Evaluation of the Effect of Donor Hyperglycemia on Recipient Peri-Transplant Liver Function

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-- Attaching core tidyverse packages ------------------------ tidyverse 2.0.0 --
v dplyr     1.1.4     v readr     2.1.5
v forcats   1.0.0     v stringr   1.5.1
v ggplot2   3.5.2     v tibble    3.3.0
v lubridate 1.9.4     v tidyr     1.3.1
v purrr     1.1.0
-- Conflicts ------------------------------------------ tidyverse_conflicts() --
x dplyr::filter() masks stats::filter()
x dplyr::lag()    masks stats::lag()
i Use the conflicted package (<http://conflicted.r-lib.org/>) to force all conflicts to becor
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Introduction

Liver disease and failure is one of the most prevalent conditions affecting populations globally, accounting for around 2 million annual deaths worldwide (Devarbhavi et al., 2023). Furthermore, cirrhosis, or the final stage of chronic liver failure, is the fourth leading cause of premature death in the US, eliciting the need for effective treatments (Khalil et al., 2023; Liu & Chen, 2022). Although invasive and non-invasive methods of treatment can address liver failure to a certain extent, systematically improving these techniques can greatly improve patient outcomes. Since liver transplants remain the common method of treating liver disease, determining the relationship between post-operative liver function in transplant recipients and external factors can significantly reduce the burden of liver disease (Khalil et al., 2023).

Current research has identified that critical environmental circumstances, such as the organ-donor shortage, have necessitated high-risk organ donors, which can lead to successful liver transplants with short-lived function (Khalil et al., 2023). Furthermore, studies have identified characteristics of the patient, such as BMI and age, that can negatively influence liver function outcomes (Pischke et al., 2017). However, there is a lack of research regarding donor risk factors that can complicate liver function after successful transplants, which must be identified to

ensure long-term treatment efficacy. Since intraoperative and peri-transplant hyperglycemia can lead to severe consequences (such as graft rejection and patient mortality), hyperglycemia should be considered a crucial factor in choosing organ donors (Rameshi et al., 2025).

Although many donor characteristics could create high-risk transplant circumstances, this paper conducts statistical analyses specifically on the association between donor hyperglycemia and recipient liver function, as it has been least explored. Since statistical modeling can provide sufficient or insufficient evidence of an association between donor hyperglycemia and liver function in the patient, the analyses in this paper are critical for developing a rich understanding behind one of the most prominent medical diseases globally. The insights from this analysis will directly inform the diagnosis of peri-operative liver function, help medical professionals create stricter guidelines for donors, and facilitate successful liver transplant outcomes overall.

Figure 1

By building upon the factors regarding liver failure from Figure 1 adapted from Rameshi et al., (2025), this analysis reveals how specific donor related factors, such as hyperglycemia, can affect peri-liver transplant function. While recipient factors and intraoperative factors have been greatly studied (as seen by the visual complexity of those two domains), this visualization outlines the lack of research on donor factors – a gap in research that this paper aims to close.

Data

The data utilized in the statistical analysis is obtained from Perez-Protto et al. (2014), which studied the relationship between donor hyperglycemia and liver function outcome to create glucose-management systems in donors. For the dataset, information on 591 liver transplants in the Cleveland Clinic was collected during a five-year period. Data regarding grafts, donors, and recipients was obtained while "grafts from living donors, donors after cardiac death, and transplants for which the donor's glucose level was measured fewer than 2 times" were excluded (Perez-Protto et al., 2014). While the dataset includes important information regarding the demographics and characteristics of both donors and patients, this analysis will primarily focus on the relationship between two variables: time-weighted average (TWA) of of glucose observations in the liver graft and delayed liver function. Additionally, to produce more accurate results, donor age, donor gender, recipient calculated model for end-stage liver disease (MELD) score, and donor intraoperative hemodynamic instability will be accounted for. Recipient calculated MELD score represents how severe the state of a recipient's liver disease is, with scores ranging from 6-40 and higher scores indicating a more severe condition. Intraoperative hemodynamic instability indicates that a donor had abnormal blood flow to organs during surgical operations.

Operationalization of Variables

For the purpose of this statistical analysis, the variable of TWA glucose observations in the liver graft above 200 mg/dL is considered as donor hyperglycemia as per the foundational paper and other literature (Oliveira et al., 2018; Perez-Protto et al., 2014). Delayed graft dysfunction, or

the patient's liver outcome, is categorized as either dysfunction by patient death or retransplant within one week peri-transplant, or by having "aspartate aminotransferase level greater than 2000 U/L or prothrombin time greater than 16 seconds any time between postoperative days 2 and 7" (Perez-Protto et al., 2014, p.107). If either of these conditions were met, liver function was described as dysfunctional, and if either were not, liver function was described as functional. For this statistical analysis, TWA glucose levels, donor age, donor gender, recipient calculated model for end-stage liver disease (MELD) score, and donor intraoperative hemodynamic instability will serve as the explanatory variables, while delayed liver function is the response variable. Although the foundational paper aimed to analyze the relationship between the same two variables, the analysis in this paper can be used to confirm or deny the findings of Perez-Proto et al. (2014). By analyzing the association between TWA glucose levels and delayed liver function specifically, the statistical analysis conducted will provide the basis for future research on donor factors regarding recipient hepatic outcomes.