Total mesopancreas excision in pancreaticoduodenectomy and its prognostic outcomes in cancer head pancreas

Original Article

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ABSTRACT

Background: Pancreatic ductal adenocarcinoma has one of the worst survival rates, even after surgical resection, 5-year survival rates only reach 20%. Many factors contribute to this poor outcome including resection margins, lympho-vascular and perineural invasion, tumor size, tumor type, tumor differentiation, and nodal metastasis.

Excision of the entire mesopancreas can result in complete clearance of retroperitoneal tissue and improve the prognosis of patients with pancreatic head cancer.

It is mandatory to excise total meso-pancreas during the surgery for pancreatic head adenocarcinoma which may increase R0 resections and increase lymph node clearance.

The aim of the study: Is to evaluate total mesopancreas excision in pancreaticoduodenectomy and its effect on surgical prognosis in cancer head pancreas.

Patients and Methods: This is a prospective study including 40 patients that have pancreatic head adenocarcinoma planned for pancreaticoduodenectomy.

Patients included in the study had resectable adenocarcinoma located in head/neck/uncinate process of the pancreas. We excluded metastatic adenocarcinoma of head/neck/uncinate process of the pancreas and locally advanced pancreatic carcinoma with vascular invasion.

Results: Recurrence occurred in 14 (35%) of patients during follow-up, this result had a statistically significant relationship with resection margin status R1 (*P<0.001*). Positive meso-pancreatic margin involvement was held accountable for 12 (30%) of the recurrent cases alone or concomitant with other margins.

The overall 1-year disease free survival rate was 56.1% of patients with a mean of 9.962 months. Disease free survival was significantly better in free meso-pancreatic margin patients (R0 MP) compared with positive meso-pancreatic margin patients (R1 MP) (11.502 vs. 7.083 months, *P<0.001*).

Evaluation of the relationship between meso-pancreatic margin status and the presence of either lympho-vascular invasion or perineural infiltration was statistically insignificant.

Conclusion: Total meso-pancreas excision during pancreaticoduodenectomy is mandatory to achieve R0 at meso-pancreatic margin aiming to reduce recurrence and improve disease-free survival.

Key Words: Hepatopancreaticobiliary, pancreatic ductal adenocarcinoma, pancreaticoduodenectomy, recurrence, total meso-pancreas.

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INTRODUCTION

Nearly 80% of all adenocarcinomas of the pancreas occur in the head of the pancreas. Even with pancreaticoduodenectomy, the prognosis for the adenocarcinoma of the head of the pancreas remains poor, the 5-year survival rate is only 20–25% and the median survival is between 10 and 20 months. Local recurrence due to the incomplete removal at the site of resection, rather than metastatic disease, is considered to be the primary reason for poor prognosis in those patients[1–4].

The mesopancreas is defined as the soft connective tissue located between the SMA and the uncinate process, or the structure situated to the right side of the SMA, and is regarded as the primary site of cancer cell infiltration[5].

However, numerous patients with pancreatic head cancer possess lymph node (LN) metastases on the left side of the SMA, lymphadenectomy involving the left side of the SMA omits the mesopancreas[6,7].

The study aims to evaluate total mesopancreas excision in pancreaticoduodenectomy and its effect on surgical prognosis in cancer head pancreas.

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PATIENTS AND METHODS:

This is a prospective study including 40 patients that had pancreatic head adenocarcinoma planned for pancreaticoduodenectomy presenting to Hepato-Pancreato-Biliary Department in National Liver Institute, Menoufia University.

The study was approved by Ethical institutional review board (IRB).

Inclusion criteria

(a) Resectable adenocarcinoma located in head/neck/uncinate process of the pancreas.

Exclusion criteria

(a) Metastatic adenocarcinoma of head/neck/uncinate process of pancreas.

(b) Locally advanced pancreatic carcinoma with vascular invasion.

The data collected and studied according to:

Preoperative data

Patients' demographics (age, sex, weight, BMI…); preoperative labs included complete blood count, complete chemistry panel, coaggulation profile, viral and tumor markers.

Preoperative diagnostic tools included pelvic-abdominal ultrasound (US), Computed tomography scan (CT) pancreatic protocol, dynamic MRI, endoscopic ultrasound, magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP) were done if needed.

Operative data

Intraoperative assessment of tumor resectability then Pancreaticoduodnectomy is performed with total excision of the meso-pancreas.

Operative technique

Under general anesthesia and nasogastric tube was presented to reduce the volume of the stomach and to decrease the distensions of small bowels. The lesser sac is opened, the hepatic flexure is mobilized. The inferior border of the pancreas is identified. Kocker maneuver is performed with exposure of the Inferior Vena Cava at the level of the proximal portion of transverse segment of duodenum (D3) till the left lateral border of the Aorta.

Porta hepatis then is dissected with identification of the Common hepatic artery and the removal of the LN accompanies it. The CHA (Common hepatic artery) is dissected to allow control of right gastric artery above and the gastroduodenal artery downwards, this allows identification of the Portal vein underneath.

The common hepatic duct is transected above the level of the cystic duct downwards.

The antrum of the stomach is transected with the specimen at the level of the third or fourth transverse vein on the lesser curvature. In some cases with small tumors, the pyloric ring is retained for pylorus preservation.

The jejunum is then transected after ligation and division of it is mesentry. Ligament of Treitz as well as the fourth and third part of the duodenum are mobilized by dividing their short mesenteric vessels. Then they are reflected underneath the mesenteric vessels.

The pancreatic head and the uncinate process are separated from the superior mesenteric confluence. The tunnel is made under the pancreas neck in front of the portal vein. The pancreatic neck is transected and reflected laterally allowing identification and ligation of venous tributaries in the portal and superior mesenteric vein.

Complete clearance of the tissues present in the triangle extending from the medial side of SMA caudally, Celiac trunk cranially and the portal vein laterally 'complete meso-pancreas excision' (Fig. 1).

Frozen sections from remnant pancreatic transection margins are done, if positive further resection is done to allow free surgical margin.

Operative time.

Estimated blood loss.

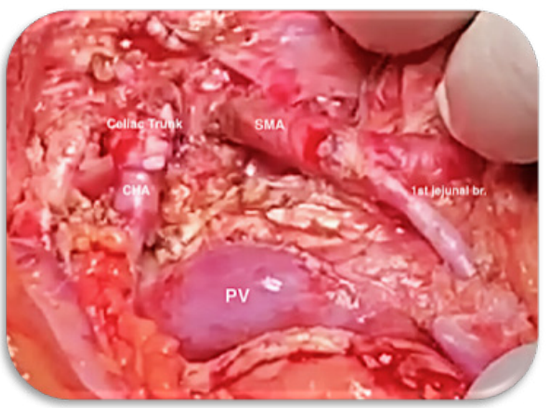

Fig. 1: Clearance of meso-pancreatic margin with the removal of all tissue between celiac trunk (cephalic), medial side of SMA, and PV laterally.

Postoperative data

Detailed histopathological assessment for tumor type, grade, lymphovascular,

Perineurial and nodal invasion. Seven distinct margins for each specimen were evaluated with 1 mm clear margin review.

Postoperative morbidities were classified according to Clavian Dindo classification. Mortality within 30 days after surgery was recorded.

Patients had follow-up of 6-18 months for local recurrence or metastasis.

Statistical analysis

Data was revised, coded and transformed into specially designed form to be suitable for personal computer entry process. Data was entered and analyzed by using SPSS (IBM Corp.Version 22.0. Armonk, NY, USA). Graphics were done using Excel program and SPSS.

Continuous variables with normal distribution are expressed as the mean and standard deviation (SD). Continuous variables with non-normal distribution are expressed as the median {interquartile range (IQR)} and {the median (range)}, and Mann–Whitney U test and Kruskal–Wallis (KW) test were used to compare between groups. Normal distribution was assessed using Kolmogorov–Smirnova test and Shapiro–Wilk test.

Categorical variables are expressed in frequency (n) and percentage (%) and analyzed using χ^2 test. However, if any of the expected cells were less than five, Fischer's exact test was used if 2×2 table otherwise Likelihood ratio was used.

Disease free survival (DFS) was assessed using the Kaplan–Meier method calculated from the date of surgery to the last follow-up or recurrence event, and differences in DFS were assessed using the Log-rank test.

A *P value* less than 0.05 was considered statistically significant.

RESULTS:

Our study included 40 patients who underwent partial pancreaticoduodenectomy with total meso-pancreas excision for cancer head pancreas. The study population consisted of 28 (70%) males and 12 (30%) females.

The study population age ranged from (35–76) years with a mean of 56.89± 9.67 years.

Preoperative labs (Table 1) Were carried out among our studied population, the results are as shown.

Radiological studies including ultrasound and CT pancreatic protocol were done for all the patients, however, some patients needed further imaging modalities for diagnosis; magnetic resonance cholangiopancreatography, ERCP, endoscopic ultrasound, MRI, and PET scan. (Table 2).

Preoperative biliary drainage

According to our center protocol, preoperative biliary drainage is done in the following situations:

(a) If the serum bilirubin more than 20 mg/dl.

(b) Renal insufficiency.

(c) Ascending cholangitis.

(d) Logistic causes.

Eleven patients were subjected to preoperative biliary drainage; nine through ERCP stenting and two had PTD.

Intraoperative data

Conventional Whipple procedure was done in 29 (72.5%) patients while 11 (27.5%) patients had pylorus preserving pancreaticoduodenectomy. Frozen sections were done from the remnant pancreatic stump for all cases to ensure free surgical margin.

The mean operative time was 7 h with a range of (5–9) h.

The mean intraoperative blood loss was 700 ml with a range of (400–1300) ml.

Pathological outcome

Ninety percent (90%) of the tumor was located in the pancreatic head proper while 10% occurred in the uncinate process.

The mean size of the pancreatic tumor was 4.5 cm and the median was 3.8 cm.

Nodal metastasis was found in 31 patients; 21 (52.5%) patients had N1 while 10 (25%) patients had N2.

The number of lymph nodes excised ranged from (8 to 47) LNs with a mean of 27.5.

Tumor staging was done using TNM classification; two (5%) were stage IA, seven (17.5%) stage IB, 21 (52.5%) stage IIB, and 10 (25%) patients were stage III.

Histopathological examination of the specimens was predominantly (90%) ductal adenocarcinoma and the rest as shown in (Table 3).

Ninety percent (90%) of the tumors exhibit perineural invasion and (40%) had lympho-vascular invasion (LVI).

R0 was achieved in 57.5% while involved resection margins R1 were positive in 42.5% (Fig. 2).

Those R1 were found among the seven examined resection margins; proximal, distal, bile duct, pancreatic, meso-pancreatic, uncinate, and anterior margin (Table 4).

12 (30%) patients had positive meso-pancreatic margin (R1 MP) involvement either alone in seven patients or concomitant with other margins.

Surgical outcome

Morbidity in the present series was graded using 'Modified Clavian Classification' for surgical complications. Twenty five patients were grade II, nine were grade IIIA and six were grade IIIB.

Seven patients suffered wound infection, five had superficial infection that was treated by administration of intravenous antibiotics while two had deep infection requiring bedside wound drainage.

Six patients had postoperative delayed gastric emptying, four patients had grade A DGE, one patient had grade B and last one had grade C. These patients required nasogastric decompression +/– administration of prokinetic drugs.

Eight patients had postoperative pancreatic fistula (POPF), two of which were grade A and the remaining four had grade B POPF and required interventional radiology for pigtail catheter insertion.

Biliary fistula occurred in three patients who required re-exploration.

One patient suffered gastric leak for which he underwent CT guided pigtail catheter insertion.

Another patient had intestinal leak for which he needed re-exploration.

One patient had wound dehiscence at the lateral part which was treated conservatively and left to heal by secondary intention.

One patient developed liver abscess after surgery. The patient underwent liver resection afterwards and he recovered well.

Postoperative primary Hemorrhage occurred in one patient who underwent re-exploration.

Eleven patients suffered from mild postoperative diarrhea.

Follow-up ranged from a minimum of 6 to 18 months. Clinical examination, CA19.9 level along with CT pancreatic protocol were the basis for recurrence detection among the reviewed patients. Patients were subjected to 3–6 months follow-up in the first couple of years then yearly afterwards.

It was noticed that recurrence after pancreaticoduodenectomy has a statistically significant relationship with resection margin status R1 (Table 5 and Fig. 3).

All patients with R1 MP 12 (30%) suffered recurrence. Recurrence among R1 MP was statistically significant. Recurrence pattern is shown below in (Fig. 4).

More than half the patients (56.1%) had 1-year DFS with a mean of 9.962 months for all studied patients as shown in (Table 6, Fig. 5).

There was a statistically significant difference in DFS between R0 and R1 groups (Log-rank $P<0.001$). DFS was significantly better in R0 group than R1 group. The median DFS for R1 group was 8 months (Table 7, Fig. 6).

Our study encountered a statistically significant difference in DFS between free and R1 MP groups (Log-rank $P<0.001$). DFS was significantly better in free group than the positive group. The median DFS for positive margin group was 8 months and not reached for free margin group. Mean DFS was 7.083 months for positive margin group compared with 11.502 months for free margin group (Table 8, Fig. 7).

Perineural invasion was found in 10 (83.3%) patients who had positive meso-pancreatic margins. However, this result was statistically insignificant. (Table 9).

Lymphovascular invasion was found in six (50%) patients who had R1 MP. However, this result was also statistically insignificant. (Table 10).

Table 1: Preoperative labs for the patients (n=40)

Lab	
Total Bilirubin	
Median (Range)	6.25 (0.6–30)
Median (IQR)	6.25 (2–10.75)
Direct Bilirubin	
Median (Range)	4. 6 (0.1–21)
Median (IQR)	4.6 (1.07–7.87)
Albumin	
Mean±SD	3.71±0.63
INR	
Median (Range)	1.05 (0.9–1.4)
Median (IQR)	1.05 (1–1.2)
Hb	
Mean±SD	12.05±1.51
TLC	
Median (Range)	7 (3–19.4)
Median (IQR)	7 (6–8.8)
PLT (Platelet)	
Mean±SD	233.22±83.38
Cr	
Median (Range)	0.9 (0.6–1.6)
Median (IQR)	0.9 (0.72–1.1)
AST (Aspartate aminotransferase)	
Median (Range)	61 (11–460)
Median (IQR)	61 (30.5–150)
ALT (Alanine aminotransferase)	
Median (Range)	64.5 (14–490)
Median (IQR)	64.5 (30–137.5)
ALP	
Median (Range)	176 (19–1200)
Median (IQR)	176 (70.25–392.75)
GGT	
Median (Range)	204.5 (8–1400)
Median (IQR)	204.5 (83–527.75)
AFP	
Median (Range)	2.55 (0.9–32)
Median (IQR)	2.55 (1.5–3.35)
CA19.9	
Median (Range)	225.5 (0.7–12000)
Median (IQR)	225.5 (75.75–783.75)
CEA	
Median (Range)	3 (0.5–93)
Median (IQR)	3 (2–4.9)

Table 2: Preoperative radiological studies for the patients (n=40).

Radiological studies	
Modalities	*n* (%)
Ultrasound abdomen	40 (100)
CT pancreatic protocol	40 (100)
MRCP	9 (22.5)
ERCP	9 (22.5)
EUS	4 (10)
Dynamic MRI	3 (7.5)
PET CT	1 (2.5)

Table 3: Tumor histopathological types

Tumor type	
Ductal adenocarcinoma, *n* (%)	36 (90)
IPMN with foci of invasive carcinoma	2 (5)
Adenocarcinoma with mucinous differentiation	1 (2.5)
Adeno-squamous	1 (2.5)

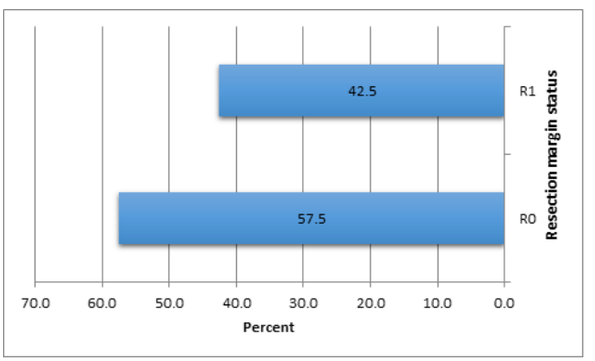

Fig. 2: Distribution of resection margin status among the studied patients (n=40).

Table 4: Positive resection margins R1 after pancreaticoduodenectomy

Positive margins	n
Total R_1 positive margins	17
Meso-pancreatic margin only	7
Meso-pancreatic +uncinate margins	3
Meso-pancreatic + pancreatic margin	2
Uncinate margin only	2
Pancreatic margin only	1
Pancreatic margin and bile duct margin	1
Anterior margin only	1

Table 5: Relationship between positive resection margins R1 and recurrence

Recurrence	Overall (*n*=40) *n* (%)	R0 (clear margins *n*=23) *n* (%)	R1 any margin (*n*=17) *n* (%)	Test value	*P* value	R1 including meso-pancreatic margin (*n*=12) *n* (%)	Test value	*P* value	R1 other margin (*n*=10) *n* (%)	Test value	*P* value
Overall											
Yes	14 (35)	0	14 (82.4)	X^2=29.140	*P*<0.001**	12 (100)	Fi=31.837	*P*<0.001**	7 (70)	Fi=7.179	*P*=0.018*
No	26 (65)	23 (100)	3 (17.6)			0			3 (30)		

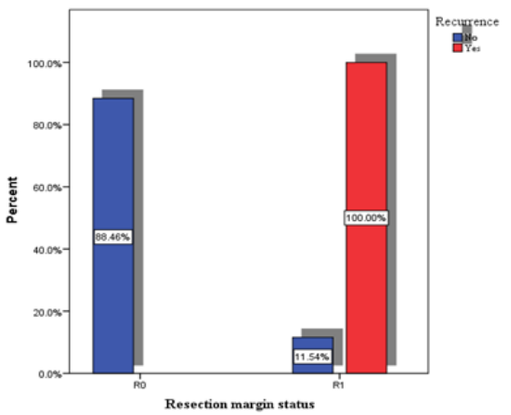

Fig. 3: Association between recurrence and resection margin status among the studied patients (n=40).

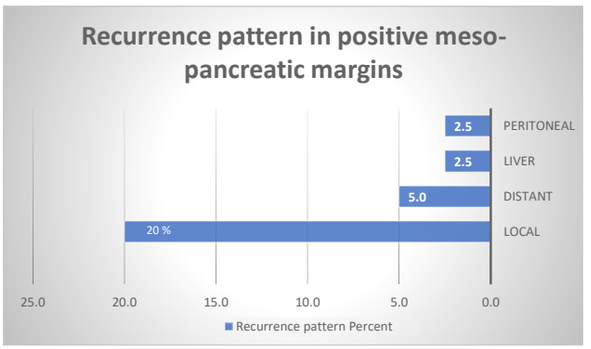

Fig. 4: Recurrence pattern among positive meso-pancreatic margin patients (n=12).

Table 6: Shows 1-year disease free survival rate was 56.1%. The mean disease free survival was 9.962 months for all studied patients

Disease free survival (DFS) Probability								
		Mean			Median			
Number of events (%)	Number of censored (%)	Estimate	95% CI lower	95% CI upper	Estimate	95% CI lower	95% CI upper	1 year DFS probability (%)
14 (35)	26 (65)	9.962	8.935	10.989	–	–	–	56.1%

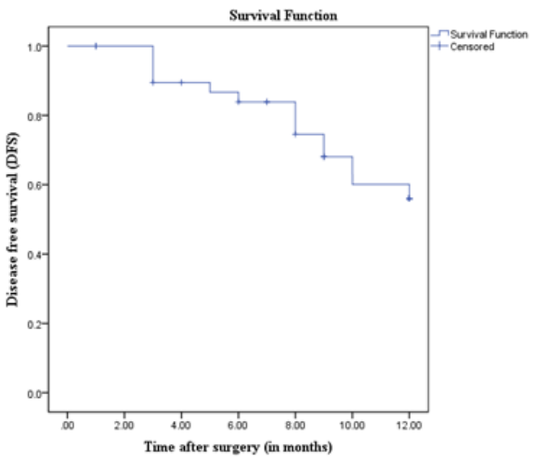

Fig. 5: Disease free survival among all patients (n=40).

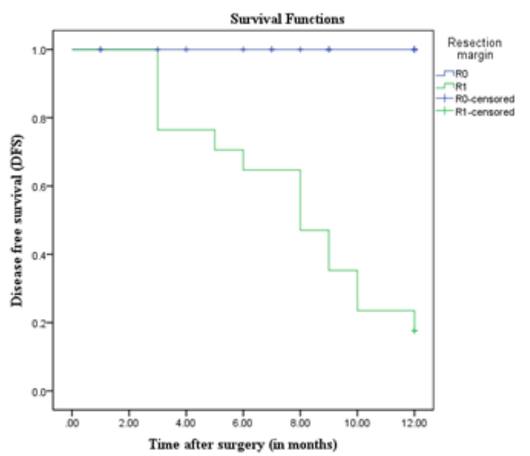

Fig. 6: Resection margin (R0/R1) specific disease free survival (n=40).

Table 7: Resection margin (R0/R1) specific disease free survival (n=40)

DFS regarding resection margin status										
			Mean			Median				
Resection margins	Number of events (%)	Number of censored (%)	Estimate	95% CI lower	95% CI upper	Estimate	95% CI lower	95% CI upper	*P* value (R0 Vs R1)	1 year DFS probability (%)
R0 (n=23)	0	23 (100)	–	–	–	–	–	–		100%
R1 (n=17)	14 (82.4)	3 (17.6)	–	–	–	8	–	–	*P<0.001*	17.6%
Overall (n=40)	14 (35)	26 (65)	–	–	–	–	–	–		

Table 8: Meso-pancreatic margin specific disease free survival

DFS regarding meso-pancreatic margin status										
			Mean			Median				
Resection margins	Number of events (%)	Number of censored (%)	Estimate	95% CI lower	95% CI upper	Estimate	95% CI lower	95% CI upper	*P* value	1 year DFS probability (%)
Free (n=28)	2 (7.1)	26 (92.9)	11.502	10.787	12.217	–	–	–		91.1
Positive (n=12)	12 (100)	0	7.083	5.353	8.814	8.000	5.866	10.134	*P<0.001*	0
Overall (n=40)	14 (35)	26 (65)	9.962	8.953	10.989	–	–	–		–

Table 9: Association between meso-pancreatic margin status and Perineural infiltration (PNI) (n=40)

	Meso-pancreatic margin status			
Perineural infiltration (PNI)	Free (*n*=28) *n* (%)	Positive (*n*=12) *n*(%)	Test value	*P* value
Absent (n=4)	2 (7.1)	2 (16.7)	Fi=0.714	*P*=0.490
Present (n=36)	26 (92.9)	10 (83.3)		

Table 10: Association between meso- pancreatic margin status and Lymphovascular infiltration (LVI) (n=40)

	Meso-pancreatic margin status			
Lymphovascular infiltration (LVI)	Free (*n*=28) *n* (%)	Positive (*n*=12) *n* (%)	Test value	*P* value
Absent (*n*=24)	18 (64.3)	6 (50)	Fi=0.847	*P*=0.570
Present (*n*=16)	10 (35.7)	6 (50)		

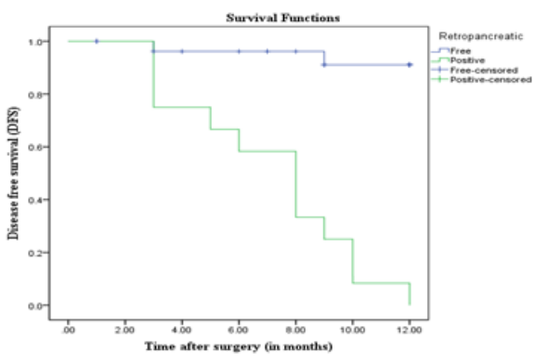

Fig. 7: Meso-pancreatic margin specific disease free survival (n=40).

DISCUSSION

Pancreatic ductal adenocarcinoma has one of the worst survival rates among human cancers, even after surgical resection, 5 year survival rates only reach 20%. Many factors contribute to this poor outcome including resection margins, lympho-vascular and perineural invasion, tumor size, tumor type, tumor differentiation, and nodal metastasis[8].

Resection margin (R-status) is an important surrogate marker for surgical radicality and another important prognostic factor that can be influenced by surgical quality, strategy, and technique. In consideration of the discontinuous spread of pancreatic cancer cells at the invasion margins and especially at sites of perineural

invasion, the new protocols for pathological work-up were accompanied by a revised strict definition of the R-status, requiring a 1 mm tumor-free margin between the closest cancer cell and any margin to call an R0 status toward the superior mesenteric artery and the celiac axis were most frequently involved[9].

The ISGPS in 2014 released the recommendation to report the resection margin status based on assessment of seven distinct margins, also supported reporting on a 1 mm free margin[10].

The first comprehensive systematic review and meta-analysis on the topic included 19 studies with a total of 4376 patients and highlighted the considerable heterogeneity of reported R0 and R1 rates: studies using the 1 mm rule and assessing at least six margins reported only 29% R0 rates, while studies still applying a 0-mm rule reported 72% R0 resections[11].

A systematic review of the literature to define recurrence patterns and resection margin status done at the University of Birmingham evaluated 23/617 studies (n=3815). In total, 16 studies (n=2564) reported margin status and the R1-rates ranged from 17 to 76%. Seven studies used 1 mm as the cut-off for a positive margin, one study 0 mm and the margin cut-off was unknown in eight studies. Specific positivity of the SMA (Superior Mesenteric artery) margin was described in six studies (n=1388). The SMA margin was positive in 15–35% of the patients in those studies. Of these six studies, three investigated the relation between a positive SMA margin and recurrence/ survival rates. Delpero *et al*.[12] reported impaired survival rates in patients with a positive SMA margin (19.5 vs. 9.6 months; *P=0.017*).15 Furthermore, a hazard ratio of 1.27 (95% CI 1.00–1.63; *P=0.05*) for a combined endpoint of recurrence and death by Fatima and colleagues. In contrast, Raut *et al*. did not find a significant relation between a positive SMA margin specifically and OS rates (HR 1.28; 95% CI 0.92–1.78; *P=0.140*)[13].

Sperti *et al*.[14] reported that 89% of patients developed recurrent disease after initial surgical resection, of which 33% were located solely in the remnant pancreas or locoregional structures. A median DFI of 10 months was seen, with a subsequent median survival of only 7 months without any intervention. Similarly, Hernandez *et al*. studied the natural history of resected pancreatic cancer and described a median DFI of 7 months and overall survival of 14 months for local recurrence[15].

R0-resection is the only effective treatment for pancreatic cancers, the frequent local recurrence within the resection bed, may be due to inadequate clearance of the peripancreatic retroperitoneal margin, the so-called meso-pancreas. Positive resection margins, especially SMA margin, are usually associated with local recurrence and impaired survival[16].

Because pancreatic cancer invasion is characterized not only by lymphatic involvement but also by perineural invasion, simple nodal excision has been traditionally considered to be oncologically inadequate. Consequently, skeletonization of the regional vessels with removal of the lymph nodes in addition to the perivascular neural and soft tissues is recommended[17].

In our study we investigated the prognostic outcome of application of total meso-pancreatic excision among forty patients during partial pancreaticoduodenectomy for pancreatic head cancer. Our main interest was the evaluation of meso-pancreatic margin status and it is impact on disease recurrence and DFS. All the specimens were examined pathologically with seven margins being evaluated for R1.

Total meso-pancreatic excision resulted in R0 achievement in 23 (57.5%) while R1 was noticed in 17 (42.5%) of patients. Most of R112 (30%) had R1 MP involvement either alone or concomitant with other margins.

Recurrence of the disease occurred in 14 (35%) patients during follow-up. All patients with positive margins R1 developed recurrence but not the opposite. This relationship between R1 and recurrence was found to be statistically significant *P value* less than 0.001**.

In context of our interest, we evaluated the relationship between R1 MP and recurrence. All patients with positive meso-pancreatic margins developed recurrence, the matter that resulted in a statistically significant relationship between R1 MP and disease recurrence *P=0.018**.

The majority of the recurrence took place in the surgical bed eight (20%) followed by distant metastasis two (5%), liver metastasis one (2.5%) and peritoneal metastasis one (2.5%).

The overall 1-year DFS rate was 56.1% of patients with a mean of 9.962 months. There was a statistically significant difference in DFS between free meso-pancreatic margin (R0 MP) and R1 MP group. DFS was significantly better in free group than positive group where the mean DFS was 7.083 months for R1 MP group compared with 11.502 months for free margin group.

Another factor that contributes to the poor prognosis of the PDAC is LVI. Takahashi and colleagues observed that LVI was commonly associated with PDAC regardless of the tumor size or stage and that it should be considered in staging regardless of the nodal status. LVI was observed in 65% of pancreatic head cancer patients and these patients suffered early nodal recurrence and LVI presence is a sole poor outcome predictive factor[18].

In a large retrospective study of 2640 patients who underwent pancreaticoduodenectomy for PDAC, LVI was noted in 56.4% of the specimen[19].

In our study 40% of the patients had LVI, five patients had N2, nine patients with N1, and two with N0. The relationship between LVI, tumor size, and staging was assessed and appeared not to be statistically significant.

A significant factor contributing to poor prognosis in PDAC is extra-pancreatic perineural invasion with a reported frequency of 53–100%. EPNI is important to identify because it carries a poor prognosis and is considered a significant factor of positive resection margin during surgery. In a study held on 59 patients, EPNI was noted in 83% of the patients and was associated with higher incidence of margin positivity especially the retro-pancreatic margin, also it was associated with higher incidence of local recurrence[20].

Although 36 (90%) patients in our study exhibit perineural invasion on pathological examination, there was no statistically significant association between PNI, resection margin, tumor size or even tumor stage.

Regional LN involvement is an important predictor of survival in patients undergoing resection for pancreatic cancer. Recent studies have suggested that the number of metastatic LN provides additional prognostic information[21].

Several studies in pancreatic cancer and other malignancies have suggested that prognosis is associated with the relationship of metastatic-to-examined LN, as assessed by the LN ratio and log of the odds of metastatic LN (LODDS)[22].

An analysis of the SEER database including 7685 patients with stage I and II pancreatic cancer found that retrieval of 20 or more regional lymph nodes was associated with increased survival in node-negative as well as node-positive cancers after adjustment for other prognostic factors. While the improved survival with greater than or equal to 20 retrieved lymph nodes in node-negative cancers may be explained by effects of stage migration, the improved survival with greater than or equal to 20 retrieved nodes in node-positive cancers points to a possible therapeutic effect of radical lymphadenectomy. In contrast to overall survival, the extent of lymphadenectomy may more directly affect local recurrence and recurrence-free survival[23].

Nodal metastasis was found in 31 patients; 21 patients (52.5%) had N1 while 10 (25%) patients had N2. The number of excised lymph nodes ranged from (8 to 47) LNs with a mean of 27.5. LN ratio had mean of 0.0625 ranging from 0 to 0.67. We noticed increased number of LNs retrieval when applying total meso-pancreatic excision in Whipple procedure.

In addition to the previously mentioned outcomes, postoperative morbidities were evaluated. pancreaticoduodenectomy is associated with a large number of specific postoperative complications that influence survival. These complications include Postpancreatectomy Hemorrhage(PPH), POPF, bile leak, intra-abdominal abscess, delayed gastric emptying, and surgical site infection[24].

POPF is one of the most common specific complications following pancreatic surgery with an incidence of 2–20%. According to the literature, the rate of DGE varies between 19 and 57% and the rate of PPH is about 1–8%[25].

Gastrointestinal dysfunction occurs frequently after pancreatectomy. Previous studies have revealed that extended lymphadenectomy and dissection of the nerve plexus could lead to severe post-operative diarrhea in patients with pancreatic cancers[26]. Dissection of the nerve plexus was performed in the patients in this study, as it was required for R0 resection[27].

Surgical site infection (SSI) incidence was investigated in a study from Pakistan, the result came out to be 7%. However, another study reported that 32% of the patients developed surgical site infections following pancreaticoduodenectomy. Pancreatic fistula and the presence of preoperative cholangitis are reported to be important predictors of organ space surgical site infection following pancreaticoduodenectomy[28].

In our series morbidity results did not exceed that reported in literature. We had seven (17.5%) patients suffered wound infection, six (15%) patients had postoperative delayed gastric emptying, eight patients had POPF (20%); two (5%) patients were grade A and the remaining four had clinically relevant grade B POPF.

Biliary fistula occurred in three (7.5%) patients.

One (2.5%) patient suffered a gastric leak while another (2.5%) had an Intestinal leak.

PPH occurred in one patient (2.5%).

Eleven (27.5%) patients suffered from mild postoperative diarrhea.

CONCLUSION

Total meso-pancreas excision during pancreaticoduodenectomy is mandatory to achieve R0 at the meso-pancreatic margin aiming to reduce recurrence and improve DFS.

Morbidities associated with total meso-pancreas excision during pancreaticoduodenectomy are comparable to those with standard whipple's operation written in literature.

CONFLICT OF INTEREST

There are no conflicts of interest.

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