Statistical Analysis Report on the Stanford Heart Transplant Data

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Abstract

This report presents a statistical analysis of the Stanford heart transplant data to determine whether heart transplantation increases survival time in patients compared to those who do not receive a transplant and the effect of prior surgery on survival time post-transplant. We employ survival analysis and Cox regression methods to analyze the data.

1 Methods

1.1 Design, Setting, and Participants

A cohort study was conducted using the Stanford heart transplant data from November 1967 to March 1974, with 103 patients officially designated as heart transplant candidates. The data set provide the information of the transplant statue, prior surgery, age, etc.

1.2 Statistical Methods

The statistical analysis was performed using STATA, employing survival analysis techniques and Cox regression to evaluate the effects of heart transplantation and prior surgery on patient survival times. The Kaplan-Meier estimator and Cox regression were utilized due to their robustness in handling censored data and quantifying the impact of heart transplants on survival, while accounting for covariates such as prior surgeries. These methods are standard for such medical data analyses, providing a reliable framework for evaluating treatment effects over time.

2 Results

We are going to show the statistical analysis result directly through graphs and tables in this part and interpret them in the discussion.

2.1 Descriptive Analysis Result

Table 1 presents the survival outcomes of 99 heart transplant candidates after 200 days follow up. We drop the data that the patient is still alive at the end of study however the follow up time is less than 200 days

Group	Survived n(%)	Died n(%)
Transplant = 0	11.76	88.24
Transplant = 1	30.77	69.23

Table 1: The proportion of survival after 200 days follow up

It shows that out of 34 patients who did not receive a transplant, 4 survived (11.76%) and 30 died (88.24%). Among the 65 patients who did receive a transplant, 20 survived (30.77%) and 45 died (69.23%).

2.2 Survival Analysis Result

In this part, we show the result of the survival analysis. The transplant status is being treated as a time varying covariate, with time at risk apportioned to the time before the transplant as transplant = 0 and time after the transplant as time= 1.

2.2.1 Kaplan-Meier survival estimates Result

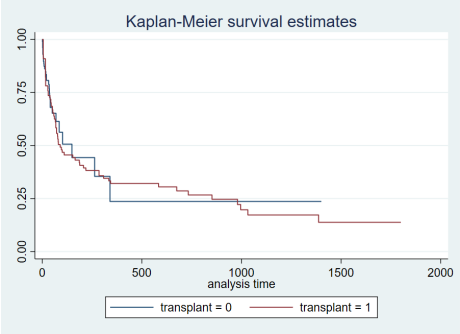


Figure 1: Kaplan-Meier survival estimates

2.2.2 Smoothed hazard estimates result

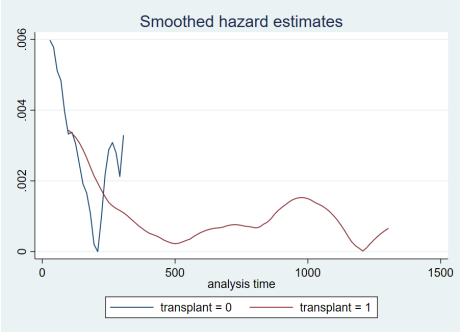


Figure 2: Smoothed hazard estimates

2.2.3 Cox regression result

	Haz.Ratio	Std.Err	z	p>|z|	95% Conf.Interval
transplant					
0	1 (base)				
1	1.133904	0.341392	0.42	0.676	[0.6284,2.0457]

Table 2: Cox regression

2.3 Subgroup Survival Analysis

We use the same survival setting but do a subgroup analysis. To find out the influence of the surgery status on the survival time.

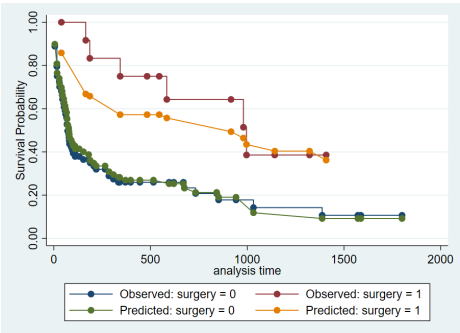


Figure 3: Subgroup Survival Analysis

3 Discussion

3.1 Interpretation of Descriptive Analysis Result

It can be observed in Table 1 that the mortality rate in the sample (after 200 days) was significantly higher in the non-transplantation group relative to the transplantation group (88% and 69%). We can therefore infer that heart transplantation has a positive impact on reducing mortality.

3.2 Interpretation of Survival Analysis

3.2.1 Interpretation of Kaplan-Meier survival estimates Result

The Kaplan-Meier survival estimate graph (Figure 1) compares the survival over time of two cohorts: those who have undergone a transplant against those who have not. Initially, both groups exhibit a sharp decline in survival probability, indicating a high event rate early on. As time progresses, the survival probability for the non-transplant group decreases more rapidly, falling below 50% relatively early in the observation period, suggesting a lower median survival time compared to the transplant group. The transplant group's survival curve demonstrates a slower decline, with a survival probability that remains above 50% for an extended period, suggesting a higher median survival time. The transplant group maintains a higher probability of survival up to 2000 days, implying that transplantation may be associated with increased survival.

3.2.2 Interpretation of Smoothed hazard estimates Result

The "Smoothed hazard estimates" graph (Figure2) shows the changing risk over time of a particular event occurring for two groups: those who have not received a transplant and those who have. The initial decline in the hazard rate for the non-transplant group suggests an early decrease in risk, which is then followed by an increase, indicating that the risk of the event rises again over time. In contrast, the transplant group exhibits a lower and more stable hazard rate, suggesting that transplantation may offer a sustained reduction in risk. This could imply that the initial treatments or conditions for the non-transplant group lose their effectiveness over time, while the benefits of receiving a transplant continue to provide a protective effect against the risk of the event.

3.2.3 Interpretation of Cox regression result

The analysis resulted in a hazard ratio of 1.134 for those who received a transplant compared to those who did not, but this finding was not statistically significant, as indicated by a p-value of 0.676 and a 95% confidence interval for the hazard ratio that includes 1 (ranging from approximately 0.628 to 2.046). Overall, the analysis suggests that transplantation does not have a statistically significant effect on the risk of the survival in this particular sample.

3.3 Interpretation of Subgroup Survival Analysis Result

In Figure 3, the observed survival rates for patients who had surgery start higher than for those who did not have surgery , suggesting that surgery may be linked to an increased initial survival probability. The predicted survival probabilities closely align with the actual observed data for both groups. This indicates that the model used for prediction is accurate and reliable in this context. Over time, both the observed and predicted survival probabilities for the non-surgery group decline steadily. In contrast, the surgery group's survival probabilities decline more gradually, maintaining a higher level of survival probability over a longer period. Towards the end of the observation period (near 2000 days), the survival probabilities for both groups tend to flatten out, indicating a decrease in the rate at which events occur. In essence, the graph suggests that undergoing surgery is associated with better survival outcomes compared to not having surgery.

4 Limitations

- This analysis doesn't consider the age and sex if the patients, further study is necessary.
- Sample Size and Selection: The study's small sample size of 103 patients limits the generalizability of the findings. Furthermore, the selection criteria for heart transplant candidates might introduce bias, as these individuals often have specific health profiles that may not represent the broader heart failure population.
- Non-randomized Design: Without randomization, confounding variables (e.g. disease severity) could skew the results. The study's retrospective design also raises the possibility of missing or inaccurate data, which can impact the validity of the findings.

5 Conclusion

The descriptive analysis showed a higher survival rate in patients who received transplants compared to those who did not, after 200 days of follow-up. This suggests a positive impact of heart transplantation on patient survival. The Kaplan-Meier survival estimates indicated a higher median survival time for the transplant group, with a more gradual decline in survival probability. Similarly, the smoothed hazard estimates demonstrated a lower and more stable hazard rate for the transplant group, implying a sustained reduction in the risk of mortality. However, the Cox regression analysis did not find a statistically significant difference in the survival of the transplant group compared to the non-transplant group. This lack of significance highlights the complexity of transplant benefits and suggests that other unmeasured factors may influence survival. The subgroup survival analysis suggested that surgery has a beneficial

impact on initial survival probabilities. However, both groups' survival probabilities eventually decline, with the surgery group maintaining higher survival over a longer period. In summary, while heart transplantation appears to be associated with improved survival rates, the benefits may not be statistically significant when considering the entire sample. These findings underscore the need for a cautious interpretation of survival benefits from transplantation and highlight the importance of considering individual patient factors when making clinical decisions regarding heart transplant candidacy. Further research is warranted to identify the specific conditions under which heart transplantation provides the most significant survival advantage.

Appendix

STATA do.file

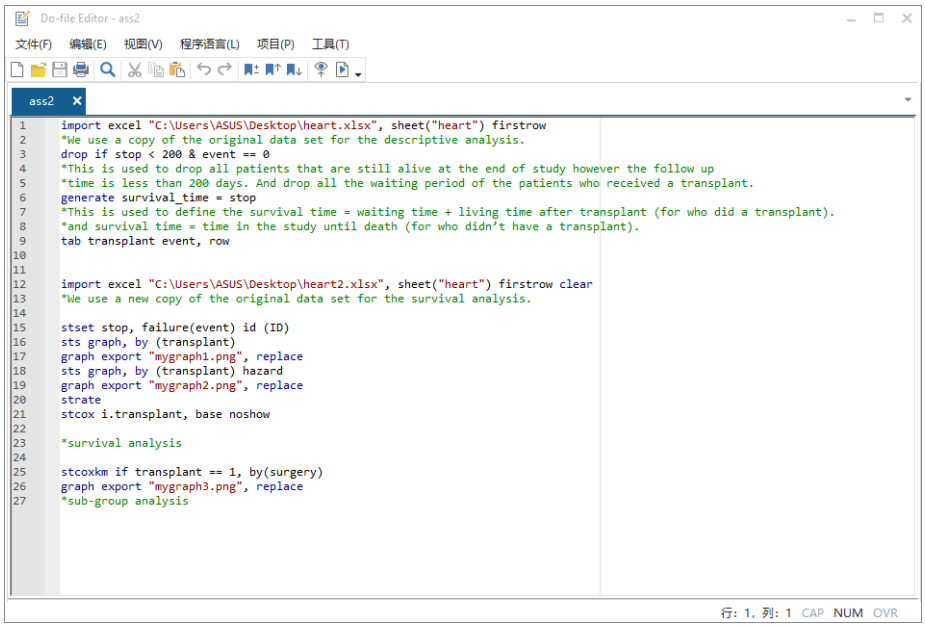


Figure 4: Subgroup Survival Analysis

Data Analysis Plan

STATISTICAL ANALYSIS PLAN	
Project name	Re-analysis of the Stanford heart transplant data
Reference number	*"N/A"*
Short name	*"N/A"*
Project CIs	*"N/A"*
Project team	*"N/A"*
Data Analysts	JINCHI CUI
Changes	*"N/A"*
Ethics approval	*"N/A"*
Target Journals	*"N/A"*

Introduction	
Background	While heart transplantation can provide many benefits, it also comes with risks, including the risk of organ rejection, infections, and complications from immunosuppressive medications. Thus, we need to know how much survival time a heart transplant increase will. To answer the question: Is it worth to receive a heart transplant although it is high risk? The Standford heat transplant data provide the information of 103 patients that were waiting for the heart transplant at the start of the study period. The data set is based on a cohort study and provide the information of the transplant statue, prior surgery, age, etc. We are going to use this information to do a statistic analysis and give advice to this question objectively.
Existing knowledge	1. Heart transplantation is a surgical procedure that replaces a patient's failing heart with a healthy donor heart. 2. For many patients with end-stage heart disease, a heart transplant can significantly extend their life expectancy. 3. Heart transplantation is often the last resort for patients who have tried all other treatments for heart failure without success.
Knowledge gaps	1. Heart transplant is the last resort for patients since it has high risk. We don't know if it can significantly increase the survival time of the patients compare to the patients without receiving a transplant. 2. Some patients come with a prior surgery, and this might influence the survival time. However, we not yet know about this clearly.
Research Questions	Exploring if receiving a heart transplant will significantly increase the survival time of the patients and the effect of a prior surgery on the survival time.
Study Hypothesis	1. Receiving a heart transplant will increase the survival time of the patients. 2. A prior surgery will have risk to decrease the length of the survival time after a heart transplant.
Study Aims	Find out if a heart transplant will increase the survival time of the patients and if A prior surgery will have risk to decrease the length of the survival time.

Method summary*	
Design, Setting, and Participants	
Study design	Cohort study
Data sets	Stanford heart transplant data
Study period	November 1967 to March 1974
Study population	103 patients included in the dataset were designated officially heart transplant candidates.
Case definitions	Patients that were gravely ill and would most likely benefit from a new heart.

Exclusion criteria	Very few candidates during the waiting period show improvement and get deselected as a heart transplant candidate, but for the purposes of this experiment those patients were kept in the data as continuing candidates.
Exposure, Main Outcomes and Measures	
Main exposures	Heart transplant, prior surgery
Main outcomes	Death or survive
Factors of interest/Covariates	1. Prior surgery 2. Transplant status (time varying covariate)
Statistical methods	Survival analysis, cox regression, hypothesis test
Subgroup analysis	Analysis the survival time of the transplant group base on their prior surgery status.
Sensitivity analysis	*"N/A"*
Analysis package	STATA
Working directory	*"N/A"*

**Please mark "N/A" to items where appropriate, denoting not applicable in the plan.*

Proposed analytical strategy

Details of methods for statistical analysis (including how to handle missing values, study endpoints, suppression rules, and other rationales for data analysis)

Datasets:

Stanford heart transplant data**.**

Study population and sample:

103 patients included in the dataset were designated officially heart transplant candidates.

Case definition

Patients that were gravely ill and would most likely benefit from a new heart.

Definitions for outcomes

The status of patients (dead or alive).

Definitions for factors of interest

Surgery: Whether or not the patient had prior surgery with levels 0 (no) and 1 (yes).
Transplant: Transplant status with levels 0 (did not receive a transplant) and 1 (received a transplant)

Statistical analysis

PART I: Overview
We are going to look the proportion of survival after 200 days follow up.

Define:
survival time = waiting time + living time after transplant (for who did a transplant).
&
survival time = time in the study until death (for who didn't have a transplant).

Modify the data set in a copy and fill in **Table I.**

(Modify means connect the separated time intervals of the same patient.)
Note: this is only done in the copy of the original data set so that it will not influence the survival analysis.

In this part, we drop the data that the patient is still alive at the end of study however the follow up time is less than 200 days.

PART II: Survival analysis base on the transplant status.

For individuals who received a transplant the survival time must be partitioned into survival time before the transplant and survival time after the transplant (already been done in the dataset). The transplant status is being treated as a time varying covariate, with time at risk apportioned to the time before the transplant as transplant = 0 and time after the transplant as time= 1. After setting up, we plot the Kaplan-Meier survival curves **(Figure I)** and he hazard function graph **(Figure II)**. And then we can estimate rates of the outcome. Finally, we do a cox regression and fill in **Table II**.

STATA CODE:

```
stset stop, failure(event) id (ID)
sts graph, by (transplant)
sts graph, by (transplant) hazard
strate
stcox i.transplant, base noshow
```

PART III: Subgroup analysis (survival analysis base on surgery status of transplant=1 group)

We use the same survival setting but do a subgroup analysis. To find out the influence of the surgery status on the survival time. We do this by setting the analysis code by(surgery). Finally, we give a plot of the Kaplan-Meier survival curves and the cox predicted curves(**Figure III**).

STATA CODE:
stcoxkm if transplant == 1, by(surgery)

References

[1] John Crowley & Marie Hu (1977) Covariance Analysis of Heart Transplant Survival Data, Journal of the American Statistical Association, 72:357, 27-36
[2] Bruce W. Turnbull , Byron Wm. Brown Jr. & Marie Hu (1974) Survivorship Analysis of Heart Transplant Data, Journal of the American Statistical Association, 69:345, 74-80, DOI: 10.1080/01621459.1974.10480130

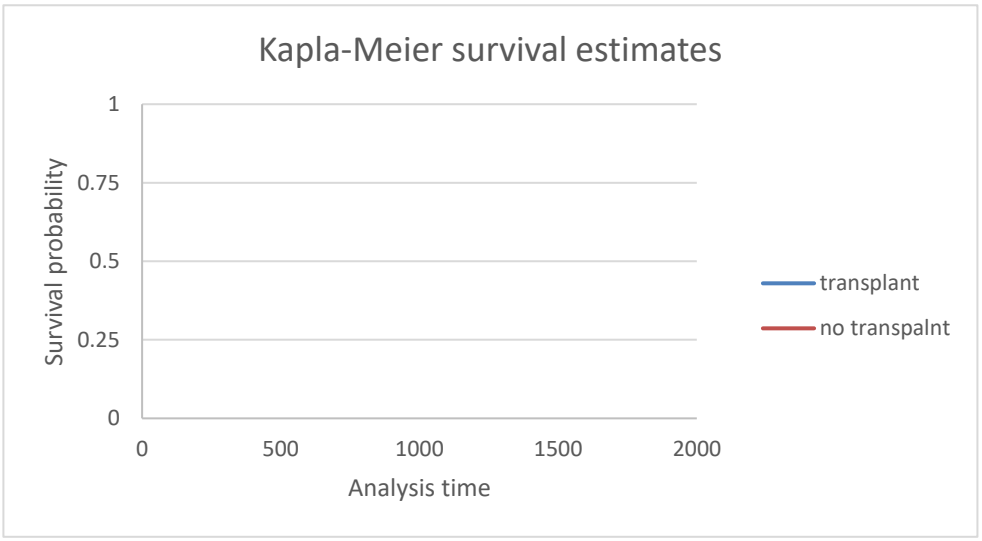
Variables	Definitions
Start	Entry time and status for this interval of time. For patients who has only one time interval, start means the first day that the patient is included in the study. For patients who has two time intervals, “start” of the first interval means the first day that the patient is included in the study. “Start” of the second interval means after that number of days, the patients received a transplant.
Stop	Exit time and status for this interval of time. For patients who has only one time interval, stop means after that number of days, the patients is out of the study (died or the study ends).For patients who has two time intervals, “Stop” of the first interval means the last day that the patient is included in the study. “Stop” of the second interval means after that number of days, the patients is out of the study (died or the study ends).
Event	1 means the patient is dead, 0 means alive.
Age	Age-48 years(Age of acceptance and age of transplant if there is a transplant).
Year	Year of acceptance (in years after 1 Nov 1967).
Surgery	Prior bypass surgery 1=yes
transplant	Received transplant 1=yes
id	Patient id
Survival time	survival time = waiting time + living time after transplant (for who did a transplant). & survival time = time in the study until death (for who didn’t have a transplant).

Analysis dissemination strategy
“N/A”

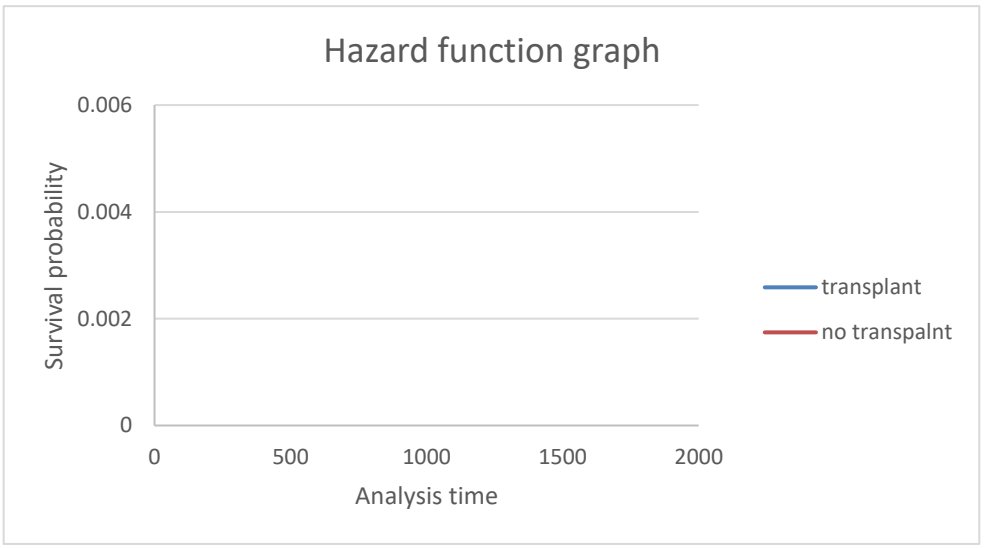
Interpretation/Notes
➢ Limitations: This analysis didn’t consider the age and sex if the patients, further study is necessary.

Dummy Tables & Figures

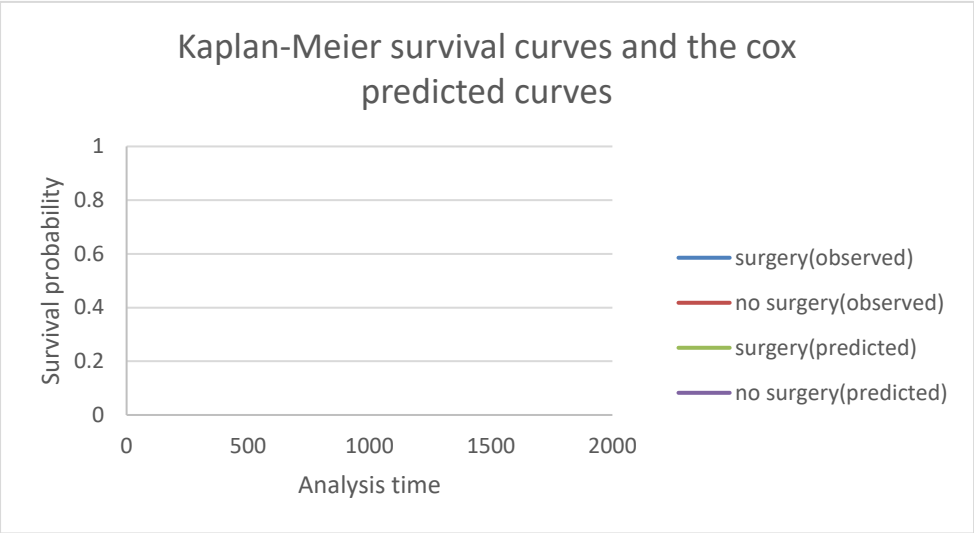
1. Figure I: Kapla-Meier survival estimates plot .



2. Figure II: Hazard function graph.



3. Figure III: Kaplan-Meier survival curves and the cox predicted curves for subgroup survival analysis based on the prior surgery status.



4. Table I: Survival status at 200 days follow up.

Group	Survived n(%)	Died n(%)
Transplant = 0		
Transplant = 1		

5. Table II：Cox regression result

	Haz.ratio	Std.err	Z	P>|Z|	[95% conf.interval]
Transplant =0					
Transplant =1					