

PATHOLOGY OF PANCREATODUODENECTOMY SPECIMENS IN INDUSTRIAL ORGANIZATION OVER THREE YEARS**Dr. Seema Chadha¹, Dr. Niharika Singh², Dr. Rakesh Kumar³, Dr. Sanjeev Singhal⁴, Dr. Shilpa Ruhela⁵,
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ABSTRACT

Background: Whipple procedure is performed for various tumors of the periampullary region. Mortality and morbidity of patients undergoing Whipple procedure has been reduced significantly. The prognosis of such patients invariably depends on precise histopathological examination of Whipple specimen including tumor type, tumor site, tumor size, tumor extent, margin status, angioinvasion, perineural invasion and lymph node status. **Material and Methods:** A retrospective descriptive study was conducted in the Department of Pathology, Northern Railway Central Hospital. Various histopathological parameters like, location of the tumor, tumor morphology, grading, lymphovascular/perineural invasion, margin status and lymph node status were assessed. Also TNM staging of the tumor was done. **Result:** Sixteen patients underwent Whipple's Pancreaticoduodenectomy procedure during the study period. Among the 16 specimens, malignant tumor was present in 12 cases (75%), whereas 4 cases (25%) were benign. Periampullary mixed carcinoma was the predominant tumor (25%) followed by pancreatic adenocarcinoma (18.75%), neuroendocrine tumor (18.75%), periampullary duodenal (12.5%), ampullary carcinoma (12.5%), and papillary adenocarcinoma of common bile duct (6.25%). Benign gastrointestinal stromal tumor were (6.25%). **Conclusion:** Pancreaticoduodenectomy specimen requires detailed histopathological evaluation for proper histological type, stage and other features which affect patient survival following Whipple's procedure. The present study showed that most of our subjects were diagnosed with malignancy, at an advanced stage, and further research is needed to develop practical methods for early diagnosis.

KEYWORDS: Whipple, Pancreaticoduodenectomy, ampullary.**INTRODUCTION**

In the year 1898 Dr. William Stewart Halsted performed first successful local resection of a periampullary tumor.^[1] The first successful regional resection of the duodenum and portion of pancreas (pancreaticoduodenectomy) for a periampullary tumor was performed by Kausch, in 1909, and was reported in 1912.^[1-3] In the year 1935, Whipple published a paper, which popularized the regional operative procedure for periampullary tumors and Brunschwig extended the indications for pancreaticoduodenal resection to include pancreatic cancer.^[1-4]

Today the Whipple procedure is performed for variety of tumors of periampullary region involving the head of the pancreas, ampulla of Vater, common bile duct and duodenum.^[5] Pancreaticoduodenectomy, or the Whipple procedure, is a complex high-risk general surgical procedure.^[1,2]

The mortality and morbidity associated with the Whipple's procedure has significantly improved by advances in surgical technique, perioperative care and large number of surgeries in big centers.^[1,2,5]

Pathological assessment of surgical specimens from pancreaticoduodenectomy (Whipple operation) needs special attention in order to accurately evaluate many factors that are prognostically important including tumor location, tumor size, tumor grade, tumor location, its extension, surgical margins status, vascular or perineural invasion and lymph node status.^[6-8]

The aim of this study was to examine the distribution and histopathologic findings in pancreaticoduodenectomy surgical specimens in a tertiary level hospital over a period of four years.

MATERIALS AND METHODS

A retrospective descriptive study was conducted in the Department of Pathology, Northern Railway Central Hospital from January 2016 to April 2019.

The specimens were fixed in 10% formalin, grossed and processed as per standard protocol. Location of the tumor, histopathologic categorization, grading, lymphovascular and perineural invasion, margin status and lymph node status were assessed. TNM staging of the tumor was done based on 8th AJCC classification.

Records of pathologic specimens were extracted and details of diagnosis and staging were evaluated.

RESULTS

Sixteen patients underwent Whipple's Pancreaticoduodenectomy procedure during a period of

40 months (January 2016 to April 2019). Ten (62.5%) patients were males and six (37.5%) were females. The mean age of the patient was 54.12 years (age ranging from 30 to 74years). Most common age group was 51 to 60 (Table 1).

Table 1: Age wise distribution of patients undergoing Pancreaticoduodenectomy.

Age(yrs)	Number (%)
30-40	1(6.25)
41-50	3(18.75)
51-60	8(50)
61-70	2(12.5)
71-80	2(12.5)

Among the 16 specimens, malignant tumor was present in 12(75%) cases; where as 4 cases (25%) were benign. Periapillary mixed carcinoma was the predominant tumor (25%) followed by pancreatic adenocarcinoma (18.75%), neuroendocrine tumor (18.75%),

periapillary duodenal (12.5%), ampullary carcinoma (12.5%), and papillary adenocarcinoma of common bile duct (6.25%). Benign gastrointestinal stromal tumor constituted (6.25%) (Table 2).

Table 2: Histopathological Diagnosis of Pancreaticoduodenectomy specimen.

DIAGNOSIS	NUMBER (%)
Malignant lesions	12(75)
Periapillary mixed	04(25)
Periapillary duodenal carcinoma	02(12.5)
Pancreatic ductal adenocarcinoma	03(18.75)
Ampullary carcinoma	02(12.5)
Papillary adenocarcinoma CBD	01(6.25)
Benign lesion	04(25)
GIST	01(6.25)
Neuroendocrine tumor	03(18.75)

Maximum tumor dimension, tumor differentiation, mean number of lymph node dissected, lymph node status, resected margin status, lymphovascular and perineural invasion among the different adenocarcinoma are demonstrated in Table 3.

Most of the periampullary, mixed and duodenal, pancreatic, ampullary and NET were moderately differentiated. There was significant difference in tumor size among periampullary and ampullary carcinomas, pancreatic tumors were the largest. Lymphovascular and perineural invasion varied in different tumor types, both

were present in most of the cases. The average numbers of lymph nodes dissected were 24.5. The lymph node involvement by tumor varied in different tumor types. Lymph nodes were involved by tumor in all the six cases of Periapillary adenocarcinoma (100%). Adequate surgical margin clearance was achieved in most of the cases except in one case of periampullary mixed carcinoma.

Pathologic staging of the malignant tumors is demonstrated in Table 4.

Table 3: Histopathological findings of tumors in Pancreaticoduodenectomy specimens.

	Periapillary mixed carcinoma (n=4)	Periapillary duodenal carcinoma (n=2)	Pancreatic Adenocarcinoma (n=3)	Ampullary carcinoma (n=2)	Papillary Adenocarcinoma CBD (n=1)	Neuroendocrine tumor (n=3)
Tumor diameter (cm)						
Mean	2.9	1.6	3.13	0.55	0.5	1.3
range	2-4.4	1.5-1.7	1.4-6	0.5-0.6		0.5-2.5
Tumor differentiation						
Well	1(25%)					1(33.3%)
Moderate	3(75%)	2(100%)	2(66.6%)	2(100)	1(100%)	2(66.6%)
Poor			1(33.3%)			

No. of lymph nodes dissected	23-39	21-36	9-28	22-26	20	7-50
Lymph node involvement						
Involved	4(100%)	2(100%)	2(66.6)			2(66.6)
Reactive			1(33.3)	2(100%)	20(100%)	1(33.3)
LVI						
Present	3(75)	1(50)	2(66.6)	2(100)		3(100)
Absent	1(25)	1(50)			1	
PNI						
Present	3(75)	1(50)	2(66.6)		1	2(66.6)
Absent	1(25)	1(50)		2(100)		1(33.3)
Resected margin status						
Involved	1(25)					
Free of tumor	3(75)	2(100)	3(100)	2(100)	1(100)	3(100)

Table 4: Pathological staging of malignant tumors.

Pathological staging of tumors (pT)	Number
pT1	3
pT2	2
pT3	8
pT4	2

DISCUSSION

In United States the periampullary adenocarcinoma which includes the four tumors account for >30,000 cancer related deaths per year. These tumors rank as the fifth leading cause of cancer deaths in this country, ranking behind lung, breast, colorectal, and prostate cancer.^[9]

In our study we observed that about 4 cases (25%) of the patients had benign pathology. A study done by Foroughi F et al observed that 7 patients (13.7%) had no malignant lesion and had benign lesions such as chronic pancreatitis or benign neoplasms mimicking malignancy.^[6] On reviewing the literature it was found that around 7% of the histology obtained at a Whipple resection were benign.^[6,10] However, in some studies this percentage was much higher. Margijske et al. reported 15% benign lesions in their series.^[6,11] Also, in analysis of 650 Whipple specimens, Yeo reported that 32% of specimens had various benign lesions including chronic pancreatitis in 71 patients (11%), neuroendocrine tumors in 31 patients (5%), pancreatic cystadenoma in 25 patients (4%), ampullary adenoma in 21 patients (3%), and gastrointestinal stromal tumors in 10 patients (2%).^[6,12]

In our study periampullary carcinoma was the predominant cancer on pancreaticoduodenectomy (PD) specimens which was similar to study done by Foroughi F et al and was in contrast to other studies by Duffy et al, Talamani et al and Howe et al which reported ampullary carcinoma as the predominant cancer.^[6,13] We found ampullary carcinoma in only 2 cases (12.5%). Western literature reveals pancreatic adenocarcinoma to be the

commonest finding in PD specimens. On review of 650 pancreaticoduodenectomies Yeo et al found 43% cases to be pancreatic adenocarcinoma.^[6,12] We found only three cases (18.75%) of pancreatic adenocarcinoma and one case of Pancreatic neuroendocrine tumor, which is lower, compared to their studies. This might be due to the small number of cases that we studied and an extensive study of larger sample size would highlight the true incidence of pancreatic malignancy in our country.

In a study done by Yeo et al they did multivariate analysis of 443 patients with periampullary adenocarcinoma. They observed four factors to adversely affect survival: 1) tumor diameter ≥ 3 cm 2) the presence of positive resection margins 3) the finding of lymph node metastases in the resected specimen and 4) the presence of a poorly differentiated tumor.^[12] They also reported ampullary carcinomas to have the smallest tumor dimension with lower incidence of positive resection margins, which is similar to our findings; we found the mean tumor diameter to be smallest in ampullary carcinoma (mean 0.55 cm).

In our study 75% of the cases were moderately differentiated, similar findings were seen by Duffy JP et al, 60% and Schmidt CM et al whereas Foroughi F et al reported 60% and Dhakhwa R et al reported 80% well differentiated tumors.^[5,6,12,13,14]

Surgical resected margins were free of tumor in 93% of cases in our study similar findings were seen by Duffy JP et al, Dhakhwa R et al and Foroughi F et al.

Margin status has been shown to correlate with survival outcomes. Yeo et al. showed in their series of 201 patients that the five-year survival in those with a negative margin was 26% (median survival 18 months) compared to those with a positive margin 8% (Median survival 10 months).^[12]

Lymphovascular invasion was present in 73% of the cases in our study, which is similar to findings reported

by Schmidt CM et al, Dhakhwa R et al and Foroughi F et al. Perineural invasion was seen in 60% of the cases in our study.^[5,6,14] In a study by Winter et al., the incidence of Perineural invasion was 91% that has been shown to be poor prognostic factor.^[5]

The number of lymph nodes dissected and involved by tumor is one of the most important prognostic factors in pancreatic and ampullary carcinomas, and this also contributes to more accurate pathologic staging and predicting survival outcomes.^[5,6,15] In our study 66% cases were positive for lymph node metastasis.

In our study most patients were diagnosed in advanced pathologic stage (T3); similar findings are reported by Dhakhwa R et al and Foroughi F et al.^[5,6] Thus it highlights the fact that more precise assessment and evaluation of signs and symptoms which will lead to early detection of malignant lesions is required.

CONCLUSION

Our study concludes that pancreaticoduodenectomy specimen requires detailed histopathological evaluation for proper histologic type, stage and other features which affect patient survival following Whipple's procedure. The present study showed that most of our patients are diagnosed with malignancy, at an advanced stage, and further research is needed to develop practical methods for early diagnosis.

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