Comparison of Pathological Radicality between Open and Laparoscopic Pancreaticoduodenectomy in a Tertiary Centre

Palanisamy Senthilnathan · Palanivelu Chinnusamy ·
Alwar Ramanujam · Srivatsan Gurumurthy Sivakumar ·
Anand Vijai Natesan · C. Chandramaliteeswaran ·
Praveen Raj Palanivelu · Parthasarathi Ramakrishnan ·
Rajapandian Subbiah

Received: 25 June 2014 / Accepted: 17 December 2014 / Published online: 4 January 2015
© Indian Association of Surgical Oncology 2015

Abstract Laparoscopic pancreaticoduodenectomy (LPD) remained a formidable challenge owing to retroperitoneal location, difficult dissection near great vessels and critical intracorporeal anastomoses. Recent reviews of literature have established the feasibility and comparable short term outcomes of laparoscopic pancreaticoduodenectomy (LPD) with that of open pancreaticoduodenectomy (OPD). This study was undertaken to compare the pathological radicality of LPD with

OPD. A prospective database of all patients who underwent standard pancreaticoduodenectomy from Mar 2006 to Feb 2011 was taken up for this study. 45 patients who underwent LPD and 118 patients who underwent OPD for periampullary and pancreatic head malignancy were taken up for analysis. The study groups were comparable in terms of age of presentation, ASA grades, comorbidity, type of surgery and BMI. There was no statistically significant difference with regard to tumor size, lymph node yield, node positivity rates, R1 rates and margin lengths. The pathological radicality of laparoscopic pancreaticoduodenectomy is comparable with that of open approach when performed by experienced minimal-access surgeons. Standardized protocols for evaluation of the resection margins should be mandatory in studies reporting outcomes of pancreaticoduodenectomy.

Electronic supplementary material The online version of this article (doi:10.1007/s13193-014-0372-x) contains supplementary material, which is available to authorized users.

P. Senthilnathan (✉) · P. Chinnusamy · A. Ramanujam ·
S. G. Sivakumar · A. V. Natesan · C. Chandramaliteeswaran ·
P. R. Palanivelu · P. Ramakrishnan · R. Subbiah
Gem Hospital and Research Centre, Minimal Access and HPB
Surgery Coimbatore, Tamil Nadu 641045, India
e-mail: senthilnathan94@yahoo.com

P. Chinnusamy
e-mail: palanivelu@mac.com

A. Ramanujam
e-mail: alwarramanujam@gmail.com

S. G. Sivakumar
e-mail: drsrivatsan@gmail.com

A. V. Natesan
e-mail: anandvij@yahoo.com

C. Chandramaliteeswaran
e-mail: yogimouli1981@gmail.com

P. R. Palanivelu
e-mail: praveenraj@me.com

P. Ramakrishnan
e-mail: parthu@me.com

R. Subbiah
e-mail: srjapandian@rediffmail.com

Keywords Adenocarcinoma · Pancreatic neoplasia ·
Resection · Pancreatic neoplasia · Outcomes · Pancreatic
neoplasia · Peri-ampullary tumours · Pancreatic neoplasia

Introduction

Though minimally invasive surgery is rapidly expanding its role in the management of abdominal malignancies, minimal invasive pancreatic surgery has had a relatively slow progress. Drainage procedures for pseudocyst and resective procedures like distal pancreatectomy and enucleation were easily adapted laparoscopically while pancreaticoduodenectomy (PD) remained a formidable challenge owing to retroperitoneal location, difficult dissection near great vessels and critical

intracorporeal anastomoses [1] It was Gagner and Pomp who first performed laparoscopic pancreaticoduodenectomy (LPD) for treating chronic pancreatitis in 1992. Though feasibility was established, the authors concluded that there was no benefit over open procedure. [2] Numerous subsequent series have demonstrated the feasibility and safety of LPD but still the concerns of prolonged operative time and surgical outcomes remained.[3] We reported our initial experience of LPD in 42 patients in 2007 followed by large series of 75 patients in 2009.[4, 5] A review of literature on LPD worldwide by Gagner et al. in 2009 reported outcomes of 146 patients. The mean operating time was 439 min, average blood loss of 143 mL; median hospital stay of 18 days; and mortalities related to the procedure was 1.3 % and a complication rate of 16 %.[6] The recent review of 285 cases of laparoscopic PD by Gumbs et al. in 2011 also reported comparable outcomes with OPD.[7] These studies have established the feasibility and comparable short term outcomes with that of open pancreaticoduodenectomy (OPD). One of the recent meta analysis has shown that in selected patients, minimally invasive pancreaticoduodenectomy is associated with lesser blood loss, decreased hospital stay, higher lymph node yield, better R0 resection in comparison with open pancreaticoduodenectomy [8] . To address this issue of oncological adequacy of technique, for which lymph node yield and R0 status are surrogate markers, a study comparing pathological radicality between open and LPD, was undertaken at our institute.

Patients and Methods

A prospective database of all patients who underwent pancreaticoduodenectomy from Mar 2006 to Feb 2011 was taken up for this study. All patients who underwent laparoscopic (LPD) and open pancreaticoduodenectomy (OPD) for periampullary and pancreatic head malignancy were included. The study group included both Classical pancreaticoduodenectomy (CPD) and Pylorus preserving pancreaticoduodenectomy (PPPD).

Clinical data and pathological reports were entered in a standard protocol format. All surgeries were performed by either of the two senior surgeons. The choice of the procedure was based on size of the tumour, location of the tumour, performance status of the patient and previous surgical history of the patient. Earlier, small periampullary tumour were selectively chosen for LPD and with growing experience our proportion of LPD cases have gone up and our selection criteria has widened. Nevertheless, patients with multiple previous surgeries, chronic pancreatitis, post neoadjuvant status and vascular resections were preferably taken up for OPD, hence such cases have been excluded from this analysis.

Fig. 1 Intra-operative picture of post resection stage of laparoscopic pancreaticoduodenectomy

Technique of LPD

The technique of LPD is described elsewhere in detail.[5] Radicality was maintained in uncinate dissection and neurolaminar tissue clearance is done lateral to superior mesenteric artery (SMA) up to the celiac axis. Inferior pancreatico-duodenal vessels are divided close to SMA. We performed standard lymphadenectomy which includes removal of nodal stations located along the hepatic pedicle (12b1, 12b2, 12c), adjacent to the anterior and posterior surface of the pancreatic head (13a, 13b, 17a, 17b), along the proximal tract of the superior mesenteric artery (14a, 14b) and anterior face of the common hepatic artery (8a). [9] An intra-operative picture of post resection stage of LPD is shown in Fig. 1. The same methodology was followed for OPD.

The specimen was marked on table for uncinate margins and retroperitoneal margins with a combination of suture placement and commercially available inks. Specimen was examined as per the guidelines of College of American Pathologists [10]. Shave sections are examined for circumferential involvement. Axial slices were taken at each resection margins to determine margin lengths. Presence of tumor within 1 mm margin was reported as R1 resection.

Fig. 2 Patient population

Table 1 Comparison of patient characteristics between LPD and OPD group

Characteristic	LPD Group <i>n</i> =45	OPD Group <i>n</i> =118	<i>P</i> value
Mean age (SD)	54 (11.6)	56 (10.8)	0.242
M:F ratio	1:1.6	1:1	0.056
Past abdominal operation	4	12	0.645
BMI	27.6	28.1	0.646

Statistical Analysis

Means were compared using Independent samples *t*-test or Mann–Whitney's *U* test. Associations between variables examined using Fisher's exact test or Chi-square test. All analysis were done using SPSS (v. 17 for Windows) and "p" value less than 0.05 was considered statistically significant.

Results

A total of 185 patients underwent pancreaticoduodenectomy between March 2006 and February 2011. Of these 18 patients had diagnosis other than periampullary and pancreatic cancer and 4 patients had vascular resections, hence were excluded from the study. Of the remaining, 45 patients underwent LPD and 118 underwent OPD. The study design is illustrated in Fig. 2.

The mean age of the patients in LPD group was 54 years and OPD group was 56 years. The study groups were comparable in terms of age of presentation, ASA grades, co-morbidity, type of surgery (CPD vs. PPPD) and body mass index (Table 1). We had higher percentage of female patients in LPD and this could be attributed to non-randomised design and patient preference. There were no significant differences in the site-wise proportion of cancers operated by LPD or OPD (Fig. 3).

There was no statistically significant difference between the two groups with regard to tumor size. The average tumor size in LPD group is 2.8 cm and in OPD group, it is 3.1 cm.

Table 2 Comparison of pathological characteristics between LPD and OPD

Parameters	LPD <i>n</i> =45	OPD <i>n</i> =118	<i>P</i> value
Tumour size (cm)	2.8	3.1	0.066
Mean no. of nodes (SD)	18.6 (3.5)	18 (3.4)	0.350
Node positivity rate	65 %	68 %	0.76

The total number of lymph nodes retrieved and node positivity rates were similar between the two study groups (Table 2).

The distribution of R1 positive margins in study groups is depicted in Fig. 4. SMA margin was the commonest margin positive in both the groups. In LPD group, 4 patients had positive margins whereas 10 patients had positive margins in OPD (*p*=0.933). There was no difference in R1 status between the study groups even when individual margins were compared separately (Table 3). Since all the R1 resections were from pancreatic head malignancy a subgroup analysis on pancreatic head tumours was done and found no significant difference in R1 rates (Table 4). The average lengths of various margins were comparable between the two groups and here again there was no statistically significant difference (Table 5).

Discussion

Apart from technical feasibility, the two major arguments against LPD were safety and oncological adequacy.[3] Two reviews by Gagner et al in 2009 [6] and Gumbs et al. in 2011 [7] have established the safety and comparable short term outcomes with open approach. This study addresses the issue of oncological adequacy by comparison of the resected specimens between laparoscopic and open pancreaticoduodenectomy. Laparoscopic pancreatic resection requires considerable expertise in both pancreatic and laparoscopic surgery. That being the fact, this series reflects the results of a surgical team with extensive experience in pancreatic and laparoscopic surgery in a tertiary care unit. In addition to our own OPD study arm, we reviewed our LPD study data with data on standard pancreaticoduodenectomy from notable randomized trials on pancreaticoduodenectomy.[11–13] The

Fig. 3 Pie chart depicting the anatomical location of tumour in LPD and OPD group

Fig. 4 Flow chart depicting the distribution of R1 positive margin status in LPD and OPD patients. (SMA-Superior mesenteric artery margin, RP-retroperitoneal margin, PANCR- pancreatic transection margin)

disease profile was comparable with published literature except that the mean age of the patients was younger. The mean tumour diameters in both arms were comparable with those studies. Our study has included both pancreatic and peri-ampullary malignancies while some of the open western series have included only pancreatic malignancies. The importance of this lies in the fact that most of the R1 positive resections are in pancreatic malignancies (Table 6). The R0 resection rate was around 91 % for both laparoscopic and open approaches in our study. We had higher proportion of R0 resections in comparison to other published data (Fig. 5). This could be due to the fact that our data does not include earlier case series which reflects our learning phase. Another pertinent issue was

Table 3 Comparison of overall and individual margin resection status between OPD and LPD groups

Resection status	LPD (<i>n</i> =45)		OPD (<i>n</i> =118)		<i>P</i> value
	N	%	N	%	
R0	41	91.1	108	91.5	0.933
R1	4	8.9	10	8.5	
SMA Margin					
R0	41	91.1	110	93.2	0.645
R1	4	8.9	8	6.8	
Retroperitoneal margin					
R0	44	97.8	116	98.3	0.823
R1	1	2.2	2	1.7	
Pancreatic transection margin					
R0	45	100	117	99.2	0.536
R1	0	0	1	0.8	

Table 4 Subgroup analysis of pancreatic head tumors overall and individual margin resection status between OPD and LPD

Resection status	LPD (<i>n</i> =21)		OPD (<i>n</i> =56)		<i>P</i> value
	N	%	N	%	0.90
R0	17	80.9	46	82.1	
R1	4	19.1	10	17.9	
<hr/>					
SMA Margin					
R0	17	80.9	48	85.7	0.82
R1	4	19.1	8	14.3	
Retroperitoneal margin					
R0	20	95.2	54	96.4	0.81
R1	1	4.8	2	3.6	
Pancreatic resection margin					
R0	21	100.0	55	98.2	0.53
R1	0	0.0	1	1.8	

Table 5 Comparison of resection margin length status

Margins (mm)	LPD Mean Length (SD)	OPD Mean Length (SD)	P value
SMA Margin	1.54 (0.8)	1.71 (0.7)	0.592
Retroperitoneal margin	1.9 (0.6)	1.8 (0.6)	0.210
Pancreatic transection margin	4.4 (0.6)	4.2 (0.5)	0.245
Bile duct margin	15.4 (0.5)	14.6 (0.6)	0.879

that in our study the more stringent and fully standardized pathological analysis like LEEPP protocol was not implemented as our study started earlier in 2006.[14] But since uniform specimen examination guidelines were followed for examining both open and laparoscopic specimen, the comparative statistics is not likely to be affected. In our study there was no significant difference in R1 positivity rates between open and laparoscopy group when compared both on overall and individual margin basis. Insufficient examination of the

Table 6 Comparative statistics with data from reported series

Parameters	LAP PD (n=45)	Open pd (n=118)	YEO et al. 2002 (n=146)	Farnell et al. 2005 (n=40)	Pedrazzoli et al. 1998 (n=40)
Mean age	54.0	56.2	66.7	64	62
PPPD	46.7 %	58.5 %	86 %	100 %	50 %
Classical	53.3 %	41.5 %	14 %	-	50 %
Site					
Pancreas	21	56	84	40	40
Ampullary	18	44	35	-	-
CBD	6	18	23	-	-

Fig. 5 Bar diagram depicting R0 and R1 status of study groups and western open PD series

margins might lead to the underreporting of R1 resections. Although most investigators report overall resection margin involvement to be an independent prognostic factor, some have concluded otherwise.[15–17].

Moderately differentiated adenocarcinoma was the commonest histological grade seen like other western studies. The lymph node harvest with LPD appears to be comparable to that of OPD (18.6 vs. 18, $p=0.35$) with magnification in laparoscopy providing added advantage of better visualisation to facilitate adequate oncological clearance. The lymph node yields were similar to published reports (Table 7).

The limitation of this study is that it is non-randomized with unequal number of patients in each group. Though this may create patient selection bias, we hope this approach would provide a realistic assessment of the learning curve and evolving impact of laparoscopic pancreaticoduodenectomy on the outcomes of pancreatic and periampullary malignancies. Finally, it can be concluded within the ambit of this non-randomized study that laparoscopic pancreaticoduodenectomy when performed by experienced

minimal-access surgeons, is technically and oncologically safe. Standardized protocols for evaluation of the resection margins should be mandatory in studies reporting outcomes of pancreaticoduodenectomy.

References

1. Kooby DA, Chu CK (2010) Laparoscopic management of pancreatic malignancies. *Surg Clin N Am* 90(2):427–446
2. Gagner M, Pomp A (1994) Laparoscopic pylorus-preserving pancreaticoduodenectomy. *Surg Endosc* 8(5):408–410
3. Cuschieri A (1994) Laparoscopic surgery of the pancreas. *J R Coll Surg Edinb* 39(3):178–184
4. Palanivelu C et al (2007) Laparoscopic pancreaticoduodenectomy: technique and outcomes. *J Am Coll Surg* 205(2):222–230
5. Palanivelu C et al (2009) Evolution in techniques of laparoscopic pancreaticoduodenectomy: a decade long experience from a tertiary center. *J Hepatobiliary Pancreat Surg* 16(6):731–740
6. Gagner M, Palermo M (2009) Laparoscopic whipple procedure: review of the literature. *J Hepatobiliary Pancreat Surg* 16(6):726–730
7. Gumbs AA et al (2011) Laparoscopic pancreaticoduodenectomy: a review of 285 published cases. *Ann Surg Oncol* 18(5):1335–1341
8. Correa-Gallego C et al (2014) Minimally-invasive vs open pancreaticoduodenectomy: systematic review and meta-analysis. *J Am Coll Surg* 218(1):129–139
9. Pedrazzoli S et al (1999) A surgical and pathological based classification of resective treatment of pancreatic cancer. Summary of an international workshop on surgical procedures in pancreatic cancer. *Dig Surg* 16(4):337–345
10. Compton CC, Henson DE (1997) Protocol for the examination of specimens removed from patients with carcinoma of the exocrine pancreas: a basis for checklists. *Cancer Committee, College of American Pathologists. Arch Pathol Lab Med* 121(11):1129–1136
11. Yeo CJ et al (2002) Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma, part 2: randomized controlled trial evaluating survival, morbidity, and mortality. *Ann Surg* 236(3):355–366
12. Farnell MB et al (2005) A prospective randomized trial comparing standard pancreaticoduodenectomy with pancreaticoduodenectomy with

Table 7 Comparison of tumour size, resection status and lymph node status

Parameters	LAP PD n=45	Open PD n=118	Yeo et al. 2002 n=146	Farnell et al. 2005 n=40	Pedrazzoli 1998 n=40
Mean tumor diameter (cm)	2.8	3.1	3.0	3.1	3.35
Differentiation	4.4 %	11 %	6 %	0 %	12.5 %
Grade 1	88 %	79 %	52 %	34 %	65 %
Grade 2	6.7 %	8.5 %	42 %	66 %	22.5 %
Grade 3					
Mean no total lymph nodes	18.6	18	17	15	13
% of Node positive	65 %	68 %	73 %	55 %	NA

- extended lymphadenectomy in resectable pancreatic head adenocarcinoma. *Surgery* 138(4):618–628
13. Pedrazzoli S et al (1998) Standard versus extended lymphadenectomy associated with pancreatoduodenectomy in the surgical treatment of adenocarcinoma of the head of the pancreas: a multicenter, prospective, randomized study. Lymphadenectomy study group. *Ann Surg* 228(4):508–517
 14. Menon KV et al (2009) Impact of margin status on survival following pancreatoduodenectomy for cancer: the leeds pathology protocol (LEEPP). *HPB* 11(1):18–24
 15. Butturini G et al (2008) Influence of resection margins and treatment on survival in patients with pancreatic cancer: meta-analysis of randomized controlled trials. *Arch Surg* 143(1): 75–83
 16. Rowsell C et al (2007) Improved lymph node retrieval in Whipple specimens as a result of implementation of a new uncinate margin protocol. *HPB* 9(5):388–391
 17. Raut CP et al (2007) Impact of resection status on pattern of failure and survival after pancreaticoduodenectomy for pancreatic adenocarcinoma. *Ann Surg* 246(1):52–60