ORIGINAL ARTICLE

A model to predict survival following pancreaticoduodenectomy for malignancy based on tumour site, stage and lymph node ratio

Bobby V.M. Dasari[1], Keith J. Roberts[1], James Hodson[2], Lewis Stevens[3], Andrew M. Smith[3], Stefan G. Hubscher[4], John Isaac[1], Paolo Muiesan[1], Robert P. Sutcliffe[1], Ravi Marudanayagam[1] & Darius F. Mirza[1]

[1]Department of HPB Surgery, [2]Institute of Translational Medicine, Queen Elizabeth Hospital, Birmingham, B15 2TH, [3]Leeds Teaching Hospitals, Leeds, and [4]Department of Cellular Pathology, Queen Elizabeth Hospital, Birmingham, B15 2WB, UK

Abstract

Background: Site of tumour origin, lymph node metastases and lymph node ratio (LNR) are identified as important factors determining prognosis in patients undergoing pancreaticoduodenectomy (PD). This study hypothesised that a prognostic index to predict survival could be developed through statistical modelling based on these pathological variables.

Methods: Patients who underwent PD between 2004 and 2013 were included. Univariable and multivariable (Cox regression) analyses were performed to identify predictors of survival, and a prognostic index was derived. The prognostic index was then validated using an external patient cohort.

Results: A total of 567 patients who underwent PD were used as a derivation cohort. Tumour site ($p < 0.001$), tumour size ($p = 0.002$), T-stage ($p < 0.001$), vascular involvement ($p = 0.002$), number of positive nodes ($p < 0.001$) and LNR ($p < 0.001$) were significantly associated with survival in univariable analysis. LNR ($p < 0.001$), tumour site ($p < 0.001$), T-stage ($p = 0.007$) remained significant predictors of survival in multivariable analysis, and were combined to derive a prognostic index. The accuracy of the prognostic index was assessed both on the original cohort, and a validation set of 194 patients from another institutional prospective database. The AUROC scores for predicting the overall survival at 3 years were 0.77 in the derivation cohort and 0.74 in the validation cohort.

Conclusion: The Pancreaticoduodenectomy Prognostic Index is a validated clinico-pathological model based on tumour site, T-stage and LNR to predict long-term survival following PD.

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Correspondence:

Darius F. Mirza, The HPB and Transplantation Unit, Queen Elizabeth Hospital, Edgbaston, Birmingham, B15 2WB, UK. Tel: +44 1213714638. Fax: +44 1214141833. E-mail: darius.mirza@uhb.nhs.uk

Introduction

Surgical resection remains the only potentially curative treatment for patients with adenocarcinomas arising from head of pancreas, ampulla, distal bile duct and ampulla. Although the median survival following pancreaticoduodenectomy (PD) has improved,[1] the actual five-year survival after resection of pancreatic ductal adenocarcinoma approaches 10%.[2–5] For ampullary carcinoma and distal cholangiocarcinoma, 5-year survival varies between 20 and 40%[6,7] and is up to 60% for duodenal adenocarcinoma.[8] Various factors, however, impact upon cancer related outcomes after PD, including tumour site, tumour size, tumour at the resection margins, lymph node metastases, and histologic grade.[3,9–11] The role of post-operative chemotherapy/radiotherapy continues to evolve and can increase survival.[12–14]

The presence of nodal metastases has been shown to be an indicator of poor prognosis.[3–5,15,16] Evidence suggests that a minimum of 11–15 lymph nodes (LNs) should be examined to provide an accurate assessment of LN metastases upon which to base

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prognostic information, following resection for pancreatic cancer.[17–19] The AJCC TNM staging system considers LN metastases as a binary outcome – they are or are not present.[20] Recent studies have demonstrated that the lymph node ratio (number of metastatic lymph nodes (LNs) divided by total number of examined nodes) provides additional prognostic information over the standard reporting of LN metastasis and its role in pancreatic carcinoma is also increasingly accepted.[17,21,22] The aim of this study was to develop a prognostic index that could be applied to the four common tumour types that require PD.

Materials and methods

This was a retrospective analysis of a prospectively maintained database of patients who underwent PD between 2004 and 2013. Patients with pancreatic ductal carcinoma, distal cholangiocarcinoma, ampullary carcinoma or duodenal carcinoma were included. Patients undergoing surgery for other pathologies were excluded. Pylorus preserving PD was the standard operation, with a Kausch Whipple procedure performed when it was deemed appropriate on oncological grounds. A standard lymphadectomy was performed to include dissection of the common hepatic artery from the splenic artery origin to the origins of the hepatic arteries. Perineural tissue and lymph nodes along the common bile duct, station 8 nodes along the hepatic artery, posterior and anterior pancreatico-duodenal nodes, nodes along the superior mesenteric vein and right lateral wall of the superior mesenteric artery were removed. The technique of pancreato-enteric anastomosis was performed at the operating surgeons discretion. Patients received adjuvant chemotherapy in line with existing practice within the United Kingdom at that time following surgery.

All specimens were reviewed by dedicated pancreatic specialist pathologists. The AJCC TNM system was used for staging the tumour.[20] Site of tumour origin was based on macroscopic assessment of tumour location. Whenever possible, this was corroborated by histological identification of in-situ neoplasia (pan-IN for ductal adenocarcinoma, Bil-IN for cholangiocarcinoma). For the purposes of the present study, the resection margins that were consistently examined were the pancreatic neck transection margin, the superior mesenteric artery surface, proximal bile duct margin, proximal duodenal margin and distal duodenal margin. Verbeke's description[23,24] of positive resection margin (tumour found within 1 mm of the margin) was used for the patients included in the latter part of the study period.

Outcomes assessed

Median follow up of the patients included in the study was 1.36 years (range, 0.02–10.05 years). Overall survival (OS) was assessed, and reported at one and three years.

Table 1 Association between clinico-pathological factors and patient survival (derivation cohort)

	N	Overall survival 1 year, 3 years	p-Value
Age			0.074
<60	149 (26%)	74%, 37%	
60–66	144 (25%)	71%, 38%	
67–74	174 (31%)	66%, 30%	
75+	100 (18%)	65%, 32%	
Smoking status[a]			0.570
Never	135 (51%)	72%, 39%	
Ex	87 (33%)	73%, 38%	
Current	43 (16%)	71%, 31%	
BMI[a]			0.528
<=25	157 (50%)	73%, 32%	
26–30	114 (36%)	68%, 41%	
31–35	30 (9%)	64%, 25%	
>35	16 (5%)	65%, 55%	
Tumour			<0.001[b]
Ductal adenocarcinoma	279 (49%)	63%, 23%	
Cholangiocarcinoma	89 (16%)	61%, 30%	
Duodenal carcinoma	32 (6%)	77%, 60%	
Ampullary carcinoma	167 (29%)	83%, 56%	
Tumour size			0.002[b]
<2.0	85 (17%)	74%, 50%	
2.0–2.4	88 (18%)	68%, 37%	
2.5–3.4	167 (34%)	70%, 32%	
3.5+	148 (30%)	63%, 25%	
T stage			<0.001[b]
1	31 (6%)	86%, 82%	
2	60 (11%)	88%, 74%	
3	393 (75%)	67%, 28%	
4	41 (8%)	71%, 29%	
R status			<0.001[b]
Negative	450 (80%)	80%, 38%	
Positive	114 (20%)	58%, 22%	
Vascular reconstruction			0.002[b]
No	493 (87%)	70%, 51%	
Yes	74 (13%)	65%, 20%	
Adjuvant chemotherapy[a]			0.074
No	133 (48%)	67%, 41%	
Yes	147 (52%)	82%, 40%	
Any pre-op comorbidity			0.132
No	344 (61%)	76%, 34%	
Yes	223 (39%)	59%, 36%	
Wound infection			0.522
No	523 (92%)	70%, 35%	

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