Predicting Time Until Renal Failure for Newly Diagnosed C3G Patients

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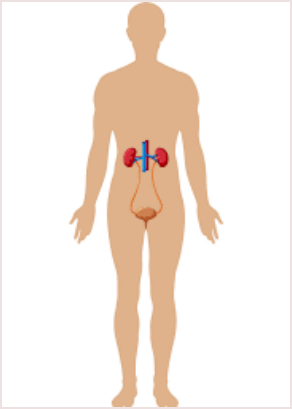


Complement-3-Glomerulopathy (C3G)

What is it?

- Group of related rare conditions that cause kidney damage

  Abnormal breakdown of C3 protein → buildup of waste products in kidneys → inflammatory response → reduced kidney function over time

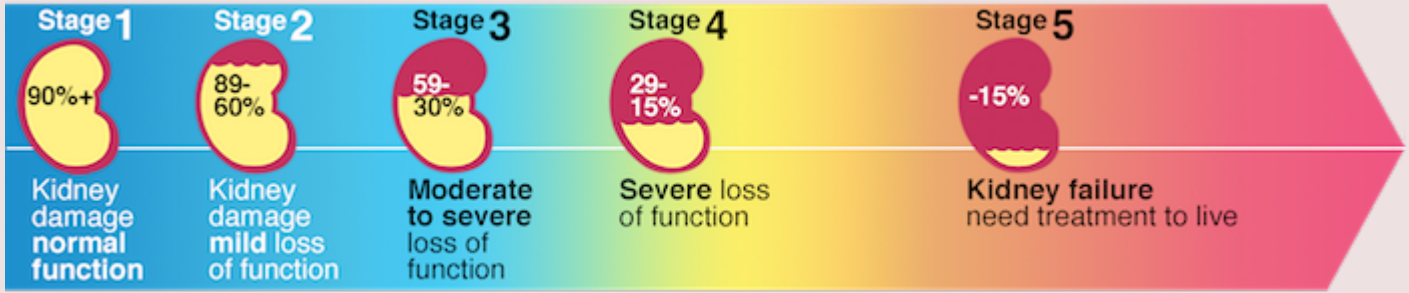
- Progresses to End-Stage Renal Disease (ESRD)
  - Dialysis or kidney transplant necessary for patient survival at this point
- Study follows cohort of C3G patients after initial diagnosis

Research question:

Can we predict when a C3G patient will reach ESRD using measures of kidney function at the time of initial diagnosis?

Measuring ESRD with GFR

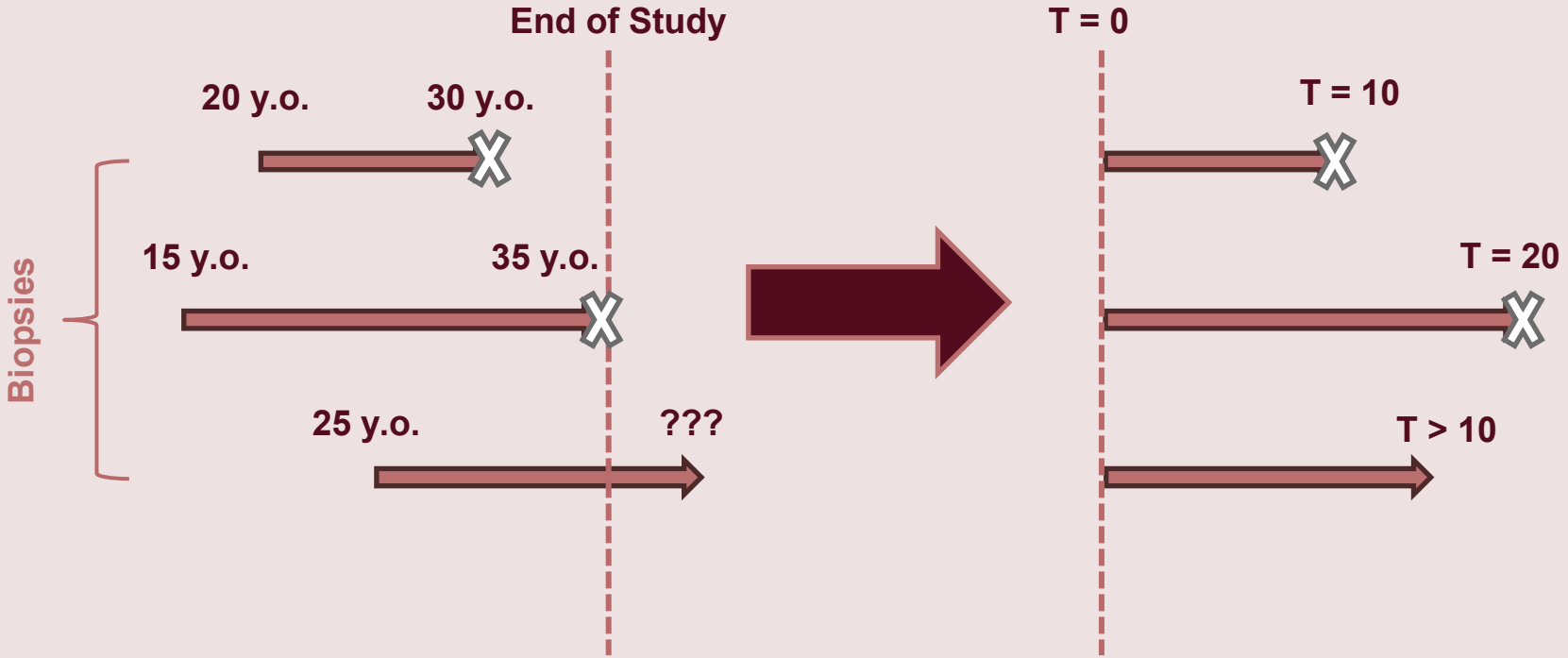
- Glomerular filtration rate (GFR)
- Rate at which blood is filtered by the kidneys per minute
- Estimated based on amounts of waste substances in the blood
- Used in our model to signify when patient has reached ESRD



Predicting Kidney Failure

Variable	Role
Creatinine	Protein waste products from normal bodily functions
Urine protein creatinine ratio (UPCR)	Ratio of proteinuria to creatinine in urine
Age of biopsy	Age when kidney biopsy was taken for C3G diagnosis
K+	Electrolyte that regulates a variety of bodily functions

Survival Data



Survival Data

Paired Data (Survival Objects):

(Time, Event)

Time in Study:

1. **Progressed to ESRD**
2. **No observed progression to ESRD/ Patient Censored**

Binary ESRD Outcome

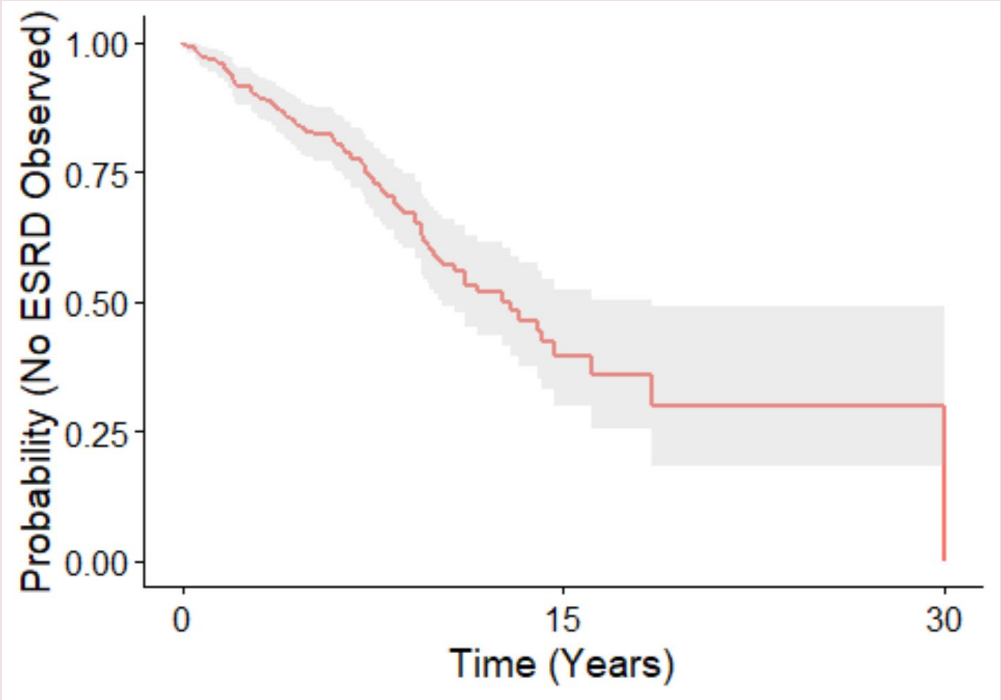
1. **ESRD (1)**
2. **No observed progression to ESRD (0)**

Methods: Kaplan-Meier Curves

- d(t): # events at time t
- n(t): # patients at risk at time t
- S(t): survival probability at time t

Equation:

$$S(t) = S(t_{-1}) \times \frac{n(t) - d(t)}{n(t)}$$



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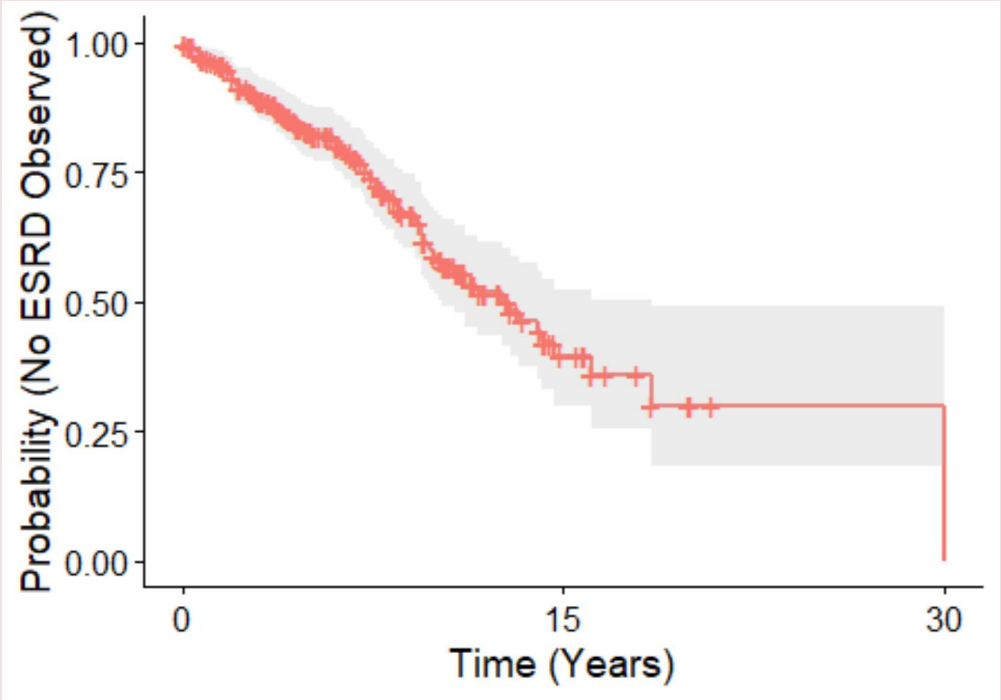
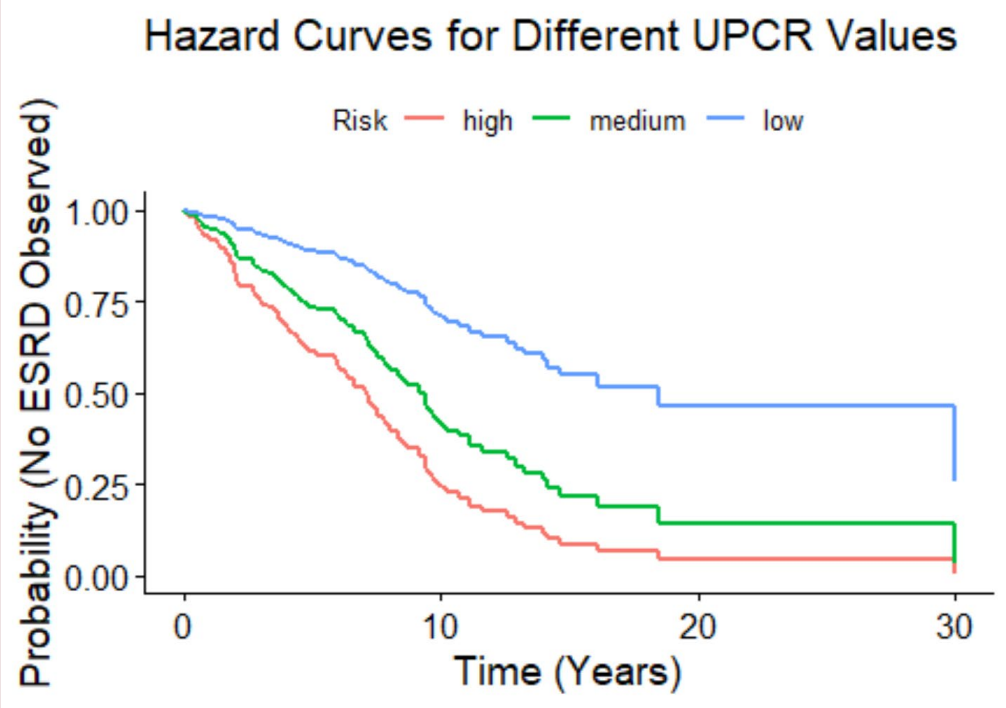


Methods: Cox Proportional Hazards

$$h_i(t) = h_0(t) \times e^{\sum \beta_j x_{ji}}$$

- i: denotes patient i
- $h_0(t)$: baseline hazard
- β_i: coefficients
- x_i: explanatory variables



Models: Cox Proportional Hazards

Significant Variables

Variable	Coefficient	Hazard Ratio
Age of Biopsy	0.016	1.016
Log(UPCR)	0.366	1.441
Potassium (K+)	0.527	1.694
GFR	-0.008	0.992
Creatinine	0.441	1.554

Equation

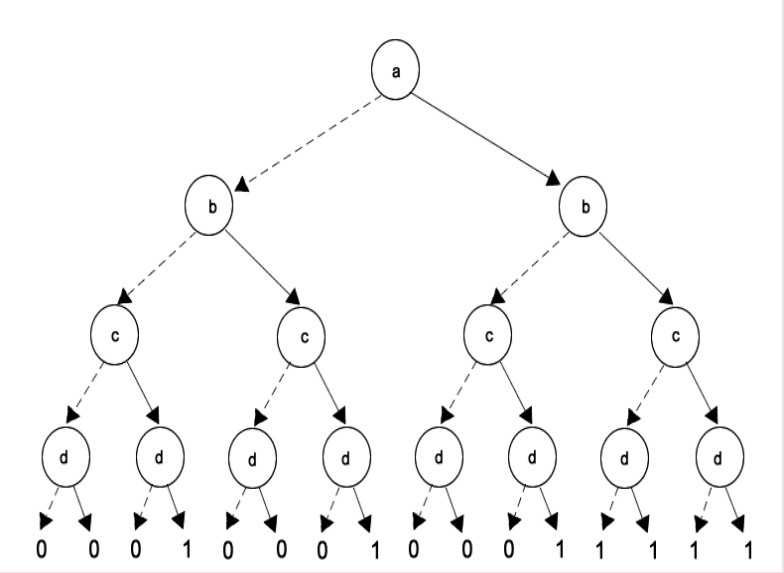
$$h_i(t) = h_0(t) \times e^{\sum \beta_j x_{ji}}$$

$$\sum \beta_i x_i = 0.016\boldsymbol{age} + 0.366\boldsymbol{log}(\boldsymbol{upcr}) + 0.527 - 0.008\boldsymbol{kgfr} + 0.441\boldsymbol{cre}$$

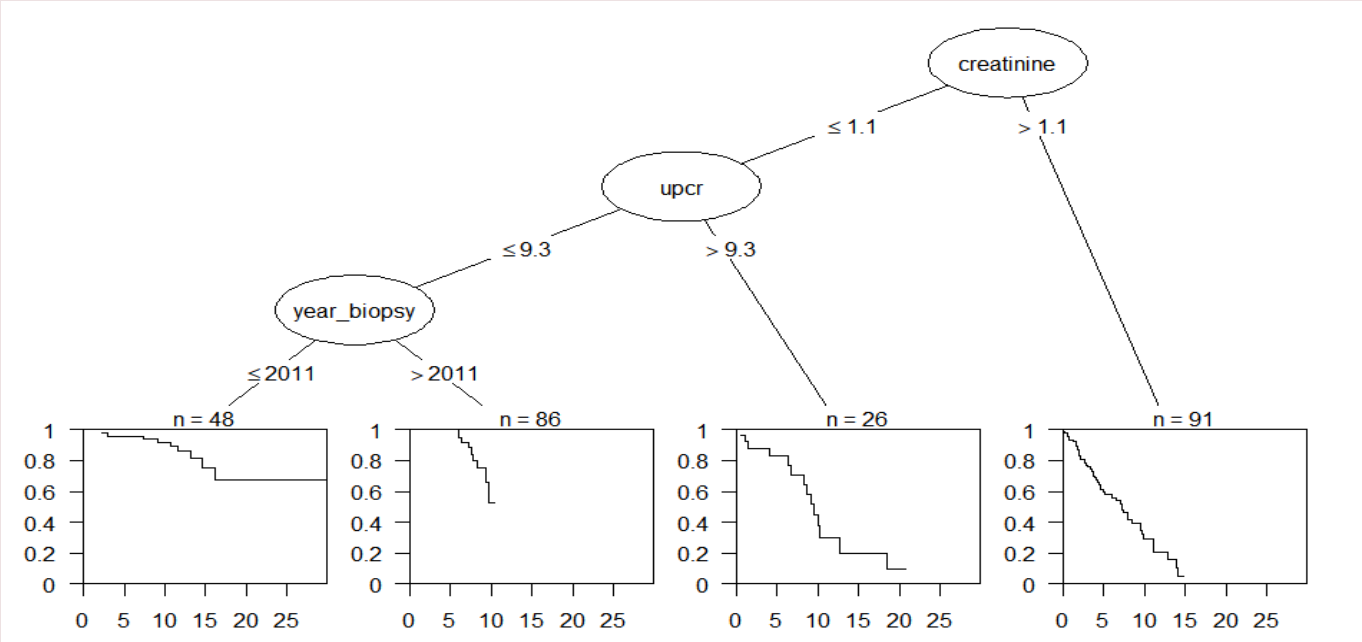
Survival Probability Calculator

Methods: Tree-Based Models

- What is a tree-based predictive model?
- How does it work?
  - Recursive partitioning
  - Impurity measures

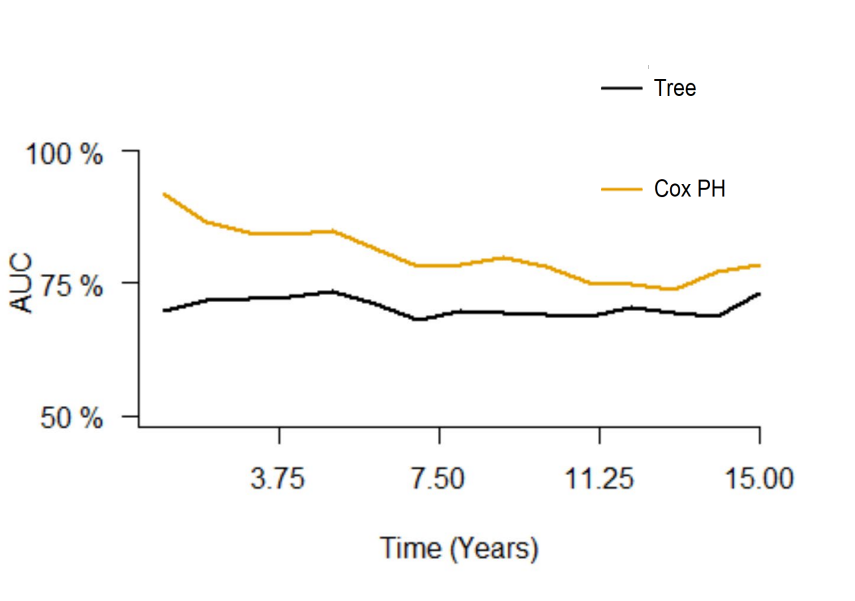


Models: Decision Tree

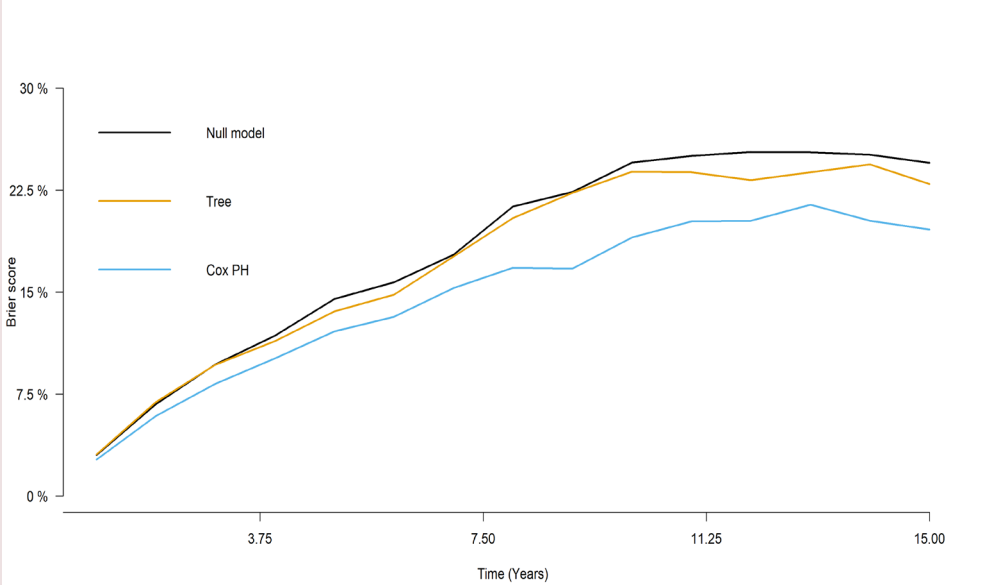


Model Validation

AUC



Brier Score



Limitations to Models

Cox Proportional Hazards

- Static Hazard Ratio Assumption
- Linearity Assumption

Trees

- Potential for Overfitting
- Instability

Future Directions

- Explore targeted subsets of patients
- Improve usability of our apps for medical utilization
- Ongoing study will more closely examine specifics of patient GFR reduction per year

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IOWA College of Public Health

NIH National Heart, Lung, and Blood Institute

Sources

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Images

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Questions?