Case Study:
The impact of tumor location on survival outcomes for patients diagnosed with pancreatic cancer and treated with surgery in Louisiana between 2004 and 2016

James Henegan

Survival Analysis Final Project

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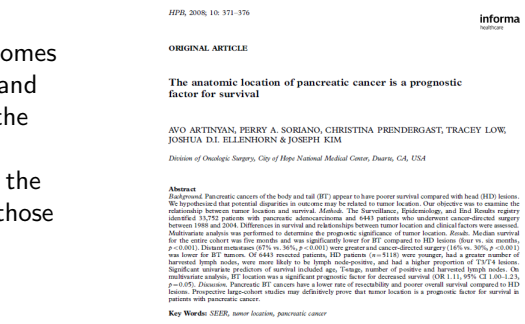
Introduction - Research Question

The purpose of this study is to investigate the relationship between tumor location and survival probability for patients diagnosed with pancreatic cancer and treated with surgery.

We restricted our attention to patients from Louisiana who had been diagnosed with the disease between the years of 2004 and 2016, inclusive.

The impact of tumor location on survival outcomes for patients diagnosed with pancreatic cancer and treated with surgery has been investigated in the past. For example, Artinyan et. al found that patients who had cancer in the body or tail of the pancreas had outcomes that were worse than those who had cancer in the head of the pancreas.



HPB, 2008; 10: 371–376

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ORIGINAL ARTICLE

The anatomic location of pancreatic cancer is a prognostic factor for survival

AVO ARTINYAN, PERRY A. SORIANO, CHRISTINA PRENDERGAST, TRACEY LOW, JOSHUA D.I. ELLENHORN & JOSEPH KIM

Division of Oncologic Surgery, City of Hope National Medical Center, Duarte, CA, USA

Abstract

Background. Pancreatic cancers of the body and tail (BT) appear to have poorer survival compared with head (HD) lesions. We hypothesized that potential disparities in outcome may be related to tumor location. Our objective was to examine the relationship between tumor location and survival. *Methods.* The Surveillance, Epidemiology, and End Results registry identified 33,752 patients with pancreatic adenocarcinoma and 6443 patients who underwent cancer-directed surgery between 1988 and 2004. Differences in survival and relationships between tumor location and clinical factors were assessed. Multivariate analysis was performed to determine the prognostic significance of tumor location. *Results.* Median survival for the entire cohort was five months and was significantly lower for BT compared to HD lesions (four vs. six months, $p < 0.001$). Distant metastases (67% vs. 36%, $p < 0.001$) were greater and cancer-directed surgery (16% vs. 30%, $p < 0.001$) was lower for BT tumors. Of 6443 resected patients, HD patients ($n = 5118$) were younger, had a greater number of harvested lymph nodes, were more likely to be lymph node-positive, and had a higher proportion of T3/T4 lesions. Significant univariate predictors of survival included age, T-stage, number of positive and harvested lymph nodes. On multivariate analysis, BT location was a significant prognostic factor for decreased survival (OR 1.11, 95% CI 1.00–1.23, $p = 0.05$). *Discussion.* Pancreatic BT cancers have a lower rate of resectability and poorer overall survival compared to HD lesions. Prospective large-cohort studies may definitively prove that tumor location is a prognostic factor for survival in patients with pancreatic cancer.

Key Words: *SEER, tumor location, pancreatic cancer*

Data Collection

Incidence – SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2018 Sub (1975-2016 Varying)

Search Criteria:

```
{Race, Sex, Year Dx, Registry, County,Year of diagnosis} = '2004','2005','2006','2007','2008','2009','2010','2011','2012','2013','2014','2015','2016'
AND {Race, Sex, Year Dx, Registry, County,SEER registry} = 'Louisiana - 2000+'
AND {Site and Morphology.Site recode ICD-O-3/WHO 2008} = '  Pancreas'
AND {Therapy.Reason no cancer-directed surgery} = 'Surgery performed'
AND {Site and Morphology.TNM 7/CS v0204+ Schema} != 'PancreasOther'
AND {Cause of Death (COD) and Follow-up.Survival months} != 0
AND {Cause of Death (COD) and Follow-up.Survival months} != 'Unknown'
AND {Race, Sex, Year Dx, Registry, County,Race recode (White, Black, Other)} != '  Unknown'
AND {Race, Sex, Year Dx, Registry, County,Race recode (White, Black, Other)} != '  Other (American Indian/AK Native, Asian/Pacific Islander)'
AND {Stage - Summary/Historic.Summary stage 2000 (1998+)} != 'Unknown/unstaged'
AND {Site and Morphology.Grade} != 'Unknown'
```

Variables:

Column

Race recode (White, Black, Other)
Sex
Year of diagnosis
Site recode ICD-O-3/WHO 2008
CS Tumor Size/Ext Eval (2004-2015)
Grade
Summary stage 2000 (1998+)
Reason no cancer-directed surgery
TNM 7/CS v0204+ Schema
Age at diagnosis
COD to site recode
Survival months
Vital status recode (study cutoff used)
Marital status at diagnosis

988 Records Returned

712 had a tumor in the head of the pancreas.

276 had a tumor in the body/tail of the pancreas

The event of interest was all-cause mortality.

The variable `TNM 7/CS v0204 Schema` attained values of `PancreasHead`, `PancreasBodyTail`, and `PancreasOther`.

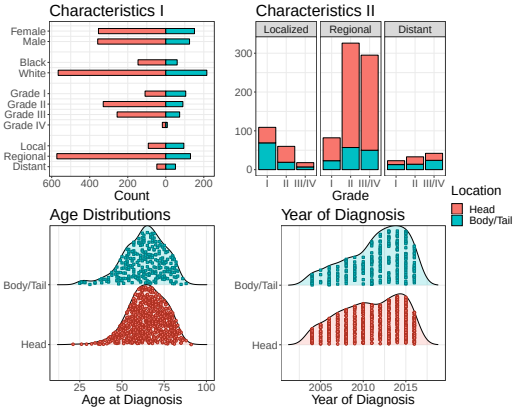
The variable `Summary stage 2000 (1998+)` attained values of `Local`, `Regional`, and `Distant`.

The variable `Grade` attained values of 1, 2, 3, and 4.

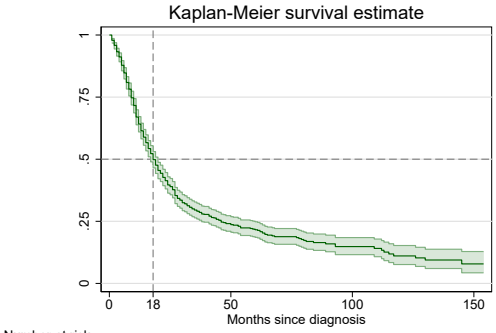
The variable `CS Tumor Size/Exit Eval(2004-2015)` was not used.

Sample Characteristics

	Tumor Location: Head of Pancreas ($N = 712$)	Tumor Location: Body/Tail of Pancreas ($N = 276$)
Age at Diagnosis (years)	64.89 ± 10.77	63.05 ± 12.22
Year of Diagnosis	2010.84 ± 3.55	2011.60 ± 3.38
Sex		
Female	354 (50%)	151 (55%)
Male	358 (50%)	125 (45%)
Race		
Black	146 (21%)	60 (22%)
White	566 (79%)	216 (78%)
Grade		
I	109 (15%)	105 (38%)
II	329 (46%)	90 (33%)
III	256 (36%)	73 (26%)
IV	18 (3%)	8 (3%)
Stage		
Local	92 (13%)	95 (34%)
Regional	573 (80%)	130 (47%)
Distant	47 (7%)	51 (18%)

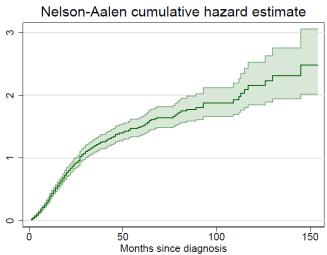


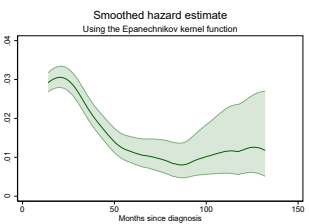
Overall Survival Data



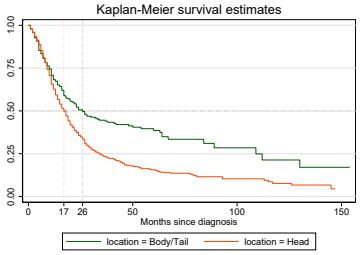
	Total ($N = 988$)
Dead	676 (68%)
Median Survival Time (Months)	18 (95% CI: 17,20)
Median Follow Up Time (Months)	49 (95% CI: 44,56)

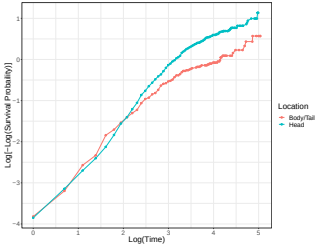
Table. Overall Survival Data.





Results, by Tumor Location





Test	p-value
Log-rank	< 0.0001
Wilcoxon	0.0022

	Tumor Location: Head ($N = 712$)	Tumor Location: Body/Tail ($N = 276$)
Dead	529 (74.30%)	147 (53.26%)
Median Survival Time (months)	17 (16,19)	26 (20,38)
Median Follow-Up Time (months)	53 (44,65)	46 (40, 52)

Variable	Unadj. HR	Unadj. HR 95% CI	Schoenfeld p-value
Tumor Location			
Head	1.58	(1.32, 1.90)	0.07
Body/Tail	—		

Table. Results from the unadjusted Cox model for Tumor Location.

Cox Model by Tumor Location, with Time Dependent Variables

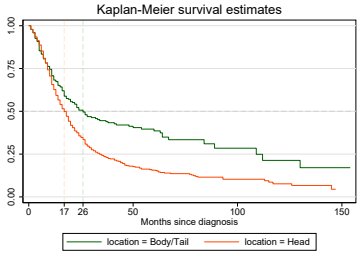
The log-log plot of the previous model caused us to consider the model $h(t, \boldsymbol{X}) = h_0(t)e^{x_1 Z_1 + x_2 Z_2}$ where

$$Z_1(t) = \begin{cases} 1, & \text{Tumor in the head of the pancreas and } t \leq 5 \\ 0, & \text{otherwise} \end{cases}$$

$$Z_2(t) = \begin{cases} 1, & \text{Tumor in the head of the pancreas and } t > 5 \\ 0, & \text{otherwise} \end{cases}.$$

The estimates obtained by this model are described below.

Variable Name	Hazard Ratio	95% CI for HR
Z_1	0.77	(0.52, 1.13)
Z_2	1.89	(1.53, 2.33)

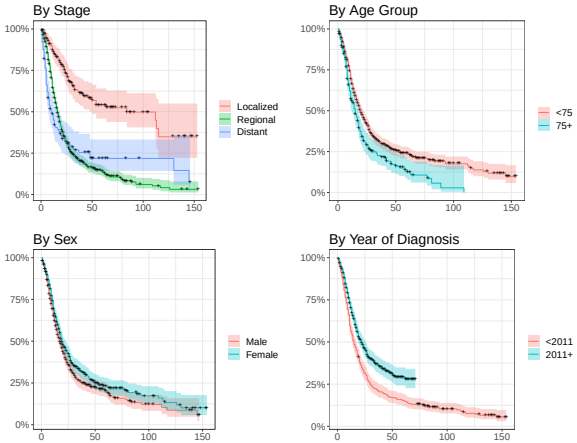


Other Unadjusted Cox Models

Variable	Log-rank p-value
Stage	< 0.0001
Age	0.0001
Sex	0.0447
Year of Diagnosis	< 0.0001

Variable	Unadj. HR	Unadj. HR 95% CI	Schoenfeld p-value
Cancer Stage			
Distant	3.45	(2.47, 4.81)	0.0012
Regional	3.27	(2.53, 4.22)	0.9877
Localized	—		
Age at Diagnosis			
≥ 75	1.43	(1.19, 1.70)	0.2675
< 75	—		
Sex			
Male	1.16	(1.00, 1.35)	0.9059
Female	—		
Year of Diagnosis			
≥ 2011	0.66	(0.57, 0.77)	0.9809
< 2011	—		

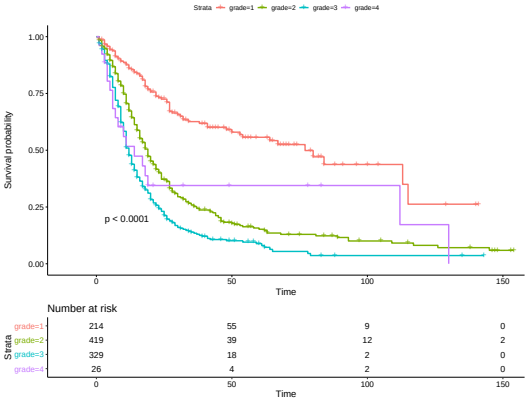
Table. Results from the unadjusted Cox models for Cancer Stage, Age at Diagnosis, Sex, and Year of Diagnosis.



Unadjusted Cox Model, by Tumor Grade

Variable	Unadj. HR	Unadj. HR 95% CI	Schoenfeld *p*-value
Tumor Grade			
I	—		
II	2.75	(2.14, 3.52)	0.47
III	4.25	(3.30, 5.47)	0.18
IV	2.76	(1.65, 4.61)	0.18

Table. Results from the unadjusted Cox model for Tumor Grade.

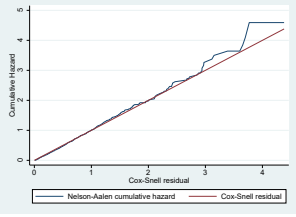


Stratified Cox Model

Cox Model, Stratified by Cancer Stage and Tumor Grade

Variable	HR	HR 95% CI	Schoenfeld p-value
Tumor Location			0.1977
Head	1.11	(0.91, 1.35)	
Body/Tail	—		
$\frac{1}{10} \times$(Age at Diagnosis, years)	1.15	(1.07, 1.24)	0.1843
Year of Diagnosis			0.7893
$\geq$ 2011	0.75	(0.64, 0.88)	
$<$ 2011	—		
			0.3465 (Global)

Table. Results from the stratified Cox Model.
Figure. Cox-Snell Residual Plot.



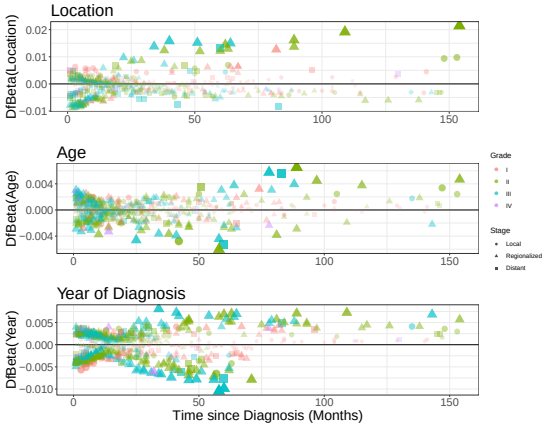


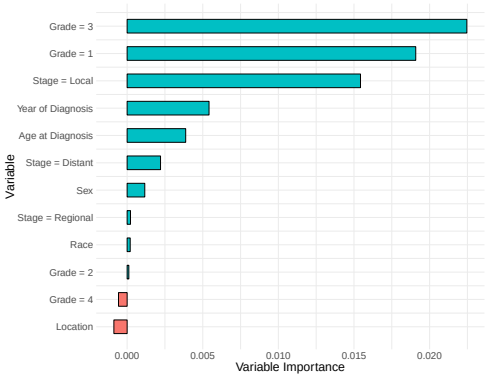
Figure. Looking for Influential Points with DFBETA residual plots.

Variable Importance

Continuing the topic of multivariate analysis . . .

Here are the results obtained from a stepwise variable selection process, in an attempt to build a Cox model using all of the recorded variables.

Step	Entered	p-value
1	Grade	< 0.0001
2	Stage	< 0.0001
3	Age at Diagnosis	0.0003
4	Year of Diagnosis	0.0011



Similarly, here are the Variable Importance results from a Random Forest Model.

Conclusions

Our results indicate that the impact of tumor location disappears when variables such as cancer grade and tumor stage are considered.

When no other variables were considered, we found that the survival outcomes for patients with cancer in the head of the pancreas were worse than the survival outcomes patients who had cancer in the body or tail of the pancreas. In this sense, our results ran opposite to the ones obtained by Artinyan et. al. However, their study was based on data collected between 1998 and 2004, while our study was based on data collected between 2004 and 2016. This suggests that survival outcomes may be influenced by year of diagnosis. This claim appears to be supported by some of our results. This aligns with the idea that the quality of clinical treatment (e.g., surgical procedures and medicine) may be improving over time.