Predictors in Determining Recurrence of Pancreatic Cancer

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http://www.pancreatic.org/site/c.htJYJ8MPIwE/b.887625/k.9A08/Pancreatic_Cancer.htm

Outline:

- Background Information
- Aim
- Experimental Designs
- Descriptive Statistics
- Events Variables
- Analytical Methods
- Conclusion
- Acknowledgments

What is Pancreatic Cancer?

- Malignant neoplasm originating from transformed cells arising in tissues forming the pancreas
- Tenth most common cancer and the fourth most common cause of cancer related deaths in the United States and the eighth worldwide
- Most diagnoses result in death

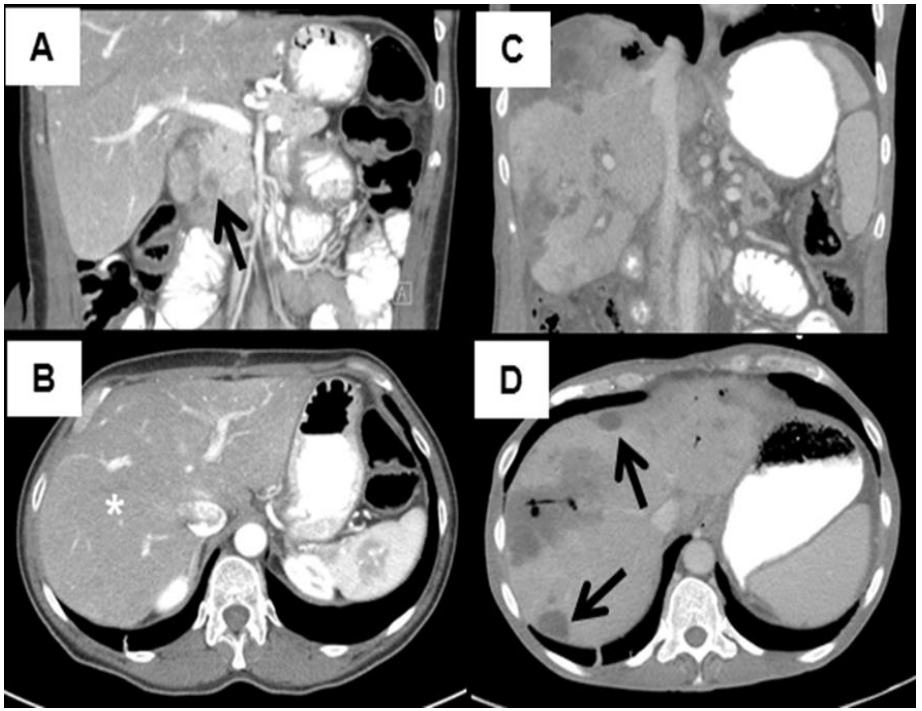
Treatments:

- Pancreatic cancer patients are generally treated with chemotherapy, radiation and surgeries
- Primary operation usually results in liver metastases

Example of early recurrence in the liver following complete resection of pancreatic cancer.

A and B

52 year old female had a tumor in the head of the pancreas. Note liver with no signs of cancer.



C. And D.

5 months post-resection, the patient presented with multiple liver metastasis including a superinfected tumor with abscess formation.

- It is currently unknown which variables are predictive of early disease and liver recurrence following pancreatectomy for pancreatic cancer.

- "Being able to predict early recurrence may change treatment strategy in patients with this disease and also provide important information to stratify patients for clinical trials." (Aeen Asghar, 2013)

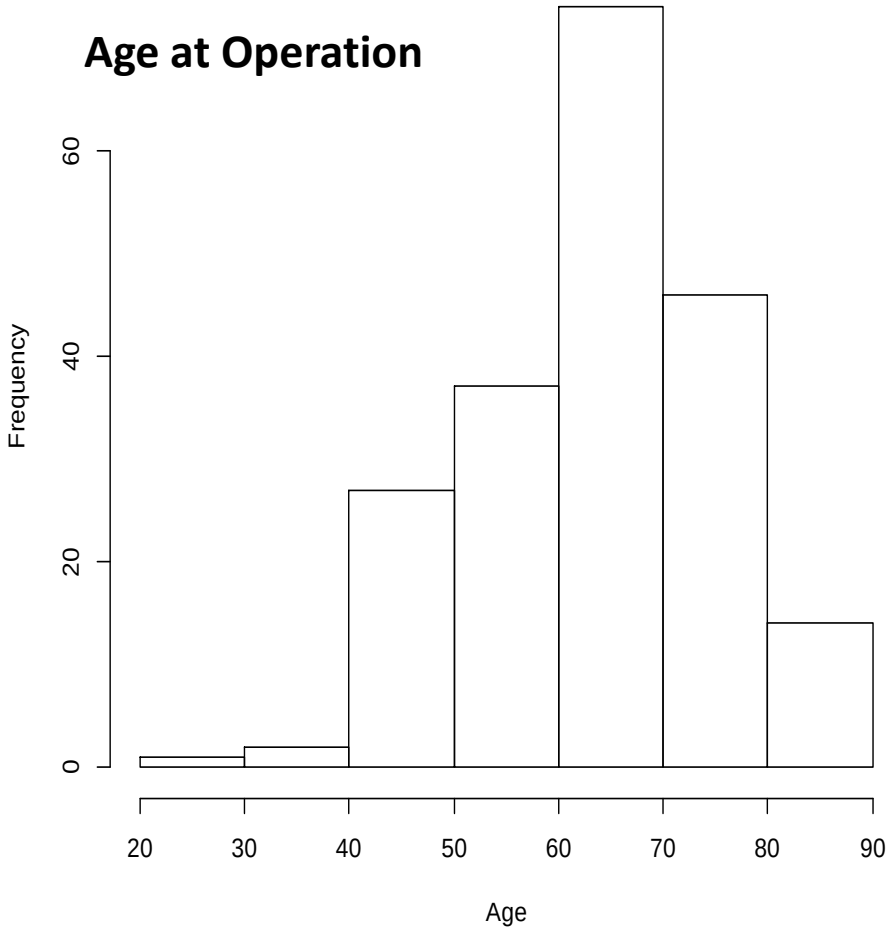
Aim:

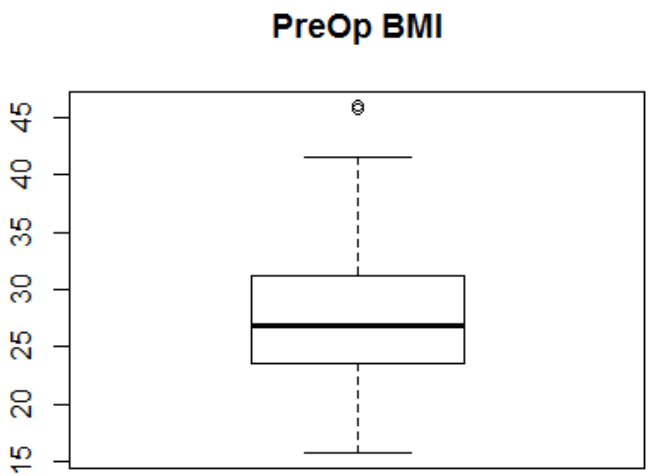
To investigate preoperative, intraoperative, and postoperative clinical and pathologic variables to determine factors that predict early recurrence following resection

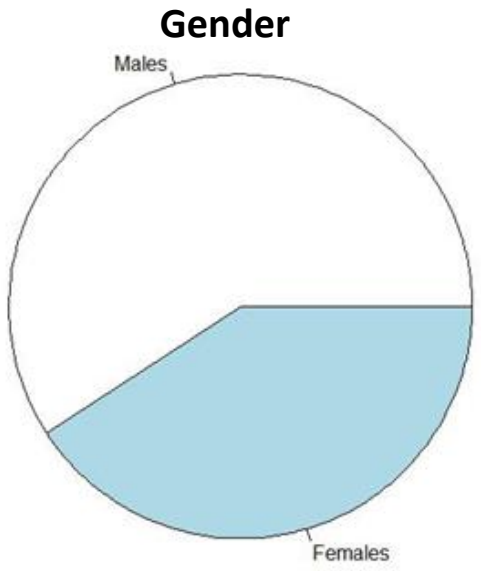
Experimental Design:

- Data set was previously collected by Aeen Asghar(BS, BA) and James J. Mezhir (MD)
- Data was collected from 1996-2013
- 201 patients
  - All underwent operation
  - Had not metastasized

Summary Statistics

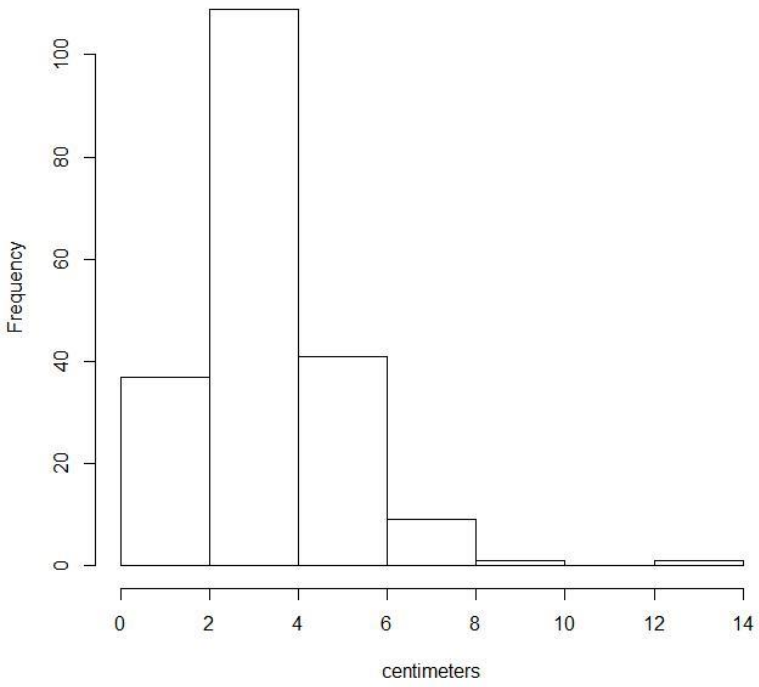




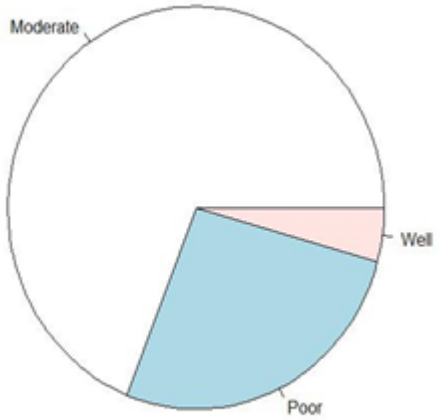


More Summary Statistics

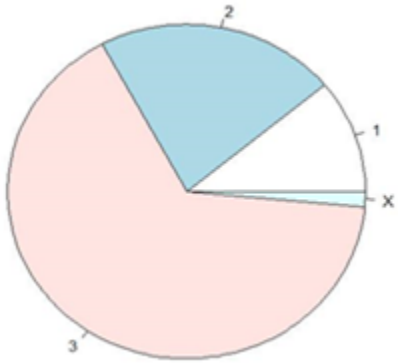
Tumor Size



Tumor Grade



Tumor Pathology (Path T)



R1: tumor < 2cm
R2: tumor outside pancreas, no major blood vessels
R3: moved into large blood vessels or nerves
Rx: unknown

Event:

Predicting:

- overall recurrence
- recurrence in the liver
- death as a result of recurrence

Event Variables:

Patients who:	Recurrence	Liver Recurrence	Death
Had Event	111	53	154
No Event	31	89	47
Unknown	59	59	0

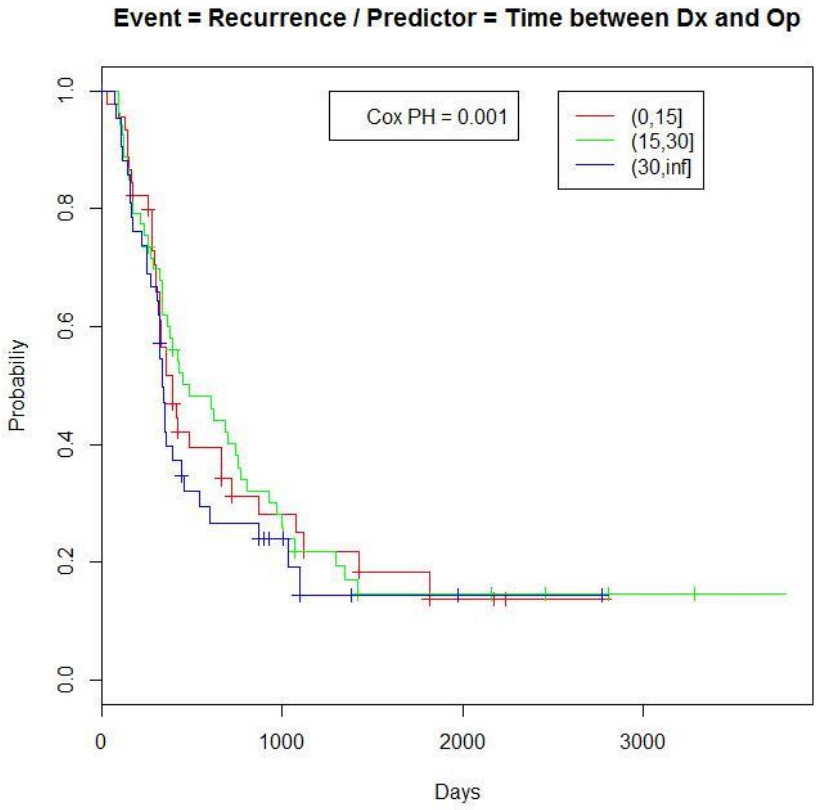
Cox Regression:

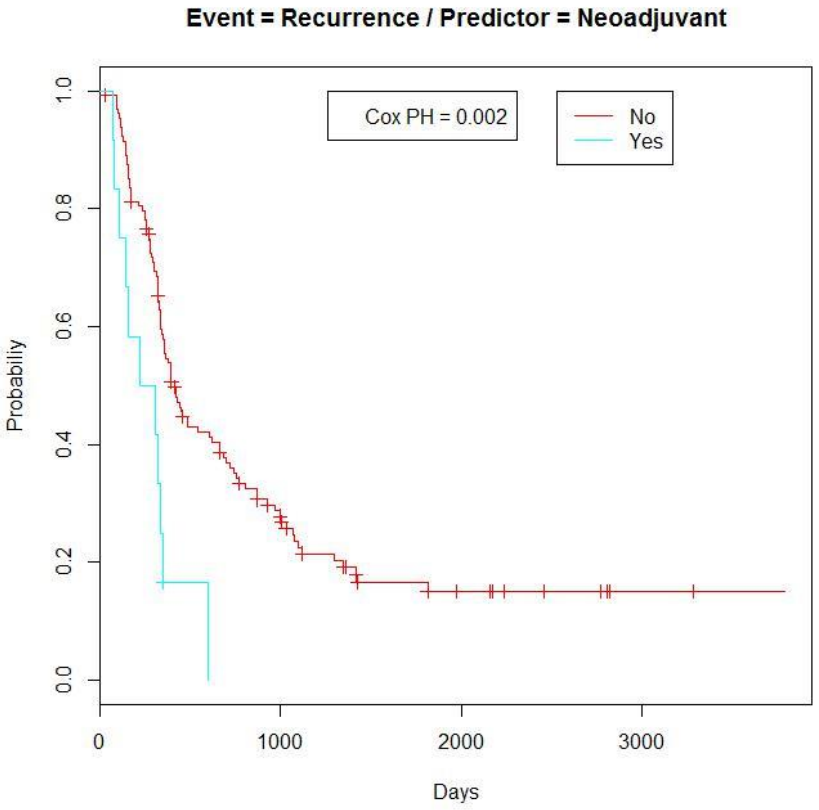
- Test significance of predictors on clinical outcomes
- Estimate their effect on risk of event

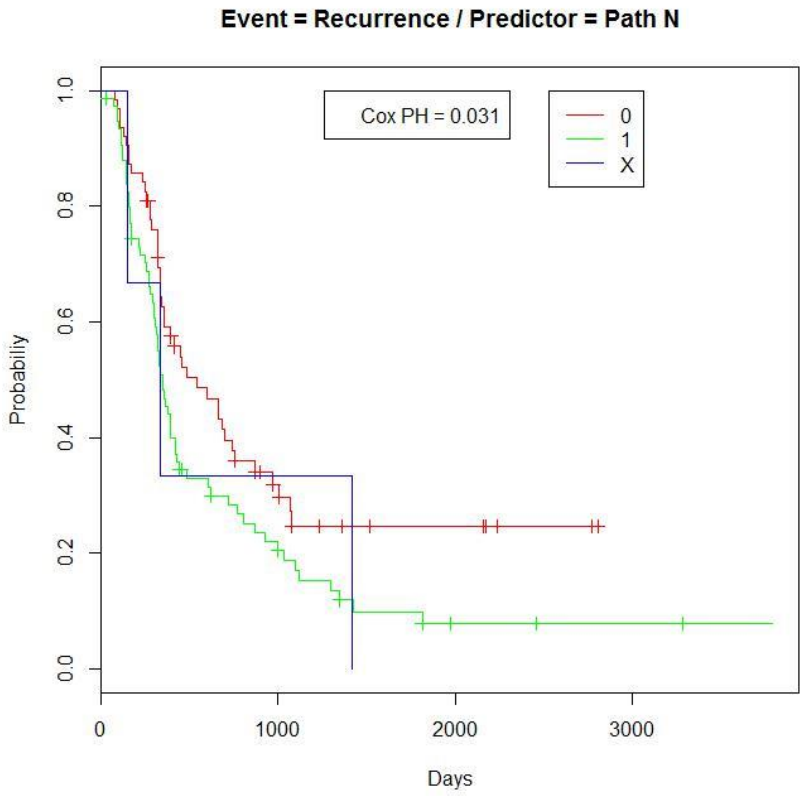
By:

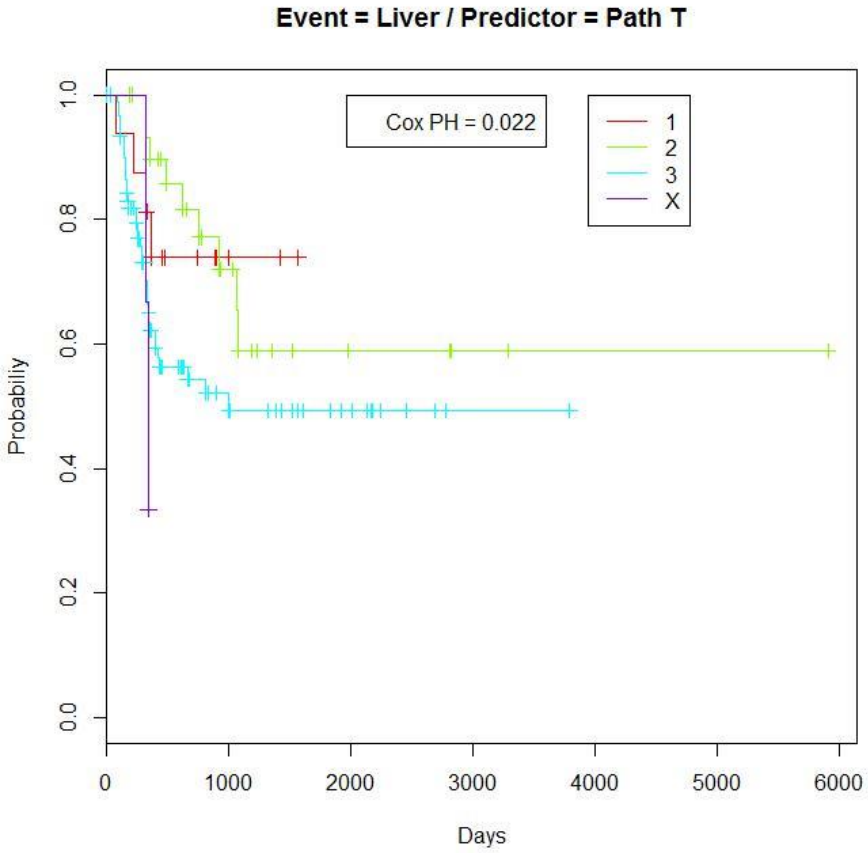
- Univariate analysis
  - Individual effect
- Multivariate analysis
  - Combined effect or adjusted effect

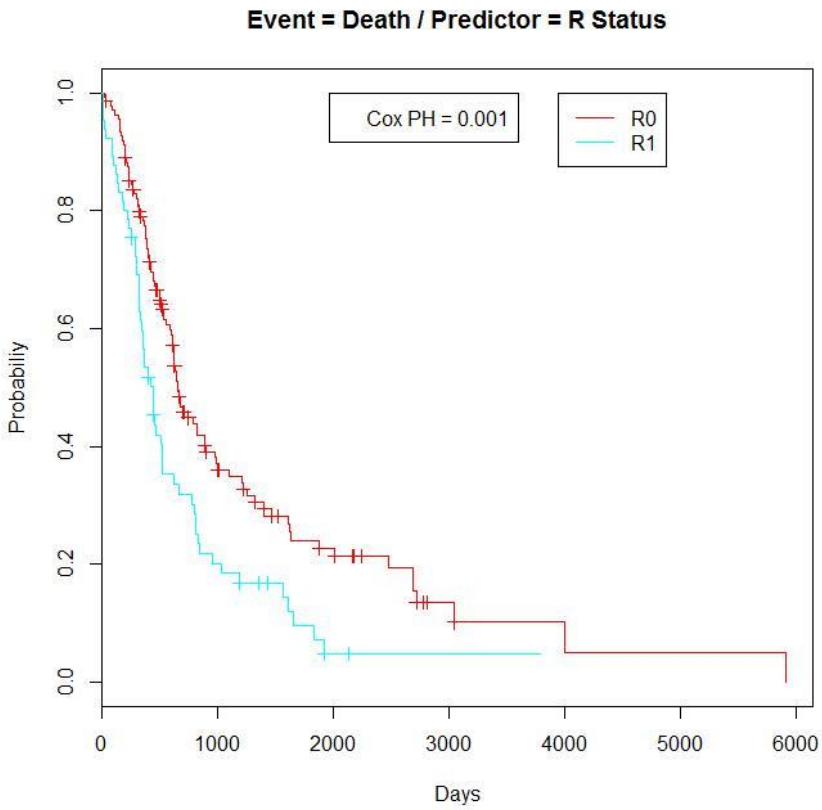
Univariate Analysis

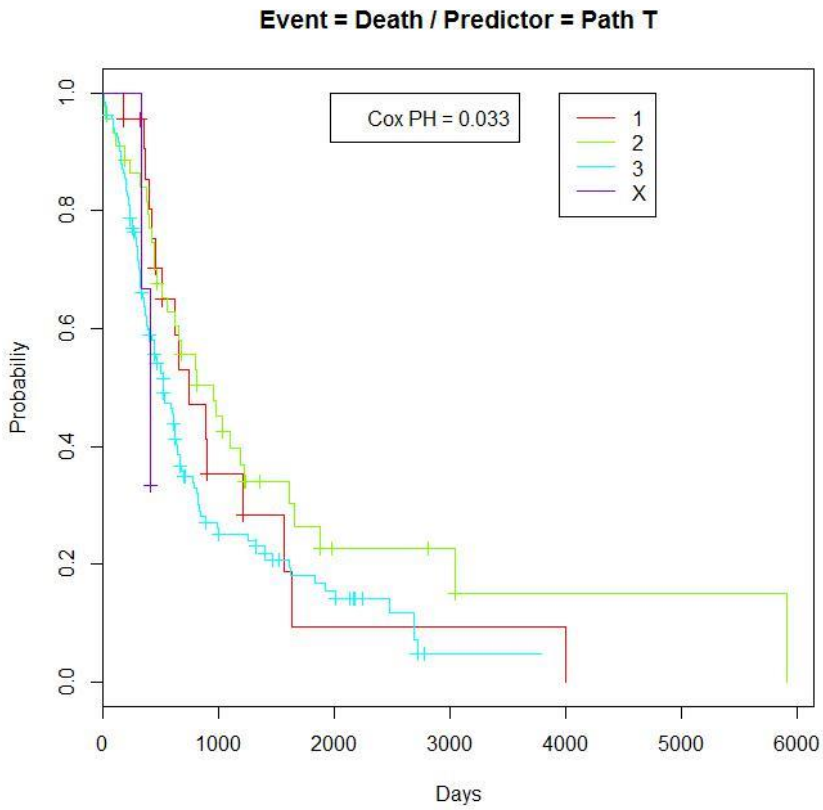

Event = Recurrence / Predictor = Time between Dx and Op
Cox PH = 0.001
(0,15]
(15,30]
(30,inf]
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1000
2000
3000
Days

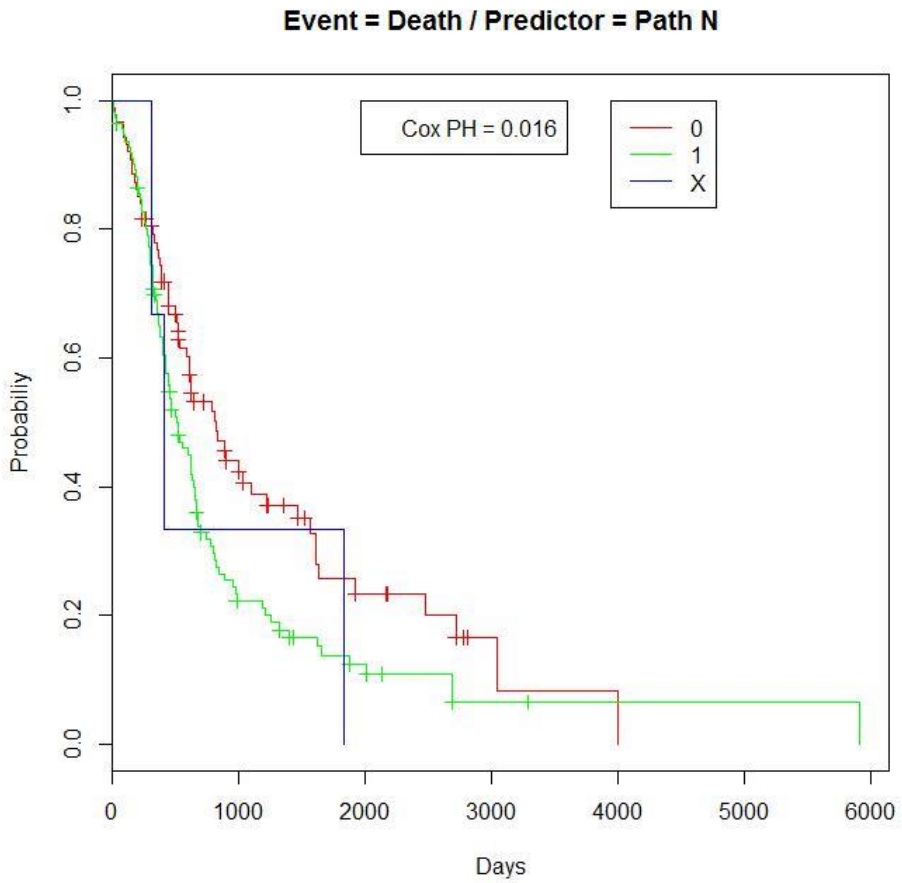

Event = Recurrence / Predictor = Neoadjuvant
Cox PH = 0.002
No
Yes
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1000
2000
3000
Days


Event = Recurrence / Predictor = Path N
Cox PH = 0.031
0
1
X
Probabiliy
0.0
0.2
0.4
0.6
0.8
1.0
0
1000
2000
3000
Days


Event = Liver / Predictor = Path T
Cox PH = 0.022
1
2
3
X
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1000
2000
3000
4000
5000
6000
Days


Event = Death / Predictor = R Status
Cox PH = 0.001
R0
R1
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1000
2000
3000
4000
5000
6000
Days


Event = Death / Predictor = Path T
Cox PH = 0.033
1
2
3
X
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1000
2000
3000
4000
5000
6000
Days


Event = Death / Predictor = Path N
Cox PH = 0.016
0
1
X
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1000
2000
3000
4000
5000
6000
Days

	Recurrence	Liver	Death
Age	0.347	0.507	0.185
Gender	0.459	0.218	0.434
PreOp BMI	0.219	0.295	0.166
Tumor Size	0.790	0.818	0.811

	Recurrence	Liver	Death
Time btwn Dx and Op	*0.001*	0.064	0.103
PreOp CA 19-9	0.061	0.400	0.071
Neoadjuvant	*0.002*	0.302	0.243
Operation Type	0.575	0.755	0.508
R Status	0.147	0.215	*0.001*
Grade	0.425	0.891	0.804
Path T	0.087	*0.022*	*0.033*
Path N	*0.031*	0.522	*0.016*
Lymph Node Ratio	0.147	0.651	0.058

Variables in blue we used for the multivariate analysis

Multivariate Analysis

Hazard Ratios

- A hazard ratio is the ratio between two hazard rates
- A hazard rate for our events are recurrence rate, liver recurrence rate, and mortality rate
- Hazard ratios show whether a specific predictor increases or decreases the risk of having an event relative to a baseline
  - Very similar to an odds ratio

Event	Predictor	Hazard Ratio	P-value
Recurrence	Path N - 0	1.00	0.048
	Path N - 1	1.40 (1.01 – 1.96)	
	Path N - X	1.96 (1.02 – 3.84)	
	Time between Diagnosis and Operation	1.06 (0.98 – 1.13)	0.134
	Neoadjuvant - No	1.00	0.710
	Neoadjuvant - Yes	1.23 (0.40 – 3.82)	

Event	Predictor	Hazard Ratio	P-value
Liver Recurrence	Path T - 1	1.00	
	Path T - 2	1.67 (1.08 – 2.59)	
	Path T - 3	2.78 (1.16- 6.70)	0.015
	Path T - X	4.65 (1.25- 17.33)	

Event	Predictor	Hazard Ratio	P-value
Overall Survival	R Status - 0	1.00	0.015
	R Status - 1	1.54 (1.09 - 2.17)	
	Path T - 1	1.00	0.118
	Path T - 2	1.22 (0.95 – 1.57)	
	Path T - 3	1.48 (0.90 – 2.46)	
	Path T - X	1.81 (0.85 – 3.86)	
	Path N - 0	1.00	0.112
	Path N - 1	1.28 (0.94 – 1.74)	
	Path N - X	1.63 (0.89 – 3.02)	

Conclusion:

- Patients characteristics are less significant in predicting recurrence than cancer progression at time of diagnose
- Doctors decide to perform surgery on lower risk patients decreasing variability among the data set

Acknowledgments:

We would like to thank Brian Smith for his guidance, knowledge and direction with our research experience.

Also, thank you Aeen and Dr. Mezhir for providing a dataset for us to analysis and master the skills we learned throughout this experience.

A special thanks to Gideon Zamba, Terry Kirk and all the TA's for their hard work and time.