Analysis of Survival Data Using Hypertabastic Models

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Abstract

Bone under repetitive stress can lead to ‘stress’ fractures. Stress fractures in elderly people are an important issue due to the growing number of elderly in society and their activeness in that age. Fatigue tests on 23 female bone samples from three individuals were analyzed. Hypertabastic survival models are a parametric method for survival analysis and life testing. A hypertabastic survival probability function of the normalized stress level and age was developed using a previously published bone fatigue stress data (Cotton, et al., *J Biomechanics* 2003). The AIC measure was used to compare the fitness of hypertabastic, Weibull, and log-logistic models. Based on this measure for model selection, hypertabastic models were selected. A hypertabastic hazard function of normalized stress level and age was also derived. Furthermore, hypertabastic proportional hazard models were used to analyze the tensile fatigue and cycle-to-fatigue of cortical bone.

Introduction

Cortical bone is the dense outer surface of bone. It supports the human body and makes up 80% of the weight of human skeleton. It protects body organs and provides levers for movements. Osteoporosis can cause cortical bone to become porous and thinner. Bone under repetitive stress can lead to ‘stress’ fractures. Stress fractures in elderly people are an important issue due to the growing number of elderly in society and their activeness in that age. Female gender has been identified as a factor. It is important to study the accumulation of permanent strain and fatigue life in cortical bones. Fatigue tests on 23 female bone samples from three individuals were analyzed. Hypertabastic survival models consist of hypertabastic proportional hazards model, hypertabastic accelerated failure models and hypertabastic proportional odds models were all introduced by Tabatabai et al. [1] as a parametric method for survival analysis and life testing. Bursac et al. [2] analyzed the performance of hypertabastic models using massive simulation and compared them with classical models of life testing. Hypertabastic survival models are very useful in the analysis of time to event data in biosciences and bioengineering. Previously, we applied hypertabastic models to analyze breast cancer [3, 4], multiple myeloma and glioma data. Hypertabastic proportional hazards model has recently been used to analyze the survival of breast cancer patients, exploring the role of a metastasis in combination with clinical and gene expression variables [3]. The hypertabastic hazard function can take different shapes depending on the values of their parameters. The hazard function for hypertabastic survival models can be increasing, decreasing, increasing and then decreasing with possibility of concavity up or down. This is not the characteristic of many parametric survival models such as exponential, Weibull, log-logistic, or log normal hazard curves. Hypertabastic accelerated failure models have been successfully applied for modeling data on bridges in the state of Wisconsin [5]. The main interest was identifying the factors that influence the time until a bridge reaches stage 5 of federal ratings.

Materials and Methods

One novel application of hypertabastic models is in the analysis of fatigue life in cortical bones. Cortical bone or as it sometimes called compact bone is the compact outer layer of the bone shaft. The cortical bone supports the whole body, protects bone marrow, store and release chemicals. Cotton et al. [6] analyzed creep strain during tensile fatigue of cortical bone and examined the creep strain accumulation rate and its stress dependency. We analyzed their data on the cortical bone taken from three females only for illustrating the usefulness of the proposed model. The age levels of females were 53, 67 and 79. Fatigue tests on 23 female bone samples from three individuals were analyzed. In order to choose the method for the survival analysis of the cortical bone data, we first applied the Weibull, log-logistic, and hypertabastic models to the cortical bone data. Based on the AIC criterion, hypertabastic models had the best fit based on AIC statistic. Thus, we applied hypertabastic models to analyze the cortical bone data. We took into consideration the effect of increased stress and age on cortical bone fatigue life. The hypertabastic survival function for proportional hazards models has the form:

$$S= [\mathrm{sech}\,[a\,(1 - (Cycle)^{b}\coth\,[(Cycle)^{b})]/b]^{\mathrm{Exp}\,(c\,(Age)+d(\,NormalizedStress)\,)},$$

where the parameters a and b govern the shape of survival and hazard functions and c and d are associated with the two covariates age and normalized stress level. The sech[.] and coth[.] are hyperbolic secant and hyperbolic tangent functions respectively.

Results

The parameter estimates for c and d were 0.052 and 23.95 respectively and the corresponding p-values were 0.022 and <0.0001 respectively. For the females at the age 80, the mean number of cycles before fatigue in cortical bone at the normalized stress level of 0.0047 (This is the sample mean of normalized stress levels of our data) was estimated to be 1928.63 cycles. For the females at age 70, and 50, the number of cycles before cortical bone fatigue was 3338.81 and 10089 cycles respectively. The results show that at the same normalized level of stress, the number of cycle before the cortical bone fails decreases drastically as the person ages. It goes from a high of 10089 cycles at the younger age of 50 to a low number of 1928.63 cycles at the age of 80. The ratio of the number of cycles before fatigue in cortical bone for 50-year-old woman to 80 year-old-woman is approximately 5.2 , the ratio of cycles for 70-year-old to 80-year- old is 1.7 and the ratio of cycles for 50-year-old cycles to 70-year old is 3. The median number of cycles before the bone starts to show signs of fatigue (holding the normalized level at 0.0047) for ages 80, 70 and 50 are 5025.31, 8462.38 and 23996.70 respectively.

Figure 1 shows the survival probability functions as a function of the number of cycles. The solid curve represents the survival function at age of 80, the dashed survival curve is at age level 70 and the dashed –dotted curve is the survival probability curve for the 50-year-old women. By comparing graphs of survival curves, we clearly see the older women have lower probability of cortical bone fatigue under the same level of stress. Figure 2 shows the corresponding hazard curves as a function of the number of cycles for women at age levels 50, 70, and 80. The graphs clearly indicate that higher age women have significantly higher failure rates when compared to younger ones. Table 1 shows the survival probability for cortical bone at different cycle-age combinations while the normalized stress level is held constant at 0.0047.

Table 1:Survival probabilities for women as a function of age and the number of cycles

Age	Cycle=50	Cycle=500	Cycle=5000	Cycle=50000
50	0.9946	0.9435	0.5880	$1x10^{-4}$
60	0.9909	0.9067	0.4090	$4.3x10^{-4}$
70	0.9848	0.8480	0.2219	$2.1x10^{-6}$
80	0.9745	0.7576	0.0798	$2.8x10^{-10}$
90	0.9575	0.6266	0.0140	$8x10^{-17}$

As examination of table 1 reveals that when the number of cycles is 50000, the survival probability of cortical bone at age 50 or higher becomes almost zero. When we consider the survival probability function as a function of normalized stress level rather than the number of cycles, the mean normalized stress for the 80 year old to break is 0.0045 while the corresponding numbers for 70 and 50 year- old- women are 0.0047 and 0.0051 respectively. Figure 3 depicts the survival probability curves for 50, 70, and 80 year- old -women as a function of normalized stress level while holding the number of cycles at the level of 1688 (This is the median of the number of cycles for our sample). The survival probability curve as the function of normalized stress level for 80-year-old is lower than the 70 and 50-year-old individuals. Similarly, figure 4 shows the hazard curve as a function of the normalized stress level for 50, 70, and 80-year-old females while holding the number of cycles at constant level of 1688. The results indicate that 80

-year-old have the highest failure curve when compared to 70 and 50-year-old women. For instance, at the normalized stress level of 0.0047 and cycle level of 2000, the failure rates for 50, 70 and 80-year olds are 4.933, 13.989 and 23.556 respectively. The failure rate for 80-year-old woman is 4.8 times higher when compared with 50-year-old woman and 1.7 times when we compared with 70 year-old women. Figure 5 is a 3-D graph of survival probability as a function of both normalized stress level and the number of cycles at age levels of 20, 50, and 80.

Conclusion

By examining the results, and for this cortical bone data, we can clearly conclude that the survival probability increases as we reduce the stress level on the bone. Age is a major factor in the survivability of cortical bone when it comes to fatigue. As the individual ages, the fatigue probability of cortical bone increases drastically. Also, the number of cycles before the cortical bone shows sign of fatigue decreases with age. It takes a lower number of cycles for an older woman bone to fracture when compared to the younger ones. We have also noticed that reducing the stress level will increase the survival probability across all age groups. We have also observed that lowering the stress level will result in lower failure rates.

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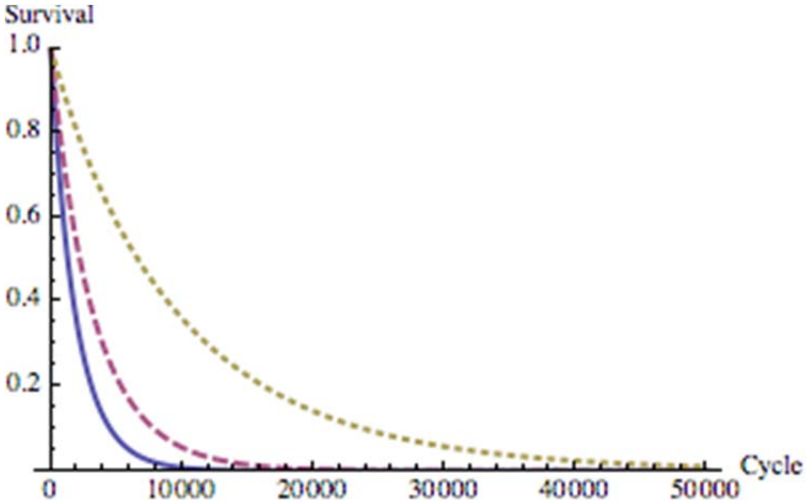

Figure 1. Survival probability curves for women with ages 50, 70, and 80 at the normalized stress level of 0.0044.

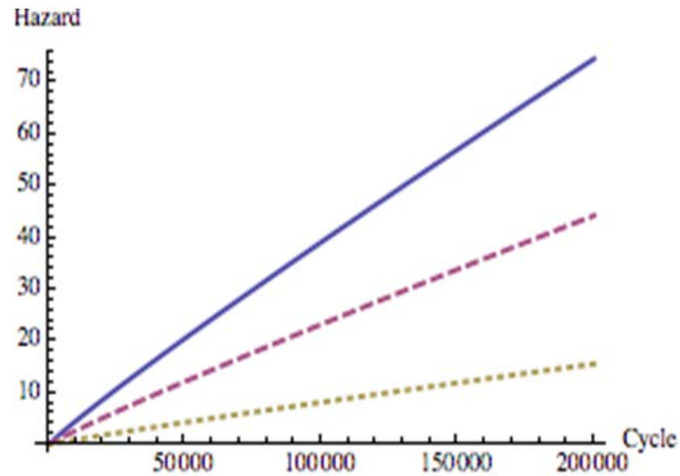

Figure 2. Hazard (failure rate) curves for women with ages 50, 70, and 80 at the normalized stress level of 0.0044.

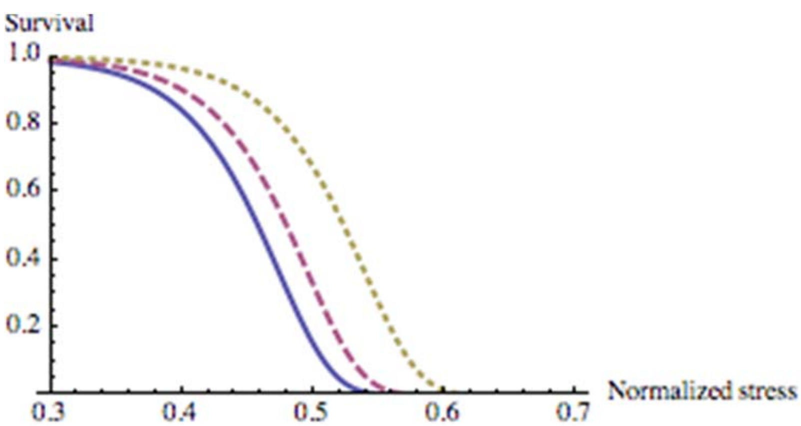

Figure 3. Survival probability curves for women with ages 50, 70, and 80 as a function of normalized stress level while holding cycle level at 1688.

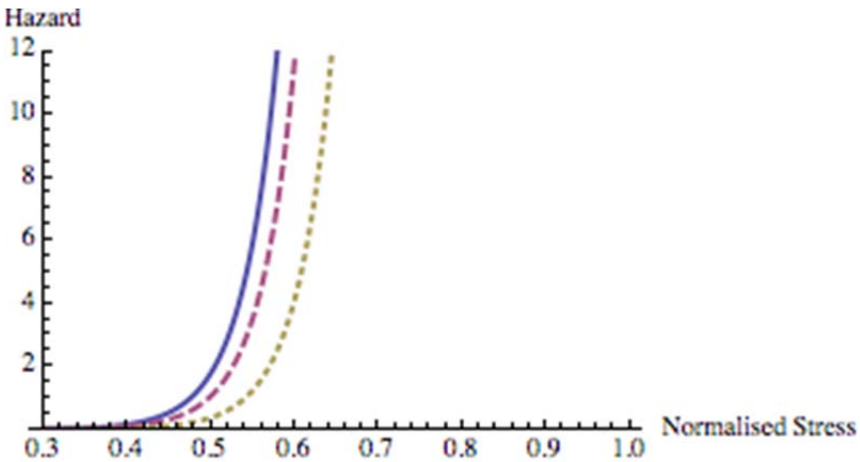

Figure 4. Hazard curves for women with ages 50, 70, and 80 as a function of normalized stress level while cycle level held at 1688.

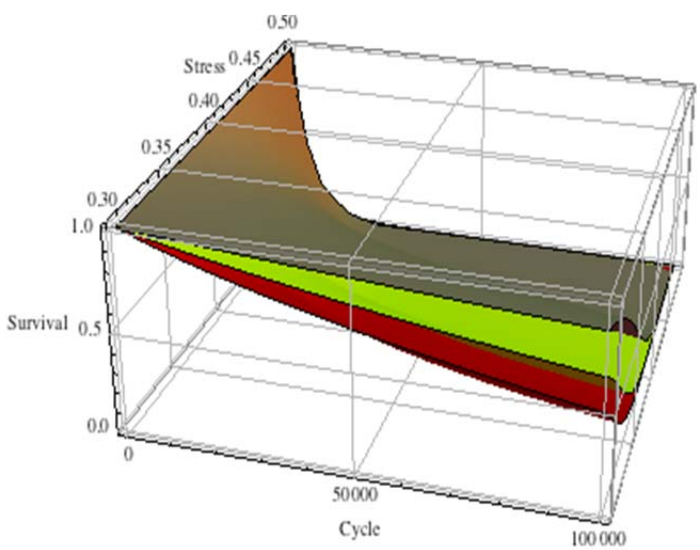

Figure 5. 3D survival graphs curves for women with ages 50, 70, and 80 as a function of the number of cycles and the normalized stress level.