Записки научных
семинаров ПОМИ
Том 294, 2002 г.

V. Bagdonavičius, M. A. Hafdi, K. E. Himdi, M. Nikulin

STATISTICAL ANALYSIS OF THE GENERALISED LINEAR PROPORTIONNAL HAZARDS MODEL

Abstract.

We analyze the finite sample properties of the modified partial likelihood estimators of the parameters of the generalised proportionnal hazards model by simulation. A goodness-of-fit test for the proportional hazards model against the GPH model is proposed. The lung cancer data are analyzed.

1. Introduction

Let $T_{x(\cdot)}$ be the failure moment under a covariate $x(\cdot) = (x_1(\cdot), \dots, x_m(\cdot))^T$ with the survival function $S_{x(\cdot)}(t)$, the hazard rate $\lambda_{x(\cdot)}(t)$, and the cumulative hazard

$$\Lambda_{x(\cdot)}(t) = \int_0^t \lambda_{x(\cdot)}(u)du = -\log(S_{x(\cdot)}(t)) \quad t \geq 0.$$

We consider the generalised proportional hazards(GPH) model (Bagdonavičius and Nikulin, 1999). It holds on a set of covariates E if for any $x(\cdot) \in E$ the hazard rate at the moment t depends not only on the values of the covariates at this moment but also on the past expressed by the cumulative hazard, i.e.,

$$\lambda_{x(\cdot)}(t) = r\{x(t)\}q\{\Lambda_{x(\cdot)}(t)\}\lambda_0(t),$$

where r and q are positive functions and λ_0 is the baseline hazard rate. In the case $q(t) \equiv 1$ we have the proportional hazards model (Cox, 1972). By $S_0(t)$ and

$$\Lambda_0(t) = \int_0^t \lambda_0(u)du = -\log(S_0(t))$$

we denote the baseline survival function and the baseline cumulative hazard, respectively.

Various parametrizations of r and q give various submodels of the GPH model. In this paper we restrict ourselves to the following parametrisation:

$$r(u) = e^{\beta^T u} \quad \text{and} \quad q(t) = e^{\gamma t}.$$

In this case the GPH model is called the generalized linear proportional hazards (GLPH) model:

$$\lambda_{x(\cdot)}(t) = e^{\beta^T x(t) + \gamma \Lambda_{x(\cdot)}(t)} \lambda_0(t). \tag{1}$$

In the following chapters we give the formulation of the estimation procedure (Bagdonavičius and Nikulin, 1999), we present a goodness-of-fit test for the proportional hazards model against the GPH model, and we give some simulation results. The simulations were programmed using the language S-plus. An application for the real data is given in Sec. 4.

2. Formulation of the semiparametric estimation procedure

Suppose that n individuals are observed under the covariates $x^{(1)}(\cdot), \ldots, x^{(n)}(\cdot)$. Let T_i and C_i be the failure and censoring times of the ith individual. Set $L_i = \min(T_i, C_i)$ and $\delta_i = \mathbf{1}_{\{L_i = T_i\}}$, where $\mathbf{1}_E$ is the indicator of the set E. Set also

$$N(t) = \sum_{i=1}^{n} N_i(t), \quad Y(t) = \sum_{i=1}^{n} Y_i(t),$$

with $N_i(t) = \mathbf{1}_{\{T_i \le t, \delta_i = 1\}}$ and $Y_i(t) = \mathbf{1}_{\{L_i \ge t\}}$. Let $\Gamma = \{\mathcal{F}_t, t \ge 0\}$ be the filtration, where $\mathcal{F}_t$ is the σ-algebra generated by $N_i(u), Y_i(v), 0 \le u \le t$. Suppose that the Γ-compensators A_i of N_i are absolutely continuous with the intensities α_i satisfying the multiplicative model:

$$\alpha_i(t) = \lambda_{x_i(\cdot)}(t) Y_i(t), \quad i = 1, \ldots, n.$$

Suppose also that all failure and censoring processes are censored at the moment τ.

Bagdonavičius and Nikulin (1999) proposed the modified partial likelihood (M.P.L.) function:

$$\widetilde{L}(\theta) = \prod_{i=1}^{n} \left[\int_0^{\tau} \frac{e^{\beta^T x_i(v) + \gamma \widetilde{\Lambda}_i(v,\theta)}}{\sum_{j=1}^{n} Y_j(v) e^{\beta^T x_i(v) + \gamma \widetilde{\Lambda}_i(v,\theta)}} \, dN_i(v) \right]^{\delta_i}, \tag{2}$$

where $\theta = (\beta^T, \gamma)^T$,

$$e^{-\gamma \widetilde{\Lambda}_i(t,\theta)} = 1 - \gamma \int_0^t e^{\beta^T x_i(u)} d\widetilde{\Lambda}_0(u,\theta),$$

and $\widetilde{\Lambda}_0(t,\theta)$ is obtained recursively from the equation

$$\widetilde{\Lambda}_0(t,\theta) = \int_0^t \left(\sum_{i=1}^n \frac{Y_i(u) e^{\beta^T x_i(u)}}{1 - \gamma \int_0^{u-} e^{\beta^T x_i(u)} d\widetilde{\Lambda}_0(v,\theta)} \right)^{-1} dN(u).$$

The maximum partial likelihood estimator $\widehat{\theta}$ of

$$\theta = (\theta_1, \ldots, \theta_{m+1})^T = (\beta_1, \ldots, \beta_m, \gamma)^T$$

maximizes (2).

Theorem 2.1. *Let θ_0 be the exact value of the parameter θ. Under regularity conditions (Bagdonavičius and Nikulin, 1999) and the* GPH *model the sequence $n^{1/2}(\widehat{\theta} - \theta_0)$ converges in distribution to the zero mean normal law.*

3. Goodness-of-fit for the PH model

Let us consider the PH model against the GLPH model :

$$\begin{aligned} &H_0 : \lambda_{x(\cdot)}(t) = e^{\beta^T x(t)} \lambda_0(t) \quad \text{against} \\ &H_1 : \lambda_{x(\cdot)}(t) = e^{\beta^T x(t) + \gamma \Lambda_{x(\cdot)}(t)} \lambda_0(t), \quad (\gamma \neq 0). \end{aligned} \tag{3}$$

3.1. Test statistic.

If the baseline cumulative hazard Λ_0 is completely known then the model (1) is parametric and the maximum likelihood estimator of the parameter θ is obtained maximizing (2). So it satisfies the system of equations :

$$U_j(\tau; \theta, \Lambda_0) = \frac{\partial \log \widetilde{L}(\theta)}{\partial \theta_j} = 0, \quad (j = 1, \cdots, m+1),$$

where

$$U_j(t; \theta, \Lambda_0) = \sum_{i=1}^n \int_0^t \frac{\partial}{\partial \theta_j} \log\{\lambda_i(t,\theta)\}\{dN_i(u) - Y_i(u)\lambda_i(u,\theta) du\}.$$

Note that if Λ_0 is unknown, then

$$w_j^{(i)}(t,\theta,\Lambda_0) = \frac{\partial}{\partial\theta_j}\log\{\lambda_i(t,\theta)\} = \begin{cases} x^{(i)}(t), & j=1,\dots,m, \\ \Lambda_i(t,\theta), & j=m+1, \end{cases}$$

and $w_{m+1}^{(i)}(t,\theta,\Lambda_0)$ depends on a finite dimensional parameter $\theta = (\beta^T,\gamma)^T$ and a infinite dimensional Λ_0. Under PH model $\gamma = 0$.

Let

$$\widehat{U}_j = \widehat{U}_j(\tau), \quad \text{where} \quad \widehat{U}_j(t) = U_j(t,(\widehat{\beta}^T,0)^T,\widehat{\Lambda}_0),$$

where $\widehat{\beta}$ is the partial likelihood estimator of the regression parameter β and $\widehat{\Lambda}_0$ is the Breslow (1975) estimator of Λ_0 under PH model.

Note that under PH model

$$\widehat{U}_j = 0, \quad (j=1,\cdots,m)$$

and

$$\widehat{U}_{m+1}(t) = \sum_{i=1}^n \int_0^t \widehat{w}_{m+1}^{(i)}(u)d\widehat{M}_i(u), \tag{4}$$

where $\widehat{M}_i(t)$ are the martingale residuals corresponding to the PH model:

$$\widehat{M}_i(t) = N_i(t) - \int_0^t Y_i(u)\,e^{\widehat{\beta}^T x^{(i)}(u)}d\widehat{\Lambda}_0(u) =$$

$$= N_i(t) - \int_0^t Y_i(u)\,e^{\widehat{\beta}^T x^{(i)}(u)}\frac{dN(u)}{S^{(0)}(u,\widehat{\beta})},$$

$$S^{(0)}(t,\beta) = \sum_{i=1}^n Y_i(t)\,e^{\beta^T x^{(i)}(t)},$$

$$\widehat{w}_j^{(i)}(t) = w_j^{(i)}(t,(\widehat{\beta}^T,0)^T,\widehat{\Lambda}_0) = \int_0^t e^{\widehat{\beta}^T x^{(i)}(u)}d\widehat{\Lambda}_0(u).$$

If $x^{(i)} = \text{const}$, then $w_j^{(i)}(t) = e^{\widehat{\beta}^T x^{(i)}}\widehat{\Lambda}_0(t)$.

The test is based on the statistics

$$\widehat{U} = \widehat{U}_{m+1}(\tau). \tag{5}$$

To construct a test, we need the asymptotic distribution of $\widehat{U}$ under the PH model.

3.2. Asymptotic properties of the test statistics. Set

$$\widehat{w}^{(i)}(t) = \widehat{w}^{(i)}_{m+1}(t), \quad S^{(1)}(t,\beta) = \sum_{i=1}^{n} x^{(i)}(t) Y_i(t)\, e^{\beta^T x^{(i)}(t)},$$

$$S^{(2)}(t,\beta) = \sum_{i=1}^{n} (x^{(i)}(t))^{\otimes 2} Y_i(t)\, e^{\beta^T x^{(i)}(t)},$$

$$E(t,\beta) = \frac{S^{(1)}(t,\beta)}{S^{(0)}(t,\beta)}, \quad \widetilde{S}^{(1)}(t,\beta) = \sum_{i=1}^{n} \widehat{w}^{(i)}(t) Y_i(t)\, e^{\beta^T x^{(i)}(t)},$$

$$\widetilde{E}(t,\beta) = \frac{\widetilde{S}^{(1)}(t,\beta)}{S^{(0)}(t,\beta)}, \quad \widetilde{S}^{(2)}(t,\beta) = \sum_{i=1}^{n} \widehat{w}^{(i)}(t) (x^{(i)}(t))^T Y_i(t)\, e^{\beta^T x^{(i)}(t)},$$

$$\tilde{\tilde{S}}^{(2)}(t,\beta) = \sum_{i=1}^{n} (\widehat{w}^{(i)}(t))^{\otimes 2} Y_i(t)\, e^{\beta^T x^{(i)}(t)},$$

where $a^{\otimes 2} = aa^T$ for all vector $a = (a_1, \dots, a_m)^T$. Denote the true value of β by β_0.

Under usual regularity conditions the Doob–Meier decomposition, delta method and the following development

$$n^{1/2}(\widehat{\beta} - \beta_0) =$$

$$\Sigma^{-1}(\beta_0) \sum_{i=1}^{n} \int_0^{\tau} \{x^{(i)}(u) - E(u,\beta_0)\} dM_i(u) + o_p(1)$$

imply that

$$n^{-1/2}\widehat{U}(t) = n^{-1/2} \sum_{i=1}^{n} \int_0^{t} \{\widehat{w}^{(i)}(u) - \widetilde{E}(u,\widehat{\beta})\} dN_i(u) =$$

$$n^{-1/2} \sum_{i=1}^{n} \int_0^{t} \{\widehat{w}^{(i)}(u) - \widetilde{E}(u,\widehat{\beta})\} dM_i(u) +$$

$$n^{-1/2} \int_0^{t} \{\widetilde{E}(u,\beta_0) - \widetilde{E}(u,\widehat{\beta})\} S^{(0)}(t,\beta_0) d\Lambda_0(u) =$$

$$n^{-1/2}\sum_{i=1}^{n}\int_{0}^{t}\{\widehat{w}^{(i)}(u)-\widetilde{E}(u,\beta_0)\}dM_i(u)-$$

$$n^{-1}\int_{0}^{t}\frac{\partial\widetilde{E}(u,\beta_0)}{\partial\beta}S^{(0)}(u,\beta_0)d\Lambda_0(u)\,n^{1/2}(\widehat{\beta}-\beta_0)+o_p(1)=$$

$$n^{-1/2}\sum_{i=1}^{n}\int_{0}^{t}\{\widehat{w}^{(i)}(u)-\widetilde{E}(u,\beta_0)\}dM_i(u)-$$

$$\Sigma^*(t)\Sigma^{-1}(\tau)n^{-1/2}\sum_{i=1}^{n}\int_{0}^{\tau}\{x^{(i)}(u)-E(u,\beta_0)\}dM_i(u)+o_p(1), \quad (6)$$

where $\Sigma(t)$ and $\Sigma^*(t)$ are respectively the limits in probability of the random matrices

$$\widehat{\Sigma}(t)=n^{-1}\int_{0}^{t}V(u,\widehat{\beta})dN(u)\ \ and\ \ \widehat{\Sigma}^*(t)=n^{-1}\int_{0}^{t}\widetilde{V}(u,\widehat{\beta})dN(u),$$

with

$$\begin{aligned} V(t,\beta) &= \frac{S^{(2)}(t,\beta)}{S^{(0)}(t,\beta)}-(E(t,\beta))^{\otimes 2}, \\ \widetilde{V}(t,\beta) &= \frac{\widetilde{S}^{(2)}(t,\beta)}{S^{(0)}(t,\beta)}-\widetilde{E}(t,\beta)E^T(t,\beta). \end{aligned} \quad (7)$$

So,

$$< n^{-1/2}\widehat{U} > (t) =$$

$$n^{-1}\sum_{i=1}^{n}\int_{0}^{t}\{\widehat{w}^{(i)}(u)-\widetilde{E}(u,\beta_0)\}^{\otimes 2}e^{\beta_0^T x^{(i)}(u)}Y_i(u)d\Lambda_0(u)-$$

$$2\Sigma^*(t)\Sigma^{-1}(\tau)n^{-1}\sum_{i=1}^{n}\int_{0}^{t}\{\widehat{w}^{(i)}(u)-\widetilde{E}(u,\beta_0)\}\{x^{(i)}(u)-E(u,\beta_0)\}^T e^{\beta_0^T x^{(i)}(u)}\times$$

$$Y_i(u)d\Lambda_0(u)+\Sigma^*(t)\Sigma^{-1}(\tau)n^{-1}\sum_{i=1}^{n}\int_{0}^{\tau}\{x^{(i)}(u)-E(u,\beta_0)\}^{\otimes 2}e^{\beta_0^T x^{(i)}(u)}\times$$

$Y_i(u)d\Lambda_0(u)\Sigma^{-1}(\tau)(\Sigma^*(t))^T + o_p(1) = \Sigma^{**}(t) - \Sigma^*(t)\Sigma^{-1}(\tau)(\Sigma^*(t))^T + o_p(1),$

where $\Sigma^{**}(t)$ is the limit in probability of

$$\widehat{\Sigma}^{**}(t) = n^{-1}\int_0^t \tilde{\tilde{V}}(u,\widehat{\beta})dN(u)$$

with

$$\tilde{\tilde{V}}(u,\beta) = \frac{\tilde{\tilde{S}}^{(2)}(t,\beta)}{S^{(0)}(t,\beta)} - \left(\widetilde{E}(t,\beta)\right)^{\otimes 2}. \tag{8}$$

Similarly, the Lindeberg condition (see Andersen et al. (1993))

$$n^{-1}\sum_{i=1}^n \int_0^\tau \{\widehat{w}_j^{(i)}(u) - \widetilde{E}_j(u,\beta_0)\}^2 \mathbf{1}_{\{|\widehat{w}_j^{(i)}(u)-\widetilde{E}_j(u,\beta_0|\geq\sqrt{n}\varepsilon\}} e^{\beta_0^T x^{(i)}} Y_i(u)d\Lambda_0(u) \xrightarrow{P} 0$$

is verified. That shows that the stochastic processus $n^{-1/2}\widehat{U}$ converge in distribution to a zero mean Gaussian process, in particular

$$n^{-1/2}\widehat{U} \xrightarrow{\mathcal{D}} N(0,D),$$

where $D = \Sigma^{**}(\tau) - \Sigma^*(\tau)\Sigma^{-1}(\tau)(\Sigma^*(\tau))^T$.

3.3. Test.

To test H_0, we shall construct the chi-squared type test (see, for example, Bagdonavičius & Nikulin (2002) and Greenwood & Nikulin (1996)). We consider the chi-squared test with approximate signification level α, based on the critical region

$$T > \chi^2_{1-\alpha}(1),$$

where

$$T = n^{-1}\widehat{U}^2\widehat{D}^{-1}, \quad \widehat{D} = \widehat{\Sigma}^{**}(\tau) - \widehat{\Sigma}^*(\tau)\widehat{\Sigma}^{-1}(\tau)(\widehat{\Sigma}^*(\tau))^T. \tag{10}$$

4. Algorithm and simulation results

For simulations, $\Lambda_0(t) = a\,t^b$ is fixed, the covariate x is dichotomous with 1 and 0 values, or is Uniform$(0,1)$ distributed. The censoring times C_x are constant, $C_x = c$, Exponential(λ) or Uniform$(0,d)$ distributed.

The parameters d, λ and c are chosen depending on the censoring probability.

The finite sample properties of the estimators were investigated using 1000 simulations for each concrete situation. The values (1,-1) and (1,1) of β were taken. The results are given in the following tables.

4.1. Dichotomous covariates.

Table 1: $C_{x(\cdot)} \sim Uniform(0,d)$.

		$\beta=1$	$\gamma=-1$	$\beta=1$	$\gamma=1$
n	p	$\widehat{\beta}$	$\widehat{\gamma}$	$\widehat{\beta}$	$\widehat{\gamma}$
100	0	1.195 (2.2223)	− 0.911 (2.4874)	1.173 (0.7584)	0.944 (0.3384)
	0.2	1.347 (2.7958)	− 1.138 (4.4658)	1.189 (0.7909)	0.840 (4.7047)
200	0	1.078 (1.3487)	− 0.781 (1.7242)	1.095 (0.8514)	1.053 (0.3134)
	0.2	1.204 (1.7077)	− 0.896 (2.0533)	1.117 (0.7517)	0.979 (0.4037)
400	0	1.029 (0.8433)	− 0.795 (1.0805)	1.027 (0.3143)	0.994 (0.1578)
	0.2	1.053 (1.0084)	− 0.826 (1.3788)	0.994 (0.3827)	1.044 (0.2621)

4.2. Random covariates.

The values between parentheses are the standard deviations of the estimators.

Various choice of the censoring time distribution gives similar results:

1. The bias of estimators decreases in n and increases in p. The bias is smaller when γ is positive.

2. The standard deviation also decreases in n and increases in p.

5. Analysis of the real data

Let us consider the survival data of 137 lung cancer patients given in Kalbfleisch et Prentice (1980). We analyze the influence of performance

Table 2: $C_{x(\cdot)} = constant$.

		$\beta=1$	$\gamma=-1$	$\beta=1$	$\gamma=1$
n	p	$\widehat{\beta}$	$\widehat{\gamma}$	$\widehat{\beta}$	$\widehat{\gamma}$
100	0	1.199 (2.4421)	– 1.016 (2.7534)	1.358 (0.8534)	0.992 (0.3118)
	0.2	1.262 (2.7923)	– 1.156 (5.4143)	1.347 (2.0697)	0.776 (2.3068)
200	0	1.128 (1.5098)	– 0.880 (1.8793)	1.055 (0.4418)	0.997 (0.2263)
	0.2	1.123 (1.5291)	– 0.838 (2.3208)	1.235 (0.8237)	0.846 (0.9606)
400	0	1.012 (0.8311)	– 0.793 (1.0766)	1.018 (0.3045)	1.006 (0.1628)
	0.2	1.006 (0.9356)	– 0.817 (1.4627)	1.171 (0.5804)	0.886 (0.6874)

status (Karnofsky rating: 10–30 completely hospitalised, 40–60 partial confinement, 70-90 able to care for self) on the survival. (The Karnofsky index is often used to measure the general health status of a patient.) In our example nine observations were censored, i.e., the proportion of censorings is 0.0657. We used the following models for the analysis:

1. PH and GLPH with the continuous covariate per (performance status).

2. PH and GLPH with the covariate $\mathbf{1}_{\{perf \leq 50\}}$ (performance status dichotomised).

Note that if for a certain number of covariates the PH model is verified, it can be not verified if a reduced number of covariates is observed. The parameter γ of the GLPH model may an information on the influence of non-observable covariates.

The goodness-of-fit test for the PH against the GLPH model was used: for two cases: the test statistic T is equal to 8.0125 and 8.4002, respectively. The critical region with the significance level $\alpha = 0.05$ is $T > 3.841$. So the PH model is rejected.

In the case of dichotomous covariates the better results with GPH

Table 3: $C_{x(\cdot)} \sim \exp(\lambda)$.

		$\beta = 1$	$\gamma = -1$	$\beta = 1$	$\gamma = 1$
n	p	$\widehat{\beta}$	$\widehat{\gamma}$	$\widehat{\beta}$	$\widehat{\gamma}$
100	0	1.247 (2.7156)	– 1.128 (3.9151)	1.157 (0.7624)	0.936 (0.3291)
	0.2	1.399 (3.2288)	– 1.412 (4.8855)	1.268 (1.4459)	0.735 (0.9799)
200	0	1.036 (1.4784)	– 0.789 (1.8093)	1.067 (0.4501)	0.991 (0.2209)
	0.2	1.103 (1.4092)	– 0.972 (2.5829)	1.123 (0.7880)	0.948 (0.6156)
400	0	1.030 (0.8647)	– 0.835 (1.0841)	1.031 (0.3002)	0.991 (0.1587)
	0.2	1.092 (0.9345)	– 0.920 (1.3562)	1.019 (0.4131)	1.026 (0.2674)

Table 4: $C_{x(\cdot)} \sim Uniform(0, d)$.

		$\beta = 1$	$\gamma = -1$	$\beta = 1$	$\gamma = 1$
n	p	$\widehat{\beta}$	$\widehat{\gamma}$	$\widehat{\beta}$	$\widehat{\gamma}$
100	0	1.196 (0.8808)	– 1.217 (2.9165)	1.122 (0.5299)	0.945 (0.2657)
	0.2	1.283 (1.0340)	– 1.422 (4.1948)	1.122 (0.6189)	0.969 (0.4287)
200	0	1.081 (0.5490)	– 1.137 (1.5307)	1.084 (0.3631)	0.951 (0.1708)
	0.2	1.115 (0.6197)	– 1.224 (2.2303)	1.045 (0.4172)	0.996 (0.2683)

model can be illustrated graphically: the Kaplan–Meier estimators $\widehat{S}_{\mathrm{KM}}$ and the estimators of the survival functions $\widehat{S}_{\mathrm{PH}}$ and $\widehat{S}_{\mathrm{GLPH}}$ obtained us-

Table 5: $C_{x(\cdot)} = constant$.

		$\beta = 1$	$\gamma = -1$	$\beta = 1$	$\gamma = 1$
n	p	$\widehat{\beta}$	$\widehat{\gamma}$	$\widehat{\beta}$	$\widehat{\gamma}$
100	0	1.208 (1.4223)	− 1.216 (4.1924)	1.129 (0.3324)	0.922 (0.2066)
	0.2	1.311 (1.6476)	− 1.432 (4.2756)	1.230 (0.7538)	0.736 (0.1995)
200	0	1.082 (0.7864)	− 1.144 (2.0897)	1.078 (0.2425)	0.957 (0.1712)
	0.2	1.120 (0.7968)	− 1.114 (2.0199)	1.085 (0.4041)	0.908 (0.5457)

Table 6: $C_{x(\cdot)} \sim \exp(\lambda)$.

		$\beta = 1$	$\gamma = -1$	$\beta = 1$	$\gamma = 1$
n	p	$\widehat{\beta}$	$\widehat{\gamma}$	$\widehat{\beta}$	$\widehat{\gamma}$
100	0	1.238 (1.5328)	− 1.387 (5.0156)	1.121 (0.3639)	0.942 (0.2171)
	0.2	1.285 (1.4721)	− 1.518 (5.0274)	1.148 (0.5186)	0.912 (0.5369)
200	0	1.114 (0.7263)	− 1.161 (1.6886)	1.082 (0.2406)	0.951 (0.1565)
	0.2	1.134 (0.8046)	− 1.191 (2.0506)	1.084 (0.3254)	0.958 (0.2538)

ing the PH and GLPH models, respectively, are presented on the Figs. 1–2. The graphs show that $\widehat{S}_{\mathrm{GLPH}}$ is much closer to $\widehat{S}_{\mathrm{KM}}$ then $\widehat{S}_{\mathrm{PH}}$.

To see the influence of the performance on the survival, the estimators of the survival functions under the GLPH model are given for $per = 20$, 50 and 70. The figure 3 shows that a high level of performance increases the probability of survival.

The obtained estimators are given in the following tables:

Table 7: Estimators $\widehat{\beta}$ and $\widehat{\gamma}$ (per dichotomous).

$Parameters$	PH	GLPH
$\widehat{\beta}$	0.9587	3.8102
$\widehat{\gamma}$	—	$-$ 2.9394

Table 8: Estimators $\widehat{\beta}$ and $\widehat{\gamma}$ (per continuous).

$Parameters$	PH	GLPH
$\widehat{\beta}$	-0.0334	$-$ 0.0866
$\widehat{\gamma}$	—	$-$ 1.9629

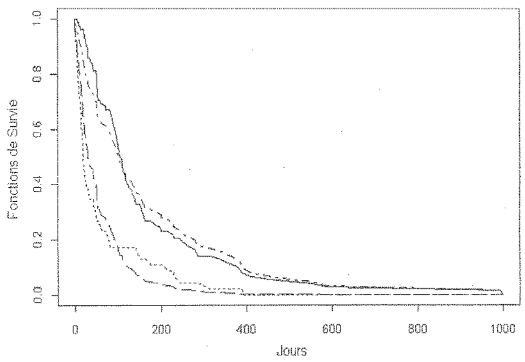

Fig. 1 Comparison of the survival functions using Kaplan–Meier (KM) and PH; KM, $per > 50$; — , KM, $per \leq 50$; — - — PH, $per > 50$; — — PH, $per \leq 50$.

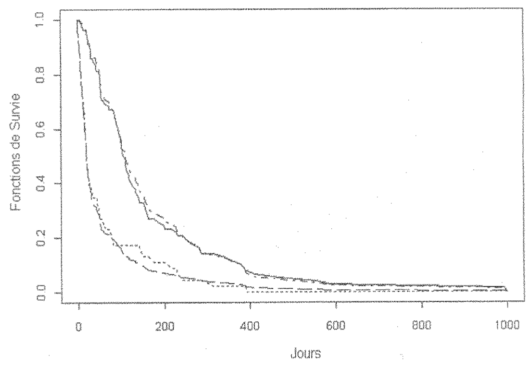

Fig. 2 Comparison of the survival functions using Kaplan–Meier (KM) and GLPH; ——, KM, $per > 50$; – – –, KM, $per \leq 50$; — - — GLPH, $per > 50$; — — GLPH, $per \leq 50$.

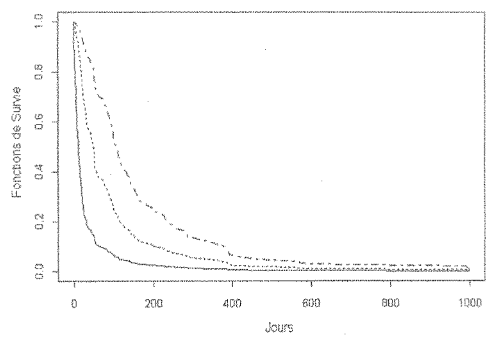

Fig. 3 Comparison of the survival functions using GLPH with per=20, 50 and 70; —— $per = 20$; – – –, $per = 50$; — - — $per = 70$.

References

1. P. K. Anderson, D. Borgan, R. D. Gill et N. Keiding, *Stochastic Models Based on Counting Processes.* Springer-Verlag, N. Y. (1993).
2. V. Bagdonaviçisus et M. Nikulin, *Generalized Proportional Hazards Model Based on Modified Partial Likelihood.* — Lifetime Data Analysis **5** (1999), 329–350.
3. V. Bagdonavičius and M. Nikulin, *Accelerated Life Models.* Boca Raton: Chapman&Hall/CRC (2002).
4. N. E. Breslow, *Analysis of survival data under the proportional hazards model.* — Internat. Statist. Rev. **43** (1975), 45–58.

5. D. R. Cox, *Regression models and life tables.* — J. R. Statist. Soc. B, **34** (1972), 187–220.
6. P. E. Greenwood, M. Nikulin, *A Guide to Chi-squared Testing.* John Wiley and Sons, New York (1996).
7. J. D. Kalbfleisch et R. L. Prentice, *The Statistical Analysis of Survival Time Data.* John Wiley and Sons, New York (1980).

Départment of Mathematical Statistics,
University of Vilnius,
University Mohammed V of Rabat, Maroc
Steklov Mathematical Institute,
St.Petersburg, Russia
E-mail: info@sinam.net,
Université Victor Segalen Bordeaux 2,
Bordeaux, France

Поступило 12 июля 2002 г.