

# Ethnoracial Disparities in Access to Transjugular Intrahepatic Portosystemic Shunt (TIPS) Creation and Hospital Survival for Acute Variceal Bleeding in the United States

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# Outline

Background

Introduction

Specific Aim 1

Specific Aim 2

Specific Aim 3

Discussion

# About Me

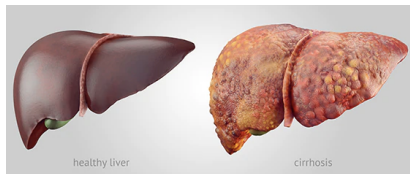
- BS in Mathematics and BA in Economics from Colorado State University (2011)
- MS in Biostatistics from CU Anschutz (2018)
- PhD candidate in the Department of Biostatistics & Informatics at CU Anschutz
- Graduate research assistant in CIDA, working in the Colorado Aging Brain Lab as well as the Translational Outcomes in Radiology Research (TORR) Lab.



# Liver Cirrhosis

A late-stage liver disease in which healthy liver tissue is replaced with scar tissue, causing permanent dysfunction.

- Estimated that 1 in 400 U.S. adults have cirrhosis of the liver.
- Causes about 26,000 deaths/year in the U.S.

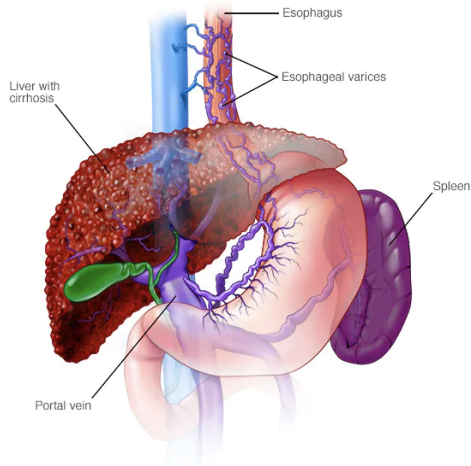


# Complications of Liver Cirrhosis

Cirrhosis increases resistance to blood flow, leading to higher blood pressure in the portal venous system, resulting in portal hypertension. This can lead to a variety of complications, including:

- Swelling in the legs and abdomen (ascites)
- Enlargement of the spleen (splenomegaly)
- Buildup of toxins in brain (hepatic encephalopathy)
- Enlarged veins (varices) in the esophagus or stomach

# Bleeding Varices

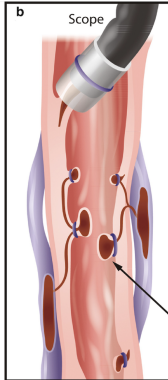


# Endoscopy

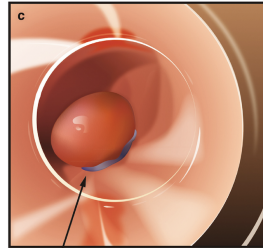
**a** Rubber Band Ligation System®



**b** Scope

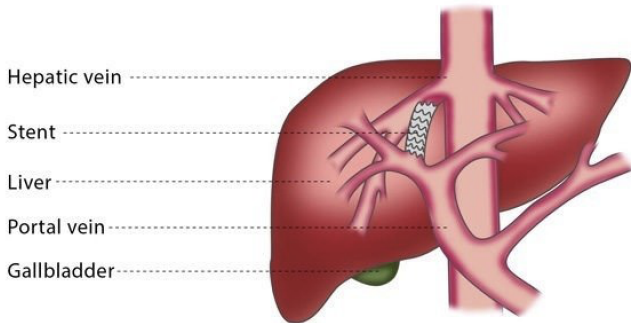


**c**



Banded varices

# Transjugular Intrahepatic Portosystemic Shunt (TIPS) Creation





# Treatment Recommendations



Endoscopy as the first-line treatment, within 12 hours of admission  
TIPS creation only in patients with: (a) endoscopic failure or (b)  
high risk for rebleeding

# Preliminary Data

## **National Trends and Outcomes of Transjugular Intrahepatic Portosystemic Shunt Creation Using the Nationwide Inpatient Sample**

Premal S. Trivedi, MD, MSE, Paul J. Rochon, MD,  
Janette D. Durham, MD, MBA, and Robert K. Ryu, MD



An incidental finding of the analysis showed that inpatient mortality for Black patients was nearly twice that of White patients (31% compared to 14%).

## GERRAF Award Specific Aims

- (1) Determine if black patients treated with TIPS for variceal bleeding have a higher odds of mortality due to higher baseline disease severity.
- (2) Determine if there are differences in treatment utilization for variceal bleeding by patient race.
- (3) Determine if time-to-treatment with TIPS following admission with variceal bleeding is associated with hospital survival and if patient race is a confounding factor.



## Unique Elements to the NIS

- Severity measures, as a way to adjust for severity of illness
  - All Patient Refined Diagnosis Related Groups (APR-DRGs), developed by 3M Information Systems
  - Elixhauser Comorbidity Software, available through HCUP Tools & Software
  - Charlson Comorbidity Index can be derived
- Hospital characteristics from the AHA Annual Survey database

**Note:** The NIS is designed to be a national representation of inpatient hospital care. Because state is not a stratification variable, state-level analyses cannot be conducted.

# Data Management

Because of the time period the study window encompasses, we encountered several data management hurdles:

- The size of the raw NIS files
- Survey weights were redesigned in 2012
- ICD-10 was introduced in Q4 of 2015

# Overview

- Data source: Nationwide Inpatient Sample (NIS)
- Study period: 2007-2016
- Inclusion criteria:
  - Encounters for patients  $\geq 18$  years of age
  - Primary diagnosis for admission of acute variceal bleeding
  - TIPS creation occurring during the inpatient encounter
- Outcome: inpatient mortality

# Study Cohort and Patient Characteristics

A total of 10,331 survey-weighted inpatient encounters were included in the analytic dataset. The following patient-level variables were pulled for inclusion in the regression analysis:

Demographics	Age, Sex, Race/Ethnicity, Primary payer, Median income bracket within zip code
Comorbid burden	APR-DRG mortality risk
Clinical risk factors	Ascites, Hepatic encephalopathy, Hepatic vein thrombus



# Hospital Processes of Care



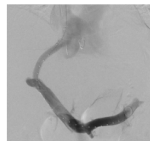
**Admission**



**Resuscitation**



**Endoscopy**



**TIPS**

The number of transfusions and endoscopies prior to TIPS creation were pulled for each encounter. The extremes of variable (none or 2+) were thought a priori to be indicators of clinical stability and associated with higher odds of mortality.

## Specific Aim 1 Regression and Results

A hierarchical logistic regression was fit for the outcome of inpatient mortality, with a random intercept included for hospital ID. SAS PROC GLIMMIX was used, with adaptive quadrature to fit the true log-likelihood function with 10 quadrature points. The following variables were found to be significantly associated with inpatient mortality, all else equal:

Covariate	Odds Ratio Estimate	95% CI	P-Value
Black race	3.01	(1.55, 3.84)	0.001
APR-DRG mortality risk: extreme	56.58	(7.73, 414.06)	< 0.001
Number of transfusions	0.50	(0.38, 0.91)	0.017
(Number of transfusions) <sup>2</sup>	1.29	(1.12, 1.48)	< 0.001

# Sensitivity Analysis

Because the NIS does not contain laboratory information, neither the MELD or Child-Pugh score could be directly calculated. However, we know that patients without ascites have a maximum possible Child-Pugh score of 13.

Covariate	Odds Ratio Estimate	95% CI	P-Value
Black race	1.25	(0.43, 3.63)	0.682
APR-DRG mortality risk: extreme	54.14	(6.95, 421.96)	< 0.001
Number of transfusions	0.49	(0.25, 0.94)	0.031
(Number of transfusions) <sup>2</sup>	1.36	(1.10, 1.69)	0.005

# Overview

- Data source: Nationwide Inpatient Sample (NIS)
- Study period: 2007-2016
- Inclusion criteria:
  - Encounters for patients  $\geq 18$  years of age, not transferred from another facility
  - Primary diagnosis for admission of acute variceal bleeding
- Outcomes: endoscopy (occurring before TIPS creation); TIPS creation

# Study Cohort and Patient Characteristics

A total of 223,204 survey-weighted inpatient encounters were included in the analytic dataset. The following patient-level variables were pulled for inclusion in the regression analysis:

Demographics	Age, Sex, Race/Ethnicity, Primary payer, Median income bracket within zip code
Comorbid burden	APR-DRG illness severity
Encounter factors	Length of stay, Weekend admission

## Specific Aim 2 Results: Endoscopy

A hierarchical logistic regression was fit for the outcome of receiving at least one endoscopy during the encounter, with a random intercept included for hospital ID. The following variables were found to be significantly associated with the outcome, all else equal:

Covariate	Odds Ratio Estimate	95% CI	P-Value
Female sex	0.930	(0.873, 0.991)	0.025
Black race	0.845	(0.755, 0.946)	0.003
Medicaid primary payer	0.872	(0.799, 0.952)	0.002
Medicare primary payer	0.815	(0.749, 0.887)	< 0.001
APR-DRG illness severity: extreme	0.810	(0.711, 0.923)	0.002

## Specific Aim 2 Results: TIPS

A hierarchical logistic regression was fit for the outcome of TIPS creation occurring during the encounter, with a random intercept included for hospital ID. The following variables were found to be significantly associated with the outcome, all else equal:

Covariate	Odds Ratio Estimate	95% CI	P-Value
Black race	0.541	(0.413, 0.708)	< 0.001
APR-DRG illness severity: extreme	3.327	(2.456, 4.506)	< 0.001

# Sensitivity Analysis

To echo the sensitivity analysis conducted in specific aim 1, patients with ascites were excluded from the dataset and the regression models were fit once again.

Black race was no longer significantly associated with receiving endoscopy (OR 0.881; 95% CI [0.763, 1.016];  $p=0.073$ ) but did remain significantly associated with receiving TIPS (OR 0.617; 95% CI [0.434, 0.877];  $p=0.007$ ).



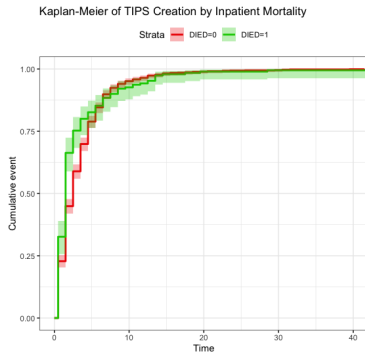
# Overview

- Data source: Nationwide Inpatient Sample (NIS)
- Study period: 2007-2016
- Inclusion criteria:
  - Encounters for patients  $\geq 18$  years of age, not transferred from another facility
  - Primary diagnosis for admission of acute variceal bleeding
  - TIPS creation occurring during the inpatient encounter
- Outcome: time of transfusion(s), time of endoscopy(ies), time of TIPS creation, inpatient mortality

# Time-to-TIPS Analysis: Death

The median survival time for patients who died was 1.5 days from admission, while it was 2.5 days for patients who did not die. The restricted mean survival times for the two groups was 3.17 and 3.28 days, respectively.

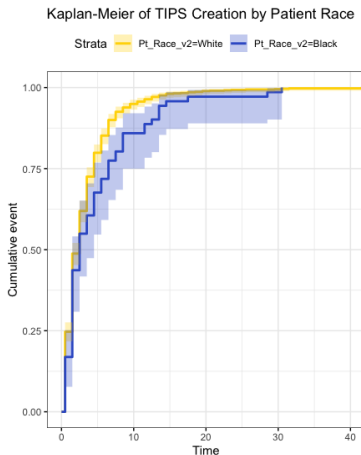
Log-rank test:  $p=0.042$ .



# Time-to-TIPS Analysis: Race

The median survival time for White and Black patients was equal at 2.5 days from admission, though Black patients had a longer restricted mean survival time than White patients (4.9 days vs. 3.4 days, respectively).

Log-rank test:  $p=0.0091$ .



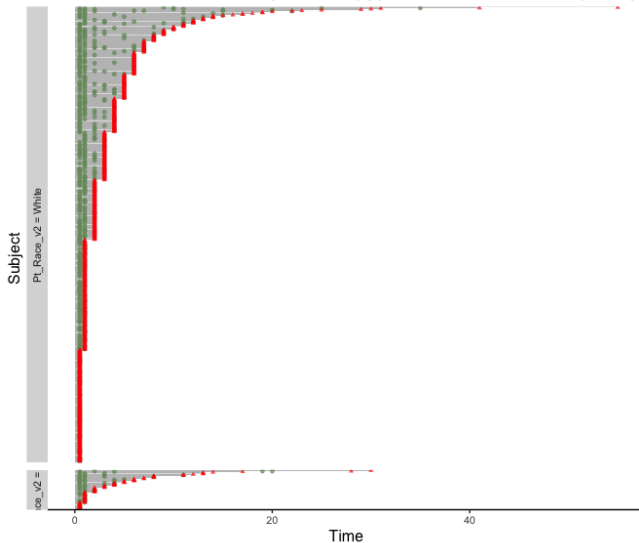
# Cox Proportional Hazards Model

A Cox proportional hazards model was fit to the data with a frailty term for hospital ID and stratified by inpatient mortality. The following variables were found to be significantly associated with the outcome, all else equal:

Covariate	Hazard Ratio Estimate	95% CI	P-Value
Black race	0.676	(0.503, 0.910)	0.010
APR-DRG risk mortality: major	0.754	(0.590, 0.964)	0.024
Number of endoscopies	0.584	(0.530, 0.644)	< 0.001

# Modeling the Hospital Care Process

Plot of Recurrent Event (Endoscopy) and Terminal Event (TIPS)



# Joint Modeling of Recurrent and Terminal Events

We attempted to fit a joint recurrent-terminal event model using the reda package but we were unable to get the model to converge, potentially due to the added complexity of the frailty term or the heavy-tailed distribution of the recurrent and terminal events.

We are currently looking for alternative ways to model the hospital care process and test whether there is a difference in the process between White and Black patients.

## Summary of Results

- Black patients had a higher odds of mortality following TIPS creation, all else equal.
  - No longer significantly associated with mortality following TIPS when looking only at patients without ascites.
- Black patients had lower odds of (1) receiving endoscopy and (2) TIPS while admitted for variceal bleeding, all else equal.
  - Looking only at patients without ascites, Black race was no longer associated with receiving endoscopy but remained significantly associated with receiving TIPS.
- Black race was also significantly associated with time-to-TIPS, having an approximately 30% lower “risk” of receiving TIPS, all else equal.

# Limitations

- No laboratory information; timing granularity of transfusions, endoscopies, and TIPS creation.
- The race variable in the NIS is actually an amalgamation of race and ethnicity.
- We were unable to fully model the hospital care process and had to examine each of the treatments (endoscopy, TIPS) separately.



## Conclusions and Future Work

Black patients with variceal bleeding experience inequitable management of their disease course, from access to endoscopy to TIPS creation, and have higher odds of death following TIPS than White patients.

Future work:

- Advancing Liver Therapeutic Approaches (ALTA) registry
- Building a statistical model for the hospital care process

# Thank You

- GERRAF
- Dr. Premal Trivedi and the TORR Lab
- Dr. Rich Lindrooth, Maggie Reid
- Dr. Elizabeth Juarez-Colunga, Bryan McNair, Dr. Peter DeWitt

**And especially everyone who came to listen to my seminar today!**