Bayesian comparison of Weibull model versus B-spline model for baseline hazard to evaluate two types of stem cell transplant

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1. Objective

To compare the effectiveness of two methods of stem cell transplant for acute myelogenous leukemia by Bayesian proportional hazards modeling using two different baseline hazards: (1) parametric Weibull model; (2) semiparametric model using a mixture of B-spline distributions.

2. Scientific Motivation

- There are two types of stem cell transplants: autologous and allogeneic. Each of the two stem cell procedures has its own distinct process and is associated with distinct benefits and risks which should be taken into account when deciding which of these stem cell treatments a patient should undergo.
- The criteria used to the procedure is based primarily on what disease the patient has.
- Clinical trials have shown that the allogeneic stem cell transplant is effective for acute myelogenous leukemia. We are interested in whether the autologous stem cell performs better or worse.

3. Description of the Data

- A sample of 101 patients with advanced acute myelogenous leukemia in the record of International Bone Marrow Transplant Registry.
- 51 patients received an autologous (auto) bone marrow transplant; 50 patients received an allogeneic (allo) bone marrow transplant.
- Data includes patients' time to death or relapse $\boldsymbol{t}$ (months); type of transplant $\boldsymbol{x}$ (0=allogeneic, 1=autologous) ;leukemia-free censoring indicator $\boldsymbol{\delta}$ (0=alive without relapse, 1=dead or relapse).

4. Statistical Model

Likelihood:

$$L(\boldsymbol{\beta}|\boldsymbol{t},\boldsymbol{x},\boldsymbol{\delta}) = \prod_{i=1}^{N}\{[\lambda_0(t_i)\exp(\beta_0+\beta_1 x_i)]^{\delta_i}\cdot \exp[-\Lambda_0(t_i)\exp(\beta_0+\beta_1 x_i)]\}$$

where

$$\Lambda_0(t) = \int_0^t \lambda_0(s)\mathrm{d}s$$

Weibull Model:

$$\lambda_0(t) = pt^{p-1} \qquad (1)$$

B-spline model:

$$\log\lambda_0(t) = \sum_{j=1}^{K}\gamma_j B_j(t) \qquad (2)$$

Priors:

$$\beta_0 \sim Flat, \quad \beta_1 \sim N(0,100^2)$$

$$p \sim Gamma(0.01,0.01), \quad \gamma_j \overset{\text{iid}}{\sim} N(0,100^2)$$

5. Methodology

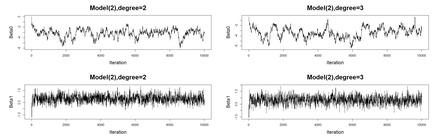
- For the semiparametric model, we used $K = 10$ knots for the B-spline basis functions. Also, we used numerical integration method (composite trapezoidal rule) to estimate the integral of baseline hazard function.
- For each of the Weibull and B-spline mixtures of degree $1, 2, 3$, we ran chains of $10,000$ iterations after discarding a burn-in of 1000.
- We performed the Gelman and Rubin test along with the trace plots which confirmed adequate convergence.
- The deviance information criterion (DIC) are adopted for model comparisons.

6. Convergence

Table 1: *Potential scale reduction factors and their 97.5% of Gelman and Rubin test for model (1)*

Parameter	Point est.	Upper C.I.
p	1.00	1.01
β_0	1.01	1.02
β_1	1.01	1.02

Figure 1: *Traceplots of β for model (2)*



Both diagnostics showed a good property of convergence of the MCMC chains.

7. Numerical results

Table 2: *Comparison of posterior means, 95% credible interval of β_1 and DIC's*

Model	$\hat{\beta}_1$	95% Set	DIC
Weibull	0.26	$[-0.30, 0.81]$	450.4
B-spline with degree$=1$	0.31	$[-0.26, 0.90]$	477.1
B-spline with degree$=2$	0.33	$[-0.22, 0.92]$	478.9
B-spline with degree$=3$	0.33	$[-0.24, 0.90]$	481.6

The Weibull model gave a posterior mean $\hat{\beta}_1 = 0.26$ with a 95% credible interval of $[-0.30, 0.81]$ suggesting no significant elevation in hazard for autologous transplant.
For semiparametric model using mixture of B-spline distributions, the transplant effect estimates were robust across the different degrees of baseline function and all methods gave the same conclusions with the Weilbull model.

8. Baseline hazard estimation

Figure 2: *Baseline hazards for the Weibull model and B-spline model with degree=1*

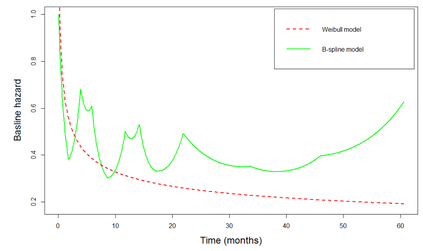


Figure 2 compares the baseline hazard functions for the parametric Weibull and the semiparametric mixtures of B-spline distributions with degree=1. The baseline hazard functions of B-spline model with degree 2 and 3 are not shown here because they have similar patterns with those of degree 1. The B-spline model is capable of providing more detailed information about the data. For example the estimated hazard drops at $t = 5, 10$ and 20 with the appearance of censored data during this periods.

9. Conclusions

- Neither model showed evidence that the autologous stem cell is more effective than the allogeneic. More criteria like the severity of the disease as well as the patient's age may be taken into account in further analysis.
- Although the weibull model has a better fit with DIC$=450.4$, where all the B-spine models have DIC's> 470, the baseline hazard in the B-spline models is no longer restricted to be monotone, adding flexibility to the model.
- Semiparametric model is useful when the baseline hazard is of great interest or when one would like to leave its shape largely unspecified.
- Further work may include trying different knots and finding more accurate and efficient numerical integration methods for model (2).