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Evaluating the Affect of Blood Products on the Incidence of Infection and Rejection in Pediatric Liver Transplant Patients

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Introduction

- Pediatric solid organ transplant (SOT) is an area of increasing medical interest and advancement.
- Scientific improvements in treatments and surgical techniques have led to better patient and graft survival.
- However, challenges remain in the management of complications, specifically infection and rejection, that arise with transplantation.
- Researchers have sought to elucidate the various factors contributing to post-transplant infection and rejection.

Introduction (con’t)

- Studies have identified specific predisposing factors, such as intraoperative (IO) blood loss and blood transfusions, that increase the risk of acute cellular rejection (ACR) and chronic cellular rejection (CCR).
- Similarly, the risk of developing a post-transplant infection is influenced by multiple circumstances, including blood transfusions and prolonged ICU stay.
- A majority of data comes from adult transplant patients, though a growing number of studies are focused on the pediatric population.

Introduction (con’t)

- The mechanisms by which IO blood product administration effects rejection and infection is not fully understood.
- Different suggestions have been made, including immunosuppressive effects of blood transfusions and blood product components.
- This study serves as the first step in pursuing future prospective research into how blood product components effect outcomes in pediatric liver transplant patients.

Aim

- Our objective was to investigate if blood products were risk factors for the development of ACR and infection in pediatric liver transplant patients.

Definitions

- Bacterial infection was determined by the presence of fever ≥ 38.3°C and a positive blood, urine, peritoneal, respiratory, wound, stool culture or gastrointestinal (GI) PCR panel.
- Blood products: Cryoprecipitate (Cryo), packed red blood cells (PRBCs), fresh frozen plasma (FFP), platelets (PLT)
- Viral infections were diagnosed by quantitative polymerase chain reaction (qPCR), respiratory viral panel (RVP) or viral culture.
- ACR was graded using the Banff criteria.

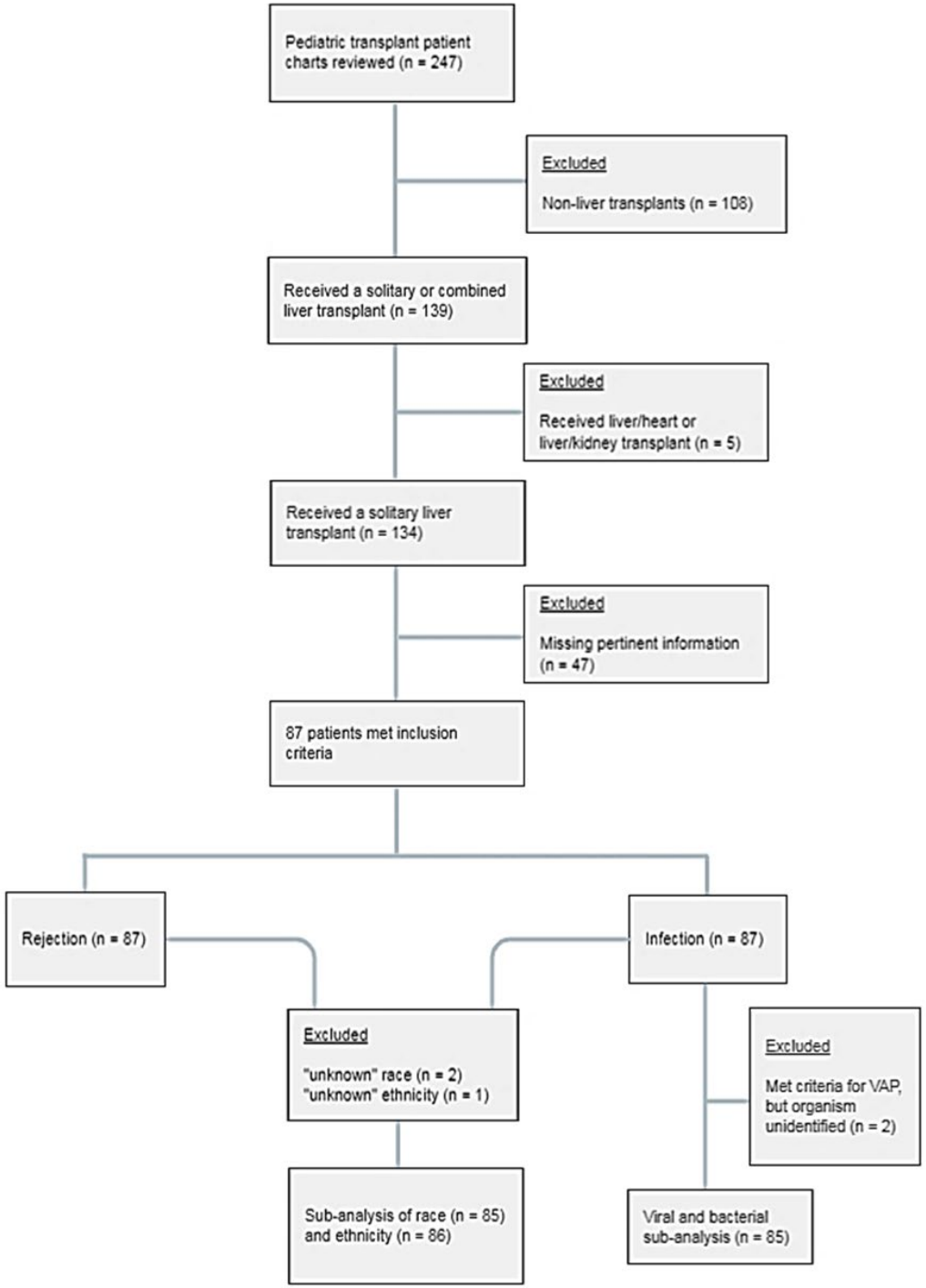
Methods

- Retrospective cohort study of pediatric liver transplant recipients at Holtz Children's Hospital between January 2008 and November 2019, following approval by the University of Miami Institutional Review Board and Jackson Clinical Trials Office (IRB number 20191201).
- Medical records of 247 pediatric liver transplant recipients were reviewed.
- Patients were included if they were ≤21 years of age at the time of transplant and had sufficient clinical data available in the electronic medical record.
- Exclusion criteria included multiorgan transplantation, repeat liver transplantation, or inconclusive biopsy findings for rejection.

Statistical analysis

- For infection analyses, patients were grouped by quartiles of total intraoperative blood product exposure per 10 mL/kg to allow visualization of dose-response relationships.
- Multivariable Cox proportional hazards regression models were constructed to evaluate the association between intraoperative blood product exposure and time to infection and rejection.
- The primary exposure variable was log-transformed total intraoperative blood product volume per 10 mL/kg to account for skewness.
- Covariates included age at transplant (months), MELD/PELD score (numeric when available), underlying disease category (cholestatic, metabolic/genetic, autoimmune/PSC, acute liver failure/unknown, malignancy, other), and Status 1 listing.
- Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported.

Results



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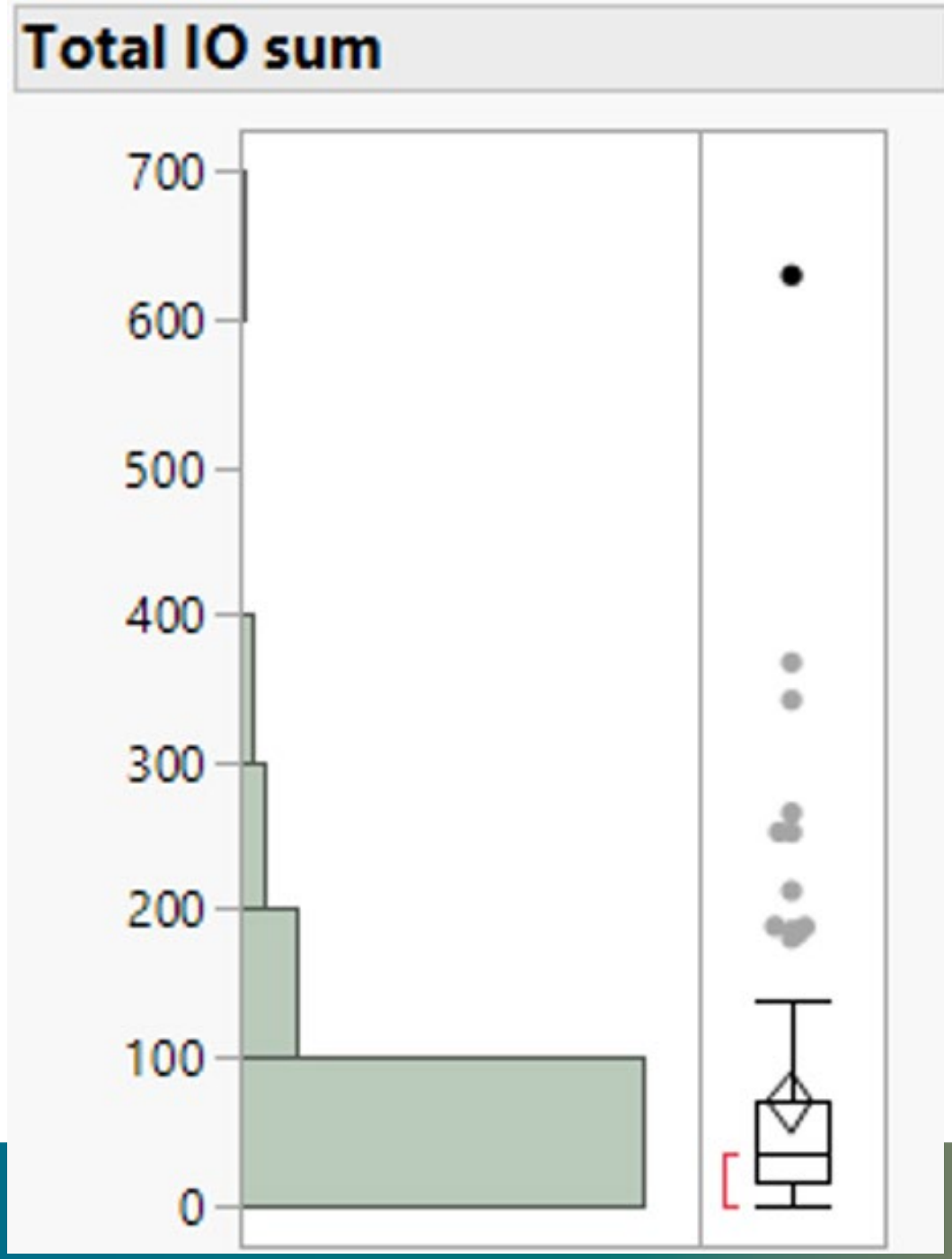
Recipient Characteristics	Overall (n = 87)
Mean age (range)	71 months (5 – 240)
Gender: Male (M), Female (F)	M – 41, F - 46
Race	
Black	33
White	52
Unknown†	2
Ethnicity	
Hispanic	30
Non-Hispanic	56
Unknown‡	1
Underlying condition	
Genetic disorders	24
Autoimmune liver disease	7
Biliary atresia	32
Primary sclerosing cholangitis	5
Cystic fibrosis/congenital hepatic fibrosis	2
Liver failure of unknown etiology	7
Tumor/malignancy	10

Organism	Number of patients with infection
Viruses	n = 32
Adenovirus	6
EBV	5
CMV	5
EBV and CMV coinfection	1
HHV-6	5
HHV-6 and Parainfluenza coinfection	1
Coronavirus (non-COVID)	2
Human metapneumovirus	1
Respiratory Syncytial Virus	1
Parainfluenza viruses	1
Rotavirus	1
Parvovirus	1
Rhino/Enterovirus	2
Bacteria	n = 15
Staphylococcus hominis	1
Methicillin-resistant *Staphylococcus aureus*	1
E. coli	4
K. pneumoniae	6
E. cloacae	1
P. aeruginosa	1
C. difficile	1



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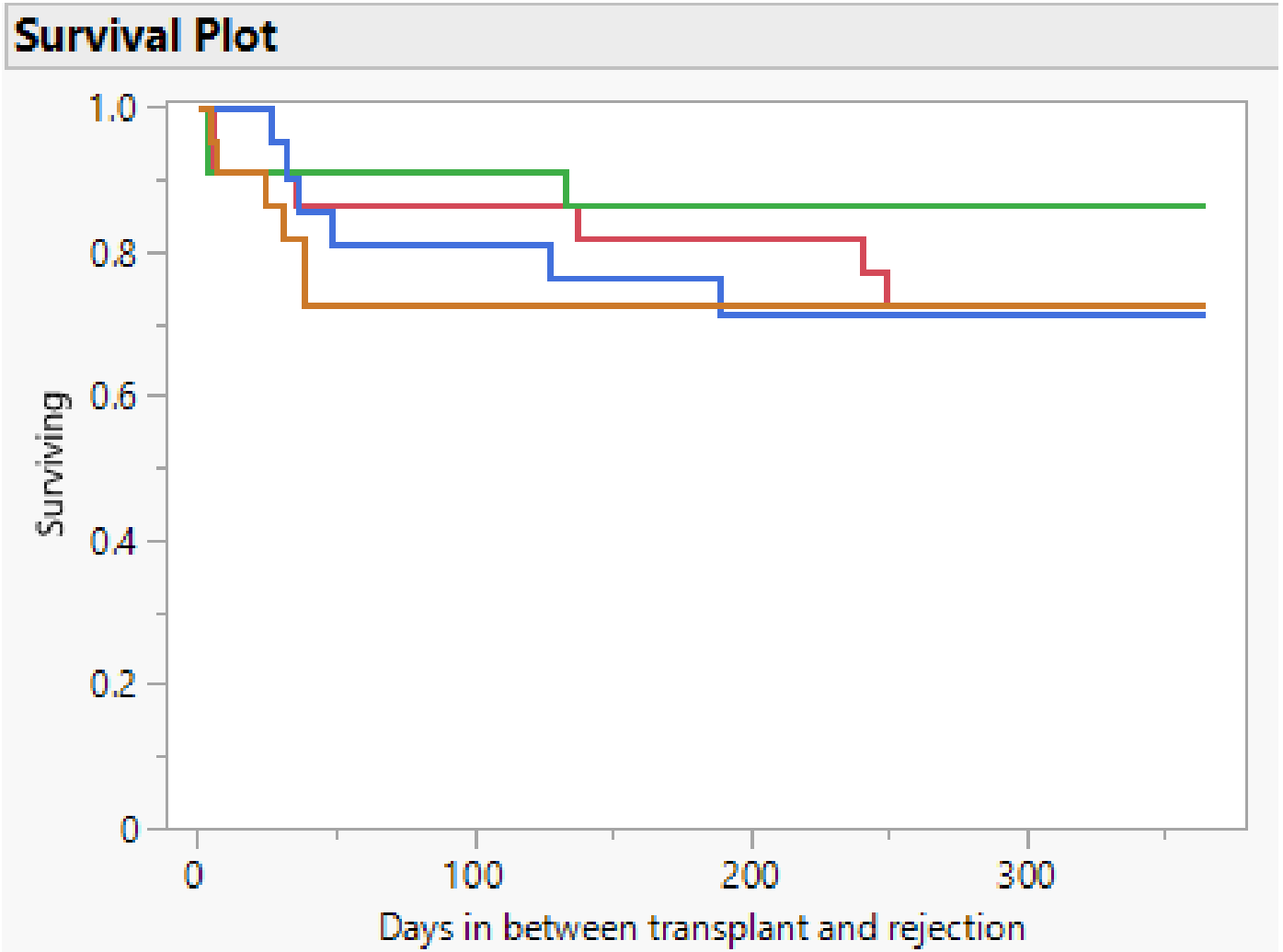

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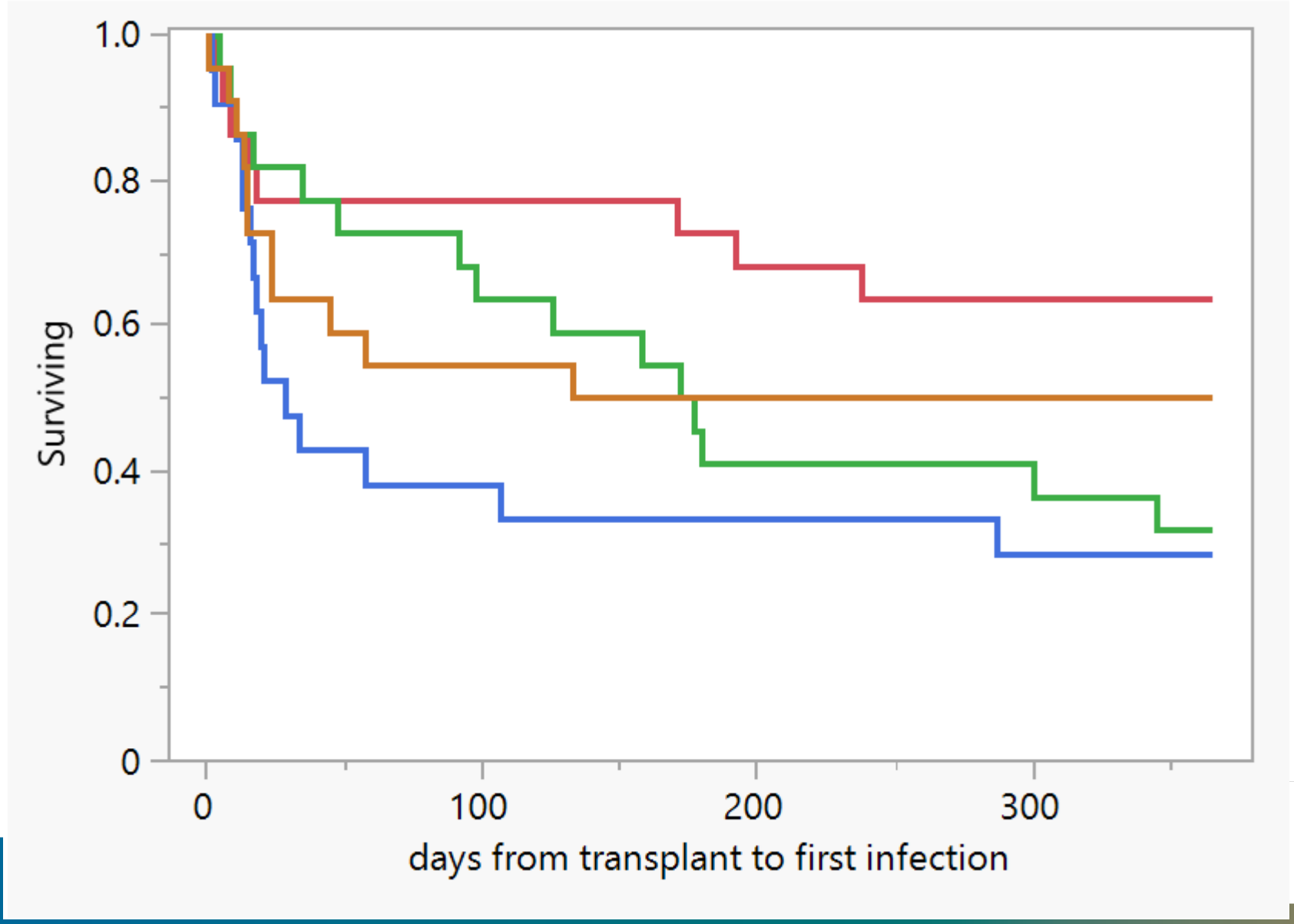
Rejection Outcome: Time to First Rejection

- Intraoperative blood product exposure not associated with rejection
- HR 1.13 (95% CI 0.71–1.73), p = 0.60

- Age, diagnosis, and Status 1 listing also not associated

Interpretation: No independent association between transfusion burden and rejection risk.

Survival Plot



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Infection Outcome: Time to First Infection

- Higher intraoperative blood product exposure (log mL/kg)

  → Earlier post-transplant infection

- HR 0.69 (95% CI 0.51–0.93), p = 0.016

- Younger age at transplant also associated with earlier infection
- No association with diagnosis or Status 1 listing

Interpretation: Transfusion burden is independently associated with infection timing.

Discussion

- Greater intraoperative blood product exposure was associated with earlier post-transplant infection but not with acute cellular rejection.
- Blood product transfusion has been associated with immunomodulatory effects, including transfusion-related immunosuppression, which may increase susceptibility to opportunistic infections.
- Pediatric patients, particularly younger children, may be especially vulnerable due to immature immune responses and greater relative transfusion exposure when standardized by body weight.

Discussion

- We did not observe a significant association between transfusion burden and rejection risk when rejection was analyzed as a time-to-event outcome.
- Absence of a detectable association may reflect limited power, heterogeneity in immunosuppression practices, or the complex and multifactorial nature of rejection.

Conclusion

- Higher intraoperative blood product exposure was associated with earlier post-transplant infection in pediatric liver transplant recipients, while no significant association with rejection was observed.
- These findings support continued efforts toward transfusion stewardship in pediatric liver transplantation and provide a foundation for future multicenter, prospective studies.

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