**A Personalized Synthetic Control Study of Overall Survival: Comparing TACE and SIRT in Hepatocellular Carcinoma**

**Aim**

The aim of this report is to compare the overall survival rates between two treatment modalities for Hepatocellular Carcinoma (HCC): Trans arterial Chemoembolisation (TACE) and Selective Internal Radiation Therapy (SIRT).

**Background**

Hepatocellular carcinoma (HCC) is a primary malignancy of the liver and is often associated with underlying liver disease, such as cirrhosis. TACE and SIRT are two common interventional treatments for unresectable HCC. TACE involves the embolization of hepatic arteries while delivering chemotherapy, whereas SIRT uses radioactive microspheres to target tumors.

**Covariates**

The following table summarizes the covariates used in the analysis for both treatment and control groups:

|  |  |  |
| --- | --- | --- |
| Covariate | TACE | SIRT |
| Gender | Yes | Yes |
| Age | Yes | Yes |
| AFP | Yes | Yes |
| Albumin | Yes | Yes |
| Bilirubin | Yes | Yes |
| Hepatitis B | Yes | No |
| Hepatitis C | Yes | No |
| Alcohol | Yes | No |
| Focality | Yes | No |
| Lesion1 | Yes | Yes |
| Lesion2 | Yes | No |
| Vascular invasion | Yes | No |
| Child-Pugh Grade | Yes | No |
| Cirrhosis | Yes | Yes |
| Cause | No | Yes |
| Morphology | No | Yes |
| Portal vein invasion | No | Yes |

**Descriptive statistics**

The following table presents the descriptive statistics of the treatment and control groups

|  |  |  |
| --- | --- | --- |
| **Covariates** | **SIRT** | **TACE** |
| Age Mean (SD) | 68.1(12.7) | 68.2(8.1) |
| AFP | 3.9(2.6) | 3.9(2.6) |
| Bilirubin | 18.9(10.2) | 16.3(11.9) |
| Albumin | 37.9(5.6) | 39.3(4.5) |
| Lesion1 | 6.3(4.3) | 5.7(3.7) |
| Lesion2 | NA | 3.3(1.9) |
| **Cirrhosis (Percent)** |  |  |
| 1 | 77.4 | 79.6 |
| 0 | 22.6 |  |
| **Gender** |  |  |
| Male | 82.1 | 87.7 |
| Female | 18.9 |  |
| **Morphology** |  |  |
| Massive or >50% | 8.9 | NA |
| Multinodular & <50% | 73.2 | NA |
| Single & < 50% | 17.9 | NA |
| **Portal Vein Invasion** |  |  |
| Yes | 21.4 | NA |
| No | 78.6 | NA |
| **Focality** |  |  |
| Unifocal | NA | 7.4 |
| Multifocal | NA | 92.6 |
| **Hepatitis B** |  |  |
| 0 | NA | 85.2 |
| 1 | NA | 14.8 |
| **Hepatitis C** |  |  |
| 0 | NA | 75.3 |
| 1 | NA | 24.7 |
| **Alcohol** |  |  |
| 0 | NA | 51.9 |
| 1 | NA | 48.1 |
| **Vascular Invasion** |  |  |
| 0 | NA | 100 |
| **Child Pugh grade** |  |  |
| A | NA | 100 |

**TACE Model**

**Model Description Using TACE Dataset**

To model overall survival using the TACE dataset, I first performed a stepwise backward selection method starting with a full Cox proportional hazards model that included the following covariates: Gender, Age, AFP, Cirrhosis, Bilirubin, Albumin, and Lesion1.

1. **Initial Model**: The full model yielded an AIC of 677.19.
2. **Stepwise Selection**:
   * In the first step, removing **Gender** resulted in the lowest AIC of 675.32.
   * The next step showed that removing **Lesion1** still kept the AIC low at 676.08.
   * Continuing this process, **Age** was removed next, resulting in an AIC of 676.24.
   * The model continued to refine, ultimately removing **Bilirubin** and **Cirrhosis**, leading to a final model with the covariates: **AFP, Cirrhosis, and Albumin**.
3. **Final Model**: The selected model was:

Surv(time, cen)∼AFP+ Cirrhosis+ Albumin

This model had an AIC of 673.10.

**Final Model**

Based on the covariates identified through the stepwise backward selection process, the final model was developed using the flexsurvspline function. The model includes the following covariates: **AFP**, **Cirrhosis**, and **Albumin**. The model specification is as follows:

This model aims to provide a flexible estimation of the survival function while accounting for the effects of the selected covariates on overall survival in patients with hepatocellular carcinoma.

|  |  |  |
| --- | --- | --- |
| **Covariate** | **Mean Estimate (SE)** | **HR (95% CI)** |
| AFP | 0.1784(0.0427) | 1.1953(1.09,1.29) |
| Cirrhosis | -0.4969(0.2838) | 0.6084(0.34,1.06) |
| Albumin | -0.0709(0.0250) | 0.9315(0.88,0.97) |

A diagram of a graph

Description automatically generated with medium confidence

**PSC Comparison**

The visualization compares distributions of AFP, Albumin, and Cirrhosis between patients treated with TACE (light blue) and SIRT (dark blue).

A diagram of a person's face

Description automatically generated

**Survival Analysis of Patients Undergoing SIRT and TACE**

A graph of a person with a blue line

Description automatically generated

The survival plot provides a comparative analysis of predicted survival outcomes for patients treated with SIRT versus those undergoing TACE. The blue line represents the predicted survival curve for patients receiving TACE. It illustrates the estimated survival probabilities over time for this treatment group. The pink line indicates the observed survival outcomes for patients treated with SIRT. The analysis reveals that patients who receive SIRT tend to have a longer survival compared to those treated with TACE. The separation between the two curves suggests that SIRT may offer a significant survival advantage, with patients undergoing SIRT demonstrating improved longevity in their treatment outcomes.

The figure below is the observed survival outcomes for patients treated with SIRT only for a better understanding.

A graph with a line

Description automatically generated

**Plotting individual treatment effects**

This figure illustrates the individual treatment effects by plotting the expected response rates for the control treatment, TACE, alongside the observed response rates from the SIRT dataset for each patient in the analysis. This comparison highlights the differences in treatment efficacy between TACE and SIRT.

A graph showing a curve

Description automatically generated