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**Determinants of survival and attempted resection in patients with non-metastatic pancreatic cancer: an Australian population-based study.**

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**ABSTRACT**

**Background**

There are indications that pancreatic cancer survival may differ according to sociodemographic factors, such as residential location. This may be due to differential access to curative resection. Understanding factors associated with the decision to offer a resection might enable strategies to increase the proportion of patients undergoing potentially curative surgery.

**Methods**

Data were extracted from medical records and cancer registries for patients diagnosed with pancreatic cancer between July 2009 and June 2011, living in one of two Australian states. Among patients clinically staged with non-metastatic disease we examined factors associated with survival using Cox proportional hazards models. To investigate survival differences we examined determinants of : 1) attempted surgical resection overall; 2) whether patients with locally advanced disease were classified as having resectable disease; and 3) attempted resection among those considered resectable.

**Results**

Data were collected for 786 eligible patients. Disease was considered locally advanced for 561 (71%) patients, 510 (65%) were classified as having potentially resectable disease and 365 (72%) of these had an attempted resection. Along with age, comorbidities and tumour stage, increasing remoteness of residence was associated with poorer survival. Remoteness of residence and review by a hepatobiliary surgeon were factors influencing the decision to offer surgery.

**Conclusions**

This study indicated disparity in survival dependent on patients’ residential location and access to a specialist hepatobiliary surgeon. Accurate clinical staging is a critical element in assessing surgical resectability and it is therefore crucial that all patients have access to specialised clinical services.

**Keywords:** Cancer care, Health service utilisation, Pancreatic cancer, Surgery, Survival.

**INTRODUCTION**

Pancreatic cancer is the 10th most commonly diagnosed cancer in more developed regions of the world. However, it has the worst prognosis of any cancer, with a five-year relative survival of less than 5%, so is the 4th most common cause of cancer death.[1](#_ENREF_1) Although survival rates have improved slightly over the past decade, current projections suggest that it will be the second leading cause of cancer death in the United States within 10 years.[2](#_ENREF_2)

Worse survival has been observed for patients who live outside metropolitan areas,[3](#_ENREF_3) have low socioeconomic status and who are elderly.[4](#_ENREF_4) While patient factors such as frailty and comorbidities may be partially responsible for these survival differences, isolation and access to quality care may also play a role. This access to care is becoming increasingly important as vascular reconstruction becomes more commonplace in major centres, particularly in combination with neoadjuvent therapies for borderline resectable tumours. Multimodality therapy which includes complete surgical removal of the tumour currently provides the only potentially curative therapeutic option,[5-7](#_ENREF_5) improving five-year survival to about 20%.[8-10](#_ENREF_8) However, due to the proximity of the pancreas to large vessels and organs, assessment of resectability is challenging and surgical resection itself is technically challenging.[11](#_ENREF_11) National Cancer Comprehensive Network (NCCN) guidelines therefore recommend multidisciplinary consultation when determining potential resectability,[12](#_ENREF_12) with the involvement of a skilled, specialised hepatobiliary surgeon as an integral part of the team.[13](#_ENREF_13), [14](#_ENREF_14) International data show that resection rates are influenced by ethnicity, insurance status, marital status, education level, socioeconomic status and geographical distance from large metropolitan areas.[15-18](#_ENREF_15) There are indications that this may be related to the expertise at the facility where patients are being staged.[19](#_ENREF_19)

Understanding factors that influence survival and that are associated with surgical resection may enable implementation of strategies to ensure all patients with pancreatic cancer who are suitable for surgery are indeed offered such potentially curative surgery as part of their management. Using data from an Australian population-based study of patients clinically staged as having non-metastatic pancreatic cancer, our aim was to investigate survival according to patient, tumour and health-service factors and to examine components associated with determination of resectability and whether or not resection was attempted.

**METHODS**

**Study population and data collection**

Data collection and regulatory approvals for the study have been described previously.[20](#_ENREF_20) Briefly, the study included patients aged ≥18 years who were notified to the Queensland Cancer Registry between 1 July 2009 and 30 June 2011 or to the New South Wales Cancer Registry between 1 July 2009 and 31 December 2010 with a diagnosis of pancreatic ductal adenocarcinoma. We obtained demographic and initial diagnosis information from the cancer registries; trained research nurses collected detailed clinical data from medical records. Date of death was obtained from medical records or cancer registries. As all patients with metastatic disease on initial clinical staging are unsuitable for curative resection, analyses were restricted to patients with no evidence of metastatic disease on clinical staging.

**Outcomes**

The main outcomes were one- and two-year mortality, defined as death of any cause within one and two years of diagnosis respectively, and survival time. Survival time was defined as the number of months from diagnosis until death or, for patients still alive, until date of last follow-up (February 2014). The date of diagnosis was taken as either the date of first diagnosis on imaging or histology/cytology, whichever came first.

To investigate survival differences, we examined factors associated with: (1) attempted surgical resection for all patients with non-metastatic disease; (2) whether patients with locally advanced disease were classified as having potentially resectable disease (restricted to this patient group as disease confined to the pancreas is automatically classified as resectable); and (3) attempted resection for those considered resectable. Whether or not a tumour was considered to be locally advanced or resectable was extracted from medical specialist or multidisciplinary team (MDT) meeting notes.

**Factors of interest**

Patient characteristics: The patient factors of interest included age at diagnosis, sex, Eastern Cooperative Oncology Group (ECOG) performance status and Charlson comorbidity index.[21](#_ENREF_21) Based on area of residence at the time of diagnosis, each person was allocated a socio-economic index for areas (SEIFA)[22](#_ENREF_22) score and Accessibility/Remoteness Index of Australia (ARIA)[23](#_ENREF_23) category. For analysis we grouped the SEIFA score into quintiles and collapsed the ARIA into three groups: major city; inner regional; and outer regional/remote/very remote.

Tumour characteristics: Tumour factors included the site within the pancreas (head/neck/uncinate process, body, tail or multiple/other) and clinical stage of the tumour (confined to the pancreas or locally advanced disease). Locally advanced disease was defined as localised (non-metastatic) disease spread beyond the pancreas.

Health service characteristics: Health-service factors included the type of specialist first seen, the volume (according to the number of patient presentations in the study) of the facility where the patient was first treated as an inpatient, whether the patient was reviewed by a MDT and if they were assessed by a hepatobiliary surgeon. A hepatobiliary surgeon was defined as a surgeon who had undergone recognised specialised hepatobiliary surgery training and/or was recognised by their peers as an experienced hepatobiliary surgeon. Receipt of any chemotherapy was also included in the analysis of the mortality and survival outcomes. Associations between investigations performed to clinically stage the patient’s tumour including computerised tomography (CT) (+/- pancreas protocol), endoscopic ultrasound (EUS), endoscopic retrograde cholangio-pancreatography (ERCP), magnetic resonance imaging (MRI) or cholangiopancreatography (MRCP), and laparoscopy, and each of resectability and attempted resection were evaluated.

**Statistical analysis**

Survival curves were generated and median survival was estimated using Kaplan-Meier methods, and the median time of follow-up was estimated using reverse Kaplan-Meier methods.[24](#_ENREF_24) The associations between all patient, tumour and health-care factors and one- and two-year mortality were examined using logistic regression and the crude odds ratios (ORs) were estimated. Hazard ratios (HRs) for overall survival were estimated using Cox proportional hazards models. All patient and tumour factors were then included in multivariable models to estimate adjusted odds ratios (AORs) or hazard ratios (AHRs). Models examining health-service factors included all patient and tumour factors and the receipt of chemotherapy.

Associations between patient/tumour/health-service factors and each of (1) attempted resection; (2) whether or not the tumour was staged as potentially resectable for patients with locally advanced disease; and (3) whether or not a resection was attempted among those who were considered resectable were examined using multivariable logistic regression. To understand associations between place of residence, age and other patient and health-service factors, Chi-squared tests were used.

Hierarchical mixed effects models, with hospital as a random intercept, were used to adjust for the effects of clustering within hospitals when assessing associations between the outcomes of interest and hospital volume.

Statistical analyses were performed in Stata13 (Statacorp, Texas). All p-values are two-sided and we considered p < 0.05 as an indication of statistical significance.

**RESULTS**

**Patient characteristics and disease stage**

Overall, 786 patients (44%) were clinically staged as having non-metastatic disease at diagnosis. The median age of these participants was 70 years (range 29 - 99) and 54% were men. The majority (69%) lived in major cities, 21% resided in inner regional areas and 10% in outer regional or remote locations. Disease was considered locally advanced for 561 (71%) patients. About two-thirds (n = 510; 65%) were classified as having potentially resectable disease after staging (225 with disease confined to the pancreas and 285 with locally advanced disease) and resection was attempted for almost three-quarters (n = 365; 72%) of these.

**Mortality and survival**

Median survival was 10 months and the proportions of patients who died within one and two years of diagnosis were 58% (n = 454) and 80% (n = 626) respectively.

Increasing age, comorbidities, low performance status, more advanced clinical stage of disease and tumours in the body of the pancreas were associated with higher mortality and poorer survival outcomes (Table 1, Figure 1).

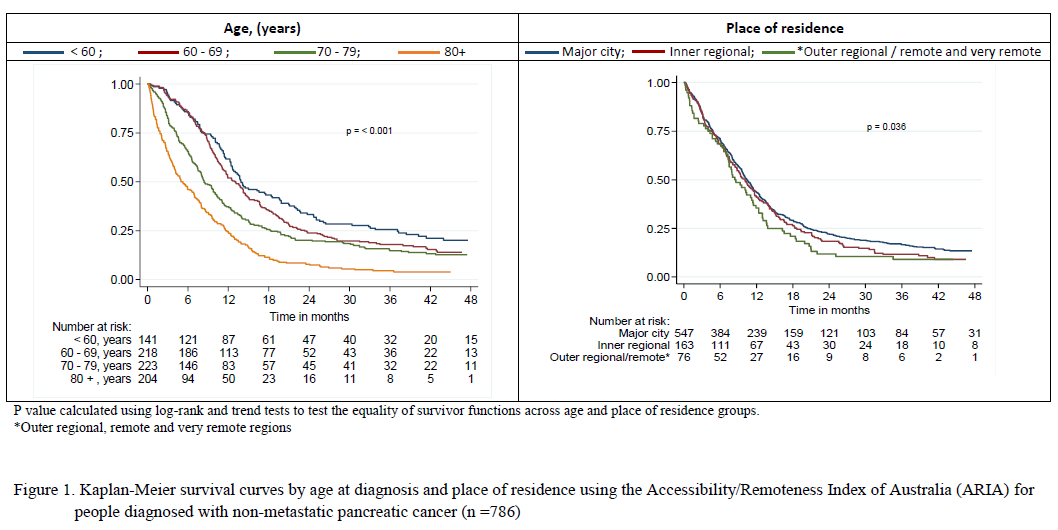


Table 1: Associations between patient, tumour and health-service characteristics and 1- and 2-year mortality and survival for patients diagnosed with non-metastatic disease (n = 786)

|  |  | 1-year mortalitya | | |  | 2-year mortalitya | | |  | Overall survivalb | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Exposure variable | Nc | % dead | Crude OR (95% CI) | Adjusted ORd (95% CI) |  | % dead | Crude OR (95% CI) | Adjusted ORd (95% CI) |  | Median(months) | Crude HR (95% CI) | Adjusted HRd (95% CI) |
| **Patient / tumour factors** |  |  |  |  |  |  |  |  |  |  |  |  |
| Age at diagnosis, years |  |  |  |  |  |  |  |  |  |  |  |  |
| < 60 | 141 | 38.3 | 1.00 | 1.00 |  | 66.7 | 1.00 | 1.00 |  | 13.9 | 1.00 | 1.00 |
| 60 - 69 | 218 | 48.2 | 1.50 (0.97, 2.30) | 1.34 (0.84, 2.15) |  | 76.2 | 1.60 (1.00, 2.56) | 1.45 (0.86, 2.45) |  | 13.0 | 1.20 (0.95, 1.52) | 1.05 (0.83, 1.34) |
| 70 - 79 | 223 | 65.8 | 2.72 (1.76, 4.20) | 2.31 (1.44, 3.73) |  | 79.8 | 1.98 (1.22, 3.19) | 1.69 (0.98, 2.91) |  | 8.4 | 1.57 (1.24, 1.98) | 1.33 (1.04, 1.69) |
| ≥ 80 | 204 | 76.0 | 5.10 (3.19, 8.13) | 3.48 (2.05, 5.91) |  | 92.2 | 5.88 (3.16, 10.91) | 3.99 (1.94, 8.24) |  | 5.0 | 2.70 (2.14, 3.42) | 2.01 (1.56, 2.60) |
| Overall p-value, p-trend |  |  | <0.001, <0.001 | <0.001, <0.001 |  |  | <0.001, <0.001 | 0.003, <0.001 |  |  | <0.001, <0.001 | <0.001, <0.001 |
| Sex |  |  |  |  |  |  |  |  |  |  |  |  |
| Men | 422 | 54.3 | 1.00 | 1.00 |  | 77.5 | 1.00 | 1.00 |  | 11.2 | 1.00 | 1.00 |
| Women | 364 | 61.8 | 1.36 (1.03, 1.81) | 1.18 (0.85, 1.63) |  | 82.1 | 1.34 (0.94, 1.90) | 1.22 (0.81, 1.85) |  | 8.8 | 1.25 (1.07, 1.45) | 1.22 (1.04, 1.42) |
| p-value |  |  | 0.03 | 0.33 |  |  | 0.11 | 0.34 |  |  | 0.004 | 0.012 |
| ECOG performance status |  |  |  |  |  |  |  |  |  |  |  |  |
| Fully active | 260 | 37.3 | 1.00 | 1.00 |  | 65.9 | 1.00 | 1.00 |  | 15.2 | 1.00 | 1.00 |
| Not fully active | 420 | 68.8 | 3.71 (2.68, 5.13) | 2.53 (1.76, 3.64) |  | 88.1 | 4.19 (2.84, 6.18) | 2.90 (1.87, 4.51) |  | 7.2 | 2.13 (1.79, 2.53) | 1.74 (1.45, 2.08) |
| p-value |  |  | < 0.0001 | < 0.001 |  |  | < 0.001 | < 0.001 |  |  | < 0.001 | < 0.001 |
| Charlson comorbidity index (score) | |  |  |  |  |  |  |  |  |  |  |  |
| Low (0) | 340 | 49.1 | 1.00 | 1.00 |  | 74.1 | 1.00 | 1.00 |  | 12.4 | 1.00 | 1.00 |
| Medium (1) | 243 | 57.6 | 1.40 (1.01, 1.96) | 1.12 (0.77, 1.63) |  | 80.3 | 1.42 (0.95, 2.11) | 1.10 (0.70, 1.73) |  | 9.9 | 1.20 (1.00, 1.43) | 1.04 (0.86, 1.25) |
| High (≥ 2) | 199 | 72.9 | 2.78 (1.91, 4.06) | 2.50 (1.64, 3.81) |  | 88.9 | 2.81 (1.70, 4.66) | 2.22 (1.26, 3.91) |  | 8.0 | 1.62 (1.34, 1.95) | 1.43 (1.18, 1.74) |
| Overall p-value, p-trend |  |  | <0.001,<0.001 | <0.001, <0.001 |  |  | <0.001,<0.001 | 0.02, 0.010 |  |  | <0.001,<0.001 | <0.001, 0.001 |
| Place of residence |  |  |  |  |  |  |  |  |  |  |  |  |
| Major city | 547 | 56.5 | 1.00 | 1.00 |  | 77.9 | 1.00 | 1.00 |  | 10.4 | 1.00 | 1.00 |
| Inner Regional | 163 | 58.9 | 1.10 (0.77, 1.58) | 1.19 (0.80, 1.79) |  | 81.6 | 1.26 (0.81, 1.96) | 1.54 (0.92, 2.59) |  | 10.1 | 1.11 (0.93, 1.34) | 1.17 (0.97, 1.42) |
| Outer regional/remote | 76 | 64.5 | 1.40 (0.85, 2.31) | 1.56 (0.88, 2.77) |  | 88.2 | 2.11 (1.02, 4.36) | 3.10 (1.34, 7.20) |  | 8.4 | 1.29 (1.00, 1.66) | 1.33 (1.03, 1.72) |
| Overall p-value, p-trend |  |  | 0.40, 0.19 | 0.27, 0.11 |  |  | 0.096, 0.03 | 0.01, 0.003 |  |  | 0.11, 0.036 | 0.04, 0.01 |
| Socio-economic Status of area of residence - quintiles | | | |  |  |  |  |  |  |  |  |  |
| Most disadvantaged | 156 | 63.5 | 1.00 | 1.00 |  | 82.0 | 1.00 | 1.00 |  | 8.8 | 1.00 | 1.00 |
| Second | 171 | 57.3 | 0.77 (0.50, 1.21) | 0.91 (0.55, 1.50) |  | 77.8 | 0.77 (0.44, 1.32) | 0.91 (0.49, 1.68) |  | 10.1 | 0.87 (0.69, 1.10) | 1.03 (0.81, 1.31) |
| Third | 158 | 54.4 | 0.69 (0.44, 1.08) | 0.68 (0.41, 1.14) |  | 78.5 | 0.80 (0.46, 1.39) | 0.81 (0.43, 1.52) |  | 10.8 | 0.85 (0.67, 1.08) | 0.81 (0.63, 1.04) |
| Fourth | 160 | 56.9 | 0.76 (0.48, 1.19) | 0.91 (0.54, 1.51) |  | 78.1 | 0.78 (0.45, 1.36) | 0.95 (0.51, 1.78) |  | 10.3 | 0.90 (0.71, 1.14) | 1.05 (0.83, 1.34) |
| Least disadvantaged | 136 | 56.6 | 0.75 (0.47, 1.20) | 0.80 (0.47, 1.35) |  | 82.4 | 1.02 (0.56, 1.86) | 1.05 (0.54, 2.05) |  | 10.4 | 0.93 (0.73, 1.19) | 1.01 (0.79, 1.31) |
| Overall p-value, p-trend |  |  | 0.57, 0.26 | 0.64, 0.46 |  |  | 0.76, 0.97 | 0.94, 0.86 |  |  | 0.70, 0.71 | 0.22, 0.86 |
| Tumour site |  |  |  |  |  |  |  |  |  |  |  |  |
| Head/neck/uncinate process | 647 | 58.4 | 1.00 | 1.00 |  | 81.1 | 1.00 | 1.00 |  | 10.1 | 1.00 | 1.00 |
| Body | 40 | 67.5 | 1.48 (0.75, 2.92) | 1.71 (0.81, 3.62) |  | 87.5 | 1.63 (0.62, 4.24) | 1.92 (0.68, 5.42) |  | 8.8 | 1.20 (0.87, 1.67) | 1.40 (1.00, 1.96) |
| Tail | 43 | 41.9 | 0.51 (0.27, 0.96) | 0.63 (0.32, 1.24) |  | 58.1 | 0.32 (0.17, 0.61) | 0.36 (0.18, 0.72) |  | 18.3 | 0.53 (0.36, 0.77) | 0.60 (0.41, 0.88) |
| Multiple/other | 33 | 51.5 | 0.76 (0.38, 1.52) | 0.77 (0.35, 1.68) |  | 81.8 | 1.05 (0.42, 2.59) | 1.13 (0.41, 3.10) |  | 11.7 | 0.93 (0.63, 1.35) | 1.10 (0.75, 1.62) |
| Overall p-value |  |  | 0.091 | 0.22 |  |  | 0.003 | 0.02 |  |  | 0.005 | 0.008 |
| Clinical Stage |  |  |  |  |  |  |  |  |  |  |  |  |
| Confined to pancreas | 225 | 45.8 | 1.00 | 1.00 |  | 68.0 | 1.00 | 1.00 |  | 13.4 | 1.00 | 1.00 |
| Locally advanced | 561 | 62.6 | 1.98 (1.45, 2.71) | 2.13 (1.48, 3.06) |  | 84.3 | 2.53 (1.76, 3.63) | 2.55 (1.68, 3.87) |  | 9.3 | 1.59 (1.34, 1.89) | 1.54 (1.29, 1.83) |
| Overall p-value |  |  | <0.001 | <0.001 |  |  | < 0.001 | <0.001 |  |  | <0.001 | < 0.001 |
| **Health Service Factors** |  |  |  |  |  |  |  |  |  |  |  |  |
| Evidence of MDT review |  |  |  |  |  |  |  |  |  |  |  |  |
| No/ Not stated | 518 | 61.8 | 1.00 | 1.00e |  | 81.9 | 1.00 | 1.00e |  | 9.3 | 1.00 | 1.00e |
| Yes | 268 | 50.0 | 0.62 (0.46, 0.83) | 0.80 (0.56, 1.14) |  | 75.4 | 0.68 (0.48, 0.97) | 0.77 (0.50, 1.18) |  | 11.9 | 0.76 (0.65, 0.89) | 0.88 (0.74, 1.04) |
| Overall P value |  |  | 0.002 | 0.22 |  |  | 0.033 | 0.22 |  |  | 0.001 | 0.14 |
| First facility volume (number of patients) | | | |  |  |  |  |  |  |  |  |  |
| 30 + | 411 | 52.1 | 1.00 | 1.00e |  | 76.2 | 1.00 | 1.00e |  | 11.4 | 1.00 | 1.00e |
| 10 - 29 | 232 | 60.3 | 1.40 (1.01, 1.94) | 1.17 (0.79, 1.72) |  | 81.0 | 1.34 (0.90, 1.99) | 0.93 (0.58, 1.49) |  | 9.3 | 1.20 (1.01, 1.43) | 1.03 (0.86, 1.24) |
| < 10 | 132 | 74.2 | 2.65 (1.72, 4.10) | 1.84 (1.07, 3.16) |  | 90.2 | 2.87 (1.55, 5.31) | 2.04 (0.91, 4.58) |  | 7.2 | 1.71 (1.39, 2.09) | 1.21 (0.95, 1.53) |
| Overall P value, P trend |  |  | 0.043, <0.001 | 0.09, 0.04 |  |  | 0.003, 0.001 | 0.17, 0.23 |  |  | <0.001, <0.001 | 0.29, 0.17 |
| First specialist seen |  |  |  |  |  |  |  |  |  |  |  |  |
| Hepatobiliary surgeon | 145 | 50.3 | 1.00 | 1.00e |  | 73.1 | 1.00 | 1.00e |  | 12.0 | 1.00 | 1.00e |
| Gastroenterologist | 235 | 54.5 | 1.18 (0.78, 1.79) | 0.83 (0.51, 1.34) |  | 78.7 | 1.36 (0.84, 2.20) | 0.96 (0.55, 1.67) |  | 11.2 | 1.23 (0.98, 1.55) | 1.02 (0.80, 1.29) |
| General Surgeon | 292 | 61.0 | 1.54 (1.03, 2.30) | 0.87 (0.54, 1.40) |  | 82.2 | 1.70 (1.06, 2.73) | 1.04 (0.59, 1.82) |  | 9.0 | 1.40 (1.13, 1.75) | 0.99 (0.78, 1.26) |
| Other specialty | 114 | 65.8 | 1.90 (1.14, 3.14) | 0.90 (0.49, 1.65) |  | 83.3 | 1.84 (1.00, 3.40) | 0.91 (0.42, 1.94) |  | 2.4 | 1.56 (1.20, 2.04) | 0.92 (0.68, 1.23) |
| Overall P value |  |  | 0.037 | 0.89 |  |  | 0.11 | 0.98 |  |  | 0.004 | 0.87 |
| Seen by hepato-biliary surgeon | |  |  |  |  |  |  |  |  |  |  |  |
| No / Not stated | 395 | 65.6 | 1.00 | 1.00e |  | 87.1 | 1.00 | 1.00e |  | 8.0 | 1.00 | 1.00e |
| Yes | 391 | 49.9 | 0.52 (0.39, 0.70) | 0.91 (0.64, 1.29) |  | 72.1 | 0.38 (0.27, 0.55) | 0.58 (0.37, 0.90) |  | 12.1 | 0.61 (0.52, 0.70) | .81 (0.69, 0.96) |
| Overall P value |  |  | < 0.001 | 0.58 |  |  | < 0.001 | 0.015 |  |  | < 0.001 | 0.013 |
| Received chemotherapy |  |  |  |  |  |  |  |  |  |  |  |  |
| No / Not stated | 387 | 74.4 | 1.00 | 1.00e |  | 88.1 | 1.00 | 1.00e |  | 5.5 | 1.00 | 1.00e |
| Yes | 399 | 41.6 | 0.24 (0.18, 0.33) | 0.34 (0.23, 0.50) |  | 71.4 | 0.34 (0.23, 0.49) | 0.50 (0.31, 0.82) |  | 14.1 | 0.57 (0.48, 0.66) | 0.58 (0.48, 0.70) |
| Overall P value |  |  | < 0.001 | < 0.001 |  |  | < 0.001 | 0.005 |  |  | < 0.001 | < 0.001 |
| Resection |  |  |  |  |  |  |  |  |  |  |  |  |
| No resection attempted | 421 | 74.8 | 1.00 | 1.00e |  | 92.4 | 1.00 | 1.00e |  | 6.8 | 1.00 | 1.00e |
| Resection attempted | 365 | 38.1 | 0.21 (0.15, 0.28) | 0.39 (0.26, 0.57) |  | 64.9 | 0.15 (0.10, 0.23) | 0.30 (0.18, 0.52) |  | 15.1 | 0.37 (0.32, 0.43) | 0.56 (0.46, 0.68) |
| Overall P value |  |  | < 0.001 | < 0.001 |  |  | < 0.001 | < 0.001 |  |  | < 0.001 | < 0.001 |

a Crude and adjusted odds ratios (ORs) estimated using logistic regression. P values are from Type 3 tests of effects using Wald’s chi-square statistic. Overall P values are for test of association.

b Median survival estimated using Kaplan-Meier methods. Crude and adjusted hazards ratios (HRs) estimated using Cox proportional hazards (PH) and stratified Cox models, respectively. P values are from Type 3 tests of effects using Wald’s chi-square statistic. Overall P values are for test of association.

cMissing data: Socio-economic status, n= 5; Performance status, n = 106; comorbidities, n = 4; First facility volume , n = 11.

dAdjusted for patient (age, performance status (ECOG), place of residence(ARIA), Charlson comorbidity index) and tumour (clinical stage, site of tumour) factors. SES not adjusted for place of residence.

eAdjusted for patient and tumour factors and receipt of chemotherapy

Place of residence groups defined by Accessibility/Remoteness Index of Australia; ECOG, Eastern Cooperative Oncology Group; SES Socio-Economic Status defined by Socio-Economic Indexes for Areas; First facility volume by number of study participant initial presentations.

MDT= multi-disciplinary team

Compared with patients from major cities, risk of dying within two years was greater for patients from inner regional areas (AOR 1.54; 95% confidence interval [CI]: 0.92 - 2.59) and outer regional/ remote areas (AOR 3.10; 95% CI: 1.34 – 7.20). Increasing remoteness was associated with poorer survival (p trend = 0.01). Compared with those from major cities, those from outer regional/remote areas were 33% more likely to die (AHR 1.33, 95% CI: 1.03 – 1.72). This difference in survival remained after adjusting for attempted surgery (p trend = 0.01, AHR 1.31, 95% CI: 1.01 – 1.70). There were no associations between socio-economic status and mortality or survival in multivariable analyses. After adjusting for patient and tumour factors women had worse overall survival than men (AHR 1.22; 95% CI: 1.04 - 1.42), but when also adjusted for attempted surgery the difference was reduced and no longer statistically significant (AHR 1.15; 95% CI 0.99 – 1.35, p = 0.07).

Each health-service factor was associated with survival and mortality. Patients reviewed by an MDT had lower odds of dying up to one or two years after diagnosis and higher overall survival, but after adjustment for patient and tumour characteristics, the estimates were no longer statistically significant (Table 1). Being seen by a hepatobiliary surgeon was associated with improved overall survival (AHR 0.80; 95% CI: 0.69 – 0.96). Compared with patients who were first admitted to a facility that managed at least 30 pancreatic cancer patients annually, those first admitted to a hospital that treated fewer than 10 had higher one-year mortality (AOR 1.84; 95% CI: 1.07 – 3.16). Estimated survival and mortality rates were more favourable for patients who had an attempted resection (AHR 0.56; 95% CI: 0.46 - 0.68). Patients who received chemotherapy were less likely to die up to a year after diagnosis compared to those who had no record of chemotherapy treatment (AOR 0.34; 95% CI 0.23 – 0.50).

**Determinants of attempted resection in all patients with non-metastatic disease**

Older age, poorer performance status, and/or higher comorbidity scores were each significantly inversely associated with the likelihood of having resection attempted (Table 2 and supplementary table 1).

Table 2. Associations between adjusted patient, tumour and health-service factors and (1) attempted resection for patients with non-metastatic diseasea (n = 786 ) ; (2) classification of disease resectabilitya for patients with locally advanced diseasea (n = 561), and(3) attempted resection for patients classified as resectablea (n = 510).

|  | 1. All Non-metastatic disease | | |  | (2) Locally advanced diseasea | | |  | 1. Classified as resectable | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Attempted resection | |  |  | Classified as resectable | |  |  | Attempted resection | |
| Variable | Total | n (%) | Adjusted ORb (95% CI) |  | Total | n (%) | Adjusted ORb (95% CI) |  | Total | n (%) | Adjusted ORb (95% CI) |
| **Patient / tumour factors** |  |  |  |  |  |  |  |  |  |  |  |
| Age at diagnosis, years |  |  |  |  |  |  |  |  |  |  |  |
| < 60 | 141 | 103 (73) | 1.00c |  | 98 | 62 (63) | 1.00c |  | 105 | 103 (98) | 1.00c |
| 60 - 69 | 218 | 135 (62) | 0.59 (0.37, 0.94) |  | 163 | 91 (56) | 0.71 (0.42, 1.20) |  | 146 | 135 (92) | 0.22 (0.05, 1.04) |
| 70 - 79 | 223 | 107 (48) | 0.33 (0.21, 0.53) |  | 161 | 76 (47) | 0.51 (0.30, 0.85) |  | 138 | 107 (78) | 0.06 (0.01, 0.27) |
| ≥ 80 | 204 | 20 (10) | 0.04 (0.02, 0.07) |  | 139 | 56 (40) | 0.38 (0.22. 0.66) |  | 121 | 20 (17) | 0.00 (0.00, 0.02) |
| Overall p value, p trend |  |  | < 0.001, < 0.001 |  |  |  | 0.002, < 0.001 |  |  |  | < 0.001, < 0.001 |
| Sex |  |  |  |  |  |  |  |  |  |  |  |
| Men | 422 | 222 (53) | 1.00d |  | 299 | 164 (55) | 1.00d |  | 287 | 222 (77) | 1.00d |
| Women | 364 | 143 (39) | 0.77 (0.55, 1.08) |  | 262 | 121 (46) | 0.74 (0.52, 1.05) |  | 223 | 143 (64) | 0.89 (0.48, 1.65) |
| Overall p value |  |  | 0.13 |  |  |  | 0.09 |  |  |  | 0.71 |
| Performance status |  |  |  |  |  |  |  |  |  |  |  |
| Fully active | 260 | 183 (70) | 1.00e |  | 160 | 95 (59) | 1.00e |  | 195 | 183 (94) | 1.00e |
| Not fully active | 420 | 134 (32) | 0.24 (0.17, 0.35) |  | 325 | 156 (48) | 0.71 (0.47, 1.05) |  | 251 | 134 (53) | 0.06 (0.02, 0.14) |
| Overall p value |  |  | < 0.001 |  |  |  | 0.09 |  |  |  | < 0.001 |
| Charlson comorbidity index (score) | |  |  |  |  |  |  |  |  |  |  |
| Low (0) | 340 | 184 (54) | 1.00e |  | 252 | 126 (50) | 1.00e |  | 214 | 184 (86) | 1.00e |
| Medium (1) | 243 | 105 (43) | 0.78 (0.54, 1.14) |  | 177 | 91 (51) | 1.15 (0.78, 1.71) |  | 157 | 105 (67) | 0.40 (0.20, 0.80) |
| High (≥ 2) | 199 | 74 (37) | 0.59 (0.39, 0.88) |  | 130 | 66 (51) | 1.10 (0.72, 1.70) |  | 135 | 74 (55) | 0.15 (0.07, 0.31) |
| Overall p value, p trend |  |  | 0.03, 0.01 |  |  |  | 0.76, 0.59 |  |  |  | < 0.001, < 0.001 |
| Place of residence |  |  |  |  |  |  |  |  |  |  |  |
| Major city | 542 | 258 (48) | 1.00d |  | 386 | 206 (53) | 1.00d |  | 362 | 258 (71) | 1.00d |
| Inner Regional | 163 | 74 (45) | 0.84 (0.55, 1.28) |  | 119 | 50 (50) | 0.90 (0.59, 1.38) |  | 104 | 74 (71) | 0.68 (0.32, 1.46) |
| Outer regional / remote | 76 | 31 (41) | 0.61 (0.33, 1.10) |  | 53 | 19 (36) | 0.48 (0.26, 0.89) |  | 42 | 31 (74) | 0.44 (0.13, 1.50) |
| Overall p value, p trend |  |  | 0.22, 0.09 |  |  |  | 0.07, 0.04 |  |  |  | 0.31, 0.13 |
| SES - quintiles |  |  |  |  |  |  |  |  |  |  |  |
| Most disadvantaged | 156 | 73 (47) | 1.00d |  | 110 | 55 (50) | 1.00d |  | 101 | 73 (72) | 1.00d |
| Second | 171 | 80 (48) | 0.77 (0.46, 1.31) |  | 123 | 65 (53) | 1.01 (0.60, 1.72) |  | 113 | 80 (71) | 0.51 (0.19, 1.32) |
| Third | 158 | 68 (43) | 0.78 (0.46, 1.34) |  | 113 | 50 (44) | 0.72 (0.42, 1.24) |  | 95 | 68 (72) | 0.95 (0.34, 2.65) |
| Fourth | 160 | 77 (48) | 0.85 (0.50, 1.45) |  | 107 | 56 (52) | 0.95 (0.55, 1.65) |  | 109 | 77 (71) | 0.56 (0.21, 1.50) |
| Least disadvantaged | 136 | 65 (48) | 0.93 (0.53, 1.64) |  | 105 | 59 (56) | 1.19 (0.68, 2.07) |  | 90 | 65 (72) | 1.56 (0.55, 4.46) |
| Overall p value, p trend |  |  | 0.86, 1.00 |  |  |  | 0.50, 0.69 |  |  |  | 0.18, 0.43 |
| Tumour site |  |  |  |  |  |  |  |  |  |  |  |
| Head/neck/uncinate process | 647 | 298 (46) | 1.00d |  | 463 | 240 (52) | 1.00d |  | 424 | 298 (70) | 1.00d |
| Body | 40 | 14 (35) | 0.46 (0.21, 0.99) |  | 29 | 8 (28) | 0.33 (0.14, 0.77) |  | 19 | 14 (74) | 0.98 (0.19, 4.99) |
| Tail | 43 | 33 (77) | 3.62 (1.58, 8.33) |  | 27 | 21 (78) | 3.09 (1.20, 7.94) |  | 37 | 32 (89) | 3.39 (0.85, 13.57) |
| Multiple/other | 33 | 13 (39) | 0.55 (0.24, 1.24) |  | 25 | 8 (32) | 0.45 (0.18, 1.10) |  | 16 | 13 (81) | 1.25 (0.19, 8.13) |
| Overall p value |  |  | 0.001 |  |  |  | 0.001 |  |  |  | 0.39 |
| **Health Service Factors** |  |  |  |  |  |  |  |  |  |  |  |
| Evidence of MDT review |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 518 | 239 (46) | 1.00f |  | 355 | 193 (54) | 1.00f |  | 356 | 239 (67) | 1.00f |
| Yes | 268 | 126 (47) | 0.60 (0.42, 0.86) |  | 206 | 92 (45) | 0.33 (0.14, 0.78) |  | 154 | 126 (82) | 1.09 (0.54, 2.21) |
| Overall p value |  |  | 0.01 |  |  |  | 0.01 |  |  |  | 0.81 |
| First facility volumeg |  |  |  |  |  |  |  |  |  |  |  |
| 30 + | 411 | 226 (55) | 1.00f |  | 275 | 153 (56) | 1.00f |  | 289 | 226 (78) | 1.00f |
| 10 – 29 | 232 | 97 (42) | 0.70 (0.47, 1.05) |  | 170 | 84 (49) | 0.92 (0.61, 1.38) |  | 146 | 97 (66) | 0.52 (0.20, 1.537) |
| < 10 | 132 | 42 (32) | 0.57 (0.34, 0.97) |  | 107 | 48 (45) | 0.88 (0.53, 1.45) |  | 73 | 42 (58) | 0.51 (0.15, 1.67) |
| Overall p value, p trend |  |  | 0.06, 0.02 |  |  |  | 0.85, 0.58 |  |  |  | 0.34, 0.19 |
| Specialist first seen |  |  |  |  |  |  |  |  |  |  |  |
| Hepatobiliary surgeon | 235 | 87 (60) | 1.00f |  | 87 | 44 (51) | 1.00f |  | 102 | 87 (85) | 1.00f |
| Gastroenterologist | 235 | 123 (52) | 0.99 (0.61, 1.61) |  | 173 | 97 (56) | 1.42 (0.83, 2.43) |  | 159 | 123 (66) | 0.75 (0.29, 1.94) |
| General Surgeon | 292 | 118 (40) | 0.70 (0.43, 1.13) |  | 222 | 108 (49) | 1.11 (0.66, 1.89) |  | 178 | 118 (66) | 0.64 (0.25, 1.63) |
| Other | 114 | 37 (32) | 0.67 (0.36, 1.25) |  | 79 | 36 (46) | 1.08 (0.56, 2.08) |  | 71 | 37 (52) | 0.58 (0.19, 1.79) |
| Overall p value |  |  | 0.24 |  |  |  | 0.52 |  |  |  | 0.77 |
| Seen by hepato-biliary surgeon | |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 395 | 106 (27) | 1.00f |  | 308 | 129 (42) | 1.00f |  | 216 | 106 (49) | 1.00f |
| Yes | 391 | 259 (66) | 3.77 (2.63, 5.39) |  | 253 | 156 (62) | 1.95 (1.35, 2.82) |  | 294 | 259 (88) | 6.78 (3.38, 13.59) |
| Overall p value |  |  | < 0.001 |  |  |  | < 0.001 |  |  |  | < 0.001 |
| Pancreas protocol computerised tomography | | |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 406 | 173 (43) | 1.00f |  | 294 | 150 (51) | 1.00f |  | 262 | 173 (66) | 1.00f |
| Yes | 380 | 192 (51) | 0.96 (0.68, 1.35) |  | 267 | 135 (51) | 0.97 (0.61, 1.23) |  | 248 | 192 (77) | 1.33 (0.71, 2.50) |
| Overall p value |  |  | 0.82 |  |  |  | 0.42 |  |  |  | 0.37 |
| Plain computerised tomography | |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 261 | 133 (51) | 1.00f |  | 189 | 104 (55) | 1.00f |  | 176 | 133 (76) | 1.00f |
| Yes | 525 | 232 (44) | 0.76 (0.54, 1.12) |  | 372 | 181 (49) | 0.79 (0.55, 1.15) |  | 334 | 232 (69) | 0.40 (0.19, 0.83) |
| Overall p value |  |  | 0.17 |  |  |  | 0.22 |  |  |  | 0.01 |
| Endoscopic ultrasound | | |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 434 | 186 (43) | 1.00f |  | 311 | 168 (54) | 1.00f |  | 291 | 186 (64) | 1.00f |
| Yes | 352 | 179 (51) | 0.85 (0.60, 1.20) |  | 250 | 117 (47) | 0.60 (0.41, 0.86) |  | 219 | 179 (82) | 1.12 (0.59, 2.10) |
| Overall p value |  |  | 0.35 |  |  |  | 0.006 |  |  |  | 0.74 |
| Laparoscopy |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 648 | 252 (39) | 1.00f |  | 455 | 201 (44) | 1.00f |  | 394 | 252 (64) | 1.00f |
| Yes | 138 | 113 (82) | 4.84 (2.92, 8.02) |  | 106 | 84 (79) | 4.70 (2.77, 7.98) |  | 116 | 113 (97) | 12.15 (3.40, 43.40) |
| Overall p value |  |  | < 0.001 |  |  |  | < 0.001 |  |  |  | < 0.001 |
| Endoscopic retrograde cholangiopancreatography | | |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 399 | 190 (48) | 1.00f |  | 276 | 134 (49) | 1.00f |  | 257 | 190 (74) | 1.00f |
| Yes | 387 | 175 (45) | 1.04 (0.74, 1.47) |  | 285 | 151 (53) | 1.26 (0.89, 1.79) |  | 253 | 175 (69) | 0.86 (0.46, 1.63) |
| Overall p value |  |  | 0.81 |  |  |  | 0.20 |  |  |  | 0.65 |
| Magnetic resonance imaging /cholangiopancreatography | | |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 642 | 285 (44) | 1.00f |  | 462 | 236 (51) | 1.00f |  | 416 | 285 (69) | 1.00f |
| Yes | 144 | 80 (56) | 1.10 (0.72, 1.68) |  | 99 | 49 (49) | 0.81 (0.51, 1.27) |  | 94 | 80 (85) | 1.42 (0.60, 3.35) |
| Overall p value |  |  | 0.67 |  |  |  | 0.36 |  |  |  | 0.43 |

a Based on clinical staging including imaging or exploratory laparoscopy.

b Adjusted odds ratios (ORs,) estimated using logistic regression.

Adjusted for: c Place of residence (major city, inner regional, outer regional/remote/very remote); d Age at diagnosis (<60, 60-69, 70-79, 80+ years) and performance status (0, 1, 2+, not stated); e Age at diagnosis; f Age at diagnosis, performance status and place of residence.

g Results from a mixed effects model with hospital as random intercept to adjust for hospital clustering.

Place of residence groups defined by Accessibility/Remoteness Index of Australia (ARIA); Performance status defined by Eastern Cooperative Oncology Group (ECOG); SES Socio-Economic Status defined by Socio-Economic Indexes for Areas; First facility volume by the number of study participant initial presentations.

Missing data: SES, n = 5; Place of residence, n = 5; Tumour site, n = 23; ECOG, n = 106; Charlson comorbidity index, n = 4; First inpatient facility volume, n = 11.

Patients from more remote areas had lower odds of attempted surgery compared with those living in major cities (AOR 0.61; 95% CI: 0.33 –1.10), although this was not statistically significant. Having tumour only in the tail of the pancreas was associated with a greater likelihood of attempted resection compared to having tumour in the head, neck or uncinate process (AOR 3.62; 95% CI: 1.58 – 0.33). Presentation at a MDT meeting and low volume of the facility where the patient was first admitted were associated with lower odds of having an attempted resection (AORs 0.60; 95% CI: 0.42 - 0.86, and 0.57; 95% CI: 0.34 - 0.97) respectively). If the patient was seen by a hepatobiliary surgeon or had a staging laparoscopy they were more likely to have surgery (AORs 3.77; 95% CI: 2.63 – 5.39 and 4.84; 95% CI: 2.92 – 8.02 respectively).

**Determinants of classification of cancer as resectable in patients with locally advanced disease**

Factors associated with having a tumour classified as potentially resectable amongst patients with locally advanced disease were younger age (< 60 versus ≥ 70 years: 63% versus 44%, p < 0.01), better ECOG performance status (fully active versus not fully active: 59% versus 48%, p = 0.02) and living in a major city (major city vs remote / outer regional: 53% versus 36%, p = 0.02) (Table 2). After adjustment for patient factors, the association with place of residence remained statistically significant (AOR 0.48; 95% CI: 0.26 –0.89) but further adjustment for health-service factors attenuated the association and it was no longer statistically significant (AOR 0.78; 95% CI: 0.38 – 1.59). Age remained associated with classification of resectability even after controlling for patient, tumour and health-service factors.

Patients presented at a MDT meeting were less likely to be assessed as having a potentially resectable tumour than those with no evidence of being reviewed by a MDT (AOR 0.33; 95% CI: 0.14 - 0.78). If patients were seen by a hepatobiliary surgeon they had almost twice the odds of being classified as having resectable disease (AOR 1.95; 95% CI 1.35- 2.82). Patients who underwent an EUS compared with those who did not were less likely to be classified as having potentially resectable disease (AOR 0.60; 95% CI: 0.41 – 0.86), whereas the opposite was observed if they had a laparoscopy (AOR 4.70; 95% CI: 2.77 – 7.98).

**Determinants of attempted surgery in patients classified as having potentially resectable disease**

Amongst those patients classified as potentially resectable we found that 28% (n = 145) did not proceed to surgery. The recorded reasons were predominantly comorbidities and/or age (88%, n = 127) with only 12% (n = 18) recorded as other or not stated. There were statistically significant associations between age, performance status and comorbidities and whether surgery was attempted (Table 2).

There was no difference in the proportion of patients who proceeded to attempted resection according to location of residence. After adjustment for age and performance status people living in more remote regions had non-significant lower odds compared to patients living in major cities. Most health system factors and investigations were significantly associated with attempted resection, but after adjusting for patient factors, only being seen by a hepatobiliary surgeon (AOR 6.78; 95% CI: 3.38 – 13.59) and having a laparoscopy (AOR 12.15; 95% CI: 3.40 – 43.40) were positively associated with attempted resection.

**Associations between age, location of residence and health system factors**

Age and place of residence were not significantly associated with each other, but both were associated with being assessed by a hepatobiliary surgeon, the specialist first seen and the facility volume where the patient was first an inpatient (Supplementary table 2). Patients living in more remote regions were less likely to undergo EUS and ERCP than those living in major cities, and older patients were less likely to undergo pancreas-protocol CT and MRI or MRCP, EUS or have laparoscopies as part of their clinical staging investigations. The likelihood of laparoscopy (8% versus 22%, p = 0.001) and EUS (33% versus 53%, p<0.001) was also lower for patients initially admitted to a low rather than high volume facility.

**DISCUSSION**

In this population-based cohort of patients with non-metastatic pancreatic cancer we found, as expected, that those with more advanced disease and those who were older, who had poorer performance status or more comorbidities were more likely to die within one or two years and had poorer overall survival. Lower survival was observed for people who lived in regional or remote areas compared with those living in capital cities, even after adjusting for differences in patient and tumour factors.

The percentage of patients with non-metastatic disease alive at one year (42%) in our cohort was considerably higher than the ~30% reported in some previous population-based studies[18](#_ENREF_18), [25](#_ENREF_25), [26](#_ENREF_26) but similar to estimates from studies using more recent registry data.[27](#_ENREF_27), [28](#_ENREF_28) Our findings that clinical disease stage, performance status, presence of comorbidities and age influence survival are consistent with international and national reports.[3](#_ENREF_3), [4](#_ENREF_4), [8](#_ENREF_8), [29](#_ENREF_29)

The proportion of our cohort classified as having potentially resectable disease was higher than that in previous international studies (65% versus 37% - 45%)[16](#_ENREF_16), [28](#_ENREF_28) with some studies suggesting that age, sex, medical insurance and site of the tumour are associated with resectability.[16](#_ENREF_16), [30](#_ENREF_30) Almost three-quarters of those identified as resectable proceeded to an attempted resection which is considerably higher than the ~20-60% in earlier reports.[16](#_ENREF_16), [18](#_ENREF_18), [28](#_ENREF_28), [31](#_ENREF_31) The higher likelihood of being classified as having resectable disease and higher rates of attempted resection in this study may be due to temporal changes in the definition of resectability as surgical techniques have improved.[32](#_ENREF_32)

The association between place of residence and survival has been observed in other settings[3](#_ENREF_3) with travelling distance to receive treatment[33](#_ENREF_33) and the lack of high-volume specialist centres in more rural areas[34](#_ENREF_34) being suggested as reasons for this. Our results suggest that the poorer survival of patients living in regional and remote areas may be at least partially due to them being less likely to be classified as having resectable disease. Although they are equally likely to undergo surgery once classified as resectable, this results in a lower overall proportion undergoing surgery. While patients living in lower socio-economic areas or more distant from health services may choose not to undergo treatment, it is important that adequate staging to determine resectability is undertaken in order that they can make an informed decision about their treatment pathways.

We found that only half of the patients were reviewed by a hepatobiliary surgeon at any time during their disease course, and the proportion was significantly higher in metropolitan areas than in regional and remote areas and in younger than in older patients. Similarly, older patients and those living in remote areas were less likely to be first admitted to a high volume hospital. These results are inconsistent with guidelines[12](#_ENREF_12), [13](#_ENREF_13), [35](#_ENREF_35) and the views of clinical experts[36](#_ENREF_36) which recommend that all patients diagnosed with non-metastatic disease should be reviewed by an experienced hepatobiliary surgeon, ideally supported by a multidisciplinary team. A recent study reported that patients with non-metastatic pancreatic cancer had a greater likelihood of having surgical treatment when clinical staging was established in a specialised pancreatic cancer centre.[37](#_ENREF_37) EUS is used to assess the tumour, vascular invasion, tissue diagnosis, lymph node disease, small volume liver disease and peritoneal ascites, all of which help to ascertain the resectability of the tumour. This may explain why patients who had this investigation were less likely to be classified as resectable. Laparoscopy, which is used selectively in most specialised units, tends to be used in patients thought to be resectable to detect potential small-volume peritoneal disease, so patients were more likely to proceed to surgery following this investigation. We also demonstrated that being seen by a hepatobiliary surgeon was associated with a greater likelihood of being diagnosed with resectable disease. While this may be due to reverse causality, being seen by a hepatobiliary surgeon appears to mediate the association between location of residence and classification of tumour resectability, suggesting that improving access to specialist care may increase the proportion of patients living in non-metropolitan areas who undergo surgery.

Review by a MDT is the standard of care for patients without metastatic disease[12](#_ENREF_12) and has been shown to improve survival.[38](#_ENREF_38), [39](#_ENREF_39) We found that review by an MDT was associated with a lower likelihood of being classified as having resectable disease, most likely because clinicians tended to present patients with borderline resectable disease to the MDT. Despite this, after adjustment for patient factors, MDT review was associated with improved overall survival, both for patients who did and did not undergo surgery (data not shown), suggesting that MDT management is an indicator of improved overall care. A follow-up study focussed specifically on multi-disciplinary care is needed to determine which patients are presented to MDTs and to understand the consequences of not being presented to a specialist MDT in a high-volume hospital.

Given the challenges of pancreatic cancer surgery and its subsequent survival even after potentially curative resection, it is appropriate that consideration of quality-of-life and other patient factors influence the decision to proceed to recommending resection. In keeping with this, we found that age, poor performance status or the presence of comorbidities were given as the reason for surgery not to proceed in patients with potentially resectable disease. Our results may, however, indicate that in some cases older patients may be considered to have non-resectable disease by default and without adequate staging or review by an expert team. In the absence of poor performance status or significant comorbidities age is not necessarily a contraindication to surgery[40](#_ENREF_40) and may indicate a nihilistic attitude amongst some clinicians.[41](#_ENREF_41) This emphasises the importance of a full staging work up so that patients can make informed decisions about their treatment, irrespective of their age.

Major strengths of our study include the large population-based sample and the comprehensive data collected. However, our classification of clinical disease stage as confined to the pancreas, locally advanced or metastatic disease, did not allow for the separate classification of borderline resectable disease. Pancreatic cancers are categorised on a continuum from resectable to unresectable according to involvement of adjacent structures and the presence of distant metastases[32](#_ENREF_32), [42](#_ENREF_42) but this categorization was performed by numerous surgeons in this study and may not be consistent. International more robust criteria for defining resectable disease were introduced after the study period.[12](#_ENREF_12), [43](#_ENREF_43) It is also possible that at least some of the associations with hospital volume, laparaoscopy and hepatobiliary surgeon review arose due to reverse-causality.

In conclusion this study found disparities in survival dependent on where patients live and where and by whom they are managed. Initial accurate clinical staging is a critical element in the provision of optimal management, with access to hepatobiliary surgeons, high volume specialist facilities and multidisciplinary teams shown to be important. Many patients do not meet the guidelines that recommend an early review by a hepatobiliary surgeon and by a MDT, with access to these services partly dependent on where patients live. Designing health services and referral patterns that ensure all patients receive appropriate staging and expert assessment, regardless of where and how they enter the health system, has the potential to lead to improvements in survival.

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Supplementary Table 1. Unadjusted associations between patient, tumour and health-service factors and (1) attempted resection for patients with non-metastatic diseasea (n = 786);

(2) classification of disease resectabilitya for patients with locally advanced diseasea (n = 561); (3) attempted resection for patients classified as resectablea (n = 510).

|  | 1. Non-metastatic disease | | |  | 1. Locally advanced diseasea | | |  | 1. Classified as resectablea | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Attempted resection | |  |  | Classified as resectable | |  |  | Attempted resection | |
| Variable | Total | n (%) | Crude ORb (95% CI) |  | Total | n (%) | Crude ORb (95% CI) |  | Total | n (%) | Crude ORb (95% CI) |
| **Patient / tumour factors** |  |  |  |  |  |  |  |  |  |  |  |
| Age at diagnosis, years |  |  |  |  |  |  |  |  |  |  |  |
| < 60 | 141 | 103 (73) | 1.00 |  | 98 | 62 (63) | 1.00 |  | 105 | 103 (98) | 1.00 |
| 60 - 69 | 218 | 135 (62) | 0.60 (0.38, 0.95) |  | 163 | 91 (56) | 0.73 (0.44, 1.23) |  | 146 | 135 (92) | 0.24 (0.05, 1.10) |
| 70 - 79 | 223 | 107 (48) | 0.34 (0.22, 0.54) |  | 161 | 76 (47) | 0.52 (0.31, 0.87) |  | 138 | 107 (78) | 0.07 (0.02, 0.29) |
| ≥ 80 | 204 | 20 (10) | 0.04 (0.02, 0.07) |  | 139 | 56 (40) | 0.39 (0.23, 0.67) |  | 121 | 20 (17) | 0.00 (0.00, 0.02) |
| Overall p value, p trend |  |  | <0.001, <0.001 |  |  |  | 0.002, < 0.001 |  |  |  | <0.001, <0.001 |
| Sex |  |  |  |  |  |  |  |  |  |  |  |
| Men | 422 | 222 (53) | 1.00 |  | 299 | 164 (55) | 1.00 |  | 287 | 222 (77) | 1.00 |
| Women | 364 | 143 (39) | 0.58 (0.44, 0.77) |  | 262 | 121 (46) | 0.71 (0.51, 0.99) |  | 223 | 143 (64) | 0.52 (0.35, 0.77) |
| Overall p value |  |  | <0.001 |  |  |  | 0.04 |  |  |  | 0.001 |
| Performance status |  |  |  |  |  |  |  |  |  |  |  |
| Fully active | 260 | 183 (70) | 1.00 |  | 160 | 95 (59) | 1.00 |  | 195 | 183 (94) | 1.00 |
| Not fully active | 420 | 134 (32) | 0.20 (0.14, 0.28) |  | 325 | 156 (48) | 0.63 (0.43, 0.93) |  | 251 | 134 (53) | 0.08 (0.04, 0.14) |
| Overall p value |  |  | <0.001 |  |  |  | 0.02 |  |  |  | < 0.001 |
| Charlson comorbidity index (score) | |  |  |  |  |  |  |  |  |  |  |  |
| Low (0) | 340 | 184 (54) | 1.00 |  | 252 | 126 (50) | 1.00 |  | 214 | 184 (86) | 1.00 |
| Medium (1) | 243 | 105 (43) | 0.65 (0.46, 0.90) |  | 177 | 91 (51) | 1.06 (0.72, 1.55) |  | 157 | 105 (67) | 0.34 (0.20, 0.56) |
| High (≥ 2) | 199 | 74 (37) | 0.50 (0.35, 0.72) |  | 130 | 66 (51) | 1.03 (0.68, 1.57) |  | 135 | 74 (55) | 0.20 (0.12, 0.34) |
| Overall p value, p trend |  |  | < 0.001, < 0.001 |  |  |  | 0.96, 0.85 |  |  |  | < 0.001, < 0.001 |
| Place of residence |  |  |  |  |  |  |  |  |  |  |  |
| Major city | 542 | 258 (48) | 1.00 |  | 386 | 206 (53) | 1.00 |  | 362 | 258 (71) | 1.00d |
| Inner Regional | 163 | 74 (45) | 0.92 (0.64, 1.30) |  | 119 | 50 (50) | 0.89 (0.59, 1.34) |  | 104 | 74 (71) | 0.99 (0.61, 1.61) |
| Outer regional / remote | 76 | 31 (41) | 0.76 (0.47, 1.23) |  | 53 | 19 (36) | 0.49 (0.27, 0.89) |  | 42 | 31 (74) | 1.14 (0.55, 2.34) |
| Overall p value, p trend |  |  | 0.51, 0.26 |  |  |  | 0.06, 0.03 |  |  |  | 0.94, 0.80 |
| SES - quintiles |  |  |  |  |  |  |  |  |  |  |  |
| Most disadvantaged | 156 | 73 (47) | 1.00 |  | 110 | 55 (50) | 1.00 |  | 101 | 73 (72) | 1.00 |
| Second | 171 | 80 (48) | 1.00 (0.65, 1.54) |  | 123 | 65 (53) | 1.12 (0.67, 1.88) |  | 113 | 80 (71) | 0.93 (0.51, 1.69) |
| Third | 158 | 68 (43) | 0.86 (0.55, 1.34) |  | 113 | 50 (44) | 0.79 (0.47, 1.34) |  | 95 | 68 (72) | 0.97 (0.52, 1.80) |
| Fourth | 160 | 77 (48) | 1.05 (0.68, 1.64) |  | 107 | 56 (52) | 1.10 (0.64, 1.87) |  | 109 | 77 (71) | 0.92 (0.51, 1.68) |
| Least disadvantaged | 136 | 65 (48) | 1.04 (0.66, 1.65) |  | 105 | 59 (56) | 1.28 (0.75, 2.19) |  | 90 | 65 (72) | 1.00 (0.53, 1.88) |
| Overall p value, p trend |  |  | 0.90, 0.81 |  |  |  | 0.48, 0.46 |  |  |  | 1.00, 0.98 |
| Tumour site |  |  |  |  |  |  |  |  |  |  |  |
| Head/neck/uncinate process | 647 | 298 (46) | 1.00 |  | 463 | 240 (52) | 1.00 |  | 424 | 298 (70) | 1.00 |
| Body | 40 | 14 (35) | 0.63 (0.32, 1.23) |  | 29 | 8 (28) | 0.35 (0.15, 0.82) |  | 19 | 14 (74) | 1.18 (0.42, 3.36) |
| Tail | 43 | 33 (77) | 3.86 (1.87, 7.97) |  | 27 | 21 (78) | 3.25 (1.29, 8.20) |  | 37 | 32 (89) | 3.49 (1.21, 10.05) |
| Multiple/other | 33 | 13 (39) | 0.76 (0.37, 1.56) |  | 25 | 8 (32) | 0.44 (0.19, 1.03) |  | 16 | 13 (81) | 1.83 (0.51, 6.54) |
| Overall p value |  |  | < 0.001 |  |  |  | 0.001 |  |  |  | 0.11 |
| **Health Service Factors** |  |  |  |  |  |  |  |  |  |  |  |
| Evidence of MDT review |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 518 | 239 (46) | 1.00 |  | 355 | 193 (54) | 1.00 |  | 356 | 239 (67) | 1.00 |
| Yes | 268 | 126 (47) | 1.04 (0.77, 1.39) |  | 206 | 92 (45) | 0.68 (0.48, 0.96) |  | 154 | 126 (82) | 2.20 (1.38, 3.51) |
| Overall p value |  |  | 0.82 |  |  |  | 0.03 |  |  |  | 0.001 |
| First facility volumeg |  |  |  |  |  |  |  |  |  |  |  |
| 30 + | 411 | 226 (55) | 1.00 |  | 275 | 153 (56) | 1.00 |  | 289 | 226 (78) | 1.00 |
| 10 – 29 | 232 | 97 (42) | 0.59 (0.42, 0.81) |  | 170 | 84 (49) | 0.78 (0.53, 1.14) |  | 146 | 97 (66) | 0.55 (0.35, 0.86) |
| < 10 | 132 | 42 (32) | 0.38 (0.25, 0.58) |  | 107 | 48 (45) | 0.65 (0.41, 1.02) |  | 73 | 42 (58) | 0.38 (0.22, 0.65) |
| Overall p value, p trend |  |  | < 0.001, < 0.001 |  |  |  | 0.13, 0.05 |  |  |  | < 0.001, < 0.001 |
| Specialist first seen |  |  |  |  |  |  |  |  |  |  |  |
| Hepatobiliary surgeon | 235 | 87 (60) | 1.00 |  | 87 | 44 (51) | 1.00 |  | 102 | 87 (85) | 1.00 |
| Gastroenterologist | 235 | 123 (52) | 0.73 (0.48, 1.11) |  | 173 | 97 (56) | 1.25 (0.74, 2.09) |  | 159 | 123 (66) | 0.59 (0.30, 1.14) |
| General Surgeon | 292 | 118 (40) | 0.45 (0.30, 0.68) |  | 222 | 108 (49) | 0.93 (0.56, 1.52) |  | 178 | 118 (66) | 0.34 (0.18, 0.64) |
| Other | 114 | 37 (32) | 0.32 (0.19, 0.54) |  | 79 | 36 (46) | 0.82 (0.44, 1.51) |  | 71 | 37 (52) | 0.19 (0.09, 0.39) |
| Overall p value |  |  | < 0.001 |  |  |  | 0.36 |  |  |  | < 0.001 |
| Seen by hepato-biliary surgeon | |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 395 | 106 (27) | 1.00 |  | 308 | 129 (42) | 1.00 |  | 216 | 106 (49) | 1.00 |
| Yes | 391 | 259 (66) | 5.35 (3.94, 7.26) |  | 253 | 156 (62) | 2.23 (1.59, 3.13) |  | 294 | 259 (88) | 7.68 (4.93, 11.95) |
| Overall p value |  |  | < 0.001 |  |  |  | < 0.001 |  |  |  | < 0.001 |
| Pancreas protocol computerised tomography | | |  |  |  |  |  |  |  |  |  |
| No / not stated | 406 | 173 (43) | 1.00 |  | 294 | 150 (51) | 1.00 |  | 262 | 173 (66) | 1.00 |
| Yes | 380 | 192 (51) | 1.38 (1.04, 1.82) |  | 267 | 135 (51) | 0.98 (0.70, 1.37) |  | 248 | 192 (77) | 1.76 (1.19, 2.61) |
| Overall p value |  |  | 0.03 |  |  |  | 0.91 |  |  |  | 0.005 |
| Plain computerised tomography | |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 261 | 133 (51) | 1.00 |  | 189 | 104 (55) | 1.00 |  | 176 | 133 (76) | 1.00 |
| Yes | 525 | 232 (44) | 0.76 (0.57, 1.03) |  | 372 | 181 (49) | 0.77 (0.55, 1.10) |  | 334 | 232 (69) | 0.74 (0.49, 1.11) |
| Overall p value |  |  | 0.07 |  |  |  | 0.15 |  |  |  | 0.15 |
| Endoscopic ultrasound | | |  |  |  |  |  |  |  |  |  |
| No / not stated | 434 | 186 (43) | 1.00 |  | 311 | 168 (54) | 1.00 |  | 291 | 186 (64) | 1.00 |
| Yes | 352 | 179 (51) | 1.38 (1.04, 1.83) |  | 250 | 117 (47) | 0.75 (0.54, 1.05) |  | 219 | 179 (82) | 2.53 (1.66, 3.84) |
| Overall p value |  |  | 0.03 |  |  |  | 0.09 |  |  |  | <0.001 |
| Laparoscopy |  |  |  |  |  |  |  |  |  |  |  |
| No / not stated | 648 | 252 (39) | 1.00 |  | 455 | 201 (44) | 1.00 |  | 394 | 252 (64) | 1.00 |
| Yes | 138 | 113 (82) | 7.10 (4.48, 11.26) |  | 106 | 84 (79) | 4.82 (2.91, 7.99) |  | 116 | 113 (97) | 21.22 (6.62, 68.03) |
| Overall p value |  |  | < 0.001 |  |  |  | < 0.001 |  |  |  | < 0.001 |
| Endoscopic retrograde cholangiopancreatography | | |  |  |  |  |  |  |  |  |  |
| No / not stated | 399 | 190 (48) | 1.00 |  | 276 | 134 (49) | 1.00 |  | 257 | 190 (74) | 1.00 |
| Yes | 387 | 175 (45) | 0.91 (0.69, 1.20) |  | 285 | 151 (53) | 1.19 (0.86, 1.66) |  | 253 | 175 (69) | 0.79 (0.54, 1.16) |
| Overall p value |  |  | 0.50 |  |  |  | 0.29 |  |  |  | 0.23 |
| Magnetic resonance imaging /cholangiopancreatography | | |  |  |  |  |  |  |  |  |  |
| No / not stated | 642 | 285 (44) | 1.00 |  | 462 | 236 (51) | 1.00 |  | 416 | 285 (69) | 1.00 |
| Yes | 144 | 80 (56) | 1.57 (1.09, 2.25) |  | 99 | 49 (49) | 0.94 (0.61, 1.45) |  | 94 | 80 (85) | 2.63 (1.44, 4.81) |
| Overall p value |  |  | 0.02 |  |  |  | 0.77 |  |  |  | 0.002 |

a Based on clinical staging including imaging or exploratory laparoscopy.

b Crude odds ratios (ORs,) estimated using logistic regression.

g Results from a mixed effects model with hospital as random intercept to adjust for hospital clustering.

Place of residence groups defined by Accessibility/Remoteness Index of Australia (ARIA); Performance status defined by Eastern Cooperative Oncology Group (ECOG); SES Socio-Economic Status defined by Socio-Economic Indexes for Areas; First facility volume by the number of study participant initial presentations.

Missing data: SES, n = 5; Place of residence, n = 5; Tumour site, n = 23; Performance status, n = 106; Charlson comorbidity index, n = 4; First inpatient facility volume, n = 11.

Supplementary Table 2: Associations between patient, tumour and health-service factors and (1) place of residence and (2) age, for patients with non-metastatic disease on clinical staging.

|  | Place of residence, n (%) (n = 781) | | | | |  | Age in years, n (%) (n = 786) | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Exposure variable | Major  city  (n = 542) | Inner  regional  (n = 163) | Outer regional/ remote  (n = 76) | | P valueb |  | < 60  (n = 141) | 60 – 69  (n =218) | 70 – 79  (n = 223) | ≥ 80  (n = 204) | P valueb |
| **Patient / Tumour factors** |  |  | |  |  |  |  |  |  |  |  |
| Age at diagnosis, years |  |  | |  | 0.44 |  |  |  |  |  |  |
| < 60 | 89 (16) | 33 (20) | | 19 (25) |  |  | Not applicable | | | |  |
| 60 - 69 | 161 (29) | 40 (25) | | 17 (22) |  |  |  |
| 70 - 79 | 158 (29) | 45 (28) | | 20 (26) |  |  |  |
| ≥ 80 | 139 (25) | 45 (28) | | 20 (26) |  |  |  |
| Sex |  |  | |  | 0.89 |  |  |  |  |  | < 0.001 | |
| Men | 292 (54) | 85 (52) | | 42 (55) |  |  | 85 (60) | 139 (64) | 110 (49) | 88 (43) |  | |
| Women | 85 (46) | 78 (48) | | 34 (45) |  |  | 56 (40) | 79 (36) | 113 (51) | 116 (57) |  | |
| ECOG performance status |  |  | |  |  |  |  |  |  |  |  | |
| 0 | 173 (32) | 56 (34) | | 27 (36) | 0.41 |  | 67 (48) | 95 (44) | 64 (29) | 34 (17) | < 0.001 | |
| 1 | 159 (29) | 57 (35) | | 24 (32) |  |  | 52 (37) | 73 (33) | 73 (33) | 42 (21) |  | |
| 2+ | 131 (24) | 30 (18) | | 19 (25) |  |  | 12 (9) | 21 (10) | 49 (22) | 98 (48) |  | |
| Not stated | 79 (15) | 20 (12) | | 6 (8) |  |  | 10 (7) | 29 (13) | 37 (17) | 30 (15) |  | |
| Charlson comorbidity index (score) | |  | |  |  |  |  |  |  |  |  | |
| Low (0) | 244 (45) | 63 (39) | | 30 (40) | 0.61 |  | 82 (58) | 92 (42) | 98 (44) | 68 (34) | 0.002 | |
| Medium (1) | 164 (30) | 55 (34) | | 23 (31) |  |  | 32 (23) | 68 (31) | 72 (32) | 71 (35) |  | |
| High (≥ 2) | 132 (24) | 44 (27) | | 22 (29) |  |  | 27 (19) | 57 (26) | 52 (23) | 63 (31) |  | |
| Remoteness of residence |  |  | |  |  |  |  |  |  |  | 0.50 | |
| Major city |  |  | |  |  |  | 89 (63) | 157 (73) | 157 (71) | 139 (68) |  | |
| Inner Regional | Not applicable | | | |  |  | 33 (23) | 40 (19) | 45 (20) | 45 (22) |  | |
| Outer regional / remote/ very remote | |  | |  |  |  | 19 (13) | 17 (8) | 20 (9) | 20 (10) |  | |
| SES |  |  | |  | < 0.001 |  |  |  |  |  | 0.62 | |
| Most disadvantaged | 82 (15) | 41 (25) | | 33 (43) |  |  | 27 (19) | 32 (15) | 51 (23) | 46 (23) |  | |
| Second | 84 (16) | 72 (44) | | 15 (20) |  |  | 34 (24) | 44 (21) | 50 (23) | 43 (21) |  | |
| Third | 110 (20) | 30 (18) | | 18 (24) |  |  | 31 (22) | 49 (23) | 38 (17) | 40 (20) |  | |
| Fourth | 133 (25) | 17 (10) | | 10 (13) |  |  | 30 (21) | 47 (22) | 46 (21) | 37 (18) |  | |
| Least disadvantaged | 133 (25) | 3 (2) | | 0 |  |  | 19 (13) | 42 (20) | 37 (17) | 38 (19) |  | |
| Tumour site |  |  | |  | 0.47 |  |  |  |  |  | 0.85 | |
| Head/neck/uncinate process | 452 (85) | 135 (88) | | 57 (78) |  |  | 115 (83) | 182 (85) | 180 (83 ) | 170 (87) |  | |
| Body | 27 (5) | 7 (5) | | 6 (8) |  |  | 8 (6) | 9 (4) | 14 (6) | 9 (5) |  | |
| Tail | 31 (6) | 5 (3) | | 7 (10) |  |  | 9 (7) | 12 (6) | 15 (7) | 7 (4) |  | |
| Multiple/other | 23 (4) | 7 (5) | | 3 (4) |  |  | 6 (4) | 11 (5) | 7 (3) | 9 (5) |  | |
| Clinical Stage |  |  | |  | 0.85 |  |  |  |  |  | 0.46 | |
| Confined to the pancreas | 158 (29) | 44 (27) | | 23 (30) |  |  | 43 (31) | 55 (25) | 62 (28) | 65 (32) |  | |
| Locally advanced disease | 389 (71) | 119 (73) | | 53 (70) |  |  | 98 (69) | 163 (75) | 161 (72) | 139 (68) |  | |
| **Health System Factors** |  |  | |  |  |  |  |  |  |  |  | |
| Evidence of MDT review |  |  | |  | 0.13 |  |  |  |  |  | < 0.001 | |
| No / not stated | 351 (65) | 105 (64) | | 58 (76) |  |  | 71 (50) | 133 (61) | 149 (67) | 165 (81) |  | |
| Yes | 191 (35) | 58 (36) | | 18 (24) |  |  | 70 (50) | 85 (39) | 74 (33) | 39 (19) |  | |
| Specialist first seen |  |  | |  | < 0.001 |  |  |  |  |  | < 0.001 | |
| Hepatobiliary surgeon | 121 (22) | 22 (14) | | 2 (3) |  |  | 24 (17) | 60 (28) | 42 (19) | 19 (9) |  | |
| Gastroenterologist | 174 (32) | 38 (23) | | 21 (28) |  |  | 52 (37) | 56 (26) | 73 (33) | 54 (26) |  | |
| General Surgeon | 170 (31) | 86 (53) | | 33 (43) |  |  | 52 (37) | 77 (35) | 78 (35) | 85 (42) |  | |
| Other | 77 (14) | 17 (10) | | 20 (26) |  |  | 13 (9) | 25 (11) | 30 (13) | 46 (23) |  | |
| First inpatient facility volume |  |  | |  | < 0.001 |  |  |  |  |  | < 0.001 | |
| 30 + | 339 (63) | 58 (36) | | 13 (17) |  |  | 84 (60) | 127 (58) | 117 (52) | 83 (41) |  | |
| 10 – 29 | 139 (26) | 54 (34) | | 36 (48) |  |  | 35 (25) | 68 (31) | 67 (30) | 62 (30) |  | |
| < 10 | 56 (10) | 49 (30) | | 26 (35) |  |  | 19 (13) | 21 (10) | 36 (16) | 56 (27) |  | |
| Reviewed by hepato-biliary surgeon | |  | |  | 0.009 |  |  |  |  |  | < 0.001 | |
| No / not stated | 262 (48) | 80 (49) | | 51 (67) |  |  | 54 (38) | 86 (39) | 101 (45) | 154 (75) |  | |
| Yes | 280 (52) | 83 (51) | | 25 (33) |  |  | 87 (62) | 132 (61) | 122 (55) | 50 (25) |  | |
| Chemotherapy |  |  | |  | 0.32 |  |  |  |  |  | < 0.001 | |
| No / not stated | 259 (48) | 83 (51) | | 43 (57) |  |  | 36 (26) | 56 (26) | 119 (53) | 176 (86) |  | |
| Yes | 283 (52) | 80 (49) | | 33 (43) |  |  | 105 (74) | 162 (74) | 104 (47) | 28 (14) |  | |
| Pancreas protocol computerised tomography | | | |  | 0.20 |  |  |  |  |  | < 0.001 | |
| No / not stated | 269 (50) | 93 (57) | | 42 (55) |  |  | 59 (42) | 101 (46) | 118 (53) | 128 (63) |  | |
| Yes | 273 (50) | 70 (43) | | 34 (45) |  |  | 82 (58) | 117 (54) | 105 (47) | 76 (37) |  | |
| Plain computerised tomography | |  | |  | 0.01 |  |  |  |  |  | 0.22 | |
| No / not stated | 196 (36) | 44 (27) | | 17 (22) |  |  | 50 (35) | 82 (38) | 64 (29) | 65 (32) |  | |
| Yes | 346 (64) | 119 (73) | | 59 (78) |  |  | 91 (65) | 136 (62) | 159 (71) | 139 (68) |  | |
| Endoscopic ultrasound |  |  | |  | < 0.001 |  |  |  |  |  | < 0.001 | |
| No / not stated | 273 (50) | 104 (64) | | 55 (72) |  |  | 61 (43) | 110 (50) | 113 (51) | 150 (74) |  | |
| Yes | 269 (50) | 59 (36) | | 21 (28) |  |  | 80 (57) | 108 (50) | 110 (49) | 54 (26) |  | |
| Laparoscopy |  |  | |  | 0.11 |  |  |  |  |  | < 0.001 | |
| No / not stated | 439 (81) | 135 (83) | | 69 (91) |  |  | 107 (76) | 174 (80) | 168 (75) | 199 (98) |  | |
| Yes | 103 (19) | 28 (17) | | 7 (9) |  |  | 34 (24) | 44 (20) | 55 (25) | 5 (2) |  | |
| Endoscopic retrograde cholangiopancreatography | | | |  | 0.02 |  |  |  |  |  | 0.69 | |
| No / not stated | 269 (50) | 79 (48) | | 50 (66) |  |  | 76 (54) | 114 (52) | 111 (50) | 98 (48) |  | |
| Yes | 273 (50) | 84 (52) | | 26 (34) |  |  | 65 (46) | 104 (48) | 112 (50) | 106 (52) |  | |
| Magnetic resonance imaging/cholangiopancreatography | | | |  | 0.93 |  |  |  |  |  | <0.001 | |
| No / not stated | 444 (82) | 132 (81) | | 63 (83) |  |  | 105 (74) | 170 (78) | 181 (81) | 186 (91) |  | |
| Yes | 98 (18) | 31 (19) | | 13 (17) |  |  | 36 (26) | 48 (22) | 42 (19) | 18 (9) |  | |

a Tumour status based on imaging or exploratory laparoscopy.

b Chi-squared test.

c Missing data: SES, n = 5; Tumour site, n = 21; Charlson comorbidity index, n = 4; Clinical stage , n = 43, First facility volume, n = 11;

SES: socioeconomic status according to socio-economic index for areas of residence; ECOG: Eastern Cooperative Oncology Group; MDT: multidisciplinary team.