Perineural infiltration and lymphovascular invasion are the most significant factors predicting cancer survival following Whipple’s Resection - An analysis of 217 pancreaticoduodenectomies

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Queenstown 2010
Predicting patient survival after pancreaticoduodenectomy for malignancy - A histopathological prognosis based on perineural infiltration and lymphovascular invasion

R Padbury, M Bhandari, David Astill, T Wilson, L Kow, M Brooke-Smith, J Toouli, J Chen

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Adelaide Community Healthcare Alliance
Adelaide, Australia
AJCC 6th Edition TNM Staging System for Pancreatic Cancer

Definitions of TNM

TX Primary tumor cannot be assessed
T0 No evidence of primary tumory
Tis Carcinoma in situ
T1 Tumor limited to the pancreas, 2 cm or less in greatest diameter
T2 Tumor limited to the pancreas, greater than 2 cm in greatest diameter
T3* Tumor extends beyond pancreas but no involvement of celiac axis or superior mesenteric artery
T4* Tumor involves the celiac axis or the superior mesenteric artery (unresectable)
NX Regional nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis
MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis

Stage grouping
Stage 0 Tis N0 M0 Localized within pancreas
Stage IA* T1 N0 M0 Localized within pancreas
Stage IB* T2 N0 M0 Localized within pancreas
Stage IIA T3 N0 M0 Locally invasive, resectable
Stage IIB* T1,2, or 3 N1 M0 Locally invasive, resectable
Stage III* T4 Any N M0 Locally advanced, unresectable
Stage IV Any T Any N M1 Distant metastases

Background

- Standard pancreatic malignancy staging based on TNM system - AJCC
- Other parameters not included
  - Tumour differentiation
  - Resection margin
  - Perineural infiltration
  - Lymphovascular invasion
Perineural infiltration

Pancreaticoduodenectomy

- N=110
- Median Follow-up = 4.9 years
- Age = 69 (20-89)
- Male:Female = 58:52
- Benign n=14
  - IPMNs, Cystadenomas, Tubular Villus Adenomas, Ganglioneuroma, Lymphoepithelial Cyst, Stone
- Malignant n=96
  - Pancreatic adenocarcinoma 60
  - Periampullary malignacies 36
    - Ampullary Carcinoma 14
    - Cholangiocarcinoma 9
    - Duodenal carcinoma 9
    - Neuroendocrine 4
HISTOPATHOLOGY

- All reports reviewed by one pathologist
- Cases of doubt or missing information the original slides were reviewed
Patient Survival

Years

Cum Survival

Periampullary malignancies

Pancreatic adenocarcinoma
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Multivariate analysis

- Perineural infiltration
  - P<0.03

- Lymphovascular invasion
  - P=0.05
Lymphovascular Invasion

Cum Survival

Years

P=0.002
Perineural infiltration

Cum Survival

Years

P<0.0001
Results: Expanded Study

- N=217
- Male : Female = 118:99
- Age = 68 (20-91)
  - Age 70-80 = 82
  - Age>80 = 14
- 30 day mortality n=7 (3.7%)
- Malignant:Benign = 185:32
- Pancreatic Adenocarcinoma n=107
- Periampullary malignancies n=78
  - Ampullary Carcinoma n=35
  - Cholangiocarcinoma n=20
  - Duodenal Carcinoma n=15
  - Neuroendocrine n=8
- Benign n=32
  - IPMNs n=5
  - Adenoma n=7
  - Trauma, stone, cyst adenomas, ganglioneuroma, lymphoepithelial cyst, chronic pancreatitis, Grove pancreatitis etc
Survival Functions

Cum Survival

Survival

Periampullary
Pancreatic

50% P<0.005
26%
Tumour Size

Survival Functions

Cum Survival

Survival

<2cm

P<0.01

2-3cm

>3cm
Survival Functions

Cum Survival

P<0.0001

Survival

Tumour Differentiation

Well

Moderate

Poor
Nodes

Survival Functions

Cum Survival

Survival

Positive

Negative

P<0.01
Resection Margin

Survival Functions

Cum Survival

Survival

P < 0.04
Perineural Infiltration

Survival Functions

Cum Survival

Survival

P<0.0001

No

Yes

Perineural Infiltration
Lymphovascular Invasion

Survival Functions

P<0.001
Multivariate Analysis

- Perineural Infiltration $P<0.03$

- Lymphovascular Invasion $P<0.05$
  - ($P=.05$ in first study)
SUMMARY

- Lymphovascular invasion and perineural infiltration independent predictors of survival in patients undergoing pancreaticoduodenectomy for periampullary malignancy
- More significant predictors of outcome than tumor size, differentiation, nodal status, resection margin status or tumour location
- High proportion of resected pancreas cancers have one or both features
CONCLUSIONS

- New pancreas specific pathological staging system required that incorporates lymphovascular invasion and perineural infiltration
- These parameters need to be considered when planning and interpreting clinical trials in patients with pancreas cancer