

## CLINICOPATHOLOGICAL ANALYSES OF PANCREAS SPECIMENS IN 49 CONSECUTIVE PATIENTS

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### ABSTRACT

**Objective:** Pancreaticoduodenectomy (Whipple) and distal pancreatectomy (DP) operations are the preferred methods for indications ranging from benign inflammatory conditions to malignant neoplasia. Pathological examination of both Whipple and DP materials requires special attention to correctly evaluate many important prognostic factors. In this study, we aimed to present the pathology results of 49 Whipple and DP materials evaluated retrospectively.

**Materials and method:** Patients were evaluated in the Istanbul Ekin Private Pathology Laboratory between January 2010 and January 2016, operated in Çanakkale Onsekiz Mart University, General Surgery Clinic between January 2016 and August 2017, and Çanakkale State Hospital, General Surgery Clinic between January 2012 and January 2018. A total of 49 Whipple procedure and DP materials, both benign and malignant, were included in the study taking into consideration the age, sex, tumor size, surgical margin status, tumor localization, lymphovascular invasion, perineural invasion, number of lymph nodes, and presence/absence of metastatic lymph nodes.

**Results:** Out of the 49 cases, 12 (24.5%) underwent DP and 37 (75.5%) pancreaticoduodenectomy (Whipple). 27 (55.1%) cases were male and 22 (44.9%) were female, and the mean age was 61.4 years. 8 (16.3%) cases were benign and 41 (83.7%) were malignant. Of the 41 malignant cases, 17 were female and 24 were male; the mean age was 61.4 years. In terms of tumor localization, 6 (%14.6) tumors were localized to the ampulla, 8 (%19.5) to the pancreas distal, 2 (%4.9) to the duodenum, and 25 (%61) to the pancreas head. In 33 (%80.5) cases, the surgical margin was intact. In 18 (%43.9) cases, metastasis was present.

**Conclusion:** In pancreatic carcinoma cases that are treated with either Whipple or DP, macroscopy should be assessed pathologically, and the entire piece should be diligently sampled. By doing so, parameters fundamentally affecting the survey, such as tumor type and lymph node status, will be evaluated more accurately. In addition, rate of resection in benign lesions can be slightly reduced by performing FNAB with ERCP or EUS to the masses detected by imaging in the preoperative period.

**Keywords:** Whipple procedure, Distal pancreatectomy, Pancreas pathology, Pancreatitis.

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### Introduction

Pancreaticoduodenectomy (Whipple) (W) is a demanding and complicated procedure that is the preferred surgical technique for pancreatic head, duodenum, choledochal lower end, ampulla malignancies, and trauma or pancreatitis<sup>(1)</sup>. This procedure was first used by Allan Whipple in 1935 for tumors of the periampullary region and subsequently began to be used for many indications<sup>(2,3)</sup>.

Distal pancreatectomy (DP) is a resection procedure preferred for indications ranging from benign inflammatory conditions to malignant neoplasia, and it includes the region extending from the midline to the left side of the pancreas and excludes the duodenum and distal bile duct<sup>(4)</sup>.

In recent years, both procedures have become highly preferred due to a significant reduction in morbidity and mortality rates<sup>(4)</sup>. However, attention should be paid to the correct pathological and clini-

cal staging of these cases due to the oncologic therapies that have changed over the years.

Pathological examination of both Whipple and DP materials requires special attention to correctly evaluate many important prognostic factors. Careful pathological assessment of the tumor size, tumor location, invasion location, surgical margin status, presence of lymphovascular/perineural invasion, and presence/absence of metastatic lymph nodes is very important<sup>(5,6)</sup>.

In this study, we aimed to present the pathology results of 49 Whipple and DP materials retrospectively evaluated over a 6-year period.

### Materials and methods

We retrospectively evaluated who underwent pancreatic surgery in a six year period. Parameters were collected from medical records of patients any histopathological analysis report A form was created for all patients. All data were recorded to the forms for each patients. Patients were excluded in the situation of missing data.

A total of 49 who underwent surgical resection of pancreas with Whipple Procedure and DP due to both benign lesions of pancreas such as serous or mucinous cystadenoma and pancreatic carcinoma. Data were collected from Istanbul Ekin Private Pathology Laboratory between January 2010 and January 2016 for six year period, Çanakkale Onsekiz Mart University, General Surgery Clinic between January 2016 and August 2017, and Çanakkale State Hospital, between January 2012 and January 2018, were enrolled the study. The parameters for each patients were recorded to the forms including age, sex, etiology (benign- malign), size of the tumor, surgical margin status, localization of the lesion, lymphovascular invasion, perineural invasion, number of lymph nodes, and presence/absence of metastatic lymph nodes.

The Analyses of the data were performed using Windows and Microsoft Excel 2016.

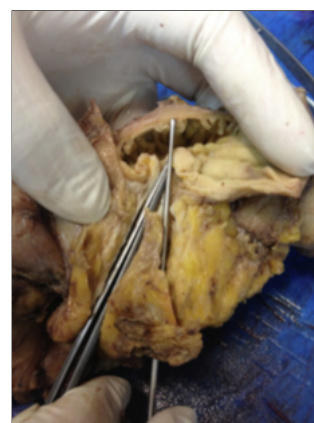
### Results

Of the 49 cases, 12 (24.5%) underwent DP and 37 (75.5%) pancreaticoduodenectomy (Whipple) (Figure 1-3).

Twenty seven (55.1%) cases were male and 22 (44.9%) were female, and the mean age was 61.4 years (age range: 38-85).



**Figure 1:** Mass localized in the ampulla of Vater, choledochal enlargement.



**Figure 2:** Mass localized in the ampulla of Vater (stille choledoch and wirsung).



**Figure 3:** Mass localized in pancreas, narrowing the choledoch in the follicular area.

Eight (16.3%) cases were benign (4 Whipple and 4 DP) and 41 (83.7%) were malignant (33 Whipple and 8 DP) (Tables 1,2).

Of the 41 malignant cases, 17 were female and 24 were male; the mean age was 61.4 years (age range: 40-85).

The smallest tumor had a diameter of 1.5 cm and largest tumor had a diameter of 12 cm, with a mean tumor diameter of 3.7 cm.

In 33 (%80.5) cases, the surgical margin was intact, whereas the tumor was adjacent to the poste-

rior surgical margin in 6 Whipple procedures (%14.6) and to the proximal surgical margin in 2 DP operations (%4.9).

Localization	Cases number, n= 8 (16.3%)	Surgical procedure
Mucinous cystadenoma	n=1	Distal pancreatectomy
Serous cystadenoma	n=1	Distal pancreatectomy
Pancreatic pseudocyst	n=2	Distal pancreatectomy
Chronic pancreatitis	n=4	Whipple procedure

**Table 1:** Tumor localization and surgical procedure in benign cases.

Localization	Malignant cases, n=41 (83.7%)	Surgical procedure
Ampulla of Vater	n=6 (%14.6)	Whipple procedure
Distal pancreas	n=8 (%19.5)	Distal pancreatectomy
Duodenum	n=2 (%4.9)	Whipple procedure
Pancreas head	n= 25 (%61)	Whipple procedure

**Table 2:** Tumor localization and surgical procedure in malignant cases.

In terms of tumor localization, 6 (%14.6) tumors were localized to the ampulla (W), 8 (%19.5) to the pancreas distal (DP), 2 (%4.9) to the duodenum (W), and 25 (%61) to the pancreas head (W) (Table 3).

Malignant cases	Benign cases
Ductal adenocarcinoma: n=38 (30:W, 8:DP)	Mucinous cystadenoma: n=1 (DP)
Neuroendocrine carcinoma: n=2 (W)	Serous cystadenoma: n=1 (DP)
Signet ring cell carcinoma: n=1 (W)	Chronic pancreatitis: n=4 (W)
	Pancreatic pseudocyst: n=2 (DP)
Total cases 41 (%83.7)	Total cases 8 (%16.3)

**Table 3:** Histopathological distribution of malignant and benign cases and preferred operating procedures.

W: Whipple procedure; DP: Distal pancreatectomy

In 23 (%56.1) cases, lymph node metastasis was not detected, whereas in 18 (%43.9) cases, metastasis was present.

The maximum number of dissected lymph nodes was 28 and the minimum number was 0 with a mean of 11.4.

Perineural invasion was present in 33 (%80.5) patients, and lymphovascular invasion was present in 19 (%46.3) patients.

According to the CAP protocol of the cases, 5 (12.2%) were stage T1c, 12 (29.3%) were stage T2, 21 (51.2%) were stage T3, and 3 (7.3%) was stage T4 (Table 4).

Stage T1	n=5 (%12.2)
State T2	n=12 (%29.3)
State T3	n=21 (%51.2)
Stage T4	n=3 (%7.3)
Total malignant cases	n=41

**Table 4:** Pathologic stage distribution of malignant cases.

Eight cases (16.3%) were benign, and 4 of these cases were chronic pancreatitis treated with Whipple procedure and the other 4 were cases treated with DP wherein 1 case showed mucinous cystadenoma, 1 case showed serous cystadenoma, and 2 cases showed pancreatic pseudocyst.

### Discussion

Whipple procedure is a surgically demanding and complex procedure that is preferred in many malignant and benign indications. Today, it is stated that Whipple procedure can also be preferred in benign neoplasms mimicking malignancy and pancreatitis cases presented as a periampullary mass<sup>(7)</sup>.

In a study conducted on 51 cases in 2012, Foroughi et al. reported that they did not detect malignancy in 7 (13.7%) cases and that these cases were benign neoplasms mimicking chronic pancreatitis and malignancy<sup>(3)</sup>. It has been reported in the literature that benign lesions can be detected in approximately 7% of cases treated with the Whipple procedure<sup>(7)</sup>.

In a study by Yeo et al. conducted on 650 cases, neoplasms mimicking pancreatitis and malignancy were detected in 32% of the cases<sup>(8)</sup>.

In our study, only 8 cases (16.3%) were benign, and 4 of these cases were chronic pancreatitis treated with Whipple procedure and the other 4 were cases treated with DP wherein 1 case showed mucinous cystadenoma, 1 case showed serous cystadenoma, and 2 cases showed pancreatic pseudocyst.

Pancreatic pseudocyst is a non-neoplastic lesion<sup>(9)</sup>. Its histopathological examination reveals no epithelium in the cyst wall, and only granulation tissue and inflammatory cells are observed. Serous cystadenomas and mucinous cystadenomas are neo-

plastic but benign lesions. Serous cystadenomas can manifest in the form of macro-micro-oligo or multicystic masses. Typically, a scar may be present in the center, and the cyst is filled with clean serous fluid. Mucinous cystadenoma is known to be a dominant condition of the female sex. The cyst content is of dense mucinous character and the cyst wall is covered with columnar epithelium secreting mucin. Ovarian stroma can be seen on the cyst wall. In addition, both cystadenomas are unrelated to the main duct system<sup>(10,11)</sup>. In our resections, the rate of benign cases (16.3%) was slightly higher than that reported in the literature. This was attributed to the small number of cases in our study.

Although preoperative imaging methods are often able to distinguish malignant/benign lesions, benign lesions sometimes mimic malignancy and may cause Whipple or DP resections. Cytological diagnosis can be made by biopsy with endoscopic retrograde cholangiopancreatography (ERCP) in masses localized in the ampulla and distal choledoch detected by imaging in the preoperative period, and biopsy can be performed on all masses localized to the pancreas by fine needle aspiration in the presence of endoscopic ultrasound (EUS)<sup>(12,13)</sup>. Performing these operations in the preoperative period will decrease the resection rate in benign lesions.

In our benign cases, no previous interventional procedures were performed, no biopsy was performed, and the cases were directly operated due to suspicion after imaging.

In our study, 41 (83.7%) of the cases were malignant. Of these, 33 underwent Whipple and 8 DP procedures.

In a study of 51 cases treated with the Whipple procedure, malignancy rate was reported to be 86.3% (3). In this study, both the number of cases and malignancy rate are consistent with our study. In the study by van Roest et al. (2008), malignancy rate was reported as 85%<sup>(14)</sup>.

In the study by Yeo et al, malignancy rate was reported to be 68%<sup>(8)</sup>. We believe that the low malignancy rate in this study was due to the fact that the lesions evaluated in the benign category were not pure benign lesions and that some lesions that already entered the neoplastic process were also evaluated in the benign category, such as neuroendocrine tumors, ampullary adenoma, and gastrointestinal stromal tumors. In our study, 2 neoplastic/benign cases out of the 8 cases in the benign category were mucinous cystadenoma and serous

cystadenoma.

Among the malignant cases in our study, ductal adenocarcinoma was the most common, whereas neuroendocrine carcinoma and stone ring cell carcinoma were less common. Ductal adenocarcinoma is the most common malignancy of the pancreas, followed by neuroendocrine tumors and histologic subtypes of signet-ring cell carcinoma<sup>(15,16)</sup>.

The majority of cancer of the pancreas about 70% arise in the head of the gland and only 20-30% in the body and tail<sup>(17)</sup>. In our study, 25 (%61) of the cases were head of pancreas.

In the literature, synchronous cases associated with pancreatic primary tumors are mentioned in some case reports. Among these, synchronous pancreatic clear cell carcinoma and gastrointestinal stromal tumor of the stomach and pancreatic ductal adenocarcinoma and thyroid medullary carcinoma have been reported<sup>(18,19)</sup>. One of these cases was our case report that was one of the ductal adenocarcinoma cases included in this study treated with the Whipple procedure<sup>(18)</sup> (Figure 4).

When surgical margin was evaluated in malignant cases, 80.5% of the cases had intact surgical margins. The tumor was adjacent to the posterior surgical margin in 14.6% Whipple procedure cases and to the proximal surgical margin in 4.9% DP procedure cases. In the literature, Foroughi et al. reported an 81.8% rate of intact pancreatic surgical margin, whereas Yeo et al. reported a rate of 71% rate<sup>(3,8)</sup>.

Foroughi et al. also reported that most of their cases were in the advanced stage (T3)<sup>(3)</sup>. In our study, most of our cases were also in the advanced stage (T1: 12.2%, T2: 29.3%, T3: 51.2%, T4: 7.3%). In the pathologic staging of pancreatic and ampullary carcinomas, it is very important to evaluate lymph node metastasis in the survey of patients<sup>(20)</sup>.

Foroughi et al. did not detect lymph nodes in 25% of the cases in their studies<sup>(3)</sup>. In our study, only one case did not involve any lymph nodes, and the maximum number of dissected lymph nodes was 28. Although lymph node metastasis was not detected in 23 (%56.1) of the cases, it was present in 18 (%43.9) cases.

As reported by Adsay et al., macroscopic sampling is very important when evaluating pancreatic resection specimens. In particular, after orienting to the resection for the surgical margin as well as to obtain the maximum number of lymph nodes, the entire wall of the piece should be sampled like peel-

ing an orange skin<sup>(21)</sup>. We always use this method when routinely performing macroscopic sampling. For this reason, we believed that we obtained slightly more lymph nodes in number compared with some studies reported in the literature.

In conclusion, in pancreatic carcinoma cases that are treated with either Whipple or DP, macroscopy should be assessed pathologically, and the entire piece should be diligently sampled. By doing so, the parameters fundamentally affecting the survey, such as tumor type and lymph node status, will be evaluated more accurately. In addition, the rate of resection in benign lesions can be slightly reduced by performing FNAB with ERCP or EUS to the masses detected by imaging in the preoperative period.

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