Surgical Oncology 27 (2018) 245–250

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Do patients with pancreatic body or tail cancer benefit from adjuvant therapy?A cohort study

Davendra P.S. Sohal*, Katherine Tullio, Alok A. Khorana

Taussig Cancer Institute, Cleveland Clinic, 9500 Euclid Avenue, R35, Cleveland, OH 44195, United States

ARTICLE INFO

Article history:
Received 21 December 2017
Received in revised form
20 February 2018
Accepted 2 May 2018

ABSTRACT

Introduction: Evidence supporting adjuvant therapy for resected pancreatic cancer is limited primarily to head tumors. We analyzed data from the National Cancer Database (NCDB) to evaluate the relationship of tumor site with benefit from adjunctive (adjuvant, neoadjuvant, perioperative) therapy (Rx).
Methods: All NCDB patients with clinical stage I and II pancreatic cancer, diagnosed from 2003 to 2013, who underwent surgical resection and had data on site of primary were included. Overall survival (OS) analyses with hazard ratios (HR), 95% confidence intervals (CI), and two-sided p-values are presented.
Results: A total of 27,930 patients met inclusion criteria; median age 66 years, 51% males, 86% white. Primary site was coded as head (74.4%), body (9.3%), or tail (16.3%). Pathologic stage was predominantly stage II (77%); 81% had negative margins. Perioperative Rx was used in 4%, neoadjuvant in 8%, adjuvant in 48%. Median OS for the cohort was 24 months; for head, body and tail tumors, it was 21.6, 34.5, and 42.5 months, respectively. In univariable analyses, adjunctive Rx was associated with improved OS in head tumors (HR, any Rx vs. no Rx: 0.87; 95% CI 0.84–0.91; $p < 0.0001$) but not in body (1.82; 1.59–2.08; <0.0001) and tail (2.28; 2.05–2.53; <0.0001) tumors; multivariable models including statistically significant predictors (Charlson-Deyo comorbidity score, tumor grade and stage, positive resection margin) confirmed these results.
Conclusions: Our study suggests that the benefit of adjunctive Rx is restricted to pancreatic head tumors; body and tail tumors have a much better prognosis. These results warrant further evaluation in prospective studies.

1. Background

Pancreatic adenocarcinoma is projected to become the second-leading cause of cancer-related death in the United States by 2030 [1]. While early detection and better treatment-related survival are controlling mortality from various other cancers, pancreatic cancer remains an exception. Improved overall survival from multi-agent chemotherapy regimens in the metastatic setting have provided an opportunity for progress [2]. This, paired with the growing acknowledgement that pancreatic cancer is a systemic disease from the time of diagnosis, is leading to a consensus that early use of systemic therapy regimens can lead to improved clinical outcomes in the curative setting as well [3,4].

What is not known clearly is the role of the primary site of the tumor. The RTOG-9704 study is the only randomized controlled trial to include patients with all primary sites and report outcomes by site. It enrolled patients after surgical resection of pancreatic adenocarcinoma and randomized them to either 5-fluorouracil or gemcitabine chemotherapy before and after 5-fluorouracil-based chemoradiation. The primary outcome – overall survival – was no different between the two study arms. When evaluated further by site, there was a trend toward improvement in overall survival in the gemcitabine arm compared with the 5-fluorouracil arm (median 20.5 vs 17.1 months) for pancreatic head tumors, but not for body or tail tumors [5,6]. Other key adjuvant therapy studies – CONKO-001, ESPAC-1, ESPAC-3, and ESPAC-4 – have shown improvement in clinical outcomes survival with adjuvant chemotherapy, but data are not reported by site of primary tumor [7–10]. Here we present a comprehensive analysis of all available data from the National Cancer Database (NCDB) on patients with resected pancreatic adenocarcinoma. Our objective is to analyze outcomes with respect to the site of the primary tumor, and to assess benefit of adjunctive (neoadjuvant, perioperative, adjuvant) therapy.

* Corresponding author.
E-mail address: sohald@ccf.org (D.P.S. Sohal).

https://doi.org/10.1016/j.suronc.2018.05.008
0960-7404/

2. Methods

2.1. Study population and data extraction

The study cohort was obtained in de-identified form from the NCDB, a hospital-based, prospectively collected nationwide oncology outcomes database recognized as the largest clinical registry in the world [11]. The NCDB collects data annually from the tumor registries of Commission on Cancer-accredited programs in the United States, comprising approximately 70% of all new invasive cancer diagnoses in the United States. Data collection is standardized based on the rules set forth by the Commission on Cancer's Facility Oncology Registry Data Standards (FORDS). Our inclusion criteria were patients diagnosed between 2003 and 2013 with clinical stage I and II pancreatic cancer who underwent surgical resection of the pancreatic primary, and where a site of primary tumor (using ICD-*O*-3 topography codes) was mentioned. These cases were identified based on FORDS site-specific procedure coding. Staging was based on the American Joint Committee on Cancer (AJCC) criteria. Site was coded as head, body, or tail. All "not otherwise specified (NOS)" and missing values were removed from respective analyses – there was no data imputation.

2.2. Statistical analyses

Descriptive analyses include medians and percentages for continuous and discrete variables, respectively. Survival analyses were performed using Kaplan-Meier estimation, and multivariable models using Cox proportional hazards modeling were created parsimoniously in step-down fashion. Sets of correlated variables were pruned to retain only the most statistically significant ones. Hazard ratios with 95% confidence intervals (CI) and two-sided p-values are provided. All analyses were performed using SAS® version 9.03 (SAS Institute, Inc., Cary, NC).

3. Results

3.1. Study population

A total of 27,930 patients met the inclusion criteria. Baseline characteristics are shown in Table 1. Of note, median age was 66 years, 51% of patients were males and 86% were white. The majority of patients were treated at academic medical centers and in large metropolitan areas. More than two-thirds of the study population (67.2%) had a Charlson-Deyo score of 0.

Table 1
Baseline characteristics of study cohort (N = 27,930).[a]

Variable	Value
Age, years	66 (18–90)
Males	14,188 (50.8%)
Race	
White	23,963 (85.8%)
Black	2674 (9.6%)
Others	1293 (4.6%)
Facility Type (missing = 614)	
Academic Program	16,192 (59.3%)
Comprehensive Community Cancer Program	8150 (29.8%)
Others	2974 (10.9%)
Primary Residence (missing = 1051)	
Metro area >1 million	14,398 (53.6%)
Metro area 250,000–1 million	5407 (20.1%)
Metro area <250,000	2596 (9.7%)
Others	4478 (16.6%)
Primary Payor	
Medicare	14,024 (50.2%)
Private Insurance	11,064 (39.6%)
Others	2842 (10.2%)
Charlson-Deyo Score	
0	18,756 (67.2%)
1	7302 (26.1%)
≥2	1872 (6.7%)
Year of Diagnosis	
2010 or earlier	14,569 (52.2%)
2011 or later	13,361 (47.8%)
Site of Primary	
Head	20,785 (74.4%)
Body	2603 (9.3%)
Tail	4542 (16.3%)

[a] For continuous variables, the median is presented, with range within parentheses. For categorical variables, the number is presented, with percentage within parentheses.

3.2. Tumor characteristics

Table 2 shows tumor characteristics in detail. The primary site was the head of the pancreas in 74.4%, body in 9.3%, and tail in 16.3% of the cases. The overall study population was almost equally split between clinical stage I and II disease; however, more head tumors had stage II disease (58.2%) compared with body and tail tumors (39% each). Overall, two-thirds of patients (67.6%) had open resections; more patients with tail and body tumors underwent laparoscopic resections, compared with head tumors (25.1%, 16.5%, and 7.7%, respectively).

The pathologic T stage was T3 in 68% of cases overall; by site, head tumors had 73.8% of cases with pT3, whereas body and tail tumors had 51% of cases with pT3. Node-positive disease was also higher in head tumors (64.6%), compared with body and tail tumors (40% each). Therefore, while 82.5% of head tumors had pathologic stage II disease, only 59% of body and tail tumors had stage II disease, with most of the rest being stage I.

A higher proportion (37%) of head tumors had poorly differentiated tumors, compared with body and tail tumors (27% and 25%, respectively). A positive resection margin was noted in 20% of cases overall; for head, body, and tail, the numbers were 22%, 17%, and 14%, respectively.

3.3. Adjunctive therapy

Of patients where further treatment details were available (N = 24,833), 39.9% received no other treatment, 8.3% received neoadjuvant therapy (5.6% neoadjuvant chemoradiation and 2.7% neoadjuvant chemotherapy), 4.2% received perioperative therapy (3% perioperative chemoradiation and 1.2% perioperative chemotherapy), and 47.6% received adjuvant therapy (23.3% adjuvant chemoradiation and 24.3% adjuvant chemotherapy). Treatment varied by site of disease. More patients with head tumors received some therapy (66%), compared with body (49%) and tail (41%) tumors. The use of preoperative therapy was also higher for head tumors (15%), compared with body (10%) and tail (3.5%) tumors.

3.4. Survival

Survival outcomes were available on 23,186 (83%) patients. The 30-day post-operative mortality was 3%; the 90-day mortality was 6%. Overall, 63.3% patients had died. Median overall survival was 24 months. Median overall survival times for head, body and tail tumors were 21.6, 34.5, and 42.5 months, respectively. Univariable analyses showed that increasing age, male sex, increasing Charlson-Deyo Score, Medicare as primary payor, head as primary site, higher tumor grade, positive resection margin, lymphovascular invasion, node-positive disease (both clinical and pathologic), higher clinical and pathologic stage, and no use of adjunctive therapy (for head tumors) were all associated with worse overall survival.