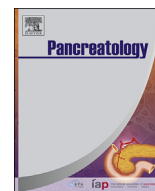




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Determinants of survival and attempted resection in patients with non-metastatic pancreatic cancer: An Australian population-based study

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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.

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1. 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]. 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].

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Worse survival has been observed for patients who live outside metropolitan areas [3], have low socioeconomic status and who are elderly [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 neoadjuvant 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], improving five-year survival to about 20% [8–10]. 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]. National Cancer Comprehensive Network (NCCN) guidelines therefore recommend multidisciplinary consultation when determining potential resectability [12], with the involvement of a skilled, specialised hepatobiliary surgeon as an integral part of the team [13,14]. International data show that resection rates are influenced by ethnicity, insurance status, marital status, education level, socio-economic status and geographical distance from large metropolitan areas [15–18]. There are indications that this may be related to the expertise at the facility where patients are being staged [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.

2. Methods

2.1. Study population and data collection

Data collection and regulatory approvals for the study have been described previously [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 are unsuitable for curative resection, analyses were restricted to patients with no evidence of metastatic disease on clinical staging.

2.2. 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.

2.3. Factors of interest

2.3.1. Patient characteristics

The patient factors of interest included age at diagnosis, sex, Eastern Cooperative Oncology Group (ECOG) performance status and Charlson comorbidity index [21]. Based on area of residence at the time of diagnosis, each person was allocated a socio-economic index for areas (SEIFA) [22] score and Accessibility/Remoteness Index of Australia (ARIA) [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.

2.3.2. 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.

2.3.3. 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) (\pm pancreas protocol), endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance imaging (MRI) or cholangiopancreatography (MRCP), and laparoscopy, and each of resectability and attempted resection were evaluated.

2.4. 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]. 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

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