International Journal of Surgery 31 (2016) 58–62

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Survival advantage with para aortic lymphadenectomy in peri-ampullary cancer: A retrospective cohort study

Abu Bakar Hafeez Bhatti [a, *], Faisal Saud Dar [a], Eraj Sahaab [a], Nusrat Yar Khan [a], Haseeb Zia [a], Atif Rana [b], Muhammad Salih [c], Najmul Hassan Shah [c]

[a] Department of HPB and Liver Transplantation, Shifa International Hospital, Islamabad, Pakistan
[b] Department of Radiology, Shifa International Hospital, Islamabad, Pakistan
[c] Department of Gastroenterology and Hepatology, Shifa International Hospital, Pakistan

HIGHLIGHTS

- Should patients with peri ampullary cancer and positive PALN undergo curative surgery is debatable.
- Acceptable survival was demonstrated in the current study.
- Positive PALN should not be a contraindication to surgery in all patients.

ARTICLE INFO

Article history:
Received 1 March 2016
Received in revised form
15 May 2016
Accepted 28 May 2016
Available online 1 June 2016

Keywords:
Lymphadenectomy
Survival
Outcome
Pancreaticodoudenctomy

ABSTRACT

Background: Metastatic para aortic lymph nodes (PALN) in patients with peri ampullary cancer entail poor prognosis. Role of curative surgery in these patients remains debatable. The objective of the current study was to evaluate outcome after extended pancreaticoduodenectomy (PD) in patients with and without positive PALN.

Methods: We reviewed 65 patients who underwent extended PD with PALN removal between 2011 and 2014. Patients were divided into two groups; those with positive PALN and those without. Patients were sub classified for pancreatic and non-pancreatic cancer. Outcome was determined based on median and estimated 3 year overall survival.

Results: Median age was 57 (32–85) years. PALN were involved in 15 (23%) patients. Overall 3 year survival for patients with and without positive PALN was 60% and 54% ($P = 0.7$). Significant difference in survival was present between patients with pancreatic cancer and positive PALN [9 (3–12) months] versus non-pancreatic cancers with positive PALN [17.5 (13–38) months] ($P = 0.02$). Four out of five patients with pancreatic cancer and positive PALN had survival >6 months and 3 out of these 5 patients were alive at the last follow up.

Conclusion: Curative surgery may benefit some patients with pancreatic cancer and positive PALN and should be considered selectively.

1. Introduction

Pancreaticoduodenectomy (PD) remains one of the most challenging surgical procedures [1]. In the last decade, impressive peri-operative outcomes with acceptable complication rate and low mortality (≤1%) have been demonstrated [2]. For pancreatic cancer in particular, long term survival is poor and majority of patients at the time of presentation have irresectable or metastatic disease [3–5]. High volume centers around the world have adopted an aggressive surgical policy in an attempt to achieve tumor free surgical resection. It has been shown that inclusion of vascular resection to PD does not increase complication rate and improves survival when compared to patients managed with palliation [6,7].

Extended lymphadenectomy (EL) which includes para aortic lymphadenectomy has been the subject of much controversy. Based on TNM classification, for patients with para aortic lymph

* Corresponding author. Shifa International Hospital, Pitras Bukhari Road, Sector H-8/4, Islamabad, Pakistan.
E-mail address: abubakar.hafeez@yahoo.com (A.B. Hafeez Bhatti).

http://dx.doi.org/10.1016/j.ijsu.2016.05.069
1743-9191/

node (PALN) metastasis, curative surgery is contra indicated [8–10]. Randomized trials have generally favored limited regional lymphadenectomy and have not demonstrated survival benefit with standard versus extended lymphadenectomy. These trials however have been criticized for small sample size, lack of objective definition of lymphadenectomy and absence of statistical determination of sample size [11]. Moreover, some recent reports have demonstrated promising role of EL in selected patients with peri-ampullary malignancy resulting in improved survival and acceptable morbidity and mortality [12]. The debate on para aortic lymphadenectomy in the setting of peri-ampullary malignancy is not over. We routinely perform para aortic lymphadenectomy in patients with peri-ampullary tumors. The objective of this study was to determine overall survival in patients with peri ampullary tumors and with positive or negative PALN who underwent extended PD.

2. Methods

We retrospectively reviewed patients who underwent PD at Shifa international hospital Islamabad between February 2011 and August 2014. A total of 66 patients underwent surgery. One patient was excluded due to significant missing data. Patients were followed until January 2016.

Patients were initially evaluated at gastroenterology or hepatobiliary surgery clinic. Baseline investigations, liver function tests and clotting profile were performed. This was followed by imaging including ultrasound and dynamic CT scan with pancreatic protocol in patients with suspected peri-ampullary malignancy. Preoperative biliary drainage was performed in patients with cholangitis. All patients with resectable and borderline resectable tumors were offered upfront surgery [13]. A treatment plan was formulized in multidisciplinary team meeting.

All surgeries were performed by or under supervision of one surgeon (FSD). Transverse abdominal incision was used as standard. Preservation of pylorus was at the discretion of surgeon based on intra-operative findings of distance between tumor and resection margin. Margins from pancreatic transection margin and bile duct margin were routinely sent for frozen section analysis. End to end anastomosis was performed for vascular resections involving <2 cm of portal vein (PV) or superior mesenteric vein (SMV), otherwise PTFE graft was used as conduit. Reconstruction was performed with Roux-en-Y loop of jejunum in cases where pylorus was not preserved. Pancreaticojejunostomy was performed in duct to mucosa fashion with PDS sutures. Single layer end to side hepaticojejunostomy was performed while double layer end to side gastrojejunostomy was fashioned with PDS sutures.

2.1. Lymphadenectomy involved removal of lymph nodes in the following areas

1) Regional lymph nodes around the pancreatic bed
2) Right and left hepatic artery
3) Proper and common hepatic artery
4) Celiac axis
5) Right side of superior mesenteric artery
6) Aortocaval window extending from inferior mesenteric artery (IMA) inferiorly to root of superior mesenteric artery (SMA) around bilateral renal hilum superiorly

Post operatively, patients were kept in ICU for 1–2 days. Naso jejunal feeding was initiated 12 h after surgery. Patients were resumed on normal diet on day 3. Drain amylase levels were sent on day 4 as a routine.

Patients were divided into two groups. Group I had positive PALN on histopathology while Group II had negative PALN. Demographics, histopathological and outcome variables were compared between the two groups. Outcome variables included complication rate, recurrence and mortality and estimated 3 year overall survival. For categorical variables, Chi square test and Fisher exact test were used. For interval variables independent *t*-test and Mann Whitney *U* test were applied. Survival was defined as time between date of death or last follow up and date of surgery. For complications, 90 day post operative period was assessed and all Grade 2 and above complications on Clavien-Dindo grading were noted [14]. Survival estimation was performed using Kaplan Meier survival curves and Log rank test was used to determine significance between variables. A P value < 0.05 was considered statistically significant. All analysis was performed on SPSS version 20.

3. Results

Median age was 57 (32–85) years. Male to female ratio was 1.8:1. The highest number of surgeries was performed in the year 2012 i.e. 22. Most commonly performed procedure was Whipple's procedure in 48 patients. Preoperative biliary drainage was performed in 31 (47.6%) patients as shown in Table 1.

Table 2 compares various demographic, histopathological and operative variables between the two groups. Out of 43 patients with nodal involvement, PALN were involved in 15 (34.8%) patients. Fourteen out of 15 (93.3%) patients with positive PALN had perineural invasion in comparison with 29 (58%) patients with negative PALN ($P = 0.01$). Lympho-vascular invasion was also more frequently seen in group I patients (73.3% versus 56%) but it did not reach statistical significance ($P = 0.06$). No significant difference in margin positivity was observed between the two groups (33.3% versus 22%) ($P = 0.1$). Mean number of nodes removed in group I was 40.4 ± 18 versus 28 ± 13.7 in group II ($P = 0.008$). Mean number of positive nodes was also significantly different between the two groups i.e. 10.6 ± 2.2versus 3.5 ± 3.5($P < 0.001$). Thirteen out of 15 (86.7%) patients in group 1 while 32/50 (64%) patients in group 2 received adjuvant chemotherapy with or without radiation ($P = 0.09$) (not shown).

Recurrence was observed in 10/15 (66.6%) patients with positive PALN versus 15/50 (30%) patients with negative PALN ($P = 0.01$). No significant difference in complications between the two groups i.e. 27% versus 34% ($P = 0.7$) or observed mortalities (40% versus 26%) ($P = 0.4$) was noted as shown in Table 3.

Median overall survival in patients with positive and negative PALN was 14 (3–38) and 12 (0.2–38) months and not significantly different ($P = 0.9$). Estimated 3 year survival in patients with and without PALN involvement was 54% and 60% and was not significantly different ($P = 0.7$) (Fig. 1). Median overall survival for pancreatic tumors was 12 (3–22) months while for non-pancreatic tumors it was 17 (0.2–38) months ($P = 0.004$). Median overall survival for pancreatic tumors with positive and negative PALN was 9 (3–12) and 12 (3–22) months ($P = 0.2$). Median survival for patients with non-pancreatic peri ampullary tumors with and without positive PALN was 17.5 (13–38) and 17 (0.2–38) months and was significantly different ($P = 0.005$). Out of 15 patients with positive PALN, 5 had underlying pancreatic malignancy. A statically significant difference in survival was present between patients with pancreatic tumors and positive PALN and non-pancreatic tumors with positive PALN ($P = 0.02$). Four out of five patients with pancreatic tumors and positive PALN had survival >6 months and 3 out of these 5 patients were alive at the last follow up. None of the patients in this group had well differentiated or early (T1/T2) tumors.