ABSTRACT Cystic neoplasms of the pancreas are a special heterogeneous group of pancreatic tumors with variable clinical and diagnostic characteristics. Its incidence has dramatically increased in recent years due to technological improvements in cross-sectional imaging methods, rising in awareness of their existence, and increased in human life-span. Aim: To evaluate the clinical, radiological, and surgical characteristics of pancreatic cystic neoplasm. Methods: The clinical findings, diagnostic features, therapeutic managements, and oncological outcomes of 16 patients with pancreatic cystic neoplasm were retrospectively evaluated. Results: There were nine female and seven male patients, with a mean age of 54 years. More than half of the patients (56.3%) were asymptomatic. Abdominal pain and icterus were the most common symptom and sign, respectively. Computed tomography and magnetic resonance imaging showed the cystic lesion in all patients. Magnetic resonance imaging revealed a connection between cystic tumor with pancreatic duct in 8 (50%) cases. Pancreaticoduodenectomy was the most performed operation. Pancreatic adenocarcinoma with cystic degeneration and solid pseudopapillary neoplasia were the most frequent diagnoses at the final histopathology. Pancreatic fistula was developed in one case. One patient died during the postoperative period. Two patients who had adenocarcinoma developed recurrence during the follow-up period. Conclusion: The discrimination of pancreatic cystic neoplasms is usually difficult preoperatively. Therefore, the structure and the localization of the lesion, and the involvement of pancreatic ductal system should be clearly demonstrated by imaging modalities for a correct surgical planning.

KEYWORDS: Diagnosis of pancreatic cystic neoplasm, management of pancreatic cystic neoplasm

Introduction
Pancreatic cystic lesions are a heterogeneous group of pancreatic tumors, with an incidence rate of approximately 1% among all tumoral lesions in pancreatic origin [1]. These lesions are mostly diagnosed in advanced age groups and have variable clinical and diagnostic characteristics. In recent years, the incidence of pancreatic cystic lesions (PCLs) have dramatically increased due to several reasons including technological improvements in cross-sectional imaging methods, rising in awareness of their existence, and increased in human life-span. PCLs can be just divided into two main groups including non-neoplastic and neoplastic cysts. Most of the PCLs are non-neoplastic (developmental or inflammatory), and approximately 15-20% represent true neoplastic cysts called as pancreatic cystic neoplasm (PCN) [2]. According to the World Health Organization (WHO), PCLs are classified as epithelial or non-epithelial lesions based on the presence of epithelial tissue [3]. Inflammatory cysts, mainly develop after an attack of acute pancreatitis, are not considered as a neoplastic cyst because of the absence of an epithelial component. PCNs can also be benign or malignant. Discrimination of the PCLs by the diagnostic modalities is rather difficult. Therefore definitive diagnosis is usually made by the histopathological examination of the resected material. In this study, the clinical and diagnostic characteristics, therapeutic managements, and the oncological outcomes of 16 PCNs were presented and discussed in the relevant literature.
Patients and Methods

Between 2011 and 2014, 16 consecutive patients who underwent pancreatic surgery for PCN at Numune Training and Research Hospital, Ankara, Turkey was included in this retrospective study. Surgical indications were the presence of symptoms related to pancreatic pathology, elevated cancer antigen 19-9 (CA 19-9), suspected malignant findings, such as size of cyst above 4 cm, rapidly increase in the size of lesion within the short time, irregularity within the cyst wall, the presence of solid component within the cyst space, and other specific signs indicating any variant of PCN on imaging methods. Patients’ age, gender, comorbid diseases, symptoms and signs, routine biochemical parameters, preoperative serum carcino embriogenic antigen (CEA) and CA 19-9, American Society of Anesthesiologists (ASA) scores, preoperative abdominal ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) findings were recorded. The types of surgery, perioperative complications, and recurrence of the follow-up time were also noted.

Statistical analysis

The Statistical package for social science (SPSS 21.0 software, IL-Chicago-USA) was used for data analyzes. Descriptive analysis was done to demographic and clinical features. The results were presented as mean ± SD/percentages for continuous variables, and number/percentage for categorical variables.

Results

Sixteen patients (9 females and seven males) with a mean age of 54 years underwent pancreatic surgery for PCN. More than half of the patients (9, 56.3%) were asymptomatic. The non-specific abdominal pain was present in 4 cases while five patients were presented with clinically apparent icterus. All patients were operated on an elective basis. Most of the patients (10, 62.5%) had an accompanying systemic disease (6 were diabetes mellitus, 5 were hypertension, 4 were chronic obstructive lung disease, 1 was ischemic heart disease). None of the patients had anemia (Hb 10 mg/dL). However, direct hyperbilirubinemia, elevated alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) were found in five patients. CEA and CA 19-9 were considered to be elevated in 3 patients with pancreatic adenocarcinoma. All the demographic, clinical, and laboratory findings were presented in Table 1. The US was the first step radiological method in all patients but did not show any pancreatic lesion in 3 patients. Moreover, US revealed a connection between the cystic lesion and pancreatic ductal system in only three patients. CT and MRI demonstrated the cystic lesion in all patients. MRI showed a connection of cystic tumor with pancreatic duct in 8 (50%) cases. On CT, a connection between the cystic lesion and pancreatic duct was revealed in 3 (18.7%) patients. Pancreaticoduodenectomy (Whipple procedure) with or without pylorus-preserving procedure was the most performed operation. Pancreatic adenocarcinoma with cystic degeneration was the most frequent diagnosis at the final histopathology. Complications related to surgery were observed in only three patients. One patient died within the postoperative period of one month. Six patients with adenocarcinoma received chemotherapy after surgery. All patients were followed-up regularly. Two patients who underwent Whipple procedure for adenocarcinoma developed locoregional recurrences. Reoperation was performed for the recurrent lesions. The perioperative findings were presented in Table 2.

Discussion

Although a large number of PCN have been described in the literature, mucinous cystic lesions including mucinous cystic neoplasm (MCN) and intraductal papillary mucinous neoplasm (IPMN), non-mucinous cystic lesions such as solid-pseudopapillary neoplasm (SPN) and serous cystic neoplasm (SCN), and ductal adenocarcinoma with cystic degeneration comprise the majority of cases [2, 4]. Accordingly, these types of PCNs were identified at the final histopathological examinations of the resected materials in our study population. SCN is known as the most frequent variant of PCN with a reported rate of 30%; however, more than half of our patients had diagnoses of cystic ductal adenocarcinoma (CDA) and SPN, probably due to the small number of patients [5]. Although PCN is less frequent than a non-neoplastic cyst, its incidence increases with age, up to 10% of patients over 70 years old [6, 7]. However, the mean age of the patients in the present study was 54. There is a sex predilection between the variants of PCNs. While SCN and MCN are mostly seen in women, IPMN affects males slightly more frequently than females [4, 8]. However, our two patients who were diagnosed as IPMN were female, and the other types were also similar regarding gender. Most of the PCLs are asymptomatic and are often detected incidentally during an abdominal radiological method for evaluation of any unrelated condition [5]. The patients with PCN become symptomatic when the lesion causes pancreaticobiliary duct obstruction. In this condition, chronic abdominal pain, jaundice, and recurrent pancreatitis are the significant clinical findings of such patients. Exocrine and endocrine pancreatic insufficiency, weight loss and anorexia are usually related to larger malignant tumors. In our study, most of the patients were asymptomatic or had mild symptoms such as abdominal discomfort, and jaundice was present in only three patients. Imaging modalities such as CT and MRI play a critical role in the diagnostic workup of PCLs. In general, cystic pancreatic pathologies are detected by these radiological modalities in 2-4% of the population above 50 years [8]. However, it is important to rule out the possible underlying malignancy in PCLs. First of all, a background history of pancreatitis with an inflammatory appearance on CT is a strong evidence of pseudocysts. It should be kept in mind that pseudocysts may also occur in patients with chronic pancreatitis [9]. The formation of a pseudocyst usually requires, at least, one month from the onset of acute pancreatitis. These lesions are mostly single and round, and their size can reach up to 20 cm in size [10, 11]. The absence of a history of pancreatitis, presence of weight loss and cachexia, elevated serum tumor markers, and some suspected radiological findings such as irregularity and calcification at the wall of the cyst and solid component within the cyst should alert physicians for the PCNs. Differentiating between the subtypes of PCNs by imaging modalities can also be challenging. However, some particular radiographical characteristics may help the radiologists to distinguish a cystic lesion from one another. For instance, the presence of central scar is a highly suggestive sign for SCN while punctate calcifications on the periphery of microcystic spaces within the lesion, called as eggshell calcifications, strongly indicates malignancy in MCN [2, 5]. Also, the presence of mural nodules and cystic dilatation of central and/or branches of main pancreatic duct above 15 mm are highly specific to IPMN [12, 13]. Unfortunately, these radiological features are found in a small number of patients, thus definitive diagnosis is often made at the histopathology. The location is also another crucial feature of PCLs. While IPMN and adenocarcinoma are often located
Table 1 The demographic data, clinical symptoms and signs, and laboratory findings of the patients.

| Characteristics | n (%) |
|----------------|-------|
| **Age**        | 54.06±14.82 (22-70) |
| **Gender**     |       |
| Female         | 9 (56.3%) |
| Male           | 7 (43.7%) |
| **Comorbidity**| 10 (62.5%) |
| **Clinical symptoms and signs** |       |
| Asymptomatic   | 9 (56.3%) |
| Icterus        | 5 (31.2%) |
| Abdominal pain | 4 (25%) |
| Nausea and vomiting | 2 (12.5%) |
| Back pain      | 1 (6.2%) |
| **Laboratory findings** |       |
| Direct hyperbilirubinemia | 5 (31.2%) |
| Elevated ALP  | 5 (31.2%) |
| Elevated GGT  | 5 (31.2%) |
| Elevated CEA  | 3 (18.7%) |
| Elevated CA 19-9 | 3 (18.7%) |

Age was presented as mean±SD (range); other variables were presented as n (%).

in the head of the pancreas, MCNs are prone to develop in the body and/or tail sections. SCN and pseudocysts occur in any part of the organ [5]. The relationship of the cystic lesions of the pancreatic duct is also important to distinguish of the different types of PCLs. SCN and MCN are not related to the pancreatic ductal system; however, IPMN may sometimes be presented with a biliary obstruction due to its closed relationship with main pancreatic duct or its branches [14]. For this reason, both CT and MRI should be used in the initial evaluation of these lesions. Moreover, MRI with MRCP can be more useful in determining the possible connection between the ductal system and the cystic lesions, identifying multifocal diseases, and visualization of lesions within the branch ducts [15, 16]. However, it was reported that similar results can be obtained by multidetector CT thanks to the recent advances in technology [6]. Also, to CT and MRI/MRCP, endoscopic ultrasound (EUS) with fine-needle aspiration (FNA) can be used for further evaluation of PCNs. Although mural nodule or solid component within the cyst can be better visualized by EUS than the conventional imaging, limited value in distinguishing between malignant and benign lesions is the primary disadvantage of this technique. However, one of the main advantages of EUS is to enable the aspiration of cyst fluid for further analysis. Cytologic properties of the cyst fluid vary between the PCNs. Positive mucin staining is a significant feature of MCN and IPMN while positivity of glycogen stain is usually related to SCN. On the other hand, CEA concentration within the cyst is usually high in MCN and IPMN [17]. Pseudocyst has α-amylase/lipase-rich cyst fluid [2]. In the present study, abdominal US, CT, and MRI were the main parts of the diagnostic work-up. Characteristic radiological features mentioned above were detected in very few patients; however, the connection between the cyst and pancreatic ductal system were identified in almost all. Except pancreatic adenocarcinoma with cystic changes, PCNs have low-malignant potential. However, the possibility of malignancy varies between the types of PCNs. Most of the SCNs are cystadenomas and have an excellent benign course [7]. However, approximately 30% of IPMN and 20% of MCN carry a risk of malignancy [7, 18]. Surgical management of PCNs differs depending on various characteristics of the lesions such as the size, type, localization, and radiological features of the cyst and the association with the pancreatic ductal system. Intraoperative findings also play a role in determining the surgical technique to be applied to the lesion. Enucleation is the treatment of choice for small cysts with low risk of malig-
Table 2 Perioperative findings and recurrences of the patients (n= 16).

| Characteristics                          | n (%)      |
|------------------------------------------|------------|
| **ASA score**                            |            |
| ASA 1                                    | 1 (6.2%)   |
| ASA 2                                    | 8 (50%)    |
| ASA 3                                    | 6 (37.5%)  |
| ASA 4                                    | 1 (6.2%)   |
| **Localization of tumors**               |            |
| Head                                     | 7 (43.7%)  |
| Body                                     | 6 (37.5%)  |
| Tail                                     | 3 (18.7%)  |
| **Type of surgery**                      |            |
| Subtotal pancreatectomy                  | 6 (37.5%)  |
| Standard Whipple procedure               | 5 (31.2%)  |
| Distal pancreatectomy                    | 3 (18.7%)  |
| Whipple procedure with pylorus preserving procedure | 2 (12.5%) |
| **Final histopathology**                 |            |
| Adenocarcinoma                           | 6 (37.5%)  |
| Solid pseudopapillary neoplasia          | 4 (25%)    |
| Serous cystic adenoma                    | 3 (18.7%)  |
| IPMN                                     | 2 (12.5%)  |
| Mucinous cystic adenoma                  | 1 (6.2%)   |
| **Postoperative complication**           |            |
| Wound infection                          | 1 (6.2%)   |
| Atelectasis                              | 1 (6.2%)   |
| Pancreatic fistula                       | 1 (6.2%)   |
| Exitus                                   | 1 (6.2%)   |
| Elevated CA 19-9                         | 1 (6.2%)   |
| **Follow-up time (mo)**                  | 19.6±6.8 (8-31) |
| **Recurrence**                           | 2 (12.5%)  |

Follow-up time was presented as mean±SD (range); other variables were presented as n (%). mo: month
nancy [19]. Since most of the PCNs are found in the body or tail of the pancreas, open or laparoscopic distal/subtotal pancreatec-
tomy are the most common performed surgical options for these tumors [20]. On the other hand, PCNs with a high risk of ma-
lignancy and located in the head of the pancreas require pancre-
atoscoduodenectomy. Lymph node dissection should be necessary when there is a strong suspicion of malignancy [21]. Similarly, pancreaticoduodenectomy with or without pylorus-preserving technique, distal and subtotal pancreas resection was the most performed surgical modality in our case series. These operations are usually associated with higher complication rate than other surgical interventions. However, only one pancreatic fistula was developed in our study group. The other complications were not serious, but mortality was observed in one patient who had serious accompanying systemic diseases. Benign PCNs usually have a good prognosis. However, since there is limited data for surveillance intervals of all PCNs, such patients, especially those with the malignant lesion, should be follow-up at appropriate intervals after surgery. In our study, during the mean follow-up time of 19 months, no recurrence was observed in patients with benign PCNs while two patients who underwent Whipple procedure for pancreatic adenocarcinoma developed a locoregional recurrence.

**Conclusion**

In conclusion, PCLs should be carefully evaluated by using ad-
vanced radiological methods such as CT, MR/MRCP, and EUS. The structure and the localization of the lesion, and the involve-
ment of pancreatic ductal system should be clearly demonstrated for a correct surgical planning before the surgical intervention as possible as. Finally, these patients should be closely followed-up after surgery because of the possibility of recurrence.

**Authors’ Statements**

*Competing Interests*

The authors declare no conflict of interest.

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