Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

[Yun Sheng] Date

Acinar cell carcinoma incidence and survival based surveillance, epidemiology, and end results data, 1973 to 2012

By

Yun Sheng

M.P.H.

Global Epidemiology

Michael Goodman

Committee Chair

Walid Shaib

Committee Member

Acinar cell carcinoma incidence and survival based surveillance, epidemiology, and end results data, 1973 to 2012

By

Yun Sheng

B.A.

China Agricultural University

2014

Thesis Committee Chair: Michael Goodman, MD, MPH

An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in Global Epidemiology

2016

Abstract

Acinar cell carcinoma incidence and survival based surveillance, epidemiology, and end results data, 1973 to 2012

By Yun Sheng

BACKGROUND: Acinar cell carcinoma (ACC) of the pancreas is a rare malignancy with little information available on the trends in incidence and survival. To date no randomized trials has been conducted to guide ACC therapy.

METHODS: Patients with ACC reported to the Surveillance, Epidemiology, and End Results (SEER) Program from 1973 through 2012 were categorized by sex, race, age, marital status, year of diagnosis, primary site, disease stage, and treatment. Then the incidence and survival were compared across different demographic and disease-related categories by calculating rate ratios (RRs) and hazard ratios (HRs) along with the corresponding 95% confidence intervals (CIs).

RESULTS: In total, 396 patients with ACC were identified. While incidence of ACC showed a gradual increase, survival remained largely unchanged. The proportion of male ACC cases increased over time from 50.7% during 1973 to 1992, up to 67.7% during 1993 to 2002, and to 72.9% during 2003 to 2012. The proportion of ACC cases originating in the head of pancreas increased over time from 27.5% during 1973 to 1992, up to 49.0% during 1993 to 2002, and down to 44.9% during 2003 to 2012. After adjusting for sex, marital status, race, disease stage, tumor site, and treatment, mortality among patients older than 70 was higher (HR= 1.72; 95% CI, 1.05-2.82) than in patients younger than 50, and mortality among patients with distant stage ACC was also elevated (HR=3.26; 95% CI, 2.00, 5.31) compared to patients with localized disease. Patients who underwent surgery (HR= 0.47; 95% CI, 0.30-0.72) or surgery and radiation (HR=0.41; 95% CI, 0.22, 0.77) had better survival than those who did not receive tumor directed treatment.

CONCLUSIONS: In recent years there has been an increase in the proportion of male ACC patients and in the percentage of ACC cases originating in the head of pancreas. Age-adjusted disease incidence appears to be higher in men than in women and in whites and American Africans compared to persons of other racial groups. Worse survival following ACC diagnosis is associated with older age and advanced disease stage. The current findings demonstrate that surgical tumor directed treatment may be associated with improved survival, although this observational can be attributed at least in part to the "immortal time bias".

Acinar cell carcinoma incidence and survival based surveillance, epidemiology, and end results data, 1973 to 2012

By

Yun Sheng

B.A.

China Agricultural University

2014

Thesis Committee Chair: Michael Goodman, MD, MP

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in Global Epidemiology

2016

INTRODUCTION

Acinar cell carcinoma (ACC) of the pancreas is a rare malignancy, accounting for about 15% in pediatric subjects and about 1% to 2% of pancreatic tumors in adults[1] with a peak incidence in the 60s. Males are affected more frequently than females with a ratio of 3.6:1 and blacks are affected less commonly than whites.[8]

Athough the majority of pancreas cells are acinar, malignant transformation of these cells is rare for unknown reasons.[2-9] Less than 50 cases of ACC are diagnosed annually in the United States.[8] ACC is composed of cells with morphological resemblance to acinar cells and exocrine enzyme production by the neoplastic cells. Significant endocrine or ductal components (not more than 25 % of the neoplastic cells) are lacking.[24] Microscopically, tumors grow in a trabecular pattern with minimal intervening stroma.[25] The staging of acinar cell carcinomas follows the staging of carcinomas of the exocrine pancreas.

Most ACC present with several non-specific symptoms, which are related to the mass effect of the neoplasm, but there may be an incidental finding on microscopic examination. Common non-specific symptoms include weight loss, abdominal pain, nausea and vomiting, melena, bile duct obstruction and jaundice, and weakness, anorexia or diarrhea.[24] Approximately 10–15 % of patients develop lipase hypersecretion syndrome; peripheral blood eosinophilia and parathyropathies may also occur.[24]

Histopathological analysis is required for definitive diagnosis of ACC. Grossly, these tumors are usually well-circumscribed, pink to tan, partly encapsulated, and homogeneous, fleshy masses. [7] ACCs often contain highly cellular with minimal stroma. They have 5 basic patterns of growth (acinar, pure solid, trabecular, gyriform and glandular); the pure solid and acinar pattern account for the majority but are often mixed with other patterns of growth.[7, 24] ACCs have round to oval

nuclei with single, prominent nucleoli. The cytoplasm is eosinophilic, abundant, and granular due to zymogen granules that produce exocrine enzymes including lipase, trypsin, and chymotrypsin. There are no specific laboratory abnormalities in patients with acinar cell carcinoma. The diagnosis of ACC is based on the presence of zymogen granules, which stain positive with periodic acid-Schiff and are diastase resistant.[15,16] "Periodic acid-Schiff is a staining technique used to identify glycogen within tissues, whereas diastase is an enzyme that catalyzes the breakdown of various forms of carbohydrate molecules such as starch into maltose."[24] In well-granulated cases, this staining pattern is supportive of ACC diagnosis. Immunohistochemical labeling for pancreatic enzyme production is helpful in confirming the diagnosis of ACC. Antibodies are available against trypsin, chymotrypsin, lipase and elastase. The first three of these are most widely employed, and labeling for trypsin (95 % of cases) and chymotrypsin has the highest degree of sensitivity, lipase (70–80 % of cases) is less commonly identified.[24]

ACC has been considered a cancer with poor prognosis due to its low resectability, frequent metastases, and high recurrence rate. To date, the most important prognostic factor is tumor stager.[28, 29] The overall mean post-diagnosis survival of ACC patients is about 47 months with a cancer-specific 5-year survival ranging from 36.2% to 72% for resected cancers.[3, 10, 11]

ACC patients tend to be younger and present with early stage disease when compared to patients with pancreatic adenocarcinoma[2-9], and the long-term survival for patients with this type of malignancy is significantly better than that of patients with pancreatic adenocarcinoma.[24] Most patients with ACC undergo surgical resection for resectable tumor, and receive chemotherapy with or without radiation for unresectable tumor with presence of distant metastases, which account for about half of ACC patients.[24]

Previous ACC studies have primarily involved retrospective chart abstractions, literature reviews, and some were limited to case reports. As the disease is so rare its treatment has not been studied in clinical trials with only a handful of reports describing various management options. Management recommendations are usually extrapolated from pancreatic adenocarcinoma literature.[2-18] Only one previous study examined population based data on ACC using the Surveillance, Epidemiology, and End Results (SEER) database (1988 to 2003).[8] Our study extend the time period from 1973 to 2012.

The present study will evaluate epidemiologic features of ACC with regard to incidence trends as well as differences in age at diagnosis, gender and race. In addition, we will examine the relationship between overall survival (OS) and treatment (surgery and radiation) stratified for stage. These results may help guide oncologists treating ACC patients.

MATERIALS AND METHODS

Data for the analysis were obtained from the National Cancer Institute's SEER Program, which is the main source for cancer statistics in the United States. 28% of the US population from specific geographic areas are represented by SEER data includes information on prevalence, incidence, and survival. SEER also compiles reports on cancer mortality for the entire country.[16] SEER data collection since the early 1970s and gradually expanded. Data for analyses were obtained from the currently operating 18 SEER registries. But incidence rate calculations to evaluate changes in incidence since 1973 were limited to the 9 original registries (San Francisco/Oakland, Connecticut, Detroit, Hawaii, New Mexico, Seattle, Utah. and Atlanta).

The International Classification of Diseases for Oncology, third edition (ICD-O-3) were used to select all cases reported to the SEER Program from 1973 through 2012 that originated from one of the following primary sites (and ICD-O-3 codes): head of pancreas (C.25.0); body of pancreas

(C.25.1); tail of pancreas (C.25.2); other specified parts of pancreas (C25.7); overlapping lesion of pancreas (C.25.8); and pancreas, not otherwise specified (C25.9). Only acinar cell carcinomas (ICD-O-3 code 8550/3) were included. Cases were excluded from the analyses if they were identified from death certificates only, of unknown age, or were not microscopically confirmed.

All patients with ACC reported during the study period from 1973 to 2012 were characterized according to sex, race, age at diagnosis, marital status, disease stage and disease site. Tumor-directed therapy was grouped into 4 categories: none, radiation alone, surgery alone, and surgery plus radiation. Only patients who were diagnosed from 1983 through 2012 were examined in the analyses of type of tumor-directed therapy, as treatment information was available from 1983 onward. Cancer staging has undergone multiple changes since the early 1970s; thus we used the "SEER historic stage A" variable, which covers our entire study period, and whose classification scheme categorizes cancer cases as localized, regional, distant, or unstaged based on definitions stated in previous study[16, 30].

Incidence rates of ACC were calculated for the entire study period by sex and race and were expressed as the number of cases per 1,000,000 person-years accompanied by 95% confidence intervals (CIs), and age-adjusted to the 2000 US Standard Population. The differences in rates between men and women and among whites, African Americans, and all other racial groups were examined by calculating rate ratios (RRs) and the corresponding 95% CIs, as described by Tiwari et al.[17] Trends in incidence were expressed as annual percentage change (APC) estimates with 95% confidence intervals (CI) and were examined further using the Joinpoint Regression Program (Control and Population Sciences, National Cancer Institute, Bethesda, Md). The APC was calculated by using the calendar year as a regressor variable and fitting a least-squares regression line to the natural logarithm of the rates. Joinpoint models were further used to analyze the

incidence data,, which were aimed at evaluating longitudinal data for a change in trend. Monte Carlo permutation method was used to test changes in trend for statistical significance.

The survival of patients with ACC was analyzed using several methods, and the total follow-up was extended to 10 years (120 months) post-diagnosis. First, we calculated 5-year and 10-year cumulative observed survival (OS), which definition defined as the proportion of patients who survived beyond a given interval. Relative survival (RS) were then calculated by dividing OS among cancer patients by the expected survival in the general population controlling for age, sex, and race characteristics. In contrast to frequency analyses, which included all records, survival analyses excluded cases that known to be alive but without documented survival time. The 5-year and 10-year OS and RS estimates were evaluated overall and by sex and race. In addition, joinpoint regression was used to examine 5-year RS estimates over time, and the resulting trend was represented by the APC and its 95% CI. These survival calculations were based on the actuarial life-table method. Data used for survival analyses extended from 1973 through the end of 2012.

We then constructed Kaplan-Meier curves and performed the corresponding log-rank tests for statistical significance to examine patient survival according to decade of diagnosis, patient sex, race, and ACC stage. And the follow-up for survival analyses was limited to 5-years. Further, multivariable Cox proportional hazards model was used to examine the association between survival and various disease-related, treatment-related and patient-related characteristics with primarily focusing on disease stage and treatment type. Other covariates in the Cox proportional hazards model included age, sex, race, marital status and disease primary site. Adjusted hazard ratios (HRs) along with the corresponding 95% CIs are reported as the results of these multivariable models. All models were examined for interactions and colinearity among covariates and proportional hazard assumptions were tested by examining log-minus-log plots for each variable.[18]

The analyses were performed using SAS 9.3 (SAS Institute, Inc., Cary, North Carolina) and SEER*Stat version 6.4.4 (National Cancer Institute, Bethesda, Md) statistical software packages.

RESULTS

In total, 396 patients with ACC were identified in the 18 SEER registries from 1973 through the end of 2012. Men accounted for 67.7% of ACC cases, approximately 84% of all patients were white and 10% were black, 65.2% of patients were married (Table 1). Nearly half of all patients (48.2%) were between ages 50 and 70 years, 38.1% of patients were over 70 years of age, and patients under the age of 50 years contributed only 13.6%. Approximately half of patients (43%) presented with a tumor originating in the head of pancreas. The distributions of patient demographic characteristics and cancer primary site did not differ appreciably over time. By contrast, there was evidence that the proportion of male ACC cases increased over time from 50.7% from 1973 to 1992, up to 67.7% from 1993 to 2002, and up to 72.9% from 2003 to 2012. The proportion of ACC cases originating in the head of pancreas also changed from 27.5% in 1973-1992, up to 49.0% in1993-2002, and down to 44.9% in 2003-2012. The stage distribution in the earlier 10-year interval (1973-1982) could not be assessed, because all cases in the time period were "unstaged".

As shown in Figure 1, there was no statistically significant time trend in the overall incidence of ACC between 1973 and 2010 (APC=0.8; 95% CI: -0.6, 2.3). There appeared to be an inflexion point after 2010; however the post-inflexion time trend was also not significant (APC=50.6; 95% CI: -29.3, 221.0). The rates of ACC in women were significantly lower than the corresponding rates among men (RR 0.46; 95% CI: 0.34-0.62). Compared to whites, the incidence was higher among African-Americans (RR 1.30; 95% CI, 0.78-2.06) and lower among individuals of all other racial groups (RR, 0.48; 95% CI: 0.21-0.94).

Overall, the 5-year and 10-year OS estimates were 19.0% (95% CI, 14.5%-23.9%) and 10.8% (95%

CI, 7.0%-15.6%), respectively (Table 2). The corresponding 5-year and 10-year RS estimates were 21.0% (95% CI, 16.1%-26.5%) and 13.5% (95% CI, 8.7%-19.3%). The OS and RS estimates generally were higher in women than in men and were higher among African American and other races than among whites (Table 2). The Kaplan-Meier curves (Figure 2) demonstrated that the survival of ACC patients was lower for persons who were diagnosed in the earliest decade (1973-1992) than for those who were diagnosed after 1992; however, subsequent time periods (1993-2002, and 2003-2012) demonstrated no discernible difference. Survival differed significantly by race, and sex (P<.05 for both), (Figures 3-4). Patients with early stage disease had better survival than those with advanced stage disease (P<.001), (Figure 5).

The independent associations of disease stage and treatment with survival, after controlling for patient demographic characteristics, are presented in Table 3. Compared with patients who had localized ACC, those with distant disease had significantly elevated mortality (lower survival), with an HR of 3.26 (95% CI, 2.00-5.31). Other factors associated with higher mortality included older age and tumor-directed treatment (Table 3). After adjusting for sex, race, marital status, disease stage, and tumor site, mortality among patients with ACC aged greater than 70 relative to those aged less than 50 counterparts was increased by 72% (95% CI, 1.05-2.82). Compared to patients who received no tumor-directed therapy mortality among those who underwent surgery HR of 0.47 (95% CI, 0.30-0.72) for patients treated by surgery only and HR of 0.41 (95% CI, 0.22-0.77) for patients treated by both surgery and radiation. By contrast, sex, race, marital status, and primary tumor site did not appear to be related to survival.

DISCUSSION

The current results demonstrate that the head of pancreas was the most common primary site of ACC followed by the tail of pancreas and body of pancreas, with a peak age-specific incidence

between ages 50 and s and 70s. We observed a modest but not statistically significant increase in the overall incidence of ACC. Although the joinpoint analyses data indicated a possible upward inflection of the trend, the inflexion was not statistically significant and may be attributable to random fluctuation of the rates over time. Additional years of data may be able to The majority of patients with ACC were men, and the age-adjusted incidence of disease found to be higher in males than in females and in whites and Blacks than in person of other racial groups.

Our results are consistent with those from earlier studies that demonstrated a preponderance of pancreatic acinar cell cancer in men, with predominantly head of pancreas involvement.[8] Unlike other reports, however, ours focused exclusively on pancreatic acinar cell histology and encompassed more extensive and contemporary data from SEER. There is other SEER-based study, which have reviewed data on ACC but also included other histologies.[8] To our knowledge, this study is the first SEER-based analysis focusing exclusively on ACC in the general population.

We also found that the 5-year survival of ACC patients was associated with age and disease stage after controlling for sex, race, marital status, disease site and treatment method. Patients older than 70 and with advanced stage disease had lower 5-year survival rate than their younger counterparts. The combination of radiation therapy and surgery and surgery alone in our data demonstrated superiority compared with radiation alone, which is accordance with previous studies.[2-9]

However, it is important to keep in mind that the analyses by treatment may have been affected by immortal time in one or more of the groups. For example patients who received surgery had to survive to the procedure and their follow up time incorporated an interval between diagnosis and surgery during which they could not have died. On the hand, patients who did not receive surgery did not have the corresponding "immortal" time interval. For this reason the observed benefit of surgery may be explained at least in part by the "immortal time bias".[22]

Other shortcomings of the present analysis are related to the limitations of the SEER data. As previously reviewed elsewhere[31-33], the main limitations of SEER data pertain to the lack of data on certain important demographic and clinical variables. Although SEER data on radiation and surgery are reasonably complete, the information pertaining to systemic treatment such as chemotherapy is usually missing and is not included in the public use files. In addition, SEER data do not contain information on additional important determinants of survival including health insurance, comorbidities and socioeconomic status. Another important data item that may need to be considered is the effect of facility-related and provider characteristics that cannot be addressed using SEER data.

On the other hand SEER-based studies often have good statistical power for detecting relatively moderate associations and allow relatively complex multivariable analyses. In contrast to institution-based, the population-based identification of patients increases the external validity of results, and the active follow-up of patients improves the accuracy of survival analyses.[31-33]

In conclusion, we observed that in recent years there has been an increase in the proportion of male ACC patients and in the percentage of ACC cases originating in the head of pancreas. Age-adjusted disease incidence appears to be higher in men than in women and in whites and American Africans compared to persons of other racial groups. Worse survival following ACC diagnosis is associated with older age and advanced disease stage. The current findings demonstrate that surgical tumor directed treatment may be associated with improved survival, although this observational can be attributed at least in part to the "immortal time bias".

.

References

1. Klimstra DS. Nonductal neoplasms of the pancreas. Mod Pathol. 2007;20:S94–S112.
2. Klimstra DS, Heffess CS, Oertel JE, Rosai J. Acinar cell carcinoma of the pancreas. A clinicopathologic study of 28 cases. Am J Surg Pathol. 1992;16(9):815-837.
3. Kitagami H, Kondo S, Hirano S, Kawakami H, Egawa S, Tanaka M. Acinar cell carcinoma of the pancreas: clinical analysis of 115 patients from Pancreatic Cancer Registry of Japan Pancreas Society. Pancreas. 2007;35(1):42-46.
4. Mansfield A, Tafur A, Smithedajkul P, Corsini M, Quevedo F, Miller R. Mayo Clinic experience with very rare exocrine pancreatic neoplasms. Pancreas. 2010;39(7):972-975.
5. Matos JM, Schmidt CM, Turrini O, et al. Pancreatic acinar cell carcinoma: a multi-institutional study. J Gastrointest Surg. 2009;13(8):1495-1502.
6. Schmidt CM, Matos JM, Bentrem DJ, Talamonti MS, Lillemoe KD, Bilimoria KY. Acinar cell carcinoma of the pancreas in the United States: prognostic factors and comparison to ductaladenocarcinoma. J Gastrointest Surg. 2008;12(12):2078-2086.
7. Seth AK, Argani P, Campbell KA, et al. Acinar cell carcinoma of the pancreas: an institutional series of resected patients and review of the current literature. J Gastrointest Surg. 2008;12(6):1061-1067.
8. Wisnoski NC, Townsend CMJr., Nealon WH, Freeman JL, Riall TS. 672 patients with acinar cell carcinoma of the pancreas: a population-based comparison to pancreatic adenocarcinoma. Surgery. 2008;144(2):141-148.
9. Holen KD, Klimstra DS, Hummer A, et al. Clinical characteristics and outcomes from an institutional series of acinar cell carcinoma of the pancreas and related tumors. J Clin Oncol. 15 2002;20(24):4673-4678.
10. Chen CP, Chao Y, Li CP, et al. Concurrent chemoradiation is effective in the treatment of alphafetoprotein-producing acinar cell carcinoma of the pancreas: report of a case. Pancreas. 2001;22(3):326-329.

11. Distler M, Ruckert F, Dittert DD, et al. Curative resection of a primarily unresectable acinar cell carcinoma of the pancreas after chemotherapy. World J Surg Oncol. 2009;7:22.
12. Kobayashi S, Ishikawa O, Ohigashi H, et al. Acinar cell carcinoma of the pancreas successfully treated by en bloc resection and intraperitoneal chemotherapy for peritoneal relapse: a case report of a 15-year survivor. Pancreas. 2001;23(1):109-112.
13. Lee JL, Kim TW, Chang HM, et al. Locally advanced acinar cell carcinoma of the pancreas successfully treated by capecitabine and concurrent radiotherapy: report of two cases. Pancreas. 2003;27(1):e18-22.
14. Mueller SB, Micke O, Herbst H, Schaefer U, Willich N. Alpha-fetoprotein-positive carcinoma of the pancreas: a case report. Anticancer Res. 2005;25(3A):1671-1674.
15. Riechelmann RP, Hoff PM, Moron RA, da Camera Lopes LH, Buzaid AC. Acinar cell carcinoma of the pancreas. Int J Gastrointest Cancer. 2003;34(2-3):67-72.
16. Seki Y, Okusaka T, Ikeda M, Morizane C, Ueno H. Four cases of pancreatic acinar cell carcinoma treated with gemcitabine or S-1 as a single agent. Jpn J Clin Oncol. 2009;39(11):751-755.
17. Sorscher SM. Metastatic acinar cell carcinoma of the pancreas responding to gemcitabine, 5-fluorouracil and leucovorin therapy: a case report. Eur J Cancer Care (Engl). 2009;18(3):318-319.
18. Suzuki A, Sakaguchi T, Morita Y, et al. Long-term survival after a repetitive surgical approach in a patient with acinar cell carcinoma of the pancreas and recurrent liver metastases: report of a case. Surg Today. 2010;40(7):679-683.
19. Prentice JKaR: The statistical analysis of failure time data 1980
20. Cox DR: Regression Models and Life Tables. Journal of the Royal Statistical Society Series B 187–220, 1972
21. Kim HJ, Fay MP, Feuer EJ, et al: Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 19:335-51, 2000 over the past 3 decades: Surveillance Epidemiology

and End Results data. J Pediatr Hematol Oncol. 2008; 30(6):425-30.

33. Saba NF, Goodman M, Ward K, et al: Gender and ethnic disparities in incidence and survival of squamous cell carcinoma of the oral tongue, base of tongue, and tonsils: a surveillance, epidemiology and end results program-based analysis. Oncology 2011; 81(1):12-20.

Tables

Table 1. Characteristics of Patients With Acinar Cell Carcinoma of the Pancreas by Decade: 18 Surveillance, Epidemiology, and End Results Registries, 1973 to 2012

Patient Characteristic	No. of Patients (%)			
	All Patients, N = 396 N (%)	1973-1992, N= 69 N (%)	1993-2002, N= 102 N (%)	2003-2012, N= 225 N (%)
Sex				
Male	268 (67.7)	35 (50.7)	69 (67.7)	164 (72.9)
Female	128 (32.3)	34 (49.3)	33 (32.4)	61 (27.1)
Race				
White	331 (83.6)	58 (84.1)	80 (78.4)	193 (85.8)
Black	41 (10.4)	9 (13.0)	13 (12.8)	19 (8.4)
Other[a]	24 (6.1)	2 (2.9)	9 (8.8)	13 (5.8)
Marital Status				
Married	258 (65.2)	43 (62.3)	66 (64.7)	149 (66.2)
Unmarried	125 (31.6)	22 (31.9)	35 (34.3)	68 (30.2)
Unknown	13 (3.3)	4 (5.8)	1 (1.0)	8 (3.6)
Age, y				
<50	54 (13.6)	11 (15.9)	18 (17.7)	25 (11.1)
50-70	191 (48.2)	38 (55.1)	44 (43.1)	109 (48.4)
≥70	151 (38.1)	20 (29.0)	40 (39.2)	91 (40.4)
Disease stage				
Localized	62 (15.7)	9 (13.0)	14 (13.7)	39 (17.3)
Regional	122 (30.8)	16 (23.2)	34 (33.3)	72 (32.0)
Distant	193 (48.7)	37 (53.6)	50 (49.0)	106 (47.1)
Untagged	19 (4.8)	7 (10.1)	4 (3.9)	8 (3.6)
Disease site				
Head of pancreas	170 (42.9)	19 (27.5)	50 (49.0)	101 (44.9)
Body of pancreas	32 (8,1)	10 (14.5)	6 (5.9)	16 (7.1)
Tail of pancreas	77 (19.4)	7 (10.1)	23 (22.6)	47 (20.9)
Others	117 (29.6)	33 (47.8)	23 (22.6)	61 (27.1)

[a] Other races included Asian or Pacific Islander, American India, Alaska Native, or unspecified

Table 2. The survival of patients with Acinar cell carcinoma is illustrated over time and by sex and race (18 Survival, Epidemiology, and End Results registries, 1973-2012). APC indicates annual percentage; CI, confidence interval; OS, Observed survival; RS, relative survival.

Patient characteristics	Survival interval	OS (95% CI)*	RS (95% CI)**
Male	5-yr	16.3 (11.2, 22.2)	18.5 (12.7, 25.2)#
	10-yr	7.0 (3.4, 12.4)	9.0 (4.3, 15.8)#
Female	5-yr	24.2 (16.0,33.4)	25.8 (17.0, 35.5)#
	10-yr	17.3 (9.7, 26.7)	20.3 (11.3, 31.1)#
White	5-yr	16.6 (12.2, 22.1)	18.7 (13.6, 24.5)#
	10-yr	10.1 (6.1, 15.3)	12.8 (7.7, 19.4)#
Black	5-yr	18.3 (7.1, 33.7)	20.6 (7.8, 37.6)#
	10-yr	7.3 (1.3, 20.6)	9.4 (1.6, 25.8)#
Other	5-yr	50.2 (25.4, 70.6)	52.2 (26.0, 73.1)#
	10-yr	32.2 (10.1, 57.1)	35.1 (10.6, 61.4)#
All groups	5-yr	19.0 (14.5, 23.9)	21.0 (16.1, 26.5)#
	10-yr	10.8 (7.0, 15.6)	13.5 (8.7, 19.3)#

* OS = percent of patients surviving beyond a given interval

** RS = OS of cancer patients divided by the expected survival in population with the same race, age, and gender characteristics.

Relative survival increased from a prior interval and has been adjusted

Table 3.Multivariable Analyses Looking at the Association Between Mortality-, Patient-, Disease-, and Treatment-Related Characteristics Among Patients With Acinar Cell Carcinoma of Pancreas: 18 Surveillance, Epidemiology, and End Results Registries, 1998-2012

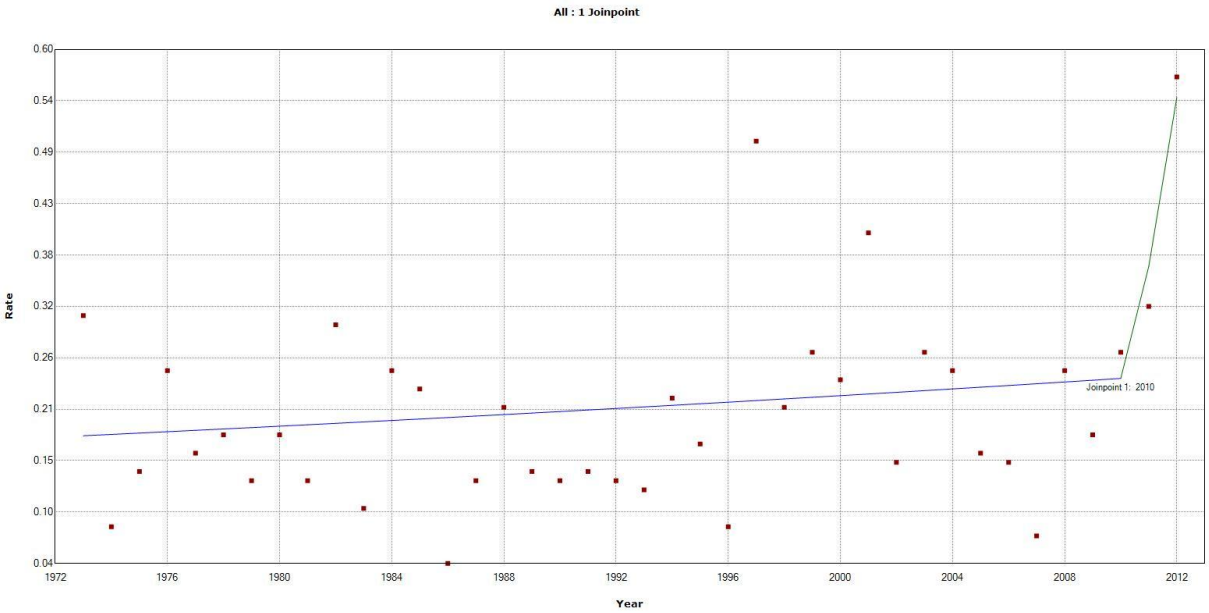
Patient Characteristic	HR	95% CL	*P*
Sex			
Male	1.00	Ref	
Female	0.78	0.55, 1.11	.162
Race			
White	1.00	Ref	
Black	1.45	0.87, 2.43	.154
Other[a]	1.06	0.48, 2.35	.878
Marital status			
Other[b]	1.00	Ref	
Married	0.93	0.65, 1.34	.702
Age, y			
<50	1.00	Ref	
50-70	1.05	0.63, 1.75	.865
≥70	1.72	1.05, 2.82	.030
Disease stage			
Localized	1.00	Ref	
Regional	1.52	0.92, 2.53	.105
Distant	3.26	2.00, 5.31	<.001
Disease site			
Head of pancreas	1.00	Ref	
Body of pancreas	1.20	0.67, 2.15	.538
Tail of pancreas	1.23	0.80, 1.89	.336
Others	1.03	0.72, 1.48	.877
Tumor-directed treatment			
None	1.00	Ref	
Surgery only	0.47	0.30, 0.72	<.001
Radiation only	0.98	0.57, 1.70	.948
Surgery and radiation	0.41	0.22, 0.77	.005

[a] Other = American Indian/AK Native, Asian/Pacific Islander

[b] Other = Single, Seperated, Divorced, Widowed, Unmarried or Domestic Partner

Abbreviations: CL, confidence limits; HR, hazard ratio; Ref, referent category.

Figures



Population groups	Rate (95% CI)*	Rate Ratio (95% CI; p-value)
Male	0.31 (0.26, 0.37)	Reference
Female	0.14 (0.11, 0.18)	0.46 (0.34, 0.62; p<0.001)
White	0.22 (0.19, 0.25)	Reference
Black	0.28 (0.17, 0.43)	1.30 (0.78, 2.06)
Other	0.10 (0.05, 0.20)	0.48 (0.21, 0.94; p=0.028)
All groups	0.21 (0.19, 0.25)	

* Rates are per 1,000,000 and age-adjusted to the 2000 US Population

Figure 1. Age adjusted rates of Acinar Cell Carcinoma over time and by sex and race (9 Surveillance, Epidemiology, and End Results registries, 1973-2012), APC indicates annual percentage change; CI, confidence interval.

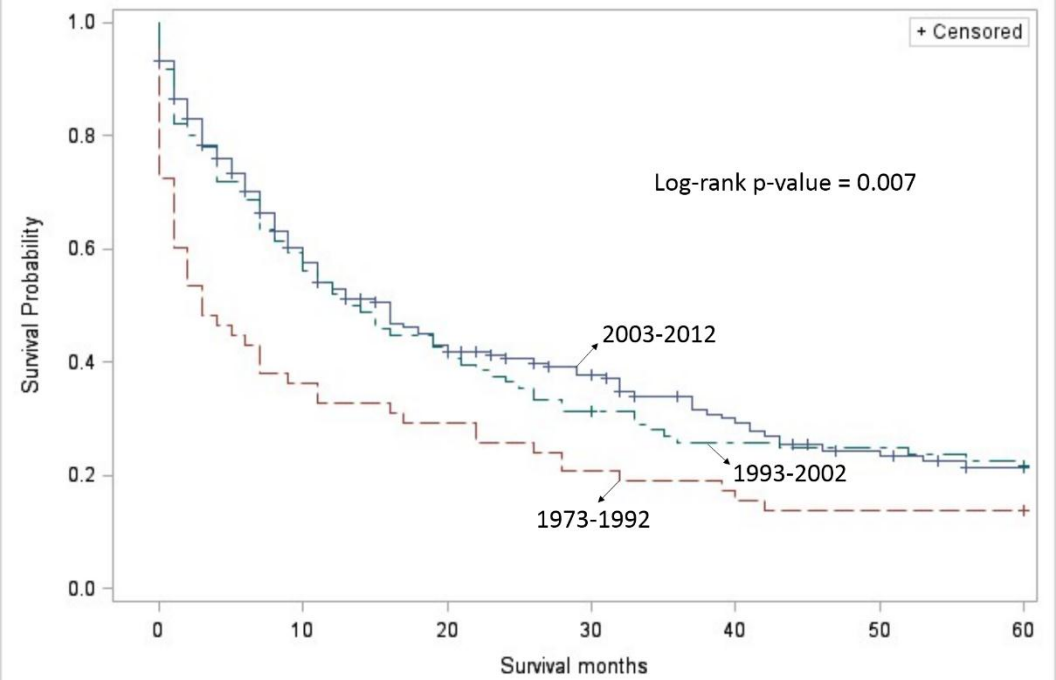


Figure 2. The survival of patients with Acinar cell carcinoma is illustrated by decade (18 Surveillance, Epidemiology, and End Results registries, 1973-2012).

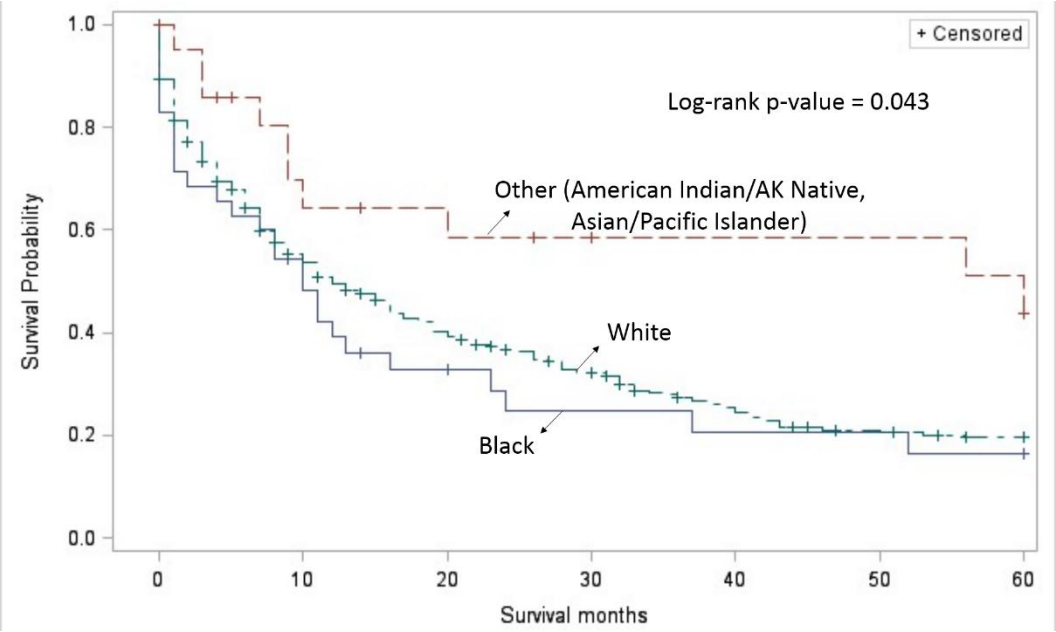


Figure 3. The survival of patients with Acinar cell carcinoma is illustrated by race (18 Surveillance, Epidemiology, and End Results registries, 1973-2012).

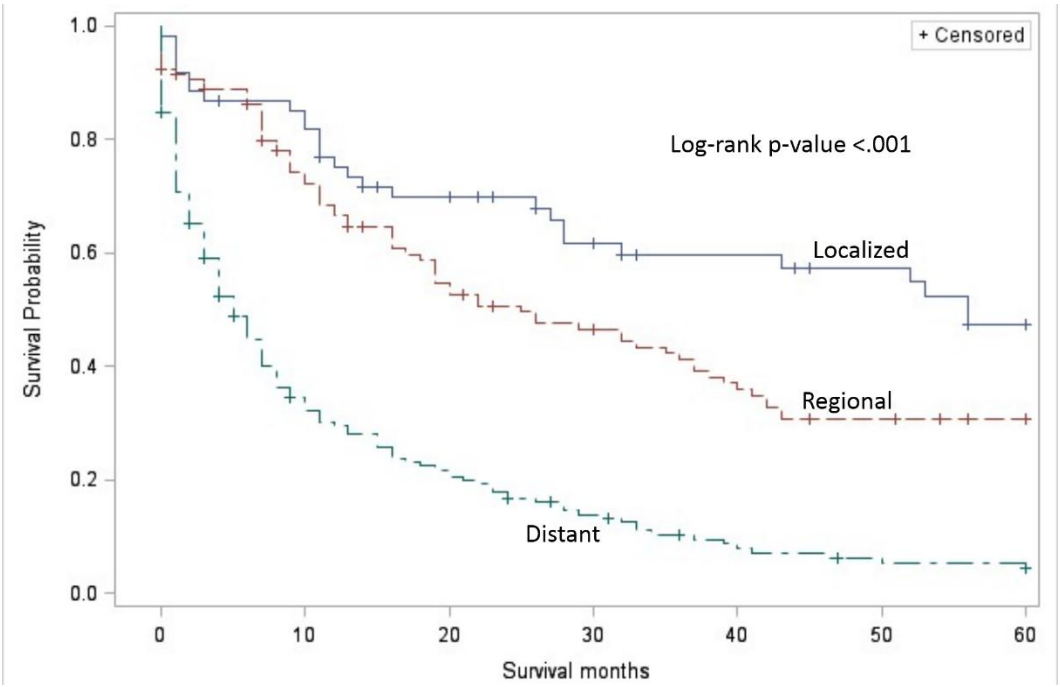


Figure 4. The survival of patients with Acinar cell carcinoma is illustrated by stage (18 Surveillance, Epidemiology, and End Results registries, 1973-2012).

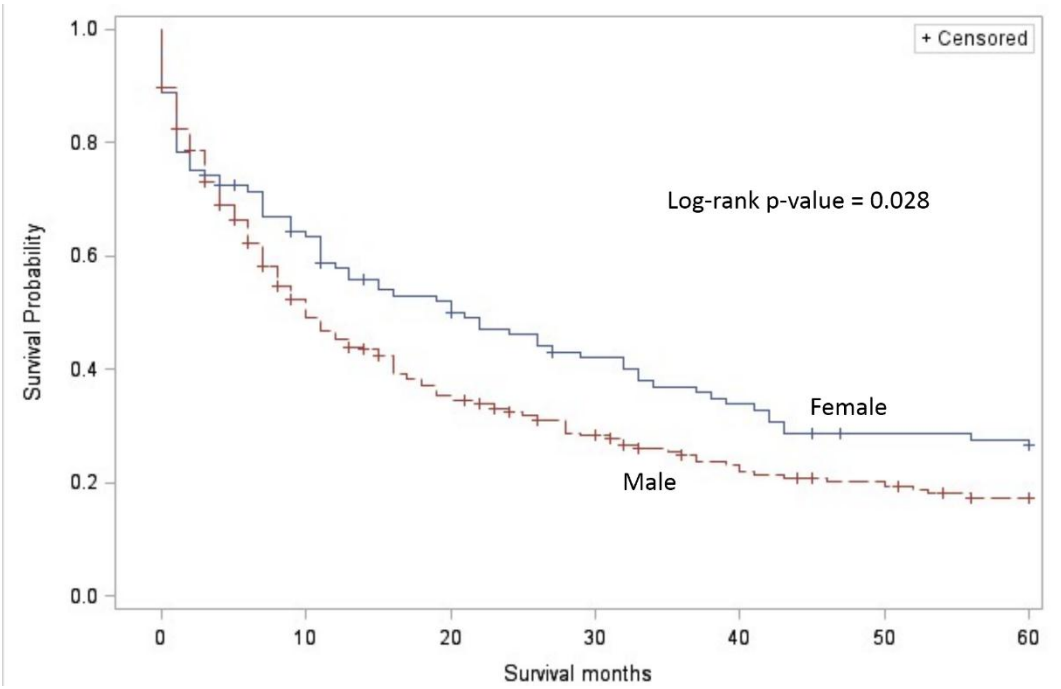


Figure 5. The survival of patients with Acinar cell carcinoma is illustrated by sex (18 Surveillance, Epidemiology, and End Results registries, 1973-2012).