Patients with a Resected Pancreatic Cystic Neoplasm: A Single Center 10-Year-Experience

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ABSTRACT

Objective: Pancreatic cystic neoplasia represents a challenging and complex spectrum of lesions within the pancreas and requires a detailed understanding of their biological behavior and clinical implications. We aimed to examine the demographic characteristics, imaging and histopathological features, and clinical outcomes of patients who underwent pancreatic surgery due to cystic neoplasms. Moreover the impact of sarcopenia and obesity on clinical outcomes was investigated.

Methods: Patients who underwent pancreatic surgery with the preliminary diagnosis of pancreatic cystic neoplasia at the General Surgery Clinic of Kartal Dr. Lütfi Kırdar City Hospital between 2010 and 2020 were retrospectively evaluated. The size, morphological features, location, and number of the cystic lesions were recorded. The presence of sarcopenia was determined by measuring the psoas muscle cross-sectional area at the L3 level with preoperative CT and calculating the psoas muscle index.

Results: The number of patients included in the study was 23 and the average age of these patients was 59.4 (SD: 14.3). 18 (78.3%) of the patients were women. The most common cyst type was mucinous cystic neoplasia (30.4%), followed by an adenoma (26%), ductal adenocarcinoma (26%) and IPMN (17.3%). The most common surgery was the Whipple procedure (56.5%). Sarcopenia was detected in 47.8% of the patients. Postoperative complications were seen in 6 (26%) patients.

Conclusion: This study provides valuable information regarding pancreatic cystic neoplasms' pathological and clinical consequences. In particular, it is one of the few studies investigating the relationship between sarcopenia, obesity and pancreatic cystic neoplasms in the current literature.

INTRODUCTION

Improvements in cross-sectional imaging techniques have led to an increased incidental identification of pancreatic cystic neoplasms (PCN).[1] PCNs include several histological subtypes, such as serous cystic neoplasms (SCN), mucinous cystic neoplasms (MCN), intraductal papillary mucinous neoplasms (IPMN) and other uncommon cystic lesions.[2] The characteristics and malignancy potential of these lesions differ from one another.[3]

Pancreatic surgery has long been associated with high morbidity and mortality rates.[4] Although perioperative care has improved over time and mortality has decreased over the years, the morbidity rate remains unchanged at approximately 50%.[5] Patients undergoing pancreatic surgery are at high risk for severe postoperative complications that significantly affect survival, such as pancreatic

fistula, gastrojejunostomy or biliary leakage and surgical site infection (SSI).[6] There is a need to identify risk factors that may predict complications after pancreatic surgery.[4]

The obese patients are at increased risk for both benign and malignant pancreatic disorders.[7-9] Additionally, it has been previously reported that obesity is associated with an increased frequency of malignant transformation in branch-channel IPMNs (BD-IPMNs) in Western countries. [10] And also obesity is associated with poor postoperative outcomes after pancreaticoduodenectomy. Weight management during treatment planning may improve outcomes in obese patients.[11]

Sarcopenia is associated with adverse outcomes and complications after surgery. Sarcopenia is the loss of muscle mass and muscle-muscle strength associated with aging and secondary sarcopenia is the loss of muscle mass and muscle-muscle strength associated with underlying diseases.[12] Examination of muscle mass in patients undergoing pancreatectomy may be an effective way to determine risk for groups of patients at high risk of sarcopenia, depending on the underlying disease.[4] Preoperative detection of sarcopenia may allow patients to be assessed for suitability for surgery.[13] Only a few studies in the literature have examined the association between sarcopenia and outcomes following pancreatic surgery.

In this study, we analyzed the clinical data of patients operated for PCN in our clinic. The study aimed to analyze the clinicopathological features of these PCNs in light of the literature. Furthermore, the second aim of the study was to determine whether obesity and sarcopenia are associated with a higher frequency of malignant PCNs and their relationship with postoperative complications.

MATERIALS AND METHODS

This retrospective cohort study encompasses the records of all consecutive adult patients who underwent pancreatic surgery with a prediagnosis of pancreatic cystic neoplasia at Kartal DR. Lütfi Kırdar City Hospital. From January 2010 to January 2021, 23 patients with pathologically confirmed pancreatic cystic neoplasm, who met the inclusion criteria and underwent surgical resection for a prediagnosis of pancreatic cystic neoplasm were included in the study. Clinical data were retrospectively acquired from hospital databases. Extensive data encompassing sociodemographic status, clinical history and presentation, laboratory and radiologic findings, surgical procedure details (type, location, size of cysts, etc.), pathology report information, postoperative complications, hospital course and follow-up datas were collected. Patients with a BMI equal to or greater than 30 kg/m^2 were classified as obese. Perioperative mortality was characterized as either "in-hospital" or "30-day mortality." Sarcopenia was assessed by measuring the cross-sectional area of the psoas muscle at the L3 level using preoperative CT and calculating the psoas muscle index. The Hounsfield unit scale (−29 to +150) was used to identify skeletal muscles from other

structures. The calculated total area was proportional to the square of the patient's height. So, sarcopenia was diagnosed by the skeletal muscle index (SMI) derived from a preoperative computed tomography scan. According to international consensus, an SMI of <545 mm^2/m^2 in men and <385 mm^2/m^2 in women indicates sarcopenia.[14]

Inclusion criteria encompassed patients aged over 18 years who had not been diagnosed with pancreatic cancer or any other malignancy before getting pancreatic surgery.

Postoperative complications were classified according to the Clavien-Dindo grading system, according to which groups 1–2 have minor and ≥3 have major complication rates. The Clavien-Dindo system, originally described in 2004, is widely used throughout surgery for grading adverse events (i.e. complications) that occur as a result of surgical procedures.[15]

Institutional Review Board approval for the study was obtained from Kartal DR. Lütfi Kırdar City Hospital Clinical Research Ethics Committee, on 27.01.2021, with decision number 514/194/11. The study is in compliance with the Declaration of Helsinki.

Statistical Analysis

Descriptive statistics are reported as mean ± standard deviation unless stated otherwise. Normally distributed continuous variables were analyzed using a 2-sample Student's t-test, whereas non-normally distributed variables have been evaluated with the Mann–Whitney U test. Categorical variables were analyzed using a Pearson $\chi2$ test and a Fisher exact test for cell counts less than 5. The One-way ANOVA Test was used for the analysis of independent groups and parametric variables. Survival analysis was conducted via the Kaplan–Meier method, comparing histologic groups by the log-rank test. A P value below 0.05 was considered statistically significant. All statistical analyses were conducted applying the SPSS Statistics version 26 software package (IBM, Armonk, NY).

RESULTS

In our study, comprising 23 patients, the mean age was 59.4 (SD: 14.3) years with women constituting the majority (78.3%). In this cohort, the mean BMI of the patients was 27.4. Clinical characteristics are described in Table 1. The most common presenting complaint was abdominal pain and symptomatology of patients described in Table 2. Most patients in this cohort have ASA (American Society of Anesthesiologists) 1 (43.5%, n=10). Second most common was ASA 2, seen in 34.8% (n=8) of patients with moderate systemic illnesses that do not impede activities. Thus, 21.7% (n=5) of patients were ASA 3.

Minimum cyst size was 1 cm, maximum 21 cm (mean: 4.7 cm, 4.05 SD). No significant correlation was found with the lesion size between PCN adenoma, borderline, in situ and adenocarcinoma (p: 0.914). Cysts were solitary in 16 patients and multiple in 7 patients. The cyst was located in

Table 1. Demographic and clinic characteristics of patients

	Number (n)	Percentage (%)
Gender		
Female	18	78.3%
Male	5	21.7%
Age		
18-65	15	65.2%
>65	8	34.7%
Obesity		
Yes	10	43.5%
No	13	56.5%
Sarcopenia		
Yes	11	47.8%
No	12	52.2%

Table 2. Symptomatology of patients

	Number (n)	Percentage (%)
Abdominal pain	18	78.3%
Dyspepsia	7	30.4%
Jaundice	5	21.7%
Weight Loss	4	17.4%
History of Pancreatitis	4	17.4%
Others	8	34.8%
(Mass, Incidental, Weakness, Nausea-vomiting)		

the head of the pancreas in 14 (60.9%) patients, in the body in 2 (8.7%) patients and in the tail in 7 (30.4%) patients. The Whipple procedure (pancreaticoduodenectomy) was the most prevalent, at 56.5% (n=13). Distal pancreatectomy with splenectomy was performed in 21.7% (n=5) of patients. Distal pancreatectomy occurred 13% (n=3) of the time. 8.7% (n=2) had total pancreatectomy with splenectomy, a more radical operation. The study includes a variety of pancreatic cystic and solid tumors, with the most frequent being mucinous cystic neoplasm (MCN), accounting for 30.4% of the cases (n=7). Intraductal papillary mucinous neoplasm (IPMN) was the second most common, representing 17.3% (n=4) of the diagnoses. Among IPMNs, a subtype featuring branch duct involvement with gastric type differentiation and associated ductal adenocarcinoma was observed in 8.7% (n=2) of the cases. Additionally, microcytic adenomas and serous cystic adenomas were each found in 8.7% of the cases (n=2). Serous cystic adenocarcinoma was 8.7% (n=2) and mucinous cystic adenocarcinoma comprised 4.3% (n=1) of the total cases. Furthermore, a diagnosis of ductal adenocarcinoma and serous cystic adenomas with neuroendocrine tumors (NET) or neuroendocrine microadenomas were also noted in 4.3% (n=1) of the cases each. In total, 23

cases were reviewed, representing a broad spectrum of both benign and malignant pancreatic lesions. Pathological examination of cysts is shown in Table 3. The mean number of positive lymph nodes was 1.17±3.8 (0-16) and the total number of dissected lymph nodes was 13.61±14.8 (0-59). Of the 23 patients with resected PCN; 12 (52.2%) had adenoma, 3(13%) had borderline neoplasms, 1 (4.3%) had carcinoma in situ, and 7 (30.4%) had invasive carcinoma. The presence of mural nodules, septa, solid components, and dilated pancreatic ducts was evaluated across different lesion categories (adenoma, borderline, in situ, invasive). The findings indicated no significant correlation between mural nodules (P=0.17) and septa (P=0.21) with invasive lesions. Nonetheless, solid components and dilated pancreatic ducts had a significant correlation with invasive lesions (P=0.01 and P=0.05, respectively).

Postoperative complications occurred in 6 individuals (26%), with 8.7% demonstrating sarcopenia. Pancreatic Fistula (Grade A, B, C - one patient for each grade), ischemic stroke in one patient, upper gastrointestinal hemorrhage occurred in 2 patients one had been followed non-operatively whereas another had required surgical intervention. The cohort had mostly mild Clavien-Dindo postoperative sequelae. Most instances (73.9%, n=17) were grade 0. 8.7% (n=2) had grade 1 problems. Grade 2 problems occurred in 4.3% of individuals (n=1). Grade 5 problems occurred in 13% (n=3) of cases. Of these patients, 1 patient died on the 44th day of intensive care follow-up due to ischemic stroke, 1 patient died on the 11th day of follow-up due to sepsis after reoperation for Grade C pancreatic fistula, 1 patient died on the 18th day of follow-up after reoperation for upper gastrointestinal bleeding. 1 patient died on the 2nd year of follow-up due to pancreatic adenocarcinoma and the other 3 patients who died were discharged without any complications and the cause of death is unknown because they did not come to follow-up. The mean hospi-

Table 3. Pathological examination of cysts

	Number (n)	Percentage (%)
Surgical border		
Positive	1	4.3%
Negative	22	95.7%
Mural nodule		
Yes	2	8.7%
No	21	91.3%
Septa		
Yes	8	34.8%
No	15	65.2%
Solid Component		
Yes	9	39.1%
No	14	60.9%
Dilated Pancreatic Duct		
Yes	5	21.7%
No	18	78.3%

tal stay was 11.9 days (3-44), the mean survival was 47.53 months (12-120), and the mean follow-up was 1262.9 days (11-3650 days).

There was no statistically significant relationship between age, gender, height, weight, BMI, sarcopenia, psoas area, SMI, lymph node involvement, obesity, comorbidities, ASA and postoperative complications. Male gender (p:0.01) and coronary artery disease (p:0.03) may be predictive of mortality. CEA (p<0.01), CRP (p:0.04) and low hgb levels (p:0.01) may be predictors of mortality. Low BMI (p:0.03) may be a predictor of mortality. However none of them appear to be significant predictors in multivariate analysis.

DISCUSSION

PCNs are more common among women,[16] as in our series 78.3% of the patients was female. Patients with PCN possess an elevated risk of developing pancreatic ductal adenocarcinoma (PDAC). Approximately 2% of the general population presently possesses pancreatic cysts, a figure that significantly increases among older adults, attributable to the prevalent utilization of advanced cross-sectional imaging modalities. The incidence of PCN increases with age, especially during the fifth decade of life.[17] In this study the mean age was 59.4.

Depending on the location size and growth rate of the PCN in the pancreas, various clinical findings such as abdominal pain, jaundice and weight loss may be observed. The presence of symptoms is a further indicator frequently linked to malignant instances, but it is not always definitive.[18-20] Our study included no asymptomatic patients. The predominant presenting complaint was abdominal pain.

For tumors located in the pancreatic head, pancreatico-duodenectomy (PD) is the preferred surgical technique.[21] Consistent with the literature, in our study, malignancies were primarily located in the pancreatic head, rendering the Whipple surgery the most prevalent intervention.

Incidentally diagnosed pancreatic cystic lesions present a challenge in their management.[3,22] One-fifth of the asymptomatic PCNs significantly increased in size after a long-term follow-up period, which was associated with initial cyst size and obesity.[23] Mizuno et al.[24] reported that the development of PCNs is linked to obesity and diabetes. Studies have also indicated that patients with a higher BMI (BMI>25 kg/m²) show a greater prevalence of malignant forms in both MCN and IPMN types with statistically significant results observed.[25] Although the prevalence of obesity was high (43.5%) in our study, no statistically significant relationship was found between postoperative complications or the prevalence of malignancy in lesions. The mean body mass index (BMI) of the patients in this cohort was 27.4.

Significantly, although there was a greater prevalence of IPMN alterations, the malignancy rate in the older, comorbid cohort remained under 5%, while their five-year overall survival rate was 79.51%. The findings indicate that although older patients with comorbidities exhibit more frequent changes in IPMN, their low malignancy risk and elevated non-pancreatic mortality must be meticulously evaluated when deciding on the need for long-term surveillance, surgical intervention, or the potential cessation of surveillance.[17] Most patients in this cohort have ASA 1.

The rates of invasive carcinoma are significantly elevated in studies examining larger lesions, ranging from 7% for cysts averaging 5 cm in size to 27–36% for lesions measuring between 8 and 10 cm.[17] The median cyst size in this study was 4.7 cm. This study showed a lack of association between lesion size and PCN adenoma, borderline, in situ and cancer.

The management of PCNs can be complex and challenging in practice.[2] There are several guidelines on this topic (The American Gastrointestinal Association guidelines, Fukuoka and European guidelines). Although there are differences among them, all guidelines agree on a few high-risk features (such as obstructive jaundice, mural nodule ≥5 mm and main pancreatic duct diameter >10 mm).[26] The reason for pancreatic resection in our series, which was smaller than 3 cm, was the presence of worrisome features mentioned in the guideline recommendations. It was observed that all other patients who underwent resection followed these recommendations. A solid component and mural nodule are independently associated with an increased malignancy risk.[27,28] In this study, solid components and dilated pancreatic ducts were significantly associated with invasive lesions.

One of the main limitations of this study is the lack of multimodal imaging data. Although endoscopic ultrasound (EUS),[29] magnetic resonance imaging (MRI),[30] and computed tomography (CT) are all essential tools in the evaluation and differential diagnosis of pancreatic cystic neoplasms (PCNs), this study was based solely on CT findings due to its retrospective design. As a result, important features such as cyst wall enhancement, mural nodules, or communication with the main pancreatic duct—more accurately detected by EUS or MRI— could not be evaluated accurately. Early diagnosis of PCNs is essential for improving patient prognosis, as delayed detection is often associated with poor clinical outcomes. In recent years, artificial intelligence (AI) has made significant contributions to imaging techniques used for PCN detection, helping to identify complex morphological features that may be difficult to detect through conventional methods. AI-assisted imaging can enhance the accuracy and speed of diagnosis, supporting clinicians in distinguishing between benign and potentially malignant lesions.[31]

A comprehensive review of 99 studies involving 9249 patients with IPMN, many of whom presented with high-risk or concerning features necessitating surgical intervention, demonstrated that the incidence of pancreatic cancer or high-grade dysplasia at the time of resection was 42%.[27] IPMNs can exhibit varying levels of malignancy.[32] Of the 23 PCN patients resected in this study, 12 (52.2%) had adenoma, 3 (13%) had borderline neoplasm, 1 (4.3%) had

carcinoma in situ and 7 (30.4%) had invasive carcinoma.

With the recent advancements in minimally invasive surgery (MIS), including both laparoscopic and robotic techniques, MIS has increasingly become a preferred approach in pancreatic surgery due to its association with reduced blood loss, shorter hospital stays, and faster recovery times compared to open surgery. Robotic-assisted procedures, in particular, offer enhanced precision which are especially valuable in the complex anatomical context of the pancreas.[33,34] Nevertheless, despite these advantages, the application of MIS in cases involving bulky or advanced pancreatic tumors remains controversial, primarily due to concerns about oncological safety, lymph node retrieval, and achieving negative margins.[35] Therefore, while MIS is increasingly recommended as a first-line surgical option for selected patients, careful case selection remains essential, especially in PCN with large volume or local invasion.[36,37]

In a meta-analysis, sarcopenic obesity in patients with pancreatic cancer was reported in 0.6% to 25.0% of patients and the incidence of major complications was reported between 8.6% and 33.9%. Postoperative pancreatic fistula rates, which we define as clinically significant, i.e. Grade B/C, ranged between 8.3% and 17.8%. Sarcopenic obesity was an independent predictor of major postoperative complications in one study, while sarcopenia was significantly associated with clinically relevant pancreatic fistulas in another study.[38,39] In our study, there was no statistically significant relationship between sarcopenia and postoperative complications. Overall, this data reflects that while most patients had uncomplicated recoveries, a subset experienced more serious outcomes, including a mortality rate of 13%, emphasizing the complexity of postoperative management in this cohort.

This study has some limitations due to its retrospective nature and the recording structure and data collection process. Even though it is increasing incidence, PCN is still an uncommon lesion which makes our patient population relatively small in number. This is a limitation of our study. Besides that, our center is not a reference center for pancreatic surgery. The variability in experience among surgeons conducting pancreatic surgery, along with differing surgical techniques and routine algorithms, as well as the inconsistent expertise of physicians performing pathological evaluations and composing reports, constitutes a limitation of the study. Another limitation is that follow-up periods are not homogeneous, as not all patients had a similar length of follow-up during the 10-year period during which data were collected for this study.

PCN comprise a range of both benign and malignant entities. Identifying the characteristics of PCNs and identifying patients with high-risk pathological subtypes for surgical intervention, while minimizing unnecessary follow-up or unnecessary surgery in those with benign lesions, keeps presenting significant challenges. Endoscopic ultrasonography demonstrated superior sensitivity relative to CT in distinguishing malignant from nonneoplastic pancreatic cysts. Despite the absence of statistical significance, this outcome may be deemed clinically significant. Moreover, EUS exhibited notable advantages in visualizing particular morphological characteristics, underscoring its potential as an important diagnostic instrument for evaluating pancreatic cystic neoplasms.[29] Concerning cystic pancreatic lesions, vascularized mural nodules are deemed "high risk stigmata" for malignancy when measuring ≥5 mm and classified as a "worrisome feature" when measuring <5 mm. Contrast harmonic-endoscopic ultrasound (CH-EUS) is effective for evaluating vascularity and distinguishing mural nodules from nonenhancing mucin plugs, with a sensitivity of 88% and a specificity of 79%.[40,41] Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) is a crucial minimally invasive technique for obtaining a cytologic evaluation to elucidate the nature of the lesion prior to surgery.[42,43] A limitation of the study is that EUS was not used as a diagnostic method in the preoperative period. And CEA, glucose, LDL cholesterol, total proteins, lymphocyte count and amylase levels in the cyst fluid were not measured and cytological examination was not performed. Glucose, CEA, LDL cholesterol, and total protein levels in cystic fluid, together with lymphocyte counts, may aid in the risk classification of IPMNs and inform clinical decision-making, which can be enhanced through metabolomic analysis.[44]

This study also has several strengths. It is the first study to investigate the effect of obesity and sarcopenia on postoperative complications in patients operated for pancreatic cystic neoplasia. The relationship between clinicopathologic features and complications was also examined. The presence of solid components and dilated pancreatic ducts, which are mentioned as high-risk features in the literature, had a significant correlation with invasive lesions. Male gender and coronary artery disease may be determinants for mortality. High CEA, high CRP and low hgb levels may be predictors of mortality. Low BMI may be a predictor of mortality.

Conclusion

This study provides valuable data on the clinical and pathological characteristics of patients undergoing pancreatic resection for PCNs. While the majority of patients experienced mild postoperative complications, the mortality rate highlights the complexity of managing pancreatic neoplasms, especially in elderly and comorbid patients.

Future studies with larger sample sizes and prospective designs are essential to further elucidate the impact of sarcopenia, obesity, and other clinical variables on surgical outcomes and to improve risk stratification and patient management strategies in pancreatic surgery.

Ethics Committee Approval

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Z.Z.K., E.T., H.F.K., F.F., M.A.O.; Design: Z.Z.K., E.T., H.F.K., F.F., M.A.O.; Supervision: Z.Z.K., E.T., H.F.K., F.F., M.A.O.; Fundings: Z.Z.K.; Materials: Z.Z.K., F.F.; Data: Z.Z.K., F.F., M.A.O.; Analysis: Z.Z.K., E.T.; Literature search: Z.Z.K., E.T., H.F.K.; Writer: Z.Z.K., F.F., E.T.; Critical Review: Z.Z.K. H.F.K.

Conflict of Interest

None declared.

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Pankreatik Kistik Neoplazm Tanısıyla Rezeksiyon Yapılmış Hastalar: Tek Bir Merkezde 10 Yıllık Deneyim

Amaç: Pankreatik kistik neoplazi, pankreas içindeki lezyonların zorlu ve karmaşık bir spektrumunu temsil eder ve biyolojik davranışlarının ve klinik etkilerinin ayrıntılı bir şekilde anlaşılmasını gerektirir. Kistik neoplazmlar nedeniyle pankreas cerrahisi geçiren hastaların demografik özelliklerini, görüntüleme ve histopatolojik özelliklerini ve klinik sonuçlarını incelemeyi amaçladık. Ayrıca sarkopeni ve obezitenin klinik sonuçlar üzerindeki etkisi de araştırıldı.

Gereç ve Yöntem: Kartal Dr. Lütfi Kırdar Şehir Hastanesi Genel Cerrahi Kliniği'nde 2010-2020 yılları arasında pankreatik kistik neoplazi ön tanısı ile pankreas cerrahisi uygulanan hastalar retrospektif olarak değerlendirildi. Kistik lezyonların boyutu, morfolojik özellikleri, yerleşimi ve sayısı kaydedildi. Sarkopeni varlığı, ameliyat öncesi BT ile L3 seviyesinde psoas kas kesit alanı ölçülerek ve psoas kas indeksi hesaplanarak belirlendi.

Bulgular: Çalışmaya dahil edilen hasta sayısı 23 ve bu hastaların yaş ortalaması 59.4 (SD: 14.3) idi. Hastaların 18'i (%78.3) kadındı. En sık görülen kist tipi müsinöz kistik neoplazi (%30.4) iken, bunu adenom (%26), duktal adenokarsinom (%26) ve IPMN (%17.3) izlemekteydi. En yaygın ameliyat Whipple prosedürüydü (%56.5). Hastaların %47.8'inde sarkopeni tespit edilmiştir. Ameliyat sonrası komplikasyonlar 6 (%26) hastada görüldü.

Sonuç: Bu çalışma pankreatik kistik neoplazmların patolojik ve klinik sonuçları hakkında değerli bilgiler sağlamaktadır. Özellikle, mevcut literatürde sarkopeni, obezite ve pankreatik kistik neoplazmlar arasındaki ilişkiyi araştıran az sayıdaki çalışmadan biridir.

Anahtar Sözcükler: Komplikasyonlar; obezite; pankreatektomi; pankreatik kistik neoplazi; postoperatif sarkopeni.