ORIGINAL ARTICLE

Radical surgical management of periampullary duodenal adenocarcinoma: A single institution experience

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Abstract

Objective: To share a single-centre experience with radical resection of adenocarcinoma of the second part of duodenum.

Methods: The retrospective review was conducted at Shaukat Khanum Memorial Cancer Hospital, Lahore, and comprised data of patients who underwent pancreaticoduodenal resection for duodenal adenocarcinoma from January 1999 to December 2012. Patient characteristics and histopathological variables were assessed. Post-op complications, median disease-free span and overall survival were assessed. Expected 5-year disease-free and overall survival were calculated using Kaplan Meier curves.

Results: Of the 12 patients whose records were included, 8(66.6%) were men and 4(33.33%) were women. Overall median age was 55years (range: 38-70 years). Jaundice was the predominant symptom in 9(75%) patients. Five complications were observed during the post-operative period. Median disease-free and overall survival was 14.5(0-140) and 17.5(1-140) months respectively. Expected 5-year disease-free and overall survival were 56% and 21% respectively. Patients who survived >24 months had underlying well differentiated tumours, negative surgical margins, absence of perineural invasion and pancreatic involvement.

Conclusion: Peri-ampullary duodenal adenocarcinoma is a rare malignancy. In selected patients, pancreatic oduodenectomy produces acceptable results.

Keywords: Survival, Duodenal cancer, Pancreaticoduodenectomy. (JPMA 64: 1260; 2014)

Introduction

Primary duodenal adenocarcinoma is a rare malignancy and accounts only for 0.5% of all gastrointestinal cancers.[1,2] Due to relative rarity, its natural course, patterns of metastasis, management options and survival is not well known. Data mainly comes from retrospective studies with small number of patients managed over decades with various treatment modalities. More importantly, patients with duodenal adenocarcinoma are grouped with peri-ampullary tumours for management leading to ambiguity in outcome data.[3,4] Patients who underwent radical surgery for duodenal cancer in a significant number of case series is small and ranges from 8 to 31patients.[5-7] Extent of surgery also remains debatable, but pancreatic oduodenectomy (PD) is preferred despite significant morbidity and mortality due to superior survival outcomes, especially in tumours of second portion of duodenum.[8] The objective of the current study was to share experience of pancreatic oduodenectomy for adenocarcinoma of the second part of duodenum treated over a period of 14 years at a cancer hospital.

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Materials and Methods

The retrospective review was conducted at Shaukat Khanum Memorial Cancer Hospital, Lahore, and comprised data of patients who underwent pancreatic oduodenal resection for duodenal adenocarcinoma from January 1999 to December 2012. Records of patients diagnosed with duodenal adenocarcinoma on histopathology of resected pancreatic oduodenectomy specimen were retrieved from the database and analysed, while those related to patients of pancreatic, ampullary and lower bile duct adenocarcinomas were excluded. All patients had peri-ampullary duodenal adenocarcinoma. Baseline investigations, liver function tests (LFTs), clotting profile and computed tomography (CT) scan of abdomen were performed in all patients. Endoscopic ultrasound (EUS), after it became available at the hospital in 2005, was performed in all patients with suspected peri-ampullary malignancy. Patients were staged according to American Joint Committee on Cancer (AJCC) staging 7th edition for small bowel cancer.[9] Endoscopic retrograde cholangiopancreatography (ERCP) with stent insertion was performed in patients with biochemical evidence of obstructive jaundice. The surgical procedure of choice was standard Whipple's operation. It involved resection of pancreatic head, duodenal cap, distal stomach and

common bile duct. Reconstruction was performed with pancreatico-enterostomy, gastro-enterostomy and hepatico-enterostomy. Patients were kept in intensive care unit (ICU) for 1 day and were shifted to floor if stable clinically. Main indications for adjuvant chemotherapy were poorly differentiated tumours, presence of perineural invasion and node positive disease. Adjuvant radiation was primarily used in patients with positive surgical margins. They were followed up 3 monthly for 1 year and 6 monthly for 4 years with yearly CT scans. After 5 years of follow-up, patients were followed annually.

Patient characteristics, including demographics, predominant symptoms, American Society of Anaesthesia (ASA) class and clinical stage at presentation were noted. Categorical variables were expressed as frequency and percentage. Continuous variables were expressed as mean ± standard deviation (SD) or median and range. Histopathological variables, including pathological tumour stage, nodal involvement, margin status, grade, perineural and lymphovascular invasion, were assessed. Mean hospital stay, median disease-free survival (DFS) and overall survival (OS) were calculated. DFS time was defined as time between surgery and development of relapse. OS time was defined as time between surgery and date of death or last follow-up. Expected 5-year DFS and OS were calculated using Kaplan Meier curves. Patients with median survival >24 months were separately analysed and their clinicopathological variables were assessed.

Results

Of the 12 patients whose records were included, 8(66.6%) were men and 4(33.33%) were women, the male-to-female ratio being 2:1. Overall median age was 55years (range: 38-70 years). Jaundice was the predominant symptom in 9(75%) patients. ERCP with stent insertion was performed in all patients, while EUS was performed in 9(75%). Most common clinical stage at presentation among the 9(75%) patients was stage I in 5(55%) (Table-1).

Various histopathological variables in patients who underwent PD were also noted (Table-2). T2 in 4(33%) patients was the most common tumour stage and 7(58%) had node negative disease. On histopathology, stage III was the most common stage and was seen in 5(42%). Negative surgical margins were achieved in all but 1(8%) patient. Perineural invasion was identified in 4(33%) patients. Mean number of nodes removed was 14.5±7.5 (range: 2-24). Nine (75%) patients had 12 or more lymph nodes removed. Mean number of positive nodes was 1.5±2.67 (range: 0-8).Focal pancreatic invasion was seen in 4(33%) patients.

Table-1: Patient characteristics.

		Number (N=12)	Percent (%)
Gender	Male	8	67
	Female	4	33
Predominant symptom	Jaundice	9	75
	Pruritis	1	8.3
	Post cholecystectomy nausea	1	8.3
	Abdominal pain	1	8.3
ASA status	I	1	8
	II	11	92
Clinical Stage*	I	5	55
	II	3	33
	III	1	12

ASA: American Society of Anaesthesiologists.

Table-2: Histopathological variables in patients who underwent pancreaticoduodenectomy.

		Number (N=12)	Percent (%)
P+T stage	T1	2	17
	T2	4	33
	T3	3	25
	T4	3	25
pN stage	N0	7	58
	N+	5	42
Pstage	Stage I	4	33
	Stage II	3	25
	Stage III	5	42
Grade	Well	5	42
	Moderate	3	25
	Poor	3	25
	Squamous differentiation	1	8
Margins	Positive	1	8
	Negative	11	92
Perineural invasion++	Present	4	44
	Absent	5	56
Lymphovascular invasion++	Present	0	-
	Absent	9	100
Pancreatic invasion	Present	4	33
	Absent	8	67

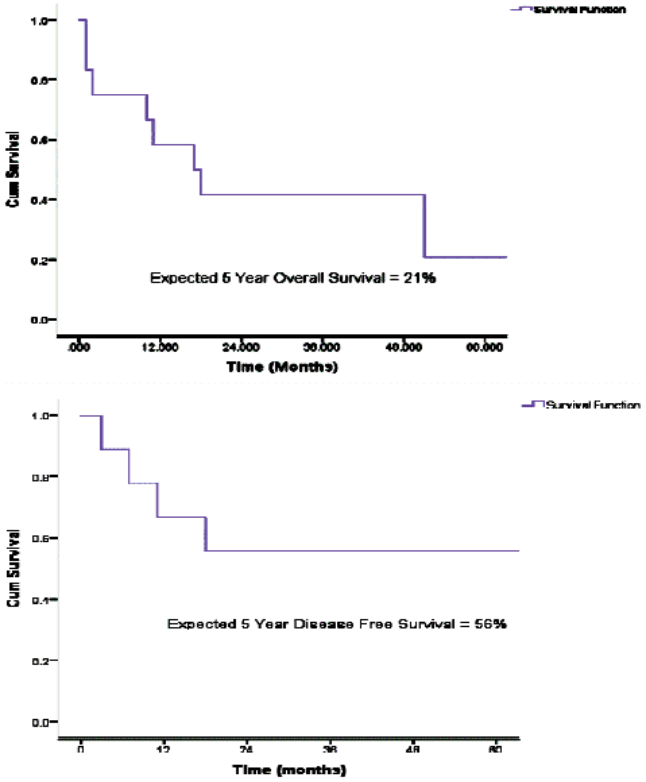
Footnote: + Pathological.
++ Variables with missing data.

Table-3: Post-op complications and sites of disease relapse in patients after pancreaticoduodenectomy.

		Number (N=12)	Percent (%)
Complications	Intra-abdominal infection	2	17
	Intra-abdominal bleed	1	8
	Wound infection	2	17
Failure sites	Liver	2	50
	Liver+ Para-aortic nodes+ Peritoneum +surgical bed	1	25
	Liver + surgical bed	1	25

Table-4: Clinicopathological characteristics, treatment modalities and outcome in patients who survived >24 months.

	Age	Gender	ASA status	Pathological stage	Grade	Surgical margins	Perineural invasion	Nodes +ve/nodes removed	Pancreatic invasion	Chemotherapy	Radiation therapy	Duration of survival (months)	Alive at last follow up
1	53	F	II	III	Well	-ve	-	1/7	-ve	Adjuvant	Adjuvant	140	Yes
2	58	M	II	I	Well	-ve	-	0/16	-ve	-	-	51	No
3	70	F	II	I	Well	-ve	-ve	0/2	-ve	-	-	33	Yes



Mentions: During follow up, four patients relapsed and all had metastasis to liver. One patient had local as well as distant relapse. One patient with positive surgical margins had diffuse metastasis in abdomen. Eight mortalities were observed in the follow up period. Median disease free and overall survival was 14.5 (0-140) and 17.5 (1-140) months respectively. The longest survival time was 140 months. Out of patients who survived >24 months, 1 developed diffuse large B cell lymphoma four years after surgical resection of duodenal adenocarcinoma. He died secondary to tumorlysis syndrome after initiation of chemotherapy for lymphoma. Expected 5 year disease free and overall survival was 56% and 21%.

Figure: Expected 5-year overall and disease free survival in patients who underwent pancreaticoduodenal resection for duodenal adenocarcinoma.

Mean hospital stay was 15.5±10.3 days. Five (42%) patients developed complications, including intra-abdominal bleeding in 1(8%), intra-abdominal infection in 2(6.6%) and wound infection in 2(6.6%) patients. One patient with intra-abdominal bleeding required re-exploration with repair of superior mesenteric artery tear. Both patients with wound infection were managed conservatively. One (8%) patient with intra-abdominal infection required CT-guided drainage and other required re-exploration with washout. Four (33%) patients relapsed in the follow-up period and all had metastasis to liver. One (8%) patient had local as well as distant relapse. One (8%) patient with positive surgical margins had diffuse metastatic disease in the abdomen. Eight mortalities were observed in the follow-up period. Median DFS and OS were 14.5 (range: 0-140) and 17.5 (range: 1-140) months respectively. Complications and sites of relapse were all noted (Table-3).

Expected 5-year DFS and OS was 56% and 21% (Figure). Also noted were various characteristics and pathological variables in patients with primary duodenal adenocarcinoma who survived for more than 24 months (Table-4). All patients belonged to ASA class II. All tumours were well-differentiated with negative surgical margins. Besides, no pancreatic involvement or perineural invasion was present. Out of three patients who survived >24 months, 1(33%) developed diffuse large B cell lymphoma four years after surgical resection of duodenal adenocarcinoma. He died secondary to tumour lysis syndrome (TLS) after initiation of chemotherapy for lymphoma.

Discussion

The study shared in-hospital experience with radical surgical management of adenocarcinoma duodenum treated over 14 years. All patients in the current study had tumours involving the second portion of duodenum. Survival comparable to published reports was achieved and distant metastasis to liver was the most frequent site of first relapse. Patients who survived longer had well-differentiated tumours, no pancreatic or perineural invasion and negative surgical margins. In the present study, 75% patients had clinical jaundice, but biochemical evidence of jaundice (raised bilirubin and alkaline phosphatase) was found in all patients. Due to suspected prolonged waiting time before surgery, all patients underwent ERCP and stent placement.

A significant number of patients with duodenal adenocarcinoma are inoperable at presentation.

Resectability rate in surgical management of duodenal adenocarcinoma can be less than 43% while PDrate might be as low as 19%.[10,11] This significantly reduces the number of patients who undergo radical surgery for duodenal cancer. Although segmental resection can be performed in cases where malignancy involves third or fourth part of duodenum, but PD is generally performed in tumours of the second portion.[11-13] Poultsides et al.[14] are credited with the largest retrospective review comprising 122 patients with diagnosis of duodenal adenocarcinomas managed with PD. Overall survival at 5 year was 48% and lymph node metastasis was the only independent predictor of survival. Positive margins were present in 8% patients. Complication rate was 36% with 13% patients developing pancreatic fistula. In the present study, one (8%) patient had margin positive resection and complication rate was 42%. None of the patients developed pancreaticojejunal leak and subsequent fistula. DFS at 5 years was 56% and overall survival was 21%. The difference in estimated DFS and OS represents patients who died in the post-operative period without developing a recurrence. Similar 5-year OS ranging from 20-30% has been reported in multiple studies.[6,7,15,16] The overall complication rate and short-term mortality of PD for peri-ampullary tumours ranges from 20% to 60% and 30-day mortality is close to 10%.[17-21] Previous reports and the current study demonstrate similar outcomes underscoring effective role of this procedure in patients with duodenal cancer. In a recent study on management of duodenal adenocarcinoma, 44 of 76 patients underwent PD.[8] Margins were positive in 7% patients and 11% patients developed a pancreatic fistula. Lymph node involvement was an independent predictor of survival, and median survival was 25 months. A correlation between serum bilirubin and morbidity/mortality could not be determined in the current study since all patients had normal bilirubin levels at the time of surgery. AJCC recommends removal of 6 lymph nodes for small bowel cancer staging. A recent study showed that if 10 lymph nodes are retrieved, the prognostic ability of AJCC staging system may improve.[22] In the current study, the mean number of lymph nodes removed was 14.5 (2-24), and 75% patients had 12 or more lymph nodes removed which was adequate for pathological staging.

Factors like grade, tumour size, nodal involvement, perineural invasion, pancreatic invasion and negative margins have been linked to outcomes in patients with duodenal adenocarcinoma.[3,12,22-26] Although prognostic factors were not determined in the present study, but patients with a median survival >24 months after resection were separately analysed. All the 3 patients had well-differentiated tumours, absence of perineural invasion, negative surgical margins and no pancreatic invasion. Distant relapse is the most common type of relapse in patients with duodenal adenocarcinoma and is seen in 59-92% patients.[5,15,26,27] Liver was the first site of relapse in all patients in the current study.

A limitation of the study was its retrospective nature and small sample size which stems from the rarity of this pathology. Since only patients who underwent PD were included, comparison with other surgical options like segmental resection could not be made. Also, since we reviewed only patients with peri-ampullary tumours, outcome of duodenal adenocarcinoma in the 1st, 3rd or 4th portion could not be determined.

Conclusion

The controversial role and extent of surgery in duodenal adenocarcinoma stems from its low incidence and late presentation. PD provides effective relief of symptoms and acceptable DFS and OS in patients who undergo successful resection with favourable prognostic variables in peri-ampullary duodenal adenocarcinoma.

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