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Review

Has survival improved following resection for pancreatic adenocarcinoma?

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ABSTRACT

Introduction: This study was undertaken to determine if survival after resection of pancreatic adenocarcinoma has improved over the past two decades.
Methods: The SEER database was queried for patients who underwent pancreatectomy for pancreatic adenocarcinoma from 1992 to 2010. AJCC Stage and survival were determined for patients. Data were analyzed using Mantel-Cox test and linear regression.
Results: 15,604 patients underwent pancreatectomy from 1992 to 2010. Survival improved from 1992 to 2010 ($p < 0.0001$); specifically, median survival increased 1992–2010 ($p < 0.0001$). However, 5-year survival rates did not change 1992–2010. More patients ($p = 0.007$) underwent resections of Stage I and relatively more patients ($p = 0.004$) underwent resections of Stage II cancers 2004–2010 with commensurately smaller tumors ($p = 0.01$).
Conclusions: From 1992 to 2010, progressively more patients underwent pancreatectomy for pancreatic adenocarcinoma with progressively smaller tumors and earlier stages. These patients lived more years (e.g., improved survival curves and median survival) but without improved 5-year survival, denoting better early and intermediate survival. Early detection, better perioperative care, more efficacious non-curative chemotherapy undoubtedly play a role, but better solutions for long-term survival must be sought.

1. Introduction

Prior to the availability of CT scanners in the early 1980's, resections for pancreatic cancer were uncommon; pancreatic cancer was seen when advanced and terminal, particularly cancers arising in the body and tail. Beginning in the mid 1980's, with the dissemination of CT scanners across America, diagnosis and staging of pancreatic cancer dramatically improved. This improvement continued as the year 2000 approached and passed with improvements in imaging, including new generations of and improved techniques with CT scanners and MR imaging, widespread application of ERCP, and nascent use of endoscopic ultrasound (EUS) becoming quite routine. As a result there were an ever growing number of people diagnosed with pancreatic cancer, particularly at earlier stages, and an ever growing number of patients eligible for and undergoing resections of their pancreatic cancers[1–8]; many centers produced large series of patients undergoing pancreatectomy with ever improving morbidity.[1–8]

Concomitantly, beginning in the 1980's, new therapies for pancreatic cancer came into clinical use (Fig. 1). In 1985, the pivotal GITSG trial documented the role of adjuvant chemoradiation therapy.[9] The 1990's had the approval of gemcitabine as therapy for pancreatic cancer, initially as an agent improving quality of life for patients ill with terminal pancreatic cancer.[10] The application of gemcitabine for pancreatic cancer quickly spread across all stages of pancreatic cancer and for adjuvant therapy. The new millennium brought targeted therapy (e.g., elotinib), more drugs (e.g., nab-paclitaxel), and new combinations of chemotherapy agents (e.g., gemcitabine with nab-paclitaxel, FOLFIRINOX) to the armamentarium against pancreatic cancer (Fig. 1).

In parallel, billions of dollars were spent on the increased number of patients at risk, improvements in imaging and diagnostics, and novel chemotherapeutic agents.[11] Given its clinical impact, funding for pancreatic cancer research seems lacking. While funding for pancreatic cancer research has marginally

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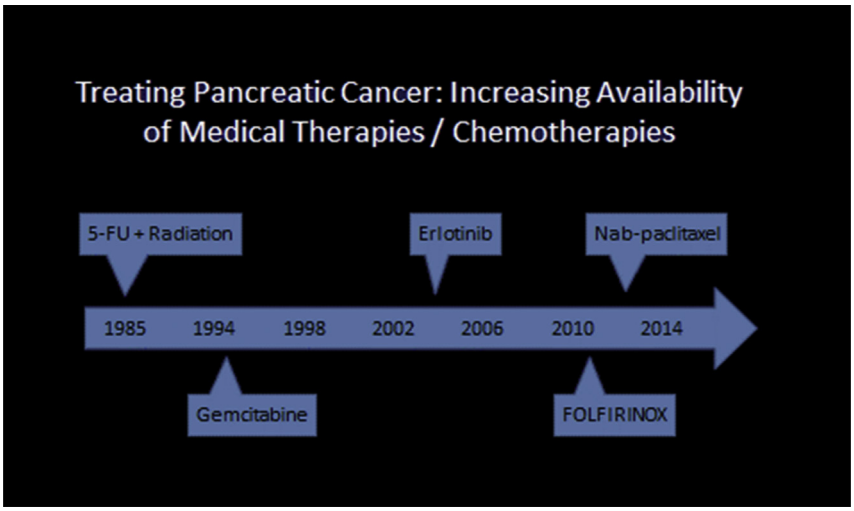

Fig. 1. Time sequence of new medical therapies for pancreatic cancer: when 'modern' therapies for pancreatic cancer appeared.

increased over the past decade, it still amounts to only 1% of all cancer research funding and only 2% of cancer site-specific funding.[12] Nonetheless, billions were spent on research to better understand all phases of pancreatic cancer, including diagnosis, operative intervention, adjunctive therapies beyond resection, and palliative care. After all the money has been spent and all the patients have been cared for and studied, what has changed?

Over the past decades many altruistic organizations have formed to combat pancreatic cancer and support patients with pancreatic cancer. A Google search on "pancreatic cancer support groups" produced over 1,750,000 "hits", documenting the place of pancreatic cancer in the public eye. As well, a Google search for "pancreatic cancer websites" produced over 4,270,000 "hits". Pancreatic cancer is no longer a 'dark' disease shrouded in mystery.

In 2015 it is projected that over 48,960 people will be diagnosed with pancreatic cancer and 40,560 people will die because of pancreatic cancer.[13] It is now projected that 1.5% of men and women will be diagnosed with pancreas cancer at some point during their lifetime, based on 2009–2011 data, with smoking, obesity, age, gender, family history, type 2 diabetes, chronic pancreatitis, cirrhosis, and chronic H. Pylori infection impacting the risk of pancreatic cancer.[13,14] Certainty, over the past two decades this cancer has achieved public awareness and a lot has been learned.

With all the effort expended and all the money spent, with all the attention given to patients with pancreatic cancer, and with the tremendous dissemination of operative techniques and knowledge, has survival after pancreatectomy for pancreatic cancer improved over the last two decades? This study was undertaken to answer this question. Our hypothesis in undertaking the study was that long-term survival after pancreaticoduodenectomy for pancreatic adenocarcinoma has improved over the last two decades.

2. Methods

With IRB approval we utilized the Surveillance, Epidemiology, and End Results (SEER) database (SEER*Stat Version 8.1.5) to identify patients undergoing pancreatectomy for pancreatic adenocarcinoma from 1992 through 2010. Demographic data was collected. As well, data on incidence, Tumor Criteria, Nodal Criteria, and AJCC Stage at the time of pancreatectomy, and survival were analyzed. Data about Tumor Criteria, Nodal Criteria, and AJCC Stage are only presented for patients undergoing pancreatectomy for pancreatic adenocarcinoma from 2004 through 2010; prior to which, this information was not collected by SEER. Cancers were stratified by presenting stage. Complete data was available through 2010.

Because of limitations of the database, median survival was determined through 2009. Five −year survival was determined through 2005, estimated survival was utilized when available or producible for illustrative purposes for 2006 through 2010.

Data were maintained on a spreadsheet (Excel, Microsoft®, Redmond, WA) and analyzed using GraphPad Prism, version 3.06 (GraphPad InStat®, GraphPad Software, Inc, San Diego, CA). Nominal and ordinal data were analyzed using contingency testing. Kaplan–Meier survival analysis (log rank test or log rank test for trends) was used to examine survival and survival differences over time. Trends were tested using regression analysis. Hazard-ratios from survival analysis, along with significance was accepted with 95% probability. Data are presented as median (mean ± standard deviation) for illustrative purposes.

3. Results

Through the SEER database, 15,604 patients underwent pancreatectomy from 1992 through 2010. Their average age was 65 years and 50% were men; 83% of patients were white (Table 1). More patients underwent pancreatectomy in the later years studied ($p < 0.0001$). With time, progressively more patients had cancers in the body and tail (Table 1, $p < 0.002$). For the years 2004–2010, tumor criteria, nodal criteria, and AJCC Stage of the cancers after pancreatectomy are known (Table 2); 53% of patients were of Stage IIB after pancreatectomy ($p = 0.007$, Table 2). Over the years 2004 through 2010, progressively more patients ($p < 0.0008$) underwent resections of Stage I tumors. Over the years 2004 through 2010, patients had commensurately smaller tumors ($p = 0.0008$). From 2004 through 2010 there was no change in the proportion of patients with N0 disease ($p = 0.16$).

Through survival curve analysis, survival improved through the years 1992–2010; more patients lived more years ($p < 0.001$). For purely illustrative purposes the patients could be divided into three relatively equal (by the number of years) cohorts (1992–97, N = 1846; 1998–2003, N = 4528; 2004–10, N = 9230); comparison of survival curves of these cohorts documented that survival