location and extension of the lesion. Pancreatic resection is recommended for symptomatic cysts, large lesions and for cysts that have potential malignancy or are malignant. Further prospective studies are required to confirm these results.

REFERENCES

1. Le Borgne J, de Calan L, Partensky C. Cystadenomas and cystadenocarcinomas of the pancreas: A multi institutional retrospective study of 398 cases. French Surgical Association. *Ann Surg* 1999;230:152-61.
2. Fernandez-del Castillo C, Warshaw AL. Cystic tumors of the pancreas. *Surg Clin North Am* 1995;75:1001-16.

3. Wilentz RE, Albores-Saavedra J, Hruban RH. Mucinous cystic neoplasms of the pancreas. *Semin Diagn Pathol* 2000;17:31-42.
4. Turner BG, Brugge WR. Pancreatic cystic lesions: When to watch, when to operate, and when to ignore. *Curr Gastroenterol Rep* 2010;12:98-105
5. Kimura W, Nagai H, Kuroda A, Muto T, Esaki Y. Analysis of small cystic lesions of the pancreas. *Int J Pancreatol* 1995;18:197-206.
6. 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.
7. Hamilton SR, Aaltonen LA, (editors). Pathology and Genetics of Tumors of the digestive system. World Health Organisation Classification of Tumors. Lyon: IARC Press: 2000.
8. Talamini MA, Pitt HA, Hruban RH, Boitnott JK, Coleman J, Cameron JL. Spectrum of cystic tumors of the pancreas. *Am J Surg* 1992;163:117-24.
9. Talamini MA, Moesinger R, Yeo CJ, Poulouse B, Hruban RH, Cameron JL, *et al.* Cystadenomas of the pancreas: Is enucleation an adequate operation? *Ann Surg* 1998;227:896-903.
10. Fernandez-del Castillo C, Targarona J, Thayer SP, Rattner DW, Brugge WR, Warshaw AL. Incidental pancreatic cysts: Clinicopathologic characteristics and comparison with symptomatic patients. *Arch Surg* 2003;38:427-33.
11. Kim YH, Saini S, Sahani D, Hahn PF, Mueller PR, Auh YH. Imaging diagnosis of cystic pancreatic lesions: Pseudocyst versus nonpseudocyst. *Radiographics* 2005;25:671-85.
12. Handrich SJ, Hough DM, Fletcher JG, Sarr MG. The natural history of the incidentally discovered small simple pancreatic cyst: Long-term follow-up and clinical implications. *AJR Am J Roentgenol* 2005;184:20-3.
13. Moesinger RC, Talamini MA, Hruban RH, Cameron JL, Pitt HA. Large cystic pancreatic neoplasms: Pathology, resectability, and outcome. *Ann Surg Oncol* 1999;6:682-91.
14. Warshaw AL, Compton CC, Lewandowski K, Cardenosa G, Mueller PR. Cystic tumors of the pancreas: New clinical, radiologic, and pathologic observations in 67 patients. *Ann Surg* 1990;212:432-43.
15. Sarr MG, Carpenter HA, Prabhakar LP, Orchard TF, Hughes S, van Heerden JA, *et al.* Clinical and pathologic correlation of 84 mucinous cystic neoplasms of the pancreas: Can one reliably differentiate benign from malignant (or premalignant) neoplasms?. *Ann Surg* 2003;138:427-34.
16. Pyke CM, vanHeerden JA, Colby TV, Sarr MG, Weaver AL. The spectrum of serous cystadenoma of the pancreas: Clinical, pathologic and surgical aspects. *Ann Surg* 1992;215:132-9.
17. Mandavilli SR, Port J, Ali SZ. Lymphoepithelial cyst (LEC) of the pancreas: Cytomorphology and differential diagnosis on fine-needle aspiration (FNA). *Diagn Cytopathol* 1999;20:371-4.
18. Bergin D, Ho LM, Jowell PS, Pappas TN, Paulson EK. Simple pancreatic cysts: CT and endosonographic appearances. *AJR Am J Roentgenol* 2002;178:837-40.
19. Meyer W, Köhler J, Gebhardt C. Cystic neoplasms of the pancreas--cystadenomas and cystadenocarcinomas. *Langenbecks Arch Surg* 1999;384:44-9.
20. Sohn TA, Yeo CJ, Cameron JL, Iacobuzio-Donahue CA, Hruban RH, Lillemoe KD. Intraductal papillary mucinous neoplasms of the pancreas: An increasingly recognized clinicopathologic entity. *Ann Surg* 2001;234:313-22.
21. Chari ST, Yadav D, Smyrk TC, DiMaggio EP, Miller LJ, Raimondo M, *et al.* Study of recurrence after surgical resection of intraductal papillary mucinous neoplasm of the pancreas. *Gastroenterology* 2002;123:1500-7.
22. Lee CJ, Scheiman J, Anderson MA, Hines OJ, Reber HA, Farrell J,

- et al.* Risk of malignancy in resected cystic tumors of the pancreas ≤ 3 or $=$ cm in Size: Is it safe to observe asymptomatic patients? A multi-institutional Report. *J Gastrointest Surg* 2008;12:234-42.
23. Javle M, Shah P, Yu J, Bhagat V, Litwin A, Iyer R, *et al.* Cystic Pancreatic Tumors (CPT): Predictors of malignant behavior. *J Surg Oncol* 2007;95:221-8.
 24. Sahani DV, Saokar A, Hahn PF, Brugge WR, Brugge WR, Fernandez-Del Castillo C. Pancreatic cysts 3cm or smaller: How aggressive should treatment be? *Radiology* 2006;238:912-9.
 25. Sarr MG, Murr M, Smyrk TC, Yeo CJ, Fernandez-del-Castillo C, Hawes RH, *et al.* Primary cystic neoplasms of the pancreas. Neoplastic disorders of emerging importance-current state-of-the art and unanswered questions. *J Gastrointest Surg* 2003;7:417-28.
 26. Allen PJ, Jaques DP, D'Angelica M, Bowne WB, Conlon KC, Brennan MF. Cystic lesions of the pancreas: Selection criteria for operative and nonoperative management in 209 patients. *J Gastrointest Surg* 2003;7:970-7.
 27. Sperti C, Pasquali C, Decet G, Chierichetti F, Liessi G, Pedrazzoli S. F-18-fluorodeoxyglucose positron emission tomography in differentiating malignant from benign pancreatic cysts: A prospective study. *J Gastrointest Surg* 2005;9:22-8.
 28. Horvath K, Chabot JA. An aggressive resectional approach to cystic neoplasms of the pancreas. *Am J Surg* 1999;178:269-74.
 29. Goh BK, Tan YM, Cheow PC, Chung YF, Chow PK, Wong WK, *et al.* Cystic lesions of the pancreas: An appraisal of an aggressive resectional policy adopted at a single institution during 15 years. *Am J Surg* 2006;192:148-54.
 30. Tanaka M, Chari S, Adsay V, Fernandez-del Castillo C, Falconi 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.
 31. Tanaka M, Fernández-Del Castillo C, Adsay V, Chari S, Falconi M, Jang JY, *et al.* International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. *Pancreatology* 2012;12:183-97.
 32. Khalid A, Brugge W. ACG practice guidelines for the diagnosis and management of neoplastic pancreatic cysts. *Am J Gastroenterol* 2007;102:2339-49.
 33. Kiely JM, Nakeeb A, Komorowski RA, Wilson SD, Pitt HA. Cystic pancreatic neoplasms: Enucleate or resect? *J Gastroint Surg* 2003;7:890-7.

Source of Support: Nil, **Conflict of Interest:** None declared.

Announcement

iPhone App



Download
iPhone, iPad
application

FREE

A free application to browse and search the journal's content is now available for iPhone/iPad. The application provides "Table of Contents" of the latest issues, which are stored on the device for future offline browsing. Internet connection is required to access the back issues and search facility. The application is Compatible with iPhone, iPod touch, and iPad and Requires iOS 3.1 or later. The application can be downloaded from <http://itunes.apple.com/us/app/medknow-journals/id458064375?ls=1&mt=8>. For suggestions and comments do write back to us.