Glucose Variability – Survival and TRM

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## Statistical Methods

Survival and Treatment Related Mortality (TRM) related summary statistics were reported as counts and percentages and median and interquartile ranges (IQR). Cox proportional hazards models were used with time-to-death as an outcome, and time-to-treated related mortality as the primary outcome and death due to other causes as a competing risk. The coefficient of variation of glucose (pre-tx, days 0-30, and days 0-100) were all log2 transformed due to skewness. log2 was chosen for ease of interpretation when transforming it back into a hazard ratio. Models were adjusted for post-tx steroids, transplant type, GVHD, and number of glucose measurements within the stated time period (also log2 transformed). Interactions between post-tx steroids and CV of glucose, as well as tx type and CV of glucose, were tested in all models.

## Primary Outcome 3: Overall Survival

**Table 1: Overall Survival Summary Statistics**

|  |  |
| --- | --- |
| Characteristic | All (n=344) |
| Patient Alive |  |
| Died | 100 (29%) |
| Alive | 244 (71%) |
| Days from Tx to Death | 263.5 (135, 499.5) |

Of the 100 patients who died in the study, the median time from tx to death was 264 days.

**Table 2a: Overall Survival: Pre-Tx Variability**

|  |  |  |
| --- | --- | --- |
| Predictor | Hazard Ratio (95% CI) | P Value |
| CV Glucose, Pre Tx\*\* | 1.18 (0.93, 1.5) | 0.177 |
| Post-tx steroids (any) | 2.93 (1.84, 4.66) | <0.0001 |
| GVHD | 0.76 (0.4, 1.42) | 0.3858 |
| Tx Type: Allogenic | 0.53 (0.32, 0.87) | 0.0114 |
| Number of Glucose measurements, Pre Tx\*\* | 0.55 (0.39, 0.78) | 0.0008 |

\*\*log2

Glucose variability pre-tx was not associated with time to death.

**Table 2b: Overall Survival: Post-Tx Days 0-30 Variability**

The association between day 0-30 glucose variability and time-to-death depended on transplant type (p=0.01). For those with allogenic transplants, for every doubling of CV glucose between days 0-30, there was a 1.40-fold (95% CI: 1.01, 1.96) increase in hazard of death. For those with autologous transplants, glucose variability was not associated with hazard of death. Other factors associated with increased hazard of death: post-tx steroids (HR: 2.36 (95% CI: 1.48, 3.78); p=0.0003).

**Table 2c: Overall Survival: Post-Tx Days 0-100 Variability**

The association between day 0-100 glucose variability and time-to-death depended on transplant type (p=0.0002). For those with allogenic transplants, for every doubling of CV of glucose between days 0-100, there was a 2.32-fold (95% CI: 1.60, 3.36) increase in hazard of death. For those with autologous transplants, glucose variability was not associated with hazard of death. Other factors associated with hazard of death: post-tx steroids HR: 1.92 (95% CI: 1.17, 3.13); p=0.009.

## Primary Outcome 4: Treatment Related Mortality (TRM)

**Table 1: TRM Summary Statistics**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristic | All (n=344) | Autologous (n=119) | Allogenic (n=225) | P Value |
| Treatment Related Mortality |  |  |  | <0.0001 |
| Treatment Related Death | 37 (11%) | 4 (3%) | 33 (15%) |  |
| Other Death | 63 (18%) | 39 (33%) | 24 (11%) |  |
| Alive | 244 (71%) | 76 (64%) | 168 (75%) |  |
| Days to Treatment Related Mortality | 189 (108, 361) | 337 (288, 905) | 152 (86, 334) | 0.08 |
| Days to Other Mortality | 377 (166, 552) | 406 (245, 592) | 158 (108, 422) | 0.001 |

**Table 2a: TRM: Pre-Tx Variability**

|  |  |  |
| --- | --- | --- |
| Predictor | Hazard Ratio (95% CI) | P Value |
| CV Glucose, Pre Tx\*\* | 1.42 (0.92, 2.21) | 0.11 |
| Post-tx steroids (any) | 3.82 (1.86, 7.85) | 0.0003 |
| GVHD | 1.28 (0.62, 2.65) | 0.5 |
| Tx Type: Allogenic | 2.08 (0.66, 6.51) | 0.21 |
| Number of Glucose measurements Pre Tx\*\* | 1 (0.35, 2.81) | 0.99 |

\*\*log2

**Table 2b: TRM: Post-Tx Days 0-30 Variability**

|  |  |  |
| --- | --- | --- |
| Predictor | Hazard Ratio (95% CI) | P Value |
| CV Glucose, Days 0-30\*\* | 1.18 (0.73, 1.9) | 0.49 |
| Post-tx steroids (any) | 3.46 (1.6, 7.47) | 0.0016 |
| GVHD | 0.98 (0.44, 2.21) | 0.96 |
| Tx Type: Allogenic | 2.18 (0.76, 6.3) | 0.15 |
| Number of Glucose measurements Days 0-30\*\* | 1.83 (1.05, 3.17) | 0.032 |

\*\*log2

**Table 2c: TRM: Post-Tx Days 0-100 Variability**

|  |  |  |
| --- | --- | --- |
| Predictor | Hazard Ratio (95% CI) | P Value |
| CV Glucose, Days 0-100\*\* | 2.36 (1.42, 3.94) | 0.001 |
| Post-tx steroids (any) | 1.96 (0.91, 4.24) | 0.087 |
| GVHD | 0.58 (0.25, 1.36) | 0.21 |
| Tx Type: Allogenic | 1.47 (0.49, 4.45) | 0.49 |
| Number of Glucose measurements Days 0-100\*\* | 2.01 (1.4, 2.89) | 0.0002 |

\*\*log2

For every doubling of CV glucose during days 0-100, the hazard of TRM increased 2.4-fold (p=0.001).