Bayesian Time-Dynamic Modeling of Post-Transplant Kidney Function in Chronic Kidney Disease Patients

Mubarizuddin Mohammed (MS CDS), Liam Daly (STAT),
Anthony Gutierrez (CS), Ali Syed (DS)
Dr. Esra Kurum (STAT Dept)

Abstract

- **Chronic Kidney Disease (CKD)** is a progressive loss in renal function over a period of months or years through **5 stages**.
- Each stage involves a decline in **Glomerular Filtration Rate:** a formula used to estimate the amount of blood filtered by kidneys (glomeruli) per minute and a **critical indicator of kidney function**.
- Patients in the final stage of CKD face **kidney failure** and must go through either **dialysis** or **kidney transplant**.
- Our analysis centers around real-world hospital data involving CKD patients that underwent **transplant** using grafts from either deceased or living donors.
- **Using statistical techniques, our primary goal is to model the trajectory of GFR in our data to observe how the kidney function evolves and compare successful and failed transplant groups.**

Motivating Data and Descriptives

Data Description

Data was sourced from the University Hospital of the Catholic University of Leuven (Belgium) between 1983 and 2000.

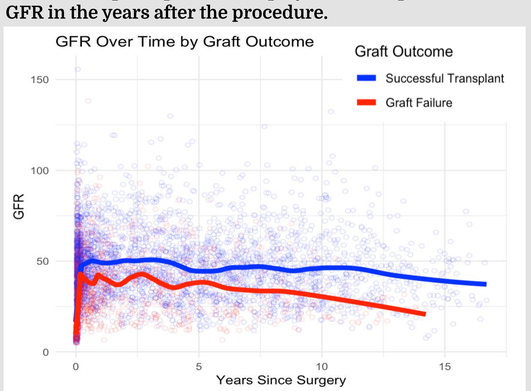
- Our dataset contains observations from 407 CKD patients over a period of 17 years.
- Transplant status: successful (281) and failed (124).

Key Predictor Variables

- **Age (years)**
- **Weight (kg)**
- **Biological sex (reference group: male)**
- **Hematocrit**: percentage of red blood cells contained in blood; higher levels are better but measurements are often lower in CKD patients.
- **Proteinuria**: indicator for a high level of protein in urine.

Relevant Findings from Exploratory Data Analysis

- Baseline distributions between successful and failed transplant groups were relatively similar, except for **GFR and proteinuria**.
  - GFR tends to be lower in failed transplant patients.
  - Significantly higher percentage of patients with failed transplants have proteinuria.
- **Failed transplant patients display a more rapid decline in GFR in the years after the procedure.**



Description of Bayesian Approaches

Frequentist:
- Provides single point estimates for model parameters based on the training data.
- Assumes all information about the model parameters comes from the data itself.

Bayesian:
- Provides distributions (posterior distributions) for model parameters, reflecting uncertainty.
- Incorporates prior beliefs about parameters, which are updated with data to form the posterior distribution.

JAGS:
- A program for analysis of Bayesian hierarchical models using **Markov Chain Monte Carlo (MCMC)** simulation.

Methodology

Time Dynamic Modeling (TDM) is a statistical method that enables researchers to explore dynamic relationships between variables over time. Time can be conceptualized in various ways, providing new insights into time varying processes and informing the development of optimal timing of interventions in Chronic Kidney Disease patients.

Through an application of TDM to our Chronic Kidney Disease data, we model the relationship between GFR and key predictor variables and observe how these relationships change after post-transplantation time. The form of the regression model is given as

$$\text{GFR}(t) = \beta_0(t) + \beta_1(t) * \text{proteinuria} + \beta_2(t) * \text{hematocrit} + \beta_3(t) * \text{weight} + \beta_4(t) * \text{age} + \beta_5(t) * \text{biological sex} + \varepsilon(t)$$

GFR(t): This represents the GFR rate at time *t*, which is a measure of kidney function. GFR is the dependent variable in our model and varies over time.

$\beta_0(t)$ represents the time-varying intercept capturing the baseline GFR level at each time *t* and it accounts for average GFR levels in absence of the other predictors; its value is expected to change over time to represent the changing kidney function.

$\beta_1(t)$ depicts the time varying-effect of proteinuria status on GFR.

$\beta_2(t)$ shows the time-varying effect of hematocrit levels on GFR.

$\beta_3(t)$ denotes the time-varying relationship between weight and GFR.

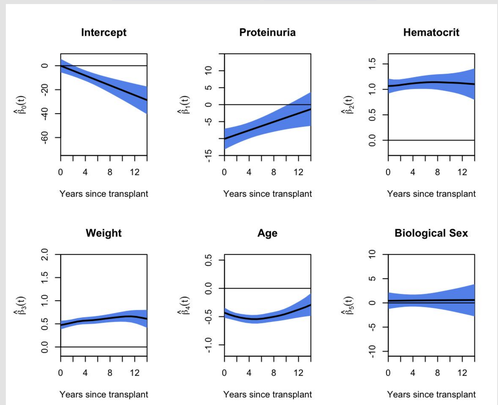
$\beta_4(t)$ measures the time-varying effect of age on GFR.

$\beta_5(t)$ represents the time-varying effect of biological sex on GFR.

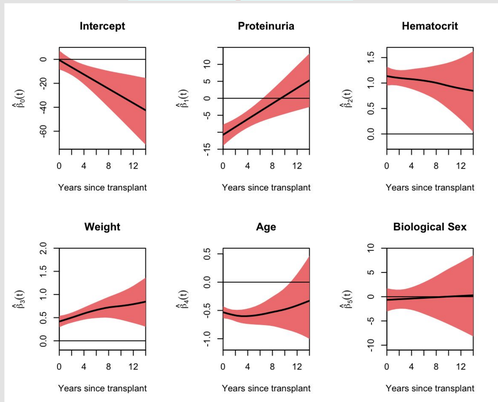
$\varepsilon(t)$ illustrates the error term at time *t*, accounting for unexplained variability in GFR. It includes all factors affecting GFR that is not captured by the predictors that are included.

Results

Successful Transplant Patients



Failed Transplant Patients



Interpretation:

1. **Intercept** declines over time for both groups, with a steeper slope for failed transplant patients. This shows an expected decrease in GFR over time for both groups.
2. **Proteinuria** initially displays the most significant time-dynamic association with GFR for both groups. However, this coefficient becomes insignificant at year 10 for successful transplant patients and at year 6 for failed transplant patients.
3. **Hematocrit** levels remain significant and positive for both groups. This suggests the impact of hematocrit on GFR is constant over time, and maintaining optimal levels is crucial.
4. **Weight** remains consistently above zero for both groups, indicating stable positive significance on GFR over time.
5. **Age** is significantly negatively associated with GFR until year 13 for successful transplant patients and year 11 for failed transplant patients.
6. **Biological sex** includes zero in the wide credible band for both groups; indicating this covariate does not have a significant effect on GFR.

Conclusion

This study aimed to investigate the temporal effects of various risk factors on the trajectory of kidney function, measured via GFR, in patients with both successful and failed transplant outcomes. The covariates analyzed included proteinuria, hematocrit, weight, age, and biological sex.

The results highlight the critical importance of monitoring proteinuria, hematocrit and weight in the management of renal patients post-transplantation.

Specifically, the findings suggest that interventions related to proteinuria should be implemented before the 10th year following a successful transplant or the 6th year after a failed transplant, as proteinuria ceases to significantly impact GFR beyond these respective periods.

Additionally, the study indicated that maintaining healthy weight and hematocrit levels positively influences GFR over the years post-transplantation.

By addressing these key factors, healthcare providers can potentially improve transplant outcomes and enhance patient survival rates. Future research should further explore the mechanisms underlying these associations to develop targeted interventions for improving transplant success.

Future Work

- *Survival analysis:* Initiate a detailed analysis of time-to-transplant failure to identify key factors contributing to higher failure post-transplant. Understanding these factors can guide the development of strategies aimed at enhancing patient survival rates.
- *Patient-Centered Outcomes:* Incorporate patient-centered outcomes, such as quality of life and functional status, into the analysis. This approach will provide a more comprehensive view of transplant success and patient well-being, ensuring that future interventions address both clinical and personal aspects of patient care.
- *Intervention Effectiveness:* Examine the effectiveness of specific interventions, including dietary modifications and new pharmacological treatments, in improving GFR and reducing the incidence of transplant failure. This investigation will help identify practical measures that can be implemented to enhance long-term transplant outcomes.

Acknowledgements

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