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Characteristics, therapy and outcome in an unselected and prospectively registered cohort of pancreatic cancer patients

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Abstract ***Purpose:*** Pancreatic cancer (PC) is associated with a dismal prognosis. Few studies have examined characteristics and outcome in an unselected population-based cohort of PC patients. Therefore, we investigated patient baseline characteristics, therapy choices and survival in a complete cohort of patients with PC.

Methods: All cases diagnosed with PC between 2007 and 2009 in the Region of Southern Denmark (pop: 1,200,000) were prospectively registered. Patient characteristics including performance status, information about haematology, liver function and therapy were retrieved from patient charts, and used to compare differently treated and untreated groups.

Results: Six-hundred-eighteen cases were registered as PC; 25 of which did not have adenocarcinomas. Patients were divided in 3 clinical groups based on initial therapy; group 1: resection ($n = 64$), group 2: chemotherapy or chemo-radiotherapy ($n = 191$), group 3: no tumour directed therapy ($n = 324$).

Median survival (mOS) (95% confidence interval (CI)) in the three groups was 25.7 months (18–30), 8.1 months (7.0–9.5) and 1.1 months (1.0–1.3) respectively. Three percent of patients participated in clinical trials.

An evaluation of baseline factors prognostic value suggested that treated patients differed significantly from non-treated patients.

Conclusion: This study reports survival in treated groups comparable to results obtained from clinical trials with highly selected patients. However the majority of patients with PC do not receive cancer directed therapy. This group was significantly different in several baseline factors, which could suggest a different biology. Improving the outcome of PC patients calls for research into the large group of untreated patients, as only a minority of patients receive cancer directed therapy.

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1. Introduction

Knowledge about treatment effect and the prognosis of cancer patients is often inferred from the results of randomised phase III trials. In randomised studies inclusion criteria are set-down to make comparisons between groups easier and reduce the amount of random noise that could otherwise mask a benefit from the investigated therapy. For these reasons patients participating in clinical trials are often more fit, younger and with less co-morbidity than the average patients, and this may lead to problems in generalising the results to a full population.[1] A problem relating to pancreatic cancer (PC) specifically is the high rate of non-histologically proven cases – typically around 40%, which are never recruited into clinical trials, and often excluded from registry reports.[2]

In PC, three major clinical groups exist, resectable disease (rPC), locally advanced (LAPC) disease and metastatic disease (mPC). The prognosis for all three groups is dismal. Even for patients with rPC, the expected median survival (mOS) based on randomised study data is less than 24 months and 5 year survival around 20%.[3] Several studies have reported outcome based n population based registries. In these studies the mOS for resected patients was as low as 11 months, and performed in approximately 10% of the patients.[4–13] In palliative therapy survival has been reported as low as 4 months for patients receiving palliative chemotherapy, with only 10–25% of the whole population being treated.[5,11] The number of patients receiving chemotherapy or chemo-radiotherapy (CRT) has not been extensively studied as registries seldom record these therapies and linkage between registries are difficult or restricted to subpopulations – e.g. the Medi-Care population.[14] As a large part of translational research is performed in resected or study populations it is important that results can be generalised to all patients.

We wanted prospectively to investigate the selection of therapies in an unselected population of patients with PC. Also we wanted to investigate if patients' baseline characteristics were comparable between different therapeutic groups, mainly treated versus non-treated.

2. Materials and methods

2.1. Data retrieval

2.1.1. Cases

We prospectively registered an unselected group of patients in the region of Southern Denmark (population 1,200,000) during the period 1st Jan. 2007 to 31th Dec. 2009. Since surgery and oncological therapy of all PC patients in the region is centralised to a single hospital, we established a database of all cases seen during the period. Afterwards we collected data on all cases of PC registered in the Danish Cancer Registry (DCR), using the unique Danish social security number which all citizens use when in contact with the health services.[15] These two databases were merged. Discordant cases were individually reviewed for inclusion, using patient charts and available registry data.

2.1.2. Patient material

We included all patients with PC (C25.0–9). However, for further analysis we excluded patients with neuroendocrine, islet cell, carcinoid and acinar cell tumours.

2.1.3. Treatment data

All treatment related data were retrieved from patients' records, and entered into the database. The registry was used according to the Danish law for clinical research and complies with the Helsinki Declaration.

2.1.4. Clinical variables

Clinical variables were collected from the patients' medical records. Data from blood samples were obtained immediately prior to diagnosis, surgery or evaluation at the department of oncology. We did not retrieve blood samples on patients having a clinical diagnosis only. Patients were staged according to the AJCC 6th edition. Information about missing values is included in Supplementary Table 1.

2.2. Statistical analysis

Overall survival was estimated using the Kaplan–Meier method, with time counted from cytological/histological diagnosis till death from any course. For patients with a clinical diagnosis only, the date of reporting to DCR was used as day 0. For patients diagnosed at autopsy, survival was set to 0.5 month. Data cutoff was January 7th 2012.

For comparisons of baseline characteristics between clinical groups ANOVA was used, with transformed variables when appropriate. In order to evaluate the co-linearity of baseline factors prognostic value a correlation analysis was performed using the Pearson rank correlation test.

To estimate the prognostic value of baseline characteristics we used a Cox regression model. A model based on all patients was built; similar models were built in each clinical group. Continuous variables were analysed assuming a linear relationship; variables with extreme outliers were truncated at the 95 percentile to improve model fit. These were white blood cells (WBC (23)), platelets (554), alanine aminotransferase (ALT (280)), alkaline phosphatase (ALP (1155)), lactate dehydrogenase (LDH (424)), bilirubin (230) and C-reactive protein (CRP (228)). Proportional hazards were tested using Schoenfeld residuals. Confidence intervals are given at the 95%, and the significance level was set to 0.05. When