

## Research Article

## A Ten-Year Retrospective Study of the Clinicopathological Profile of Pancreatic Neoplasms at The dr. Cipto Mangunkusumo Hospital

Jessica Prisscila,<sup>1</sup> Nur Rahadiani,<sup>2\*</sup> Marini Stephanie,<sup>2</sup> Amelia F. Manatar,<sup>2</sup> Ening Krisnuhoni<sup>2</sup>

<sup>1</sup>Anatomical Pathology Residency Program, <sup>2</sup>Department of Anatomical Pathology, Faculty of Medicine Universitas Indonesia-dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

\*Corresponding author: nur.rahadiani@ui.ac.id  
Received 5 December 2023; Accepted 6 September 2024  
<https://doi.org/10.23886/ejki.12.648.153>

### Abstract

Pancreatic neoplasms exhibit diverse clinical and pathological features, necessitating collaboration between clinicians, radiologists, and anatomical pathologists to enhance diagnostic accuracy and patient management. This study aimed to provide a clinicopathological overview of pancreatic neoplasms in the Indonesian population from 2012 to 2022. A descriptive-analytical cross-sectional study was conducted using secondary data from the Department of Anatomical Pathology, dr. Cipto Mangunkusumo Hospital and electronic medical records. A total of 62 resected pancreatic epithelial neoplasms were analyzed, with solid neoplasms (85%) and cystic neoplasms (15%) predominant. Clinicopathological profiles were associated with neoplasm types based on stage. Pancreatic ductal adenocarcinoma (PDAC), solid pseudopapillary neoplasms (SPN), pancreatic neuroendocrine tumor (PanNET), and pancreatic neuroendocrine carcinoma (PanNEC) were the most common solid neoplasms. Meanwhile, mucinous cystic neoplasm (MCN) was the most common cystic neoplasm. Both solid and cystic neoplasms were more prevalent among women, with 58% of patients under 50 years old. Patients with PDAC and mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) have a higher proportion of <10-month survival rates and advanced stages. Although many clinicopathological features align with existing literature, further research with larger patient cohorts and comprehensive data is warranted.

**Keywords:** clinicopathological, cystic, pancreatic neoplasm(s), solid.

## Studi Retrospektif Sepuluh Tahun tentang Profil Klinopatologi Neoplasma Pankreas di Rumah Sakit dr. Cipto Mangunkusumo

### Abstrak

Neoplasma pankreas menunjukkan beragam fitur klinis dan patologis sehingga memerlukan kerjasama antara klinisi, radiologis, dan patologis anatomi dalam meningkatkan akurasi diagnosis dan pengelolaan pasien. Penelitian ini bertujuan untuk memberikan gambaran klinikopatologis neoplasma pankreas pada populasi Indonesia tahun 2012-2022. Studi deskriptif-analitis, potong-lintang dilakukan menggunakan data sekunder dari Departemen Patologi Anatomi, Rumah Sakit dr. Cipto Mangunkusumo dan catatan medis elektronik. Sejumlah 62 reseksi keganasan epitel pankreas, didapatkan neoplasma solid (85%) lebih mendominasi dibandingkan neoplasma kistik (15%). Profil klinikopatologis berhubungan dengan jenis terutama berdasarkan stadium. Pancreatic ductal adenocarcinoma (PDAC), solid pseudopapillary neoplasms (SPN), pancreatic neuroendocrine tumor (PanNET), dan pancreatic neuroendocrine carcinoma (PanNEC) merupakan neoplasma padat paling banyak terdapat, sedangkan mucinous cystic neoplasm (MCN) merupakan tipe neoplasma kistik yang paling umum. Baik neoplasma padat maupun kistik lebih sering ditemukan pada perempuan, dengan 58% pasien berusia di bawah 50 tahun. Pasien dengan PDAC dan mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) memiliki proporsi tingkat kelangsungan hidup <10 bulan dan stadium lanjut yang lebih tinggi. Meskipun banyak fitur klinikopatologis yang sejalan dengan literatur yang ada, penelitian lebih lanjut dengan sampel yang lebih besar dan data yang komprehensif masih diperlukan.

**Kata kunci:** klinikopatologis, kistik, neoplasma pankreas, padat.

## Introduction

Pancreatic neoplasms are a diverse group of tumors that arise within the pancreas. They encompass benign, borderline, and malignant neoplasms from the ductal, acinar, neuroendocrine, and other types, presented with varying clinical and pathological features.<sup>1</sup> Pancreatic neoplasms have a relatively low incidence rate compared to neoplasms of other organs, but their malignant counterparts, especially pancreatic ductal adenocarcinoma (PDAC) are associated with high mortality rates.<sup>2,3</sup> Pancreatic neoplasms also occur in relatively specific age and sex manners depending on the type of tumor. Based on these variations, good cooperation among clinicians, radiologists, and pathologists will increase the accuracy of the diagnosis and determine the more suitable follow-up treatment for each case.<sup>1,4</sup>

Pancreatic neoplasms can be divided into solid and cystic based on their predominant features. Computed tomography scan (CT Scan) or magnetic resonance imaging (MRI) can help determine the precise location of the tumor, the three-dimensional tumor size, the solid/cystic appearance, the possibility of tumor differentiation, the presence of calcifications, the tumor's relationship with surrounding tissues (such as the great vessels and spleen), and the possibility of metastasis in both the lymph nodes and distant organs. Pathological examinations are divided into pre- and post-operative examinations. The pre-operative examination includes cytopathological examination through fine needle biopsy and histopathological examination of cytological preparations made into paraffin blocks (cell blocks). Post-operative examination includes histopathological examination of resected specimens. Through this post-operative examination, diagnosis, histological type, degree of differentiation, pathological stage, invasion of blood vessels or adjacent organs, and the status of the incision margins are then reported, which may be necessary for determining further patient management.<sup>1,5,6</sup>

This study aims to contribute valuable insights into the Indonesian population's clinicopathological landscape of pancreatic neoplasms. The findings of this preliminary study will enhance our understanding of the disease and facilitate the development of more effective strategies for diagnosis, treatment, and patient support, thus ultimately improving the care provided to individuals affected by pancreatic neoplasms.

## Methods

This retrospective study is a descriptive-analytic with a cross-sectional design. A total of 62 samples were obtained from archived secondary data from the Department of Anatomical Pathology and hospital medical records for 10 years between January 2012 and December 2022. The present study (protocol no. 23061015) was approved by the Medical Ethics Committee of the Faculty of Medicine, Universitas Indonesia/dr. Cipto Mangunkusumo Hospital (no. KET976/UN2.F1/ETIK/PPM.00.02/2023).

All cases were collected based on the inclusion criteria, namely all primary pancreatic neoplasm cases resected between January 2012 and December 2022. The exclusion criteria were cases in which macroscopic examination was performed in another hospital, and not all slides were sent for review. Clinical and pathological data searches were conducted for cases that met the inclusion and exclusion criteria in examination forms, clinical data, and slides with hematoxylin and eosin (H&E) staining.

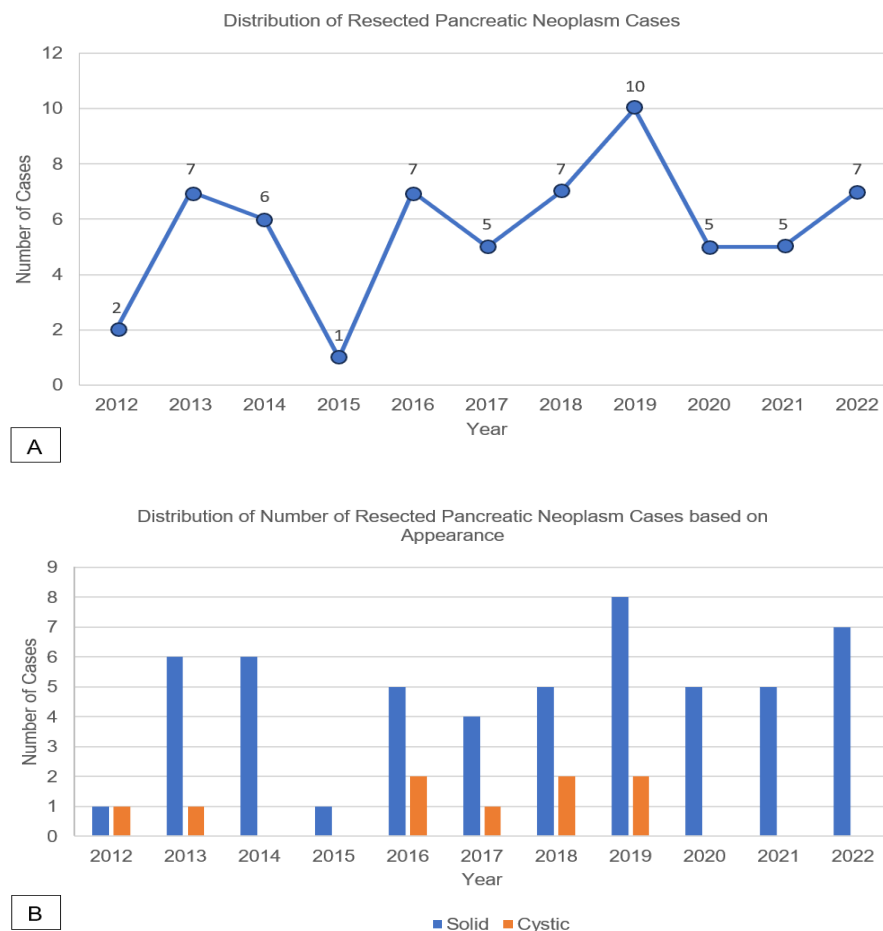
Data on age, sex, preoperative serum CA19-9 levels, and metastatic status (at the time of diagnosis) were obtained from the patients' histopathological examination forms and electronic medical records. Patient survival data were obtained through direct telephone and/or electronic messages with patients or their families on two occasions. Staging data were obtained from secondary data based on the American Joint Committee on Cancer (AJCC) 8<sup>th</sup> staging system and/or the 2019 WHO classification of digestive system tumours.<sup>6</sup>

All the collected data were processed using the Statistical Package for the Social Sciences/SPSS version 25.0 (IBM Corp.). Bivariate analysis was performed on each clinicopathological feature of the neoplasm group using the Chi-Square or Fisher's exact test.  $P < 0.05$  was considered to be statistically significant.

## Results

### *Data Distribution per Year*

The overall distribution of pancreatic neoplasms based on the predominant appearance of the tumor for every year is shown in Figure 1. In the last five years (2017-2022), the number of resected pancreatic neoplasms at dr. Cipto



**Figure 1. Distribution of The Number of Resected Pancreatic Neoplasm Cases Per Year**  
**A. Overall number of cases; B. The number of cases by year is based on the appearance of the tumors**

Mangunkusumo Hospital increased, with 39 cases, compared to 23 cases in the previous five years (2012–2017). Solid neoplasms were the majority of cases over the past decade (2012–2022), with 53 cases (85%), compared to cystic neoplasms, with 9 cases (15%).

**Clinical Characteristics**

Data on the clinical and pathological profile characteristics, including age, sex, pre-operative serum CA 19-9 levels, metastatic status, patient survival, tumor size based on a macroscopic examination, histological type, number of lymph nodes, number of lymph nodes with metastatic tumor, lymphovascular invasion, perineural invasion, incision margin status, and stage are shown in Table 1.

Out of 62 cases, the majority were females aged ≤50 with a median age of 48.5 years (age range, 17–71 years). Most cases had normal pre-operative serum CA 19-9 levels (≤37 U/ml). Distant

metastases were found in two cases: one to the liver and one to the appendix. The majority of the patients survived for >10 months.

Of the 62 cases, most tumors were >4 cm in size, with a median of 5 cm (ranged 1–35 cm). On macroscopic examination, solid tumors were more common (Figure 2). In contrast, Pancreatic Ductal Adenocarcinoma (PDAC), Solid Pseudopapillary Neoplasm (SPN), Pancreatic Neuroendocrine Tumor (PanNET), and Pancreatic Neuroendocrine Carcinoma (PanNEC) were the most diagnosed sequentially. In tumors with a cystic appearance (Figure 2), Mucinous Cystic Neoplasm (MCN) and Cystadenoma/Cystadenocarcinoma were the most diagnosed. A total of three cases were classified with an “other” diagnosis as they could not be confirmed with certainty at the time of diagnosis and required immunohistochemical (IHC) examination to determine the diagnosis, consisting of high-grade sarcoma with a differential diagnosis of rhabdomyosarcoma

**Table 1. Clinicopathological Characteristics of The Patients (n = 62)**

Parameter	n	%
Age		
≤50 years	36	58
>50 years	26	42
Sex		
Male	24	39
Female	38	61
Pre-operative serum CA 19-9 levels		
≤37 U/ml	22	36
>37 U/ml	15	24
No data	25	40
Metastatic status		
No metastasis	41	66
With metastases	2	3
No data	19	31
Patient survival		
≤10 months	8	13
>10 months	23	37
No data	31	50
Histological type		
Pancreatic ductal adenocarcinoma (PDAC)	24	36
Pancreatic neuroendocrine tumor (PanNET)	8	12
Pancreatic neuroendocrine carcinoma (PanNEC)	6	9
Mixed neuroendocrine – non-neuroendocrine Tumor (MiNEN)	1	1,5
Acinic cell carcinoma (ACC)	1	1,5
Pancreatoblastoma	0	0
Solid pseudopapillary neoplasm (SPN)	10	15
Mucinous cystic neoplasm (MCN)	5	8
Intraductal papillary mucinous neoplasm/IPMN	0	0
Cystadenoma/cystadenocarcinoma	4	6
Intraductal papillary neoplasm	0	0
Others	3	5
Tumor size based on macroscopic examination		
≤2 cm	9	15
2.1–4 cm	17	27
>4 cm	36	58
Number of lymph nodes		
0	30	48
1–11	27	44
≥12	5	8
Number of lymph nodes with tumor metastases		
No lymph node	30	48
0	16	26
1–3	8	13
≥4	8	13
Lymphovascular invasion		
Absent	50	81
Present	12	19
Perineural invasion		
Absent	53	85,5
Present	9	14,5
Incision margin		
Negative margin	17	27
Positive margin	45	73
Stage based on AJCC 8 <sup>th</sup> /WHO Digestive System 2019 (n=41)		
Stage 0	1	2
Early (stage I and II)	35	56
Advanced (stage III and IV)	5	8
Not assigned	21	34

and Gastrointestinal Stromal Tumor (GIST) in one case, Acinic Cell Carcinoma (ACC) with a differential diagnosis of SPN and PanNET in one case, and PanNET with a differential diagnosis of ACC in one case. In some of the resected lymph nodes, tumor metastases were observed. In most cases, there was no lymphovascular or perineural invasion, and most had a free surgical margin.

Based on the tumor size, the number of lymph nodes containing tumors, and metastatic status, the staging of 41 (out of 62) cases could be determined. The data showed that the majority of cases were at an early stage. The staging for the rest of the cases was undetermined.

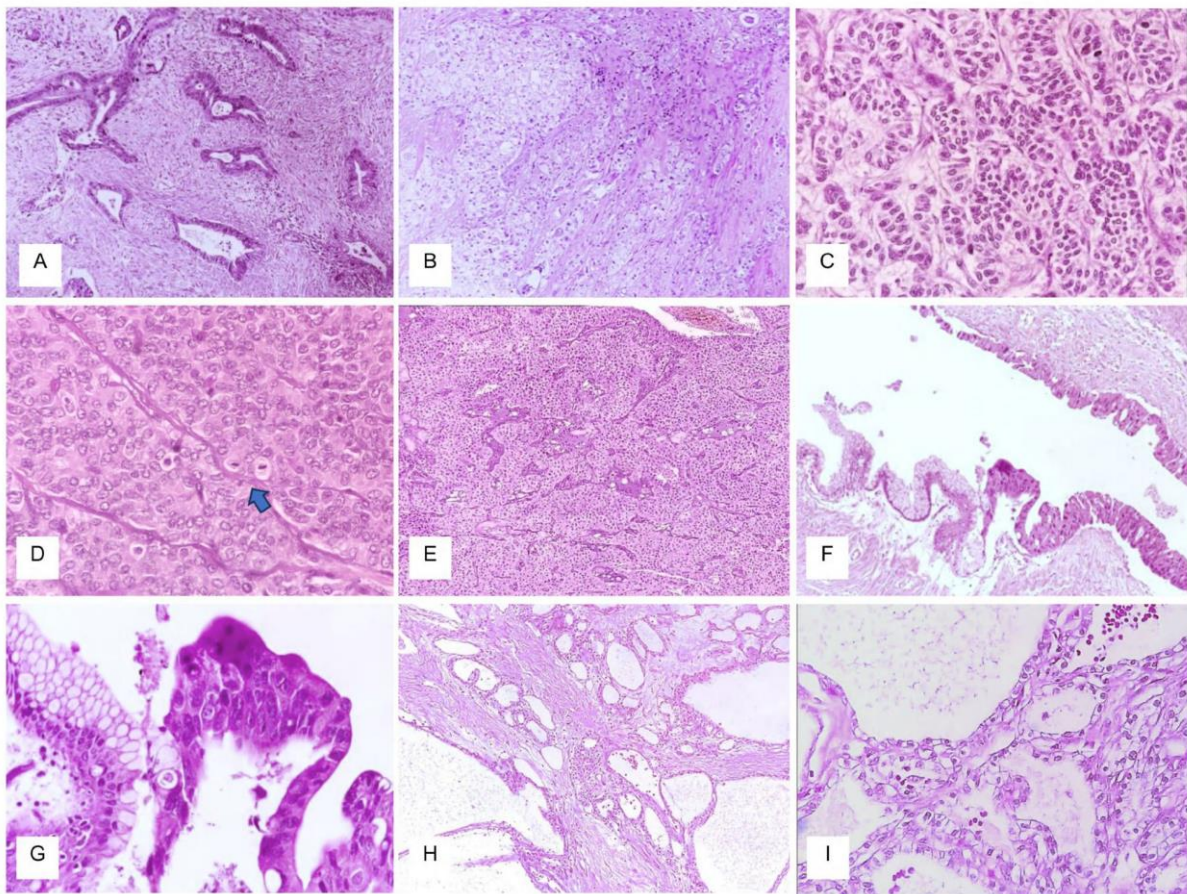
**Clinicopathological Characteristics of Pancreatic Neoplasms**

Bivariate analysis was performed on each solid and cystic neoplasm group clinicopathological characteristics (Table 2). It was found that there was only a significant association in stage in the pancreatic neoplasm group (p<0.05). The results showed that solid pancreatic neoplasms were more commonly diagnosed in the later stage compared to cystic neoplasms. The clinicopathological characteristics of each entity included in the solid and cystic neoplasms group are shown in Tables 3 and 4.

The present study showed that more than half of PDAC cases were diagnosed in patients aged >50 years (mean 54±8.8 years), but numerous cases were diagnosed in patients aged ≤50 years, with the youngest being 37 years. In contrast, 90% of SPN cases were diagnosed in patients aged ≤50 years, with a mean age of 30±10.7 years, and the youngest being 17 years. In Pancreatic Neuroendocrine Neoplasm/PanNEN, the proportion of patients aged ≤50 years and >50 years was equal, with a mean age of 40±16 years in PanNET and 4.6±18.5 years in PanNEC.

Carcinoma cases (PDAC, MiNEN, ACC) were more prevalent in males, whereas SPN and PanNEN were more common in females. Upon further investigation, it was discovered that five out of seven female PanNET patients had functional tumours that produced hormones. No cases of pancreoblastoma were found among the patients.

The findings, moreover, showed an increase in CA 19-9 levels (>37 U/ml) in the majority of PDAC cases (median 379.8 U/ml;



**Figure 2. Types of Pancreatic Solid and Cystic Neoplasms**

A) PDAC: Well-differentiated (H&E, 100x); (B) Poorly differentiated (H&E, 100x). (C) PanNET: Tumor cells arranged in an organoid pattern with salt and pepper chromatin (H&E, 400x). (D) PanNEC: Tumor cells are arranged in a solid pattern, with cells showing nucleoli, abundant cytoplasm, and lots of mitoses (arrows) (H&E, 400x). (E) SPN: Tumor cells arranged in a solid growth pattern with sclerotic stroma among them (H&E, 100x); (F) MCN: Cystic cavity lined by mucinous epithelial (H&E, 100x); (G) Mucinous epithelial with low-grade (left) and high-grade (right) dysplasia (H&E, 400x). Cystadenoma/Cystadenocarcinoma; (H) Cystic cavities lined by non-mucinous epithelial (H&E, 100x); (I) Cuboidal epithelia with clear cytoplasm (H&E, 400x)

minimum 2 U/ml–maximum 12,000 U/ml) and the only MiNEN case. Metastases to distant organs were observed in one case of PDAC and one case of MiNEN to the appendix and the liver, respectively. No cases of metastases were observed in cases of PanNET and PanNEC. PDAC patients had the lowest survival time compared with the other pancreatic solid neoplasms, with a mean of  $6.8 \pm 1.2$  months. On the other hand, SPN was associated with a higher survival rate, with all cases surviving for  $>10$  months.

The results suggested that in the macroscopic findings, most tumors were  $>2$  cm, namely PanNEC with a mean of  $10.3 \pm 4.8$  cm, SPN with a median of 7.3 cm (ranged 3.3–13 cm), PanNET with a mean of  $3.8 \pm 2.3$  cm, and PDAC with a median of 3.5 cm (ranged 1–12 cm). Most lymph nodes in carcinoma cases found in the resection specimens

were  $<12$ , mostly in PDAC cases (median 4, minimum 0 and maximum 16), typically containing tumor metastases. Tumor metastases in the lymph nodes were also found in PanNEC, MiNEN, and ACC cases. Regarding SPN, no tumor metastases were found in the lymph nodes. Lymphovascular and perineural invasion were also found in similar proportions in cases of PDAC and PanNET. The highest proportion of cases with a positive incision margin was found in MiNEN and PDAC, followed by PanNET, PanNEC, and SPN. Regarding the stage, most solid tumours diagnosed at an advanced stage were PDAC and MiNEN.

MCN cases were diagnosed at a younger age (mean  $36 \pm 8.4$  years) compared to serous cystadenoma/cystadenocarcinoma (mean  $50.3 \pm 10.4$  years), found mainly in females (Table 4). Additionally, the preoperative serum CA 19-9 levels were low ( $\leq 37$  U/ml) for both types of tumors, and no

**Table 2. The Clinicopathological Characteristics of Pancreatic Tumor Based on Predominan Features**

Parameter	Solid (n=53)	Cystic (n=9)	p-value	OR (95% CI)
<b>Age</b>				
≤50 years	30	6	0,722 <sup>2</sup>	Reference
>50 years	23	3		1,533 (0,346-6,794)
<b>Sex</b>				
Male	23	1	0,135 <sup>2</sup>	6,133 (0,715-52,583)
Female	30	8		Reference
<b>Pre-operative serum CA 19-9 levels</b>				
≤37 U/ml	16	6	0,204 <sup>2</sup>	Reference
>37 U/ml	14	1		5,250 (0,562-49,080)
No data	23	2		
<b>Metastatic status</b>				
No metastasis	36	3	1,000 <sup>2</sup>	Reference
With metastases	2	0		(-)
No data	16	6		
<b>Patient Survival</b>				
≤10 months	8	0	0,550 <sup>2</sup>	Reference
>10 months	19	4		(-)
No data	26	5		
<b>Tumor size based on macroscopic examination</b>				
≤2 cm*	8	1	0,282 <sup>2</sup>	Reference
2.1-4 cm*	16	1		1,778 (0,099-31,976)
>4 cm	29	7		0,440 (0,048-4,116)
<b>Number of lymph nodes</b>				
0	25	5	0,728 <sup>2</sup>	Reference
1-11*	24	3		1,600 (0,344-7,441)
≥12*	4	1		0,800 (0,073-8,752)
<b>Number of lymph nodes with tumor metastases</b>				
No lymph node	25	5	0,600 <sup>2</sup>	
0	13	3		Reference
13*	8	0		(-)
≥4*	7	1		1,615 (0,140-18,581)
<b>Lymphovascular invasion</b>				
Absent	41	9	0,185 <sup>2</sup>	Reference
Present	12	0		(-)
<b>Perineural invasion</b>				
Absent	44	9	0,333 <sup>2</sup>	Reference
Present	9	0		(-)
<b>Surgical Margin</b>				
Negative margin	17	0	0,053 <sup>2</sup>	Reference
Positive margin	36	9		(-)
<b>Stage</b>				
Stage 0	0	1	0,049 <sup>2</sup>	Reference
Early/Stage I-II*	32	1		(-)
Advanced/Stage III-IV*	7	0		(-)
Not assigned	14	7		(-)

<sup>1</sup>Chi-square test, <sup>2</sup>Fischer's exact test, \*Combined when analyzed  
OR: odds ratio, CI: confidence interval

Table 3. Clinicopathological Characteristics of Solid Pancreatic Neoplasms (n = 53)

Parameter	PDAC (n=24)	PanNET (n=8)	PanNEC (n=6)	MiNEN (n=1)	ACC (n=1)	SPN (n=10)	Other (n=3)
Age							
≤50 years	10	4	3	1	0	9	3
>50 years	14	4	3	0	1	1	0
Sex							
Male	16	1	2	1	1	1	1
Female	8	7	4	0	0	9	2
Pre-operative serum CA 19-9 levels							
≤37 U/ml	3	4	3	0	1	5	0
>37 U/ml	11	1	1	1	0	0	0
No data	10	3	2	0	0	5	3
Metastatic status							
No metastasis	13	7	5	0	0	10	0
With metastases	1	0	0	1	0	0	0
No data	10	1	1	0	1	0	3
Patient survival							
≤10 months	6	1	1	0	0	0	0
>10 months	2	4	2	0	1	9	1
No data	16	3	3	1	0	1	2
Tumor size based on macroscopic examination							
≤2 cm	6	1	0	0	1	0	0
2.1–4 cm	10	4	1	0	0	1	0
>4 cm	8	3	5	1	0	9	3
Number of lymph nodes with tumor metastases							
No lymph node	4	7	3	0	0	8	3
0	8	1	2	0	0	2	0
1–3	7	0	1	0	0	0	0
≥4	5	0	0	1	1	0	0
Lymphovascular invasion							
Absent	16	6	5	0	1	10	3
Present	8	2	1	1	0	0	0
Perineural invasion							
Absent	17	7	5	1	1	10	3
Present	7	1	1	0	0	0	0
Surgical margin							
Negative margin	12	2	1	1	0	1	0
Positive margin	12	6	5	0	1	9	3
Stage based on AJCC 8 <sup>th</sup> /WHODigestive System 2019							
Stage 0	0	0	0	0	0	0	0
Early/Stage I–II	11	7	5	0	0	10	1
Advanced/Stage III–IV	4	0	0	1	0	0	0
Not assigned	9	1	1	0	1	0	2

**Table 4. Clinicopathological Characteristics of Cystic Pancreatic Neoplasms (n=9)**

Parameter	Hystological type	
	MCN (n=5)	Serous Cystadenoma/ Cystadenocarcinoma (n=4)
Age		
≤50 years	5	1
>50 years	0	3
Sex		
Male	0	1
Female	5	3
Pre-operative serum CA 19-9 levels		
≤37 U/ml	4	2
>37 U/ml	1	0
No data	0	2
Metastatic status		
No metastasis	3	2
With metastases	0	0
No data	2	2
Patient survival		
≤10 months	0	0
>10 months	2	2
No data	3	2
Tumor size based on macroscopic examination		
≤2 cm	0	1
2.1-4 cm	0	1
>4 cm	5	2
Number of lymph nodes		
0	3	2
1-11	2	1
≥12	0	1
Number of lymph nodes with tumor metastases		
No lymph node	3	2
0	2	1
1-3	0	0
≥4	0	1
Lymphovascular invasion		
Absent	5	4
Present	0	0
Perineural invasion		
Absent	5	4
Present	0	0
Surgical margin		
Negative margin	0	0
Positive margin	5	4
Stage		
Stage 0	1	0
Early/Stage I-II	1	0
Advanced/Stage III- IV	0	0
Not assigned	3	4



metastatic features were observed in any of the MCN and serous cystadenoma/cystadenocarcinoma cases. In this study, all patients had a survival of >10 months.

All cystadenoma or cystadenocarcinoma cases were smaller (mean  $4.9 \pm 3.3$  cm) than MCN cases mean  $11.6 \pm 5.5$  cm). Only 1 case of serous cystadenoma/ cystadenocarcinoma was found with  $\geq 12$  lymph nodes and tumor metastasis in it. No metastasis to distant organs, lymphovascular invasion, or perineural invasion were found. All cases had a free surgical margin. Based on all available data, all cystic neoplasms were diagnosed at an early stage. At the same time, there were no cases of PMN nor intraductal papillary neoplasm detected in the patients.

## Discussion

Most primary pancreatic tumors have a characteristic radiological and gross appearance and are generally divided into solid or cystic tumors. Pancreatic malignancy may arise from the exocrine (95%) and endocrine components of the pancreas, with the most common type being PDAC (80%). PDAC primarily (90%) arises from Pancreatic Intraepithelial Neoplasm/PanIN, with 10% arising from cystic lesions, namely IPMN and MCN.<sup>7-9</sup>

There were 62 cases of primary pancreatic neoplasms, consisting of 53 cases of solid neoplasms and 9 cases of cystic neoplasms. There has been an increase in the prevalence of pancreatic neoplasm resections in the last five years (2017–2022) compared to the preceding five years (2012–2017), dominated by solid neoplasms. In the first five years, several pancreatic neoplasm resections were performed in 2013, when the national health insurance system (Jaminan Kesehatan Nasional/ JKN) began to be implemented. This potentially affected the number of pancreatic neoplasm cases undergoing examination and treatment at RSCM. In the last five years, most pancreatic neoplasm resections were performed in 2019 and decreased in 2020, possibly due to pandemic restrictions on the number of patients who could visit the hospital before increasing again in 2021–2022.

In this study, staging showed a significant association with both neoplasm groups, in which cystic neoplasms were more often diagnosed at an earlier stage than solid neoplasms, in line with the research conducted by Jones et al.<sup>10</sup> The most commonly resected pancreatic neoplasms in

the solid neoplasm group were PDAC, SPN, PanNET, PanNEC, MiNEN, and ACC. Whereas in cases of cystic neoplasms, the most common type was MCN, followed by serous cystadenoma/ cystadenocarcinoma. Most cases of pancreatic solid neoplasms, especially PDAC, that underwent resection were those that had not metastasized and were diagnosed in the earlier stages. Whereas in cases of cystic neoplasms, resection was performed as the primary curative measure.<sup>1,5</sup> A significant number of SPN cases were found in this study, even though in the literature, SPNs are generally found in only ~1.5-3% of pancreatic neoplasm cases.<sup>11,12</sup> However, based on studies conducted in Asian populations, the prevalence of SPN cases is found to be higher in Eastern countries.<sup>11,12</sup>

This study's proportion of PDAC cases was slightly higher in patients aged <50 years, whereas WHO in 2019 states that most patients are diagnosed at 55-85 years with a median age of 70.<sup>6</sup> Based on previous literature, cases diagnosed with pancreatic carcinoma at a younger age (<50 years) can be classified as early-onset pancreatic cancer (EOPC), which is more common in patients of Asian descent.<sup>13</sup> This should be considered along with a history of smoking, obesity, and alcohol consumption, which are known risk factors for pancreatic cancer.<sup>6,14</sup>

The sex distribution of PanNEN patients in this study differed from that in previous literature, in which PanNEN was more common in males. This may be due to the majority of PanNEN patients who were female suffered from functional tumours/ hormone-producing tumours that caused clinical symptoms.<sup>15-17</sup>

This study showed that tumor metastases to distant organs were found only in patients with PDAC and MiNEN in the solid neoplasm group. In PDAC cases, distant metastases were found only in two cases, and no metastasis was found in PanNEN cases. Based on the literature, PDAC is a very aggressive type of pancreatic neoplasm, in which invasion and metastasis in PDAC cases can occur even before the tumor causes clinical symptoms and is clinically detectable.<sup>1,18</sup>

In PanNEN cases, the literature states that 50% of cases exhibit metastatic features at diagnosis.<sup>1,6</sup> In this study, the lack of metastatic findings is possibly due to poor patient compliance, resulting in a lack of follow-up, limited access to clinical and

radiological data of patients at RSCM in the first period (2012-2017), and patient survival, which was generally low ( $\leq 10$  months) in PDAC patients, making long-term follow-up not possible.

One of the findings that appear highly specific for PDAC was the tumour cells' ability to grow along the edges of channels, including vascular channels, nerve fibres, pancreatic ducts, interlobular connective tissue, and peripancreatic fat. The presence of perineural invasion is considered a specific finding in PDAC cases. This perineural invasion is generally found around or outside the pancreas, which contains numerous nerve fibers; similarly, vascular invasion, common in the peripancreatic tissue, and lymphatic channel invasion, which may be associated with lymph node metastasis.<sup>6</sup> In this study, lymphovascular invasion was only found in 8 PDAC cases, whereas perineural invasion was observed in 7 cases and lymph node metastases in 12 cases. The low incidence of lymphovascular invasion, which was disproportionate to the high incidence of metastases to the lymph nodes, may be caused by two factors. First, tumor cells displace endothelial cells and grow along the vascular channels, which makes it more difficult to determine vascular invasion. Second, inadequate sampling in the peripancreatic area usually contains more vessels and nerve fibers.<sup>1,18</sup> These may explain why there were fewer observed lymphovascular and perineural invasions.

The present study has numerous limitations. First, the population in the present study was small, all from a single center consisting of patients with a resected pancreatic neoplasm over the last 11 years. Second, due to the limitations in data collection, a high frequency of non-available data is inevitable. Therefore, a further prospective study with a larger cohort and more comprehensive clinicopathological data collection is warranted to understand better the clinicopathological characteristics of patients with pancreatic neoplasms in Indonesia.

## Conclusion

This study showed that the cases were predominantly solid neoplasms (85%) rather than cystic neoplasms (15%), with 58% of patients under 50 years old. Women appear to have a higher prevalence of both solid and cystic neoplasms, with 57% and 89% of cases, respectively. There was a significant relationship between the stage and both pancreatic neoplasm groups. Among pancreatic neoplasms, PDAC was the most frequently

resected neoplasm in the solid group, followed by SPN, PanNET, and PanNEC. At the same time, MCN was the predominant diagnosis in cystic neoplasms. Of all the cases of pancreatic neoplasms, PDAC cases had the worst prognosis, with most of the available data showing survival times of less than 10 months.

Most of the clinicopathological features obtained in this study are in agreement with the literature and previous studies, except for the age and sex distribution. Further study in a more extensive series of patients with more comprehensive clinicopathological data is warranted to understand better the clinicopathological characteristics of patients with pancreatic neoplasms in Indonesia.

## Conflicts of Interest

The authors declare no conflicts of interest to report regarding the present study.

## Acknowledgments

The authors thank Nadia Carolina Notoprawiro for formatting the manuscript.

## References

1. Campbell FVC. Pathology of the pancreas: a practical approach. London: Springer; 2013. 7–45 p.
2. World Health Organization. International agency for research on cancer GLOBOCAN 2020. Indonesia. 2021. Available from <https://gco.iarc.who.int/media/globocan/factsheets/populations/360-indonesia-fact-sheet.pdf>
3. World Health Organization. International agency for research on cancer GLOBOCAN 2020. Pancreatic cancer fact sheet. 2020. Available from <https://gco.iarc.fr/en>.
4. Tempero MA, Malafa MP, Al-Hawary M, Behrman SW, Benson AB, Cardin DB, et al. Pancreatic adenocarcinoma, Version 2. JNCCN. 2021;21:439–57. doi: 10.6004/jnccn.2021.0017.
5. Herranz Pérez R, De la Morena López F, Santander Vaquero C. Neoplasias quísticas pancreáticas, enfoque diagnóstico. Rev Colomb Gastroenterol. 2019;34:52. Espana. doi: 10.22516/25007440.242.
6. World Health Organization. WHO classifications of tumours: digestive system tumours, 5<sup>th</sup> ed. Geneva: WHO. 2019.p.296–8.
7. Odze RD GJ. Surgical pathology of the GI tract, liver, biliary tract, and pancreas, 3<sup>rd</sup> ed. Philadelphia: Elsevier; 2015.p.1081–8.
8. Kumar AA editors. Robbins pathologic basis of disease, 9<sup>th</sup> ed. Philadelphia: Elsevier; 2014.p.890–5.
9. Ducreux M, Cuhna AS, Caramella C, Hollebecque A, Burtin P, Goéré D, et al. Cancer of the pancreas: ESMO clinical practice guidelines for diagnosis,

- treatment and follow-up. *Ann Oncol.* 2015;26:56–68. doi: 10.1093/annonc/mdv295.
10. Jones NB, Hatzaras I, George N, Muscarella P, Ellison EC, Melvin WS, et al. Clinical factors predictive of malignant and premalignant cystic neoplasms of the pancreas: a single institution experience. *HPB.* 2009;11:664–70. doi: 10.1111/j.1477-2574.2009.00114.x.
  11. Kiani AZ, Khan HM, Ali Z, Sheikh HS, Khan AS, Atiq M. A single institution experience with solid pseudopapillary neoplasm of the pancreas: clinicopathological correlation and review of the literature. *Asian Pac J Cancer Care.* 2023;8:49–57. doi: 10.31557/apjcc.2023.8.1.49-57.
  12. Yao J, Song H. A review of clinicopathological characteristics and treatment of solid pseudopapillary tumor of the pancreas with 2450 cases in Chinese population. *BioMed Research International.* 2020;2020:2829647. doi: 10.1155/2020/2829647.
  13. Ntala C, Debernardi S, Feakins RM, Crnogorac-Jurcevic T. Demographic, clinical, and pathological features of early onset pancreatic cancer patients. *BMC Gastroenterol.* 2018;18:139. doi: 10.1186/s12876-018-0866-z.
  14. Teng Y, Saito E, Abe SK, Sawada N, Iwasaki M, Yamaji T, et al. Female reproductive factors, exogenous hormone use, and pancreatic cancer risk: the Japan public health center-based prospective study. *Eur J Cancer Prev.* 2017;26:378–84. doi: 10.1097/cej.0000000000000358.
  15. Muscogiuri G, Barrea L, Feola T, Gallo M, Messina E, Venneri MA, et al. Pancreatic neuroendocrine neoplasms: does sex matter? *TEM.* 2020;31:631–41. doi: 10.1016/j.tem.2020.02.010.
  16. Zheng R, Zhao H, An L, Zhang S, Chen R, Wang S, et al. Incidence and survival of neuroendocrine neoplasms in China with comparison to the United States. *Chin Med J.* 2023;136:1216–24. doi: 10.1097/CM9.0000000000002643.
  17. Fu M, Yu L, Yang L, Chen Y, Chen X, Hu Q, et al. Gender differences in pancreatic neuroendocrine neoplasms: a retrospective study based on the population of Hubei Province, China. *Front Endocrinol.* 2022;13:1-9. doi: 10.3389/fendo.2022.885895
  18. Kim J. Cell dissemination in pancreatic cancer. *Cells.* 2022;11:1-16. doi: 10.3390/cells11223683.