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Post-Transplant Survival Estimation Using Preoperative Albumin Levels

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Abstract

Background—Hypoalbuminemia has been recognized as a prognostic indicator in patients with heart failure. We recently reported a strong association between pre-operative albumin level and post-operative outcomes in patients undergoing ventricular assist device implant as well as those undergoing heart transplant (HTx). The purpose of this study was to create a post-transplant survival probability equation based on preoperative albumin concentration using parametric survival model.

Methods—Pre-operative albumin concentration and post-transplant survival data were obtained from 822 consecutive patients undergoing HTx at Columbia University Medical Center between 1999 and 2010. Available data from the United Network of Organ Sharing (UNOS) (n=13,671) was also analyzed.

Results—Parametric survival estimation model based on our institutional data showed that preoperative albumin concentration (Alb) alone can allow us to estimate survival probability (S) at post-transplant day (t), indicated S(t), by the following formula; $\lambda=\exp(-6.46455-0.580872\times Alb)$, $S(t)=\exp(-\lambda \times t)$. The survival probabilities of patients with an Alb of 3.0, 3.5 and 4.0 mg/dL at 2000 days post-HTx were 58.0, 66.5, and 73.7%, respectively. Based on the UNOS data, we can create the formula as; $\lambda=\exp(-8.22281-0.106462\times Alb)$, $S(t)=\exp(-\lambda \times t)$.

Conclusions—Pre-transplant serum albumin level is a useful marker to estimate post-transplant survival.

Keywords

Heart transplantation; albumin; survival

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Disclosure

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

Hypoalbuminemia has been recognized as a marker of poor outcomes in patients with chronic diseases including those with advanced heart failure. We recently reported that pre-operative hypoalbuminemia is associated with poor prognosis following LVAD surgery, although post-operative normalization of albumin level would improve their survival [1]. We also reported that pre-transplant serum albumin concentration is a strong prognostic marker for 1-year post-transplant survival in heart transplant (HTx) recipients [2]. However, an association between pre-transplant serum albumin and long-term outcome in HTx recipients has not yet been fully elucidated. In the present investigation, we aimed to create a post-transplant survival probability equation based on a preoperative albumin level using parametric survival model to estimate survival reflecting multiple factors such as nutrition, inflammation, hepatic function and overall catabolic state.

We reviewed a total of 822 consecutive patients undergoing HTx at Columbia University Medical Center between 1999 and 2010. Pre-transplant clinical data including serum albumin concentration were obtained. For patients with multiple laboratory measurements prior to the transplants, the results obtained at the closest date to the surgery were used for the analysis. A parametric model of survival using an arbitrary value of albumin was analyzed and a formula to estimate survival provability based on pre-transplant albumin value was created. We also analyzed an available data from the United Network of Organ Sharing (UNOS). Patients with available albumin levels before HTx were selected for the current study (n=13,671). In the same manner, a parametric survival estimation formula was created based on the UNOS data. Survival probability of S(t) and the moment mortality of λ were determined by a parametric analysis as follows;

$$S(t)=\exp(-\lambda t);\ \lambda=\exp(\beta 0+\Sigma \beta j x j)$$

β0, constant number; βj, partial regression coefficient of covariable xj.

Univariate parametric analysis for post-transplant mortality based on our institutional data revealed that an serum albumin value before transplant (mg/dL) was associated with a hazard ratio (HR) of 0.559 with 95% confidence interval (CI) ranged from 0.453 to 0.689. Multivariate analysis including pre-and peri-operative parameters revealed the strongest association between pre-operative albumin level and post-transplant mortality (HR 0.540, 95%CI 0.421–0.693, $p<0.00001$) followed by pre-operative total bilirubin concentration (mg/dL) and donor age (years) (HR 1.297, 95%CI 1.166–1.444, $p<0.0001$; HR 1.011, 95% CI 1.000–1.022, $p=0.0464$, respectively). A survival probability of post-transplant day S(t) in patients with an albumin value of 'Alb (mg/dL)" was calculated by the following formula: $\lambda=\exp(-6.46455-0.580872\times Alb)$, $S(t)=\exp(-\lambda \times t)$. This formula indicates that the survival probabilities at post-operative day 2000 of a patient with pre-operative albumin of 3.0, 3.5 and 4.0 mg/dL were 58.0, 66.5, and 73.7%, respectively (Figure 1).

Univariate parametric analysis based on the UNOS dataset revealed that pre-transplant serum albumin levels were associated with post-transplant mortality with a HR of 0.899 (95% CI 0.865–0.934). The survival probability at post-transplant day S(t) was calculated using the following formula:$\lambda=\exp(-8.22281-0.106462\times Alb)$, $S(t)=\exp(-\lambda \times t)$. This formula indicates that the survival probabilities at post-operative day 2000 of a patient with pre-operative albumin of 3.0, 3.5 and 4.0 mg/dL calculate to 67.7, 69.1 and 70.4 %,

respectively (Figure 2). The value of βj (partial regression coefficient) based on the UNOS dataset was −0.106462; this absolute value was smaller than the βj derived from our single center cohort which was −0.580872. Therefore, the contribution of pre-transplant albumin levels to post-transplant mortality based on an analysis of the UNOS dataset was smaller than that based on our single center database.

We previously demonstrated pre-transplant hypoalbuminemia is a predictor for 1-year post-transplant survival [2]. The death after HTx occurs most frequently within one year after transplant [3]. The pre-transplant condition of patients has the most significant impact on the post-transplant prognosis in the early post-operative phase rather than in the chronic phase. However, in the present paper, we show a clear association between pre-transplant albumin levels and overall (long-term) post-transplant survival and that pre-transplant albumin levels alone enables us to estimate a patient's post-transplant survival at a certain post-transplant duration. We admit that the numbers of patients and available data were different between the two analyses we performed. Our institutional analysis was based on 822 consecutive transplant recipients, and UNOS analysis was based on 13,671 patients (31.9%) with albumin data available for a total of 42,803 patients who underwent transplant between October 1987 and February 2010. The UNOS dataset is based on self-reported, transplant center-specific data provided to the UNOS data collection center. Unfortunately, for many patients without pre-operative albumin data in the UNOS database, data on other laboratory values were missing as well. Therefore, the analysis based on the UNOS dataset does not represent the entire cohort of transplant recipients, which may be a reason for differences in the relationships between albumin and survival derived from our institutional dataset and the UNOS dataset. Nevertheless, we can successfully show an association between pre-transplant low serum albumin levels and higher mortality in strictly linear and incremental manners in both analyses.

In conclusion, prediction model using pre-transplant albumin alone allows estimation of post-transplant survival. Pre-transplant albumin is useful in discussing post-transplant prognosis of a possible transplant candidate, which will be important information when considering his or her transplant eligibility.

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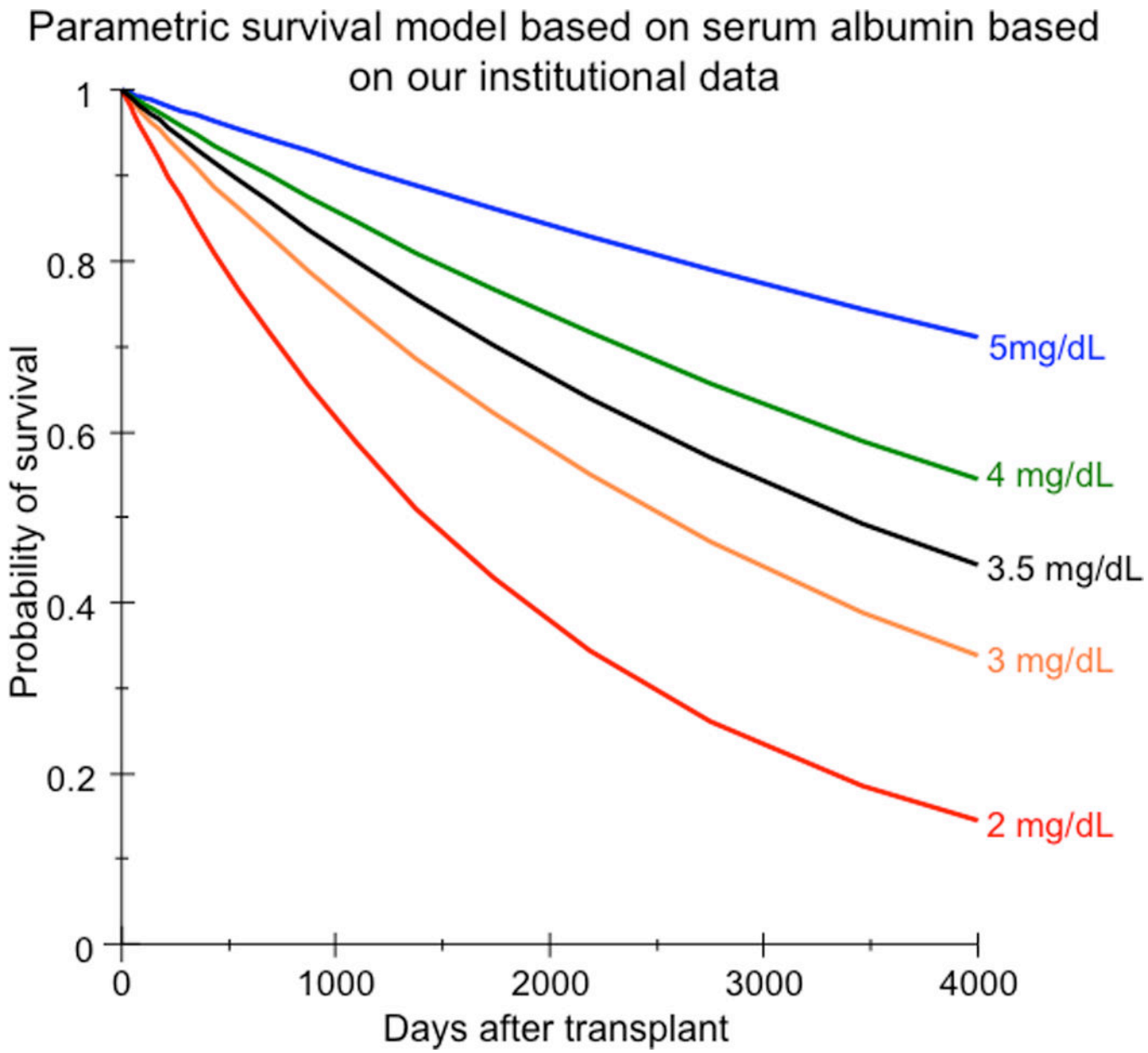

Figure 1. Post-transplant survival probability curve using parametric analysis based on our institutional data with a pre-operative albumin value as a reference

Patients with pre-operative albumin at 5 mg/dL (blue line), 4mg/dL (green line), 3.5mg/dL (black line), 3mg/dL (orange line), and 2.5mg/dL (red line) were shown in the graph. Survival probability at day t ; $S(t)=\exp(-\lambda t)$, Moment mortality: $\lambda=\exp(-6.46455-0.580872\times\text{albumin})$, therefore if albumin in 3.5 mg/dL, $\lambda=\exp(-6.46455-0.580872\times3.5)=0.0002039569$, then the survival probability of this patient at day 2000 is $S(2000)=\exp(-0.0002039569\times2000)=0.6650362$ (approximately 67%). In a similar manner, for a patient with albumin 2.5 mg/dL, S(2000) is 48.2% and a patient with albumin 4.5 mg/dL, S(2000) is 79.6%.

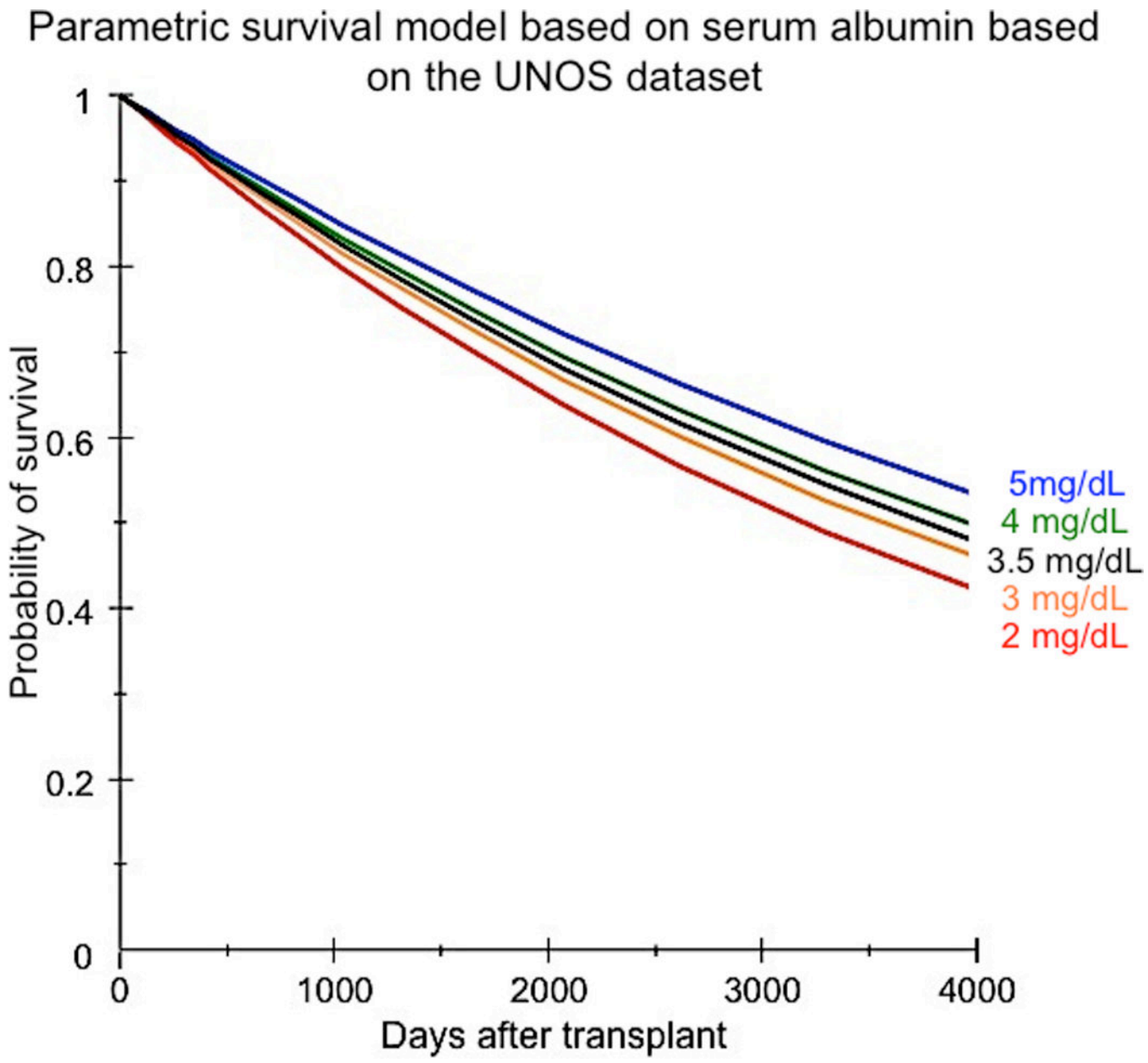

Figure 2. Post-transplant survival probability curve using parametric analysis based on UNOS data with a pre-operative albumin value as a reference

Patients with pre-operative albumin at 5 mg/dL (blue line), 4mg/dL (green line), 3.5mg/dL (black line), 3mg/dL (orange line), and 2.5mg/dL (red line) were shown in the graph. Survival probability at day t ; S(t)=exp(-λt), Moment mortality: λ=exp(−8.22281–0.106462×Alb). The survival probability of a patient with albumin 3.0 mg/dL at day 2000 showing S(2000)=82.3%, a patient with albumin 2.5 mg/dL at day 2000 showing S(2000)=66.3%, and a patients with albumin 4.5 mg/dL at day 2000 showing S(2000)=71.7%.