Survival Analysis of Infection Control Measures in Burn Patients

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1 Introduction

Infection with *Staphylococcus aureus* is a critical concern in burn patients, often contributing to prolonged hospital stays, increased morbidity, and higher healthcare costs [4]. Therefore, effective infection control measures are of great importance. This study investigates the impact of replacing routine bathing with total body washing using antimicrobial agents on infection risk, leveraging survival analysis techniques to rigorously evaluate the time to infection. The dataset, originally published by Ichida *et al.* (1993), provides data on infection times, patient characteristics, and clinical interventions [2].

To highlight differences in infection-free survival between patients receiving routine bathing and those undergoing total body washing, the Kaplan-Meier estimator was used [3].

To further identify factors influencing infection risk,the Cox Model was used [1]. Both time-independent covariates (e.g. patient gender, race) and time-dependent covariates (e.g. surgical excision of burn tissue, prophylactic antibiotic treatment) are employed for a comprehensive analysis of *Staphylococcus aureus* infection on burn patients.

This report aims to present a clear and actionable evaluation of the infection control measures through the lens of survival analysis, with insights that inform clinical decision-making and contribute to better patient care.

2 Results and Discussion

2.1 Kaplan-Meier Analysis

Fig. 1 highlights differences in infection-free survival between routine care and antimicrobial cleansing. After 30 days, 76% of patients in the cleansing group remained infection-free compared to 66% in the routine care group. By the end of the study, 70% of cleansing patients remained infection-free, versus 30% in the routine care group. Nelson-Aalen curves confirmed these trends, showing slightly higher infection-free percentages for both groups. Furthermore, The log-rank test supports this difference with ($\chi^2 = 3.8$, $p = 0.05$). Patients in the antimicrobial cleansing group had fewer observed infections (20) than expected (26.6), while those in the routine care group experienced more infections (28) than expected (21.4).

These results suggest that antimicrobial cleansing offers a protective benefit in reducing infection risks, highlighting its potential as an effective intervention for burn patients.

2.2 Cox Proportional Hazards Model

The constructed final model was determined to include Treatment, Race, and the time-dependent covariate surgical excision, as these variables demonstrated clinical relevance and statistical significance.

Patients who received antimicrobial cleansing were 40.4% less likely to develop an infection compared to those who received routine care (p = 0.082). While this result was not statistically significant, it suggests a potential protective effect of a cleansing against *Staphylococcus aureus* infection. White patients were significantly more likely to develop an infection compared to non-White patients, with an 8.86-fold higher likelihood of infection (p = 0.031). The wide confidence interval (95% CI: 1.22–64.34) for this result reflects some uncertainty, likely due to variability or a smaller sample size (n = 154). Finally, surgical excision was associated with a 60% lower likelihood of infection (p = 0.059), indicating a marginally significant effect.

Overall, the model demonstrated good predictive performance, with a concordance index of 0.696, meaning it correctly predicted the order of infection risk in approximately 70% of cases. The likelihood ratio test confirmed the statistical significance of the model as a whole (p = 0.0004).

2.3 Residual Analysis

2.3.1 Deviance Residuals

The analysis of deviance residuals revealed several cases where the observed time to infection deviated significantly from the model's predictions. A positive deviance residual indicates that the infection occurred later than predicted. To be specific, observation 214 is a non-white male with 20% burns involving trunk who received cleansing care and had a deviance residual of 2.769.

Observation 70 is a white female patient with 36% burns involving the trunk and lower legs who underwent surgical excision and received antibiotic treatment, yet had a deviance residual of -2.124. Observation 160 is a male patient with 5% burns to the trunk and lower legs who received surgical excision but no antibiotics, with a deviance residual of -2.740. Both observation 118 and 160

Observations About Respiratory Tract Burns Patients with respiratory tract burns show an interesting trend toward prolonged infection-free survival. For instance, observation 214, a male patient with burns classified as "Flame," involving the trunk and respiratory tract, received antimicrobial cleansing and had a deviance residual of 2.769. This suggests that infection occurred much later than predicted. The apparent resilience of patients with respiratory tract burns could indicate a different response to infection risk compared to skin burns alone. However, the limited number of cases with respiratory burns in this dataset restricts drawing definitive conclusions.

DFBETA values measure the influence of individual observations on the model's coefficients. Large DFBETA values indicate that a specific observation has a strong effect on a particular predictor. # Conclusion Provide actionable recommendations based on the analysis.

3 Appendices

4 Data Description

The dataset `burn` consists of 154 observations of burn patients and 17 variables that capture patient characteristics, clinical interventions, and infection status with time to infection.

4.1 Outcome Variables

- **T3 (time to infection)**: The time (in days) until infection with *Staphylococcus aureus*.
- **D3 (infection status)**: A binary variable indicating whether the patient developed an infection within the course of the study (1 = infected, 0 = not infected).

4.2 Time-Dependent Covariates

- **T1 (time to surgical excision)**: The time (in days) to surgical excision of burn tissue.
- **D1 (surgical excision status)**: A binary variable indicating whether surgical excision was performed (1 = excised, 0 = not excised).
- **T2 (time to antibiotic treatment)**: The time (in days) to the administration of prophylactic antibiotic treatment.

- **D2 (antibiotic treatment status)**: A binary variable indicating whether antibiotics were administered (1 = treated, 0 = not treated).

4.3 Baseline Characteristics

- **Treatment**: Categorical variable indicating the bathing regimen (Routine or Cleansing with antimicrobial agents).
- **Gender**: Categorical variable indicating the patient's gender (Male or Female).
- **Race**: Categorical variable indicating the patient's race (Nonwhite or White).
- **PercentBurned**: Numeric variable representing the percentage of the patient's body surface area affected by burns.

4.4 Burn Site Characteristics

- **SiteHead**: Binary factor indicating whether the head was burned (Burned or Not Burned).
- **SiteButtock**: Binary factor indicating whether the buttocks were burned (Burned or Not Burned).
- **SiteTrunk**: Binary factor indicating whether the trunk was burned (Burned or Not Burned).
- **SiteUpperLeg**: Binary factor indicating whether the upper leg was burned (Burned or Not Burned).
- **SiteLowerLeg**: Binary factor indicating whether the lower leg was burned (Burned or Not Burned).
- **SiteRespTract**: Binary factor indicating whether the respiratory tract was burned (Burned or Not Burned).

4.5 Burn Type

- **BurnType**: Categorical variable specifying the type of burn (Chemical, Scald, Flame, or Electric).

5 Methods

5.1 Kaplan-Meier Survival Analysis

The Kaplan-Meier estimator was used to estimate and visualize the probability of remaining infection-free over time for patients undergoing either routine bathing or antimicrobial washing. Additionally, Nelson-Aalen estimate was also plotted for a comprehensive view of survival difference between groups.

Survival curves were compared using the `survdiff` function in package `survival`, which performs a log-rank test to assess whether the differences between the two groups are statistically significant.

Additionally, cumulative hazard functions were plotted against time to estimate the cumulative infection probability at different time points. Complementary log-log survival curves were plotted against log-transformed time to assess if the ratio of hazard rates between two treatment groups remains constant over time.

5.2 Cox Proportional Hazards Model

5.2.1 Model with Time-Independent Covariates

An initial Cox proportional hazards model was constructed using time-independent covariates to evaluate their relationship with the risk of infection. The primary predictor of interest was **Treatment**. Additional time-independent variables were sequentially introduced into the model.

To address the violation of the proportional hazards assumption identified in the unstratified model, the variable **SiteRespTract** was stratified. This allowed for differing baseline hazard functions for patients with and without burns in the respiratory tract.

Model refinement was performed using the `drop1` function to identify covariates that did not significantly contribute to model performance. Multicollinearity among covariates was assessed using variance inflation factors, ensuring that redundant predictors were identified and addressed without compromising the integrity of the model.

5.2.2 Model with Time-Dependent Covariates

To incorporate time-dependent predictors, the dataset was expanded using counting process notation. Two key time-dependent covariates were included: 1. **Surgical excision of burn tissue (T1, D1)**. 2. **Prophylactic antibiotic treatment (T2, D2)**.

A Cox model was constructed combining time-dependent and time-independent covariates. The time-dependent variables captured the dynamic effects of these interventions on infection risk, while time-independent variables provided baseline hazard adjustments.

5.3 Model Checking and Diagnostics

Model checking was performed using a comprehensive suite of diagnostic techniques:

5.3.1 Proportional Hazards Assumption

The proportional hazards assumption was evaluated using Schoenfeld residual plots which test whether the residuals show systematic trends over time and `cox.zph` function from package `survival`. Where violations were detected, appropriate adjustments were made, such as stratification to allow baseline hazard functions to differ between groups.

5.3.2 Goodness-of-Fit

Cox-Snell residuals were used to assess overall model fit. A cumulative hazard plot was constructed to compare observed data with the expected hazard under the model. A straight 45-degree line indicated good fit, while deviations suggested potential inadequacies.

5.3.3 Outlier Analysis

Residual analysis was performed to evaluate how well the Cox model aligned with the observed data and to identify unusual observations. Two types of residuals – deviance residuals and DFBETA values – were analyzed.

Deviance residuals are derived from martingale residuals and measure how much an individual's observed time to infection deviates from the model's prediction, with positive values indicating later-than-expected infections.

DFBETA values measure the influence of individual observations on the model's coefficients. Large DFBETA values indicate that a specific observation has a strong effect on a particular predictor.

Using thresholds based on two standard deviations from the mean for each residual type, observations were flagged as unusual.

References

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