



Surgical outcomes of resected cystic neoplasms of pancreas: Experience from a tertiary care centre in India

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ABSTRACT

Objective: Cystic neoplasms of the pancreas form a rare heterogeneous group of pancreatic tumors with variable clinical and diagnostic characteristics. Its incidence has increased in recent years due to improvements in cross-sectional imaging methods and awareness amongst surgeons.

Material and Methods: This study aimed to study the demographic, clinical, imaging, and histopathologic characteristics, incidence of malignancy and outcome of surgical resection of pancreatic cystic neoplasms. Retrospective analysis of 91 patients who underwent surgical resection for cystic neoplasm of the pancreas between 2006 to 2017 at a tertiary care institute was done.

Results: There was a female preponderance in the study with a mean age of 47.2 years. Abdominal pain (46.1%) and jaundice (23.1%) were the most common symptoms. Computed tomography and endoultrasound (EUS) were the most commonly used imaging methods in the study and demonstrated good surgical correlation. Pancreaticoduodenectomy (37.1%) was the most commonly performed procedure followed by distal pancreaticosplenectomy (31.8%). Of the lesions, 9.8% were found malignant. Solid pseudopapillary epithelial neoplasm (SPEN) (37.3%) was the most common neoplasm followed by serous (21.9%), intraductal papillary mucinous neoplasm (IPMN) (15.3%) and mucinous neoplasm (14.3%). Preoperative radiological diagnostic correlation was found to be 75-100% implying the importance of imaging in cystic neoplasms of the pancreas. Morbidity and mortality in the study group were 28.5% and 2.1%, respectively.

Conclusion: Pancreatic cystic neoplasms were mostly benign with female preponderance and presented in the younger age group with prevalence of SPEN higher than IPMN in our subcontinent. These can be reliably diagnosed on preoperative cross-sectional imaging, and surgical resection is associated with favourable outcome and acceptable morbidity.

Keywords: Pancreatic cystic neoplasms, clinico-pathological co-relation, surgical resection

INTRODUCTION

Pancreatic cystic neoplasms (PCN) are a rare entity of pancreatic cystic diseases that are diagnosed less frequently as compared to epithelial neoplasms of pancreas. It is found to have a prevalence of 2.6% in patients undergoing abdominal CT and 13% in patients undergoing MRI for unrelated complaints (1,2). The reported incidence in the United States has been found to be one in 100 hospitalized patients (3).

PCNs constitute around 50% of cystic diseases of the pancreas, which is substantial, and includes a spectrum of benign, premalignant and malignant entities (4). Hence, the management also ranges from observation in benign cystic lesions up to surgical resection in malignant neoplasms. Most borderline premalignant lesions pose a therapeutic dilemma, wherein the risk of post-surgical morbidity is to be weighed against malignant transformation. The role of surgery becomes crucial because cystic neoplasms have a better prognosis after resection as compared to solid tumors (5).

WHO has classified PCNs as serous cystic neoplasm (SCN), mucinous cystic neoplasm (MCN), solid pseudopapillary neoplasm (SPEN) and intraductal papillary mucinous neoplasm (IPMN). SCNs are not known to be malignant, whereas MCN, and IPMN have a high risk of malignant transformation. SPEN, on the other hand, has been found to be locally invasive in few cases (4).

Surgical resection has been the gold standard of management of PCN for more than a decade although the indications have changed dramatically. Increased incidence of cross-sectional imaging (CT/MRI) and advent of endoscopic ultrasound have positively contributed to increased detection rates of PCN and have also led to decreased incidence of unnecessary resections (6).

Although many earlier studies (mainly from the United States and China) (7,8) stating the prevalence, clinico-pathological features and surgical outcomes of PCN

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have been reported, data with respect to Indian subcontinent is sparse. Prolonged asymptomatic state and non-specific symptoms might be probable causes for delay in referral to dedicated tertiary care centres. Authors believe that this is the largest single centre study pertaining to PCNs as applicable to the Indian subcontinent. The present study was undertaken to study the demographics, clinical profile of cystic neoplasms of the pancreas, to identify variables associated with potentially malignant and malignant lesions and the outcomes of surgical resection in such lesions in a retrospective cohort study.

MATERIAL and METHODS

Ninety-one patients who underwent resection for suspected/proven pancreatic cystic lesions at a tertiary care centre between June 2006 to June 2017 were included in this retrospective cohort study after approval from institutional ethics committee and review board. Data was collected through the institutional database. The study included patients with radiologically suspected cystic neoplasms of the pancreas who underwent resection. Non-surgical patients were excluded.

CT scan was done as the first cross sectional radiological imaging for all patients. MRI/MRCP and endoscopic ultrasound (EUS) were done in selective cases. Cyst fluid CEA and serum CA 19-9 levels were done in cases where imaging could not clearly differentiate MCN from SCN.

Parameters that were recorded included age at presentation, sex, symptoms, radiological findings, location of tumor, type of surgery, surgical complications, histology, recurrence rate and mortality. Postoperative complications were graded according to the Clavien-Dindo classification (9). Grading of pancreatic complications was done according to the International Study Group of Pancreatic Surgery guidelines (10). Follow-up was done on outpatient basis for a minimum period of two years. Follow-up data was collected from the outpatient records and/or telephonic conversations.

The collected data was analysed using SPSS 19.0 software (SPSS, Chicago, Illinois, USA). As there were no control groups in this study, only descriptive measures were used. All patients

undergoing surgery for PCN during the study period were taken as sample size. The results are reported as mean, median and percentage.

RESULTS

Surgical data from a high-volume tertiary care centre was studied over a period of eleven years (2006-2017) during which total pancreatic resections performed were 693. Out of these, 91 resections were performed for PCNs. Eighty one cases were histologically proven to be PCN, whereas 10 cases were found to be benign lesions (e.g. simple cyst, pseudocyst, neuroendocrine tumor (NET), hydatid cyst etc.).

SPEN was found to be the most common (n= 34; 37.3%), followed by SCN (n= 20; 21.9%), IPMN (n= 14; 15.3%) and MCN (n= 13; 14.3%). PCNs typically showed a female preponderance with SPEN showing the highest female to male ratio (33:1; 97%). IPMN and benign cysts showed a fairly uniform distribution between males and females. Median age of presentation was lowest for SPEN (29 y), followed by SCN (52 y), IPMN (56 y) and MCN (58 y) (Table 1).

Abdominal pain was the most common presenting feature occurring in 42 patients (46.1%) followed by jaundice seen in 21 patients (23.1%). Of the patients, 19.7% were detected incidentally and 10.9% of the patients presented with a mass (Table 1).

Pancreatic head and body were more common tumor locations compared to tail in this study (n= 37 and 36 vs 16) (Table 2).

Preoperative CT was performed as the first line cross sectional radiological imaging for all cases (Figures 1,2). MRCP was performed in 12 cases wherein CT indicated a diagnosis of IPMN. EUS was performed in a total of 47 cases. CT and EUS, as combined diagnostic modality, had good surgical correlation leading to high diagnostic accuracy (Table 2). Imaging features suggestive of SCN and MCN were well-demarcated multicystic lesions with or without mural nodules. IPMNs were characterized by the dilatation of the main pancreatic duct, branch duct or both. SPEN characteristically showed both solid and cystic components without local infiltration.

Table 1. Patient demographics and clinical symptoms

	SCN	MCN	SPEN	IPMN	Miscellaneous	Total
Number of patients	20 (21.9%)	13 (14.3%)	34 (37.3%)	14 (15.3%)	10 (10.9%)	91
Median age (yrs)	52 (36-65)	58 (40-68)	29 (17-36)	56 (49-74)	43 (39-65)	
Sex (M:F)	5:15	2:11	1:33	6:8	4:6	
Incidental finding	6	2	4	3	3	18 (19.7%)
Abdominal pain	14	4	20	2	2	42 (46.1%)
Jaundice	6	1	4	8	2	21 (23.1%)
Mass		2	4	1	3	10 (10.9%)

SCN: Serous cystic neoplasm, MCN: Mucinous cystic neoplasm, SPEN: Solid pseudopapillary neoplasm, IPMN: Intraductal papillary mucinous neoplasm.

Table 2. Tumor characteristics and diagnostic correlation

Type	Head	Body/Neck	Tail	Size (cm), mean
SCN	7	4	9	6.1 (3.1-13.2)
MCN				
Benign	2	4	2	7.1 (2.5-11.7)
Malignant	1	3	1	7.5 (3.8-9.7)
SPEN	13	18	3	7 (2.9-12.4)
IPMN				
Non-invasive	6	4		5.6 (2.7-10.6)
Invasive	4			5.8 (4.1- 9)
Miscellaneous	4	2	4	6.2 (4-11.1)
Total	37	36	16	

Radiological and pathological correlation				
Type	CECT (N)	MRI/MRCP (N)	EUS (N)	Correlation with surgical diagnosis (%)
SCN	20		12	15/20 (75%)
MCN	13		9	10/13 (76.9%)
SPEN	34		10	32/34 (94%)
IPMN	14	12	8	14/14 (100%)
Miscellaneous	10		8	9/10 (90%)

CECT: Contrast enhanced CT, MRI: Magnetic resonance imaging, EUS: Endoultrasound.

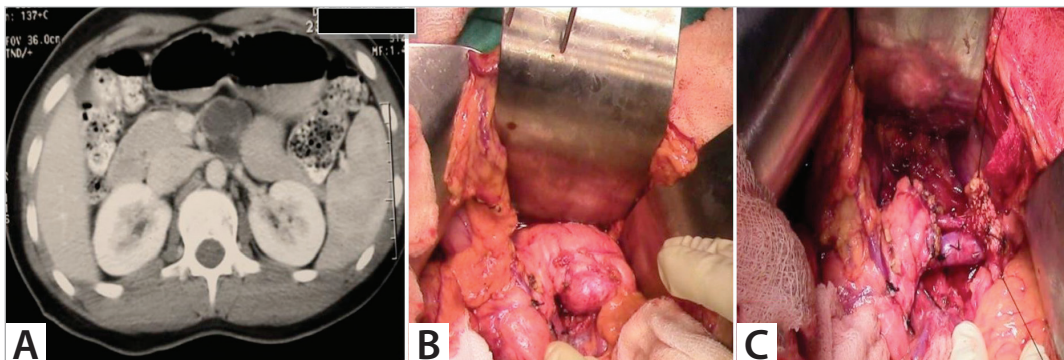


Figure 1. MCN. **A.** CECT showing a cystic lesion in body of pancreas. **B.** Intraoperative image of tumor and **C.** central pancreatectomy.

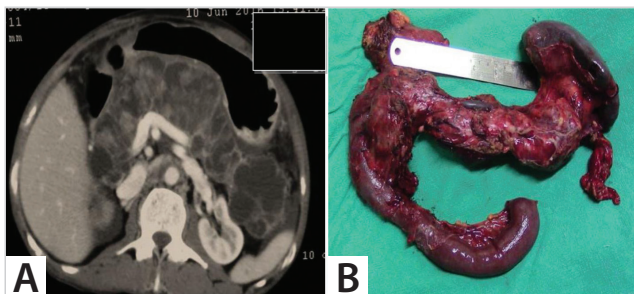


Figure 2. IPMN. **A.** CECT showing multiple cystic SOL involving the entire pancreas. **B.** Total pacreatectomy with splenectomy specimen.

EUS guided cyst fluid analysis/FNAC was done only in doubtful cases. It was found that elevated CEA levels correlated well with MCN. However, its absence did not rule out MCN. Elevated serum CA 19-9 and amylase levels were found to be poor predictors of cystic neoplasms (Table 3).

Indications for surgery included patients who were symptomatic and who fulfilled the criteria as per modified Fukuoka guidelines (11,12). Pancreatoduodenectomy (PD) was the most commonly performed surgical procedure (34; 37.3%), followed by distal pancreatectomy (DP, 29; 31.8%). Spleen preservation was done in nine cases (9.8%) that allowed a safe resection margin.

Table 3. Tumor marker characteristics

Type	Performed	Elevated cyst fluid amylase	Elevated cyst fluid CEA	Elevated serum CA19-9
SCN	10	-	4	3
MCN	7	-	5	3
SPEN	-			
IPMN	4	1	1	-
Miscellaneous	5	2	1	1

Table 4. Type of resection and complications

Type of resection	n				
Pancreatoduodenectomy (PD)	34				
PD with portal vein resection	1				
Distal pancreatectomy (DPS)	29				
Spleen preserving distal pancreatectomy (SPDP)	9				
Central pancreatectomy	7				
Total pancreatectomy	2				
Enucleation	5				
Inoperable/palliative procedure/drainage	4				
Complications associated with type of procedure					
Type of resection	POPF-A	POPF-B	POPF-C	PPH	DGE
Pancreatoduodenectomy (PD)	9	4	2	2	9
PD with portal vein resection	-	-	-	-	-
Distal pancreatectomy (DPS)	3	1	-	1	1
Spleen preserving distal pancreatectomy (SPDP)	2	-	-	-	-
Central Pancreatectomy	3	1	-	-	1
Total Pancreatectomy	-	-	-	-	-
Enucleation	-	-	-	-	-
Total (n)	17	6	2	3	11

POPF: Post-operative pancreatic fistula, PPH: Post-pancreatectomy hemorrhage, DGE: Delayed gastric emptying.

Central pancreatectomy was done in seven cases (7.6%) where adequate distal pancreas was preserved. Enucleation was performed in five (5.4%) cases where tumors were less than 3 cm, located away from the main pancreatic duct. PD with sleeve resection of the portal vein had to be performed in one case of malignant MCN with local infiltration of the portal vein. Total pancreatectomy was performed in two cases (2.2%) of IPMN that showed diffuse involvement of the pancreas (Table 4, Figures 1,2). Standard lymphadenectomy was performed as per ISGPS definition (13).

Assessment of the margin status on frozen section is crucial in IPMN resections. The authors routinely perform frozen section for margin status in IPMN. However, not so for other PCNs. There is an ongoing debate on the management of those patients with positive margins for benign IPMN with low-grade dysplasia. In our centre, such cases are not subjected to additional

resections, whereas IPMN with high-grade dysplasia are treated with extended resections.

On histopathological evaluation, invasive lesions were found in nine cases (9.8%), out of which five were MCNs and four IPMNs (Table 2).

Postoperative pancreatic fistula was the most common complication encountered, type A was the most frequent (19%), followed by type B and C (6.5% and 2.1% respectively). Post pancreatectomy haemorrhage was reported in three cases and delayed gastric emptying occurred in 11 patients (Table 4).

Major complications were classified according to the Clavien-Dindo classification and included type B and C pancreatic fistula, post pancreatectomy haemorrhage and post-operative death within the first 30 days of hospitalisation. The authors found a total morbidity of 28.5%.

Table 5. Comparative analysis of large scale studies on PCN vs the present study

Characteristics	USA (31)	French (23)	China (20)	Our study
Institution	Single	Multi	Multi	Single
No of patients	1424	398 (396 PCNs)	2251	91
M:F ratio	1:2.3	1:6	1:2.4	1:4
Age at presentation (years)	63	54.5	47.5	47.6
Symptomatic (%)	51.5	57	-	80.3
Size (median in cm)	3	5.6	-	6.5
Location (%)				
Head	42	32.5	-	40.6
Body & Tail	58	67.5	-	59.4
Histology (%)				
SCN	23	32.6	30	21.9
MCN	11	28.5	16.2	14.3
SPEN	2	4.2	31.6	37.3
IPMN	27	10	22	15.3
Incidence of malignancy (%)	23	19.6	0.6-31.2	9.8
Morbidity (%)	35	-	-	28.5
Mortality (%)	0.7	2.7	-	2.1

Patients were followed up on outpatient basis for a minimum period of two years. Ten patients were lost to follow up, and 10 patients with benign cystic lesions on histopathology were excluded from follow-up. A total of 71 patients were followed up for a period ranging from two years to eight years (median follow-up of five years).

A total of two postoperative mortalities were reported (2.1%) due to pancreatic fistula leading to multi organ failure. One patient, who underwent total pancreatectomy for IPMN, died at home six months after surgery probably due to hypoglycaemic attack.

Recurrence was reported in two patients who underwent resection for MCN. The first patient presented with hepatic metastases and second one presented with loco-regional recurrence with encasement of hepatic artery and portal vein. Both patients were referred to the medical oncology department for palliative chemotherapy. Both patients died within six months of completion of chemotherapy.

DISCUSSION

Pancreatic cystic neoplasms have been a subject of keen academic interest since the past few years. Probable reasons for this are increased detection rate and change in surgical guidelines (11,12). Rate of surgical resection has increased in the past few years (7,14).

In the present study, SPEN was found to be the most commonly occurring PCN. This was in conformance with three other prior studies, one of which is from the author's institution (7,15,16)

(Table 5). This could either mean increased surgical resections for SPEN due to symptomatic presentation and large size as found in our study, or might indicate a true increase in the prevalence of SPEN. Greater incidence of SPEN has been found in the Indian and Chinese population as compared to the western countries (17-20).

The prevalence of SCN has not changed significantly as they are largely considered to be benign. In the present study, major surgical indications for radiologically proven SCN were large symptomatic tumors and a diagnostic suspicion of other premalignant lesions. Mucinous tumors were reported in 14.3% of the patients that correlated with the Chinese experience (20). Surgical correlation was evident in 76.9% cases, which, however, did not affect the decision to resect as it was known to be premalignant. Prevalence of IPMN was found to be rather low (15%) as compared to data from the USA and China (17,20). This could indicate the confounding role of ethnic, genetic and racial factors. Furthermore, as a tertiary care referral centre, mostly symptomatic and large tumors were referred for further management to the study center. Additionally, PCNs on observation were not included in this study, which may have underestimated the actual prevalence of PCNs.

All PCNs except IPMN showed female preponderance similar to previous studies (20,21). A significantly higher rate of occurrence of MCN in females could be due to the possible role of human chorionic gonadotrophin (22). The mean age of presentation was found to be lesser in this study (47.1 y) as compared to the American literature (14,21). Increased prevalence of SPEN in this

study and symptomatic presentation overall could have led to earlier diagnosis. MCN and SPEN commonly occurred in the body as has been indicated in a previous study although the overall occurrence was similar in both the head and the body region (2). MCN and SPEN present with larger masses more frequently. The authors are of the opinion that tumors located in the body tend to develop symptoms later as compared to those located in the head region. A French study has also confirmed the above finding (23).

Abdominal pain was the most common presenting feature followed by jaundice and mass. About 19.7% of the cases were detected incidentally on cross sectional CT for unrelated complaints, which also meant that about 80% of the patients were symptomatic at presentation that may have contributed to earlier diagnosis and younger age at presentation.

A good diagnostic correlation with surgical diagnosis was observed in this study with CT and EUS. Ours being an academic centre, EUS and MRCP could be done liberally in conjunction with CT without cost constraints. Elevated cyst fluid CEA levels correlated well with MCN. Although CEA levels >192-200 ng/mL strongly indicate mucinous cysts, it does not distinguish between benign lesions and malignant ones (24). In addition, serum CA 19-9 levels >37 IU/mL is a strong predictor of invasive cancer in IPMN (25). It, however, lacks specificity. Hence, it is prudent to combine these tumor markers with EUS morphology (26). The overall incidence of malignancy was found to be 9.8% in this study, which was lower than previous studies (14,21). Authors believe that a comparatively smaller sample size may have resulted in this variation.

Type of surgery was guided by location and size of the tumor (27). A reported perioperative mortality of 2.1% has been noted in this study. A similar mortality rate has been reported by a Swiss study of 650 patients (28).

Recurrences are relatively uncommon in benign and borderline malignant PCNs; however, invasive lesions are reported to have recurrence rates similar to those of adenocarcinomas. Due to high recurrence rates and similar to conventional pancreatic ductal adenocarcinoma, a structured follow-up is recommended after surgery for all resected cystic lesions with high-grade dysplasia or invasive carcinoma (12). The risk of recurrence of non-invasive IPMN is much lower when compared to invasive IPMN and is estimated around 5-9% (29). The recurrence of non-invasive lesions is almost always non-invasive and occurs after a median of more than four years after resection (30).

The authors also compared their data from the present study to other previously published large studies on PCN (20,23,31). There were a few noteworthy features that were distinct to this study. For instance, the authors found a higher percentage of SPEN, a comparatively younger age at presentation and a lower

incidence of invasive malignancy as compared to some of the prior publications. Demographic differences are noticed in the Indian population as compared to Western and Chinese population.

Although this is believed to be the largest single institution study on PCNs in India, it is not without flaws. A smaller sample size, exclusion of non-surgical cases on observation may have underestimated the true prevalence of this disease.

CONCLUSION

This study confirms that most cystic neoplasms of the pancreas are benign and can be reliably diagnosed with preoperative imaging in the form of CECT and EUS. Rate of surgical resection has increased due to improved detection on cross sectional imaging, and most patients can be offered surgery with acceptable morbidity. This study may act as a potential starting point for future studies with a more archetypal study population.

Ethics Committee Approval: This study was approved by NH Institutional Ethics Committee (Review letter no: 1911/2022, Date: 28.06.2022).

Informed Consent: Informed consent was obtained from the son of the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - DS; Design - NB; Supervision - NB; Data Collection and/or Processing - DS; Analysis and/or Interpretation - DS; Literature Review - NB; Writer- DS, NB; Critical Review - DS, NB.

Conflict of Interest: No conflict of interest was declared by the authors.

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Pankreasın cerrahi uygulanmış kistik neoplazilerinin sonuçları: Hindistan'daki üçüncü basamak bir bakım merkezinin deneyimi

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ÖZET

Giriş ve Amaç: Pankreasın kistik neoplazmaları, değişken klinik ve tanısal özelliklere sahip, nadir görülen, heterojen bir pankreatik tümör grubu oluşturur. Son yıllarda kesitsel görüntüleme yöntemlerindeki gelişmeler ve cerrahlar arasındaki farkındalık nedeniyle insidansı artmıştır. Bu çalışma, pankreas kistik neoplazmalarının demografik, klinik, görüntüleme ve histopatolojik özelliklerini, malignite insidansını ve cerrahi rezeksiyon sonuçlarını incelemeyi amaçladı.

Gereç ve Yöntem: 2006-2017 yılları arasında üçüncü basamak bir sağlık kuruluşunda pankreas kistik neoplazmı nedeniyle cerrahi rezeksiyon uygulanan 91 hastanın retrospektif analizi yapıldı.

Bulgular: Çalışmada yaş ortalaması 47,2 idi ve kadın ağırlıklıydı. Karın ağrısı (%46,1) ve sarılık (%23,1) en sık görülen semptomlardı. Bilgisayarlı tomografi ve endoskopik ultrason (EUS) çalışmada en sık kullanılan görüntüleme yöntemleriydi ve iyi bir cerrahi korelasyon gösterdi. Pankreatikoduodenektomi (%37,1) en sık uygulanan prosedüdü ve bunu %31,8 ile distal pankreatikospalenektomi izledi. Lezyonların %9,8'i malign bulundu. Solid psödopapiller epitelyal neoplazm (SPEN) (%37,3) en sık görülen neoplazmdı, bunu seröz (%21,9), intraduktal papiller müsinöz neoplazm (IPMN) (%15,3) ve müsinöz neoplazm (%14,3) izledi. Preoperatif radyolojik tanı korelasyonunun %75-100 olması pankreasın kistik neoplazmalarında görüntülemenin önemini göstermektedir. Çalışma grubunda morbidite ve mortalite sırasıyla %28,5 ve %2,1 idi.

Sonuç: Pankreatik kistik neoplazmalar çoğunlukla iyi huyluydu ve kadın ağırlıklıydı ve alt kıtamızda SPEN prevalansı IPMN'den daha yüksek olan genç yaş grubunda ortaya çıktı. Bunlar, preoperatif kesitsel görüntülemeye güvenilir bir şekilde teşhis edilebilir ve cerrahi rezeksiyon, olumlu sonuç ve kabul edilebilir morbiditeyle ilişkilidir.

Anahtar Kelimeler: Pankreasın kistik neoplazileri, klinik-patolojik ilişki, cerrahi rezeksiyon

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