Survival Analysis applied to Continuous Ambulatory Peritoneal Dialysis (CAPD) and Hemodialysis (HD) Data

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Abstract

A survival analysis was performed over 246 patients on CAPD and 140 patients on HD that followed a dialysis program between the years 1980 and 2000 on the dialysis service of the Division of Nephrology in the Hospital Universitario de Caracas and on the unit of Hemodialysis of the Hospital de Clinicas Caracas, Venezuela. To perform the survival analysis two (2) censoring variables were used: death and dropout associated with medical reasons. Several Cox's Proportional Hazard Models were performed to model survival with combinations of type of dialysis and censoring type to find significant predictor selected from several continuous and dichotomous covariates. The best models are presented and analysed according to the "state of art" techniques on survival analysis. Adequacies of the models were verified using the methods based on counting processes: Residuals and testing proportional hazard. A competing risk analysis with several dropout causes is also performed.

1. Introduction

Applications of survival analysis in dialysis are not a new issue. However, many of them are limited to estimation of survival or hazard functions and adjusting regression model to find predictor of mortality and hazard ratios, some of these papers are Maiorca et al. (1988, 1991), Held et al. (1993), and Maggiore et al. (1996).

The counting process approach to survival analysis (Fleming and Harrington 1991, Andersen et al. 1993) has extended the possibilities of the survival models. Therneau et al. (1990) introduced some martigale-based residuals for survival analysis, these residuals have been incorporated in commercial software from a few year ago (Therneau and Grambsch, 2000).

The purpose of this paper is to present a survival analysis based on a classical analysis and on the verification of the assumptions of the regression model based on the newest techniques available.

2. Data

The data that was analysed corresponds to 246 patients on continuous ambulatory peritoneal dialysis (CPAD) on the Service of the Division of Nephrology of the Hospital Universitario de Caracas and to 140 patient on the unit of hemodialysis (Hd) of the Hospital de Clinicas Caracas, Venezuela. Patients were followed from the beginning of their dialysis up to the ocuurence of some of the following events of interest: Their death by causes associated with the dialysis or dropout by medical reasons associated with the dialysis. Because in not all the patients the occurrence of some of the events was observed during the follow up period, some of the observations are censored.

The follow up period of the patients on CPAD was from 1980 to 1997. In this kind of dialysis 100 dichotomous an 16 continuous covariates were considered.

The period for HD patients was from 1986 to 2000. For HD 86 dichotomous and one continuous covariates were included.

The survival analysis was performed defining the events of interest: Death by causes associated with the dialysis, dropout by medical reasons associated with the dialysis, and a combination of death and dropout.

3. Statistical analysis

The survival analysis was performed for each type of dialysis and event of interest. Estimations of the survival function were obtained using the Kaplan-Meier estimator (Kaplan and Meier 1958). Several Cox's model (Cox 1972) were used to identify the significant covariates, these models were obtained using a stepwise approach. With the final model in each case the assumptions of the model were verified according to Therneau and Grambsch (2000). In the cases that a violation of the proportional hazard was detected, stratified model were used.
Competing risk model were also obtained using both events of interest: Death and dropout.
The analysis was performed using S-PLUS for Windows.

4. Results

The results for the combination of type of dialysis Cox's models and for the competing risk model is presented in the following sections.

4.1 Cox's models for CPAD

The Cox's models adjusting for CPAD are presented in table 1. In all these models the significance for at least 10% and assumptions of the model were verified in each of the models.

Table 1. Cox's models for CPAD

Event	Model	Covariates	Coefficient	p-value
Death	1	Age	0.0315	0.0011
		Quetelet index	-0.0969	0.013
		Diabetes	0.5492	0.087
Dropout *	1	Heart disease	1.1214	0.0039
		Weight	-0.0153	0.05
	2	Heart disease	1.117	0.0039
		Body surface	-0.997	0.043
Death or Dropout *	1	Heart disease	0.669	0.057
	2	Diabetes	0.376	0.078
	3	Quetelet index	-0.0345	0.094

* Model stratified by high blood pressure

4.2 Models for HD

The Cox's models adjusting for HD are presented in table 2. In all these models the significance for at least 10% and assumptions of the model were verified in each of the models.

Table 2. Cox's models for HD

Event	Model	Covariates	Coefficient	p-value
Death	1	Ischaemic heart disease	0.903	0.01
		Age	0.03	0.014
	2	Ischaemic heart disease	1.129	0.00014
		Congestive cardiac failure	0.923	0.06
Dropout	1	Heart disease	-0.764	0.092
	2	Sex	-0.773	0.066
Death or Dropout	1	Ischaemic heart disease	0.673	0.0039

4.3 Competing risk models

The competing risk model for CPAD and HD are presented in table 3, in both models death is competing with dropout. Both models were significant for at least 5% by the Wald and robust score test, likelihood and score test can not be used in this context. The assumptions of the models were also verified

Table 3. Competing risk models

Type of dialysis	Covariates	Coefficient	p-value
CPAD *	Chronic Hepatitis C	-0.7742	0.01
	Heart disease	0.7109	0.014
	Quetelet index	-0.0455	0.048
HD	Ischaemic heart disease	0.603	0.013
	Congestive cardiac failure	0.734	0.026

* Stratified model by high blood pressure

5. Graphical verification of the assumptions of the models

The verification of the assumptions of the regression model were done using graphical display, these graphics are not presented in this paper and would be presented at the conference.

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