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LINEAR RANK TESTS FOR COMPETING RISKS MODEL

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Abstract: Linear rank invariant tests are developed for testing the equality of q dependent cause-specific hazard rates in competing risks model. Asymptotic locally optimal tests are provided using counting process techniques. The performance of the proposed tests and other existing tests is assessed in a simulation study. An example is given to illustrate the proposed tests.

Key words and phrases: Competing risks model, linear rank tests, optimal tests, survival analysis.

1. Introduction

In the competing risks setting, a unit is exposed to several risks at the same time, but eventual failure of the unit is due to only one of these risks, which is called a cause of failure. In many practical situations, it is important to know whether several risks are equal or not.

One formulation of the competing risks model is in terms of conceptual or latent failure times for each failure type (Cox (1959)). It assumes that the competing risks are independent of each other. This approach has been criticized on the basis of unwarranted assumptions, lack of physical interpretation and identifiability problems.

Alternatively, Prentice, Kalbfleisch, Peterson, Flournoy, Farewell and Breslow (1978) proposed cause-specific hazard rates, and showed that they were the basic estimable quantities in the competing risks framework. The competing risks may be dependent on each other. Under this framework, suppose failure time T is continuous and there are q competing risks. The overall hazard function for an individual is given by

$$\lambda_{all}(t; z) = \lim_{\Delta t \to 0} P\{t \le T < t + \Delta t | T \ge t; z(t)\}/\Delta t,$$

where $z(t)$ denotes the value of the regression vector at time t. The cause-specific hazard functions are defined by

$$\lambda_j(t; z) = \lim_{\Delta t \to 0} P\{t \le T < t + \Delta t, \delta = j | T \ge t; z(t)\}/\Delta t$$

for $j = 1, \ldots, q$, where δ represents failure cause. Assuming that the q failure types are distinct, the overall hazard function can be expressed in terms of cause-specific hazard functions as

$$\lambda_{all}(t; z) = \sum_{j=1}^{q} \lambda_j(t; z).$$

Suppose now that n study subjects give rise to data (t_i, δ_i, c_i), $i = 1, \ldots, n$, where t_i is the failure or censoring time, and $\delta_i = (\delta_{i1}, \ldots, \delta_{iq})$ is the failure cause indicator vector, with value $\delta_{ij} = 1$ if the cause of failure for subject i is j, and $\delta_{ij} = 0$ otherwise. Let δ_i be a scalar cause indicator such that $\delta_i = j$ if $\delta_{ij} = 1$. Let c_i be a censoring indicator which takes value 1 if failure occurs and value 0 otherwise. The cause of failure δ_i may be specified arbitrarily if $c_i = 0$. As usual, an independent censoring mechanism is assumed.

The likelihood function under an independent censoring mechanism is, up to a constant of proportionality,

$$\prod_{i=1}^{n} [\lambda_{\delta_i}(t_i; z_i)]^{c_i} \exp\{-\sum_{j=1}^{q} \int_0^{t_i} \lambda_j(u; z_j(u)) du\}.$$

The likelihood function is completely specified by the cause-specific hazard functions $\lambda_j(t; z)$, $j = 1, \ldots, q$, and they are the basic estimable quantities in the competing risks framework. The marginal hazard rates are usually not estimable.

A common hypothesis of interest is

$$H_0 : \lambda_1(t) = \cdots = \lambda_q(t), \tag{1.1}$$

against the alternative hypothesis $H_1 : \lambda_i(t) \neq \lambda_j(t)$ for at least one pair of i, j, $1 \leq i < j \leq q$.

Various authors have proposed tests of H_0 for the case in which there are two independent competing risks and without censoring: Bagai, Deshpandé and Kochar (1989a, b) developed distribution-free rank tests; Yip and Lam (1992) suggested a class of weighted log rank-type statistics; Neuhaus (1991) constructed asymptotically optimal rank tests for q competing risks against stochastic ordering when there was no censoring.

The case of dependent competing risks has been considered only recently. Aly, Kochar and McKeague (1994) proposed Kolmogrov-Smirnov type tests for testing the equality of two dependent competing risks with censoring data. Dykstra, Kochar and Robertson (1995) considered a model for q dependent competing risks with grouped data or with discrete failure times. The likelihood ratio test statistic was constructed for testing the null hypothesis of the equality of cause-specific hazard rates against ordered alternatives.

In Section 2 we introduce our linear rank invariant tests for the q competing risks problem, they are log-rank type tests. In Section 3, we give large sample properties of the proposed linear rank tests, and also give asymptotic locally optimal tests within the log-rank type test class. In Section 4, we present simulation results and give an example. Finally, in Section 5, we give a brief discussion.

2. Linear Rank Invariant Tests

Linear rank invariant tests for testing the equivalence of q dependent competing risks are developed in this section. The statistics arise as score statistics based on the marginal probability of a generalized rank vector.

The data set (t_i, δ_i, c_i), $i = 1, \ldots, n$, is defined as in Section 1. Consider the following linear model for the cause-specific hazards:

$$f_j(t) = f(t + b_j), \qquad j = 1, \ldots, q, \quad \text{with } b_1 = 0, \tag{2.1}$$

or equivalently $\lambda_j(t) = \lambda(t + b_j)$, $j = 1, \ldots, q$, with $b_1 = 0$. Equation (2.1) is the location shift model if the competing risks are independent.

The likelihood function under an independent censoring mechanism, up to a constant of proportionality, may be written as

$$\prod_{i=1}^{n} \{[\lambda(t_i + \mathbf{b}^T \delta_i)]^{c_i} \exp[-\sum_{j=1}^{q} \int_0^{t_i} \lambda(u + b_j) du]\},$$

where $\mathbf{b} = (0, b_2, \ldots, b_q)$. The null hypothesis at (1.1) can be re-expressed under model (2.1) as $H_0 : \mathbf{b} = \mathbf{0}$, and the alternative hypothesis is $H_1 : \mathbf{b} \neq \mathbf{0}$.

Let $t_{(1)} < \cdots < t_{(k)}$ represent the ordered event times in the sample. In some arbitrary order, let $t_{(i1)}, \ldots, t_{(im_i)}$ denote the right-censored times in $[t_{(i)}, t_{(i+1)})$ for $i = 0, \ldots, k$, with $t_{(0)} = 0$, $t_{(k+1)} = \infty$. Note that we assume no ties among the event times, but there may be ties between right-censored observations and uncensored observations.

The accumulated probability of possible underlying rank vectors is then

$$P(r) = \int_{\tau_{(1)} < \cdots < \tau_{(k)}} \prod_{i=1}^{k} \{\lambda(\tau_{(i)} + \mathbf{b}^T \delta_{(i)})[\exp\{-\sum_{j=1}^{q} \int_0^{\tau_{(i)}} \lambda(u + b_j) du\}]^{m_i+1} d\tau_{(i)}\}. \tag{2.2}$$

This expression arises because the possible rankings corresponding to each censored time $\tau_{(i)}$ map out an integral over the whole line segment $[\tau_{(i)}, \infty)$ (Prentice (1978)). Note that at $\mathbf{b} = \mathbf{0}$, (2.2) can be integrated directly, leading to a value of $P(r)$ equal to $(n_1 \cdots n_k)^{-1}$, where $n_i = q[(m_i + 1) + (m_{i+1} + 1) \cdots + (m_k + 1)]$.

The score function for testing $\mathbf{b} = \mathbf{0}$ based on (2.2), as proved in Appendix 1, is

$$v = \sum_{i=1}^{k} d_i (\delta_{(i)} - (1/q)\mathbf{1}), \tag{2.3}$$

where $\mathbf{1}$ is a q-vector $(1,\ldots,1)$, and

$$d_i = \int_{\tau_{(1)}<\cdots<\tau_{(k)}} [\lambda'(\tau_{(i)}/\lambda(\tau_{(i)}] \prod_{j=1}^{k} \{n_j\lambda(\tau_{(j)})[S(\tau_{(j)})]^{m_j+1} d\tau_{(j)}\}. \tag{2.4}$$

The covariance matrix of v under the null hypothesis is s^2, where

$$s^2 = \sum_{i=1}^{k} d_i^2 \begin{bmatrix} q^{-1}(1-q^{-1}) & -q^{-2} & \cdots & -q^{-2} \\ -q^{-2} & q^{-1}(1-q^{-1}) & \cdots & -q^{-2} \\ \vdots & \vdots & \vdots & \vdots \\ -q^{-2} & -q^{-2} & \cdots & q^{-1}(1-q^{-1}) \end{bmatrix}.$$

The linear rank score test statistic U^2 is a weighted log-rank type test:

$$U^2 = v^T(s^2)^- v = \left\{ q \sum_{h=1}^{q} \left[\sum_{i=1}^{k} d_i(\delta_{(ih)} - 1/q) \right]^2 \right\} / \left\{ \sum_{i=1}^{k} d_i^2 \right\}, \tag{2.5}$$

where sign $^-$ denotes generalized inverse.

When $q = 2$, from (2.5), we have

$$U = \sum_{i=1}^{k} d_i(\delta_{(i1)} - 1/2) / \sqrt{\sum_{i=1}^{k} d_i^2/2^2},$$

which follows a standard normal distribution under H_0. An extreme minimum value density, $f(t) = \exp(t - e^t)$, yields $\lambda'(t)/\lambda(t) = 1$; then we have $d_i = 1$. We denote this test as T_1. A logistic density, $f(t) = e^t/(1+e^t)^2$ gives $\lambda'(t)/\lambda(t) = S(t)$, so that, from (2.4), we have $d_i = \prod_{j=1}^{i} n_j/(n_j+1)$. We denote this test as T_2. The weight function d_i is asymptotically equivalent to the Kaplan-Meier estimator $\prod_{j=1}^{i}(n_j-1)/n_j$.

3. Large Sample Properties and Asymptotic Locally Optimal Tests

In this section, we prove that the test U^2 at (2.5) has a χ^2 distribution with $q-1$ degrees of freedom under the null hypothesis. We also give asymptotic locally optimal tests within the log-rank type test class.

3.1. General testing

For a dependent counting process $N(t) = (N_1(t),\ldots,N_q(t))$, $t \in \Gamma = [0,\tau]$, for a given terminal time τ where for $j = 1,\ldots,q$, $N_j(t) = \sum_{i=1}^{n} N_{ij}(t) = \sum_{i=1}^{n} I(T_i \le t, \delta_{ij} = 1)$, T_i is failure or censoring time, the cause-specific intensity process is $\mathbf{a}(t) = (a_1(t),\ldots,a_q(t))$, with $a_h(t) = \lambda_h(t)Y(t)$, $h = 1,\ldots,q$, where λ_h is cause-specific hazard rate and $Y(t) = \sum_{i=1}^{n} I(T_i \ge t)$. It is assumed that $\int_0^t \lambda_h(s)ds < \infty$, $h = 1,\ldots,q$, $t \in \Gamma$. It is also assumed that there are no ties in failure times. Then the counting process $M_h(t) = N_h(t) - \int_0^t a_h(s)ds$ is a local square integrable martingale. We denote $N(t) = \sum_{l=1}^q N_l(t)$ and define stochastic processes

$$Z_h(t) = \int_0^t K(s)[dN_h(s) - 1/qdN..(s)], \quad h = 1,\ldots,q, \tag{3.1}$$

where $K(s)$ is locally bounded and only depends on $(N..(s), Y(s))$. When $Y(s)$ is zero, $K(s)$ is also zero. Under (1.1), $Z_h(t)$ is a local square integrable martingale. We denote the optional variation process of $\mathbf{Z}(t)$ as $[Z_h, Z_j](t)$. Then $[Z_h, Z_j](t) = \int_0^t K(s)^2 q^{-1}(I(h = j) - 1/q)dN..(s)$, which is a consistent estimator of Σ, the covariance matrix of $\mathbf{Z}(t)$. A reasonable test statistic for hypothesis (1.1) is the quadratic form

$$\mathbf{X}^2(t) = \mathbf{Z}(t)^T([\mathbf{Z},\mathbf{Z}](t))^- \mathbf{Z}(t). \tag{3.2}$$

By virtue of the Martingale Central Limit Theorem, $\mathbf{X}^2(t)$ has asymptotically a χ^2 distribution with $q-1$ degrees of freedom under hypothesis (1.1), provided certain regularity conditions are fulfilled (Andersen, Borgan, Gill and Keiding (1991, Chap.V2)).

We can write $\mathbf{X}^2(t)$ as follows:

$$\begin{aligned} X^2(t) &= \{\sum_{h=1}^q [Z_h(t)]^2\} / \int_0^t K(s)^2 q^{-1} dN..(s) \\ &= \left\{ q \sum_{h=1}^q \left[\sum_{i=1}^k K(t_{(i)})(\delta_{(ih)} - 1/q) \right]^2 \right\} / \left\{ \sum_{i=1}^k K(t_{(i)})^2 \right\}. \end{aligned}$$

Test statistics $X^2(t)$ and U^2 of (2.5) are equivalent when the two weight functions $K(t_{(i)})$ and d_i are the same. Therefore, U^2 also has asymptotically a χ^2 distribution with $q-1$ degrees of freedom under hypothesis (1.1).

3.2. Asymptotic locally optimal tests

In this subsection, the behavior of test statistic $\mathbf{X}^2(t)$ is studied under a sequence of local alternative hypotheses, and the optimal tests are derived.

Consider $a_h^{(n)}(t) = \lambda_h^{(n)}(t) Y^{(n)}(t)$ with

$$\lambda_h^{(n)}(t) = \lambda(t) + \varphi_h \gamma(t)\lambda(t)/cn + \rho_h^{(n)}(t), \tag{3.3}$$

where φ_h are constants, $\gamma(t)$, $\lambda(t)$ are fixed functions on $[0,\tau]$, $\{c_n\}$ is a sequence of constants increasing to infinity as $n \to \infty$, and $\{\rho_h^{(n)}\}$, $h = 1,\ldots,q$, are sequences of functions satisfying $\sup_{[0,\tau]} |c_n \rho_h^{(n)}(t)| \to 0$ for each h as $n \to \infty$.

Theorem 1. *A test based on* $\mathbf{X}^2(t)$ *in* (3.2) *is an asymptotic locally optimal test under a sequence of local alternative hypotheses* (3.3) *when the weight process* $K^{(n)}(s)$ *is asymptotically proportional to* $\gamma(s)$.

The proof of Theorem 1 is in Appendix 2.

Under local Lehmann alternative $\lambda_h^{(n)}(t) = \lambda(t)\theta_h$, where $\theta_h \to 1$, we have $\gamma(t) = 1$, $c_n = \varphi_h n^{-1/2}$, $\rho_h^{(n)}(t) = 0$. Therefore, from Theorem 1, asymptotic local optimality for the Lehmann alternative is achieved when the weight process $K^{(n)}(s)$ is asymptotically proportional to 1.

Next, we show how to get the optimal weight process $K^{(n)}(s)$ for censored data using a survival function estimator. We also show that rank tests T_1 and T_2, derived from extreme minimum value and logistic distributions respectively, are indeed the optimal tests for these distributions. We assume that the distribution functions $F_1^{(n)}, \ldots, F^{(n)}q$ form a generalized local location family in the sense that

$$F^{(n)}h(t) = \Psi(g(t) + n^{-1/2}\varphi_h),$$

where Ψ is a fixed absolutely continuous distribution function with positive continuously differentiable density Ψ on $(-\infty, \infty)$, and g is a fixed non-decreasing differentiable function from $(0, \infty)$ onto $(-\infty, \infty)$. Note that, $F^{(n)}h(t)$ has hazard function $\lambda^{(n)}h(t) = h(g(t) + n^{-1/2}\varphi_h)g'(t)$, where $h = \psi/(1 - \Psi)$ is the hazard function corresponding to Ψ. Therefore, a Taylor expansion gives (3.3) with $c_n = \sqrt{n}$, $\lambda(t) = h(g(t))g'(t)$, and $\gamma(t) = h'(\Psi^{-1}(F(t)))/h(\Psi^{-1}(F(t)))$, where $F(t) = \Psi(g(t))$ is the common distribution function under the null hypothesis.

An optimal test can be obtained by using the weight process

$$K^{(n)}(t) = I(Y^{(n)}(t) > 0)h'(\Psi^{-1}(\hat{F}^{(n)}(t-)))/h(\Psi^{-1}((n)(t-))),$$

where $\hat{F}^{(n)} = 1 - \hat{S}^{(n)}$, and $\hat{S}^{(n)}(t)$ is the Kaplan-Meier estimator based on the combined sample $\hat{S}^{(n)}(t) = \prod_{s \le t}\{1 - \Delta N..^{(n)}(s)/[qY^{(n)}(s)]\}$.

For the two-sample case, that is, $q = 2$, (3.2) reduces to

$$X^2(\tau) = 4\left\{\sum_{h=1}^{q}\left[\sum_{i=1}^{k} K(t_{(i)})(\delta_{(ih)} - 1/2)\right]^2\right\} / \left\{\sum_{i=1}^{k} K(t_{(i)})^2\right\}. \tag{3.4}$$

For the extreme value distribution, $\Psi(t) = 1 - \exp(-e^t)$, $h(t) = e^t$ and $r(t) = 1$. Thus, from (3.4), the optimal test can be achieved when $K^{(n)}(t_{(i)}) = I(Y^{(n)}(t_{(i)}) > 0)$, which is also the linear rank test T_1 under the extreme minimum value distribution. For the logistic distribution, $\Psi(t) = h(t) = e^t/(1 + e^t)$, $h'(t) = \Psi(t)(1 - \Psi(t))$ and $r(t) = 1 - \Psi(t)$. The optimal choice of weight process is, therefore, $K^{(n)}(t_{(i)}) = I(Y^{(n)}(t_{(i)}) > 0)\hat{S}^{(n)}(t_{(i)-})$. It is, asymptotically, the linear rank test T_2 under the logistic distribution.

4. Simulation Studies and an Example

4.1. Simulation

Simulation studies were carried out to investigate the finite sample performance of proposed tests T_1, T_2 and existing tests D_{3n}, D_{4n} (Aly, Kochar and McKeague (1994)). Let X and Y denote the failure times for two different causes. Three underlying distributions were studied.

(i) Block and Basu's (1974) absolutely continuous bivariate exponential (ACBVE) distribution has density

$$f(x,y) = \begin{cases} \frac{\lambda_1\lambda(\lambda_2+\lambda_0)}{\lambda_1+\lambda_2} e^{-\lambda_1 x-(\lambda_2+\lambda_0)y}, & \text{if } x < y, \\ \frac{\lambda_2\lambda(\lambda_1+\lambda_0)}{\lambda_1+\lambda_2} e^{-\lambda_2 y-(\lambda_1+\lambda_0)x}, & \text{if } x > y, \end{cases}$$

where $\lambda = \lambda_0 + \lambda_1 + \lambda_2$. Different values of λ_2 correspond to different departures from H_0; X and Y are independent if and only if $\lambda_0 = 0$. We set $\lambda_0 = 1$, $\lambda_1 = 1$, $\lambda_2 = 1$, 1.5 and 2.

(ii) Independent logistic distributions with $f(t) = e^t/(1 + e^t)^2$.

(iii) Independent extreme minimum value distributions with $f(t) = \exp(t - \exp(t))$.

The censoring distributions were taken respectively to be independent exponential, logistic and extreme minimum value distributions. The cumulative censoring percentages were taken to be 0%, 25%-35% and 50% - 70%. The asymptotic significance level was 5%. Simulations were repeated 5000 times. The sample size was 100.

The results in Table 1-3 show that T_1 and T_2 are very close under the logistic and extreme minimum value distributions. Test T_2 is more powerful than T_1 under the ACBVE distribution. Test D_{3n} is more powerful than D_{4n} under all three distributions. Test D_{3n} is close to T_2 under all three distributions when there is no censoring. When there is censoring, especially when the censoring is heavy, both D_{3n} and D_{4n} have size lower than 5% and lower power than T_1 and T_2. The relative low reject rate for T_1 in the uncensored case may be due to sample variation.

4.2. Example

Non-Hodgkin's Lymphoma (NHL) occurs in approximately 2% of all patients infected with the human immunodeficiency virus (HIV), and may account for 11% of NHL in the United States. Furthermore, patients surviving HIV infection may be particularly prone to lymphoma, as evidenced by the 20%-30% actuarial risk of lymphoma at 3 years in one series of patients treated with antiretroviral therapy. There are two causes of death for HIV positive NHL patients: opportunistic infection (OI) and NHL. The two causes of death may be dependent. Our proposed methods are applied to compare the risks of these two potential causes of death.

Table 1. The observed rejection rates for tests T_1, T_2, D_{3n} and D_{4n} at an asymptotic level of 5%. The underlying distribution of (X, Y) is the ACBVE distribution.

λ_2	T_1	T_2	D_{3n}	D_{4n}
Uncensored				
1	4.9	5.2	4.9	3.4
1.5	64.0	80.4	77.8	68.4
2	95.8	99.5	99.5	98.5
Lightly censored 25%-35%				
1	5.4	5.3	4.4	3.8
1.5	70.6	77.7	70.9	60.2
2	97.8	99.4	98.7	96.8
Heavily censored 50%-70%				
1	4.5	4.7	2.7	2.0
1.5	67.8	70.6	55.6	43.3
2	97.2	98.0	95.0	89.6

Table 2. The observed rejection rates for tests T_1, T_2, D_{3n} and D_{4n} at an asymptotic level of 5%. The underlying distributions of X and Y are independent extreme minimum value distributions.

A	T_1	T_2	D_{3n}	D_{4n}
Uncensored				
0	4.9	4.9	4.5	3.7
-0.2	24.8	24.9	23.9	19.4
-1	99.9	99.8	99.8	99.8
Lightly censored 25%-35%				
0	4.9	5.0	4.1	3.4
-0.2	21.3	20.1	17.3	14.3
-1	99.6	99.2	99.3	98.6
Heavily censored 50%-70%				
0	4.5	4.4	1.0	0.1
-0.2	11.7	12.0	3.2	2.0
-1	86.5	85.6	71.7	59.5

We considered a set of mortality data provided by Dr. J. Sparano of the Albert Einstein Cancer Center. A total of 62 HIV-associated NHL patients were treated with chemotherapy. The data analyzed was that of the first 12 months of follow-up.

Table 3. The observed rejection rates for tests T_1, T_2, D_{3n} and D_{4n} at an asymptotic level of 5%. The underlying distributions of X and Y are independent logistic distributions.

a	T_1	T_2	D_{3n}	D_{4n}
Uncensored				
0	4.7	5.2	4.6	3.9
-0.2	14.4	16.4	15.1	12.0
-1	94.6	96.7	95.7	92.4
Lightly censored 25%-35%				
0	5.1	5.3	4.0	3.4
-0.2	14.4	14.8	11.8	9.4
-1	93.2	94.7	91.9	86.5
Heavily censored 50%-70%				
0	4.9	4.6	3.1	2.2
-0.2	11.5	11.6	7.3	5.2
-1	80.8	82.2	70.9	59.1

Among the 62 patients, 18 died of NHL, 7 died of OI, 37 were censored. The Kaplan-Meier survival curves are plotted in Figure 1, where death from other causes was considered censored. The cause-specific hazard rate functions are given in Figure 2. They were estimated by smoothing the increments of the Nelson-Aalen estimator using a bandwidth of 2 months. We performed both test T_1 and test T_2 on this data set.

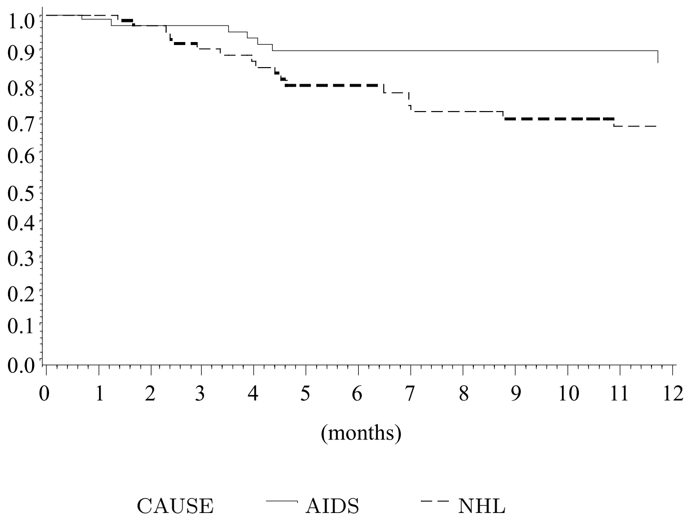

Figure 1. Kaplan-Meier survival curves.

For test T_1, we have $U = 2.2$, P_value= 0.007. The NHL death cause-specific hazard rate was significantly higher than the OI death cause-specific hazard rate. For test T_2, we have $U = 2.07$, P_value= 0.010. The NHL death cause-specific hazard rate was also significantly higher than the OI death cause-specific hazard rate. Both tests showed that the HIV positive NHL patients had significantly higher risk of dying of NHL than OI within the first year of diagnosis of NHL. The relative smaller P_value from T_1 may be due to the proportionality of two cause-specific hazard rates within that period of time (Fig. 2).

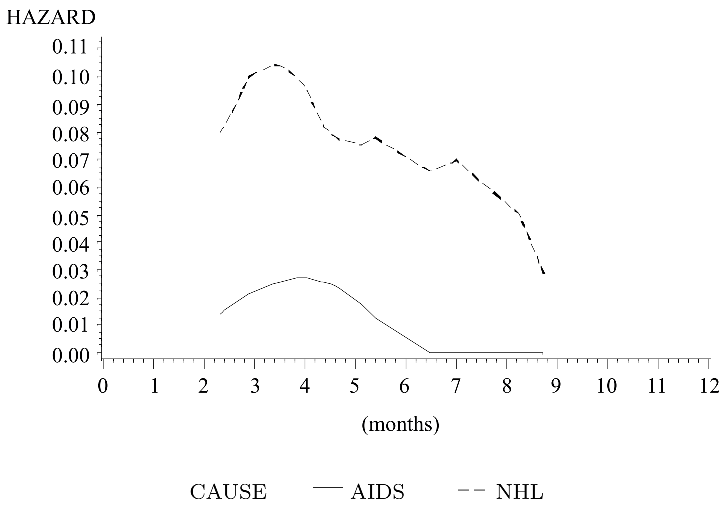

Figure 2. Cause-specific Hazard rate functions.

5. Discussion

In this note, we have proposed linear rank statistics for testing the equality of q dependent cause-specific hazard rates in competing risks model with censored data. We have also provided asymptotic locally optimal tests among the proposed log-rank type linear rank tests using martingale techniques. Assuming two independent competing risks with no censoring, the tests of Bagai, Deshpande and Kochar (1989a, b) and Yip and Lam (1992) result as special cases of our tests T_1 and T_2. Bagai , Deshpande and Kochar (1989a, b) also studied statistics which are linear combinations of T_1 and T_2. Aly, Kochar and McKeague (1994) studied dependent cause-specific hazard rates, and proposed tests D_{3n} and D_{4n}. Under both dependent and independent competing risks, our simulation studies show that T_1 and T_2 are more powerful than D_{3n} and D_{4n} when there is censoring.

Quantitative assessment for the competing risks, and handling of missing cause-of-failure are other interesting topics. We expect to report on these topics elsewhere.

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Appendix

Proof of (2.3).

$$\begin{aligned}
v &= \partial \ln(P(r))/\partial \mathbf{b}|_{b=0} = [P(r)]^{-1}\partial(P(r))/\partial \mathbf{b}|_{b=0} \\
&= \prod_{i=1}^{k}\{n_i\}\frac{\partial}{\partial b}\int\limits_{\tau_{(1)}<\cdots<\tau_{(k)}}\sum_{i=1}^{k}\{\lambda(\tau_{(i)}+\mathbf{b}^T\delta_{(i)})[S(\tau_{(i)})]^{m_i+1}d\tau_{(i)}\}|_{b=0} \\
&= \int\limits_{\tau_{(i)}<\cdots<\tau_{(k)}}\sum_{i=1}^{k}\{n_i\delta_{(i)}\lambda'(\tau_{(i)})[S(\tau_{(i)})]^{m_i+1} \\
&\quad +n_i\mathbf{1}(m_i+1)\lambda(\tau_{(i)})[S(\tau_{(i)})]^{m_i+1}S(\tau_{(i)})[-\int_0^{t_{(i)}}\lambda'(u)du]\}d\tau_{(i)} \\
&\quad \prod_{j\neq i}\{n_j\lambda(\tau_{(j)})[S(\tau_{(i)})]^{m_j+1}d\tau_{(j)}\} \\
&= \int\limits_{\tau_{(1)}<\cdots<\tau_{(k)}}\sum_{i=1}^{k}\{\delta_{(i)}\lambda'(\tau_{(i)})/\lambda(\tau_{(i)})-\mathbf{1}(m_i+1)\lambda(\tau_{(i)})\} \\
&\quad \prod_{j=1}^{k}\{n_j\lambda(\tau_{(j)})[S(\tau_{(j)})]^{m_j+1}d\tau_{(j)}\} \\
&= \sum_{i=1}^{k}(\delta_{(i)}d_i+m_iD_i\mathbf{1}),
\end{aligned}$$

where $D_i = -\frac{m_i+1}{m_i}\int_{\tau_{(1)}<\cdots<\tau_{(k)}}\lambda(\tau_{(i)})\prod_{j=1}^{k}\{n_j\lambda(\tau_{(j)})[S(\tau_{(j)})]^{m_j+1}d\tau_{(j)}\}$.

It is easy to see that $d_i = n_i(D_{i-1}-D_i)$. Then we have

$$v=\sum_{i=1}^{k}\delta_{(i)}d_i-\mathbf{1}\sum_{i=1}^{k}(m_i+1)\sum_{j=1}^{k}d_i/n_i=\sum_{i=1}^{k}\delta_{(i)}d_i-\mathbf{1}(1/q)\sum_{i=1}^{k}d_i=\sum_{i=1}^{k}d_i[\delta_{(i)}-(1/q)\mathbf{1}].$$

Proof of Theorem 1. The $Z_h^{(n)}(t)$ of (3.1) may be written as a local square integrable martingale term $W_h^{(n)}(t)$ and a convergent term $V_h^{(n)}(t)$:

$$Z_h^{(n)}(t) = W_h^{(n)}(t) + V_h^{(n)}(t),$$

where $W_h^{(n)}(t) = \int_0^t K^{(n)}(s) \sum_{l=1}^q (I(h=l) - 1/q) dM_l^{(n)}(s)$,

$$V_h^{(n)}(t) = c_n^{-1} \int_0^t K^{(n)}(s) Y^{(n)}(s) \gamma(t) \lambda(t) \{\varphi_h - (1/q) \sum_{l=1}^q \varphi_l\} ds + R_{1h}^{(n)}(t),$$

$$|R_{1h}^{(n)}(t)| = o(b_n^{-1}) \int_0^t K^{(n)}(s) Y^{(n)}(s) ds.$$

Under the sequence of local alternatives specified in (3.3), $W_h^{(n)}$ is a local square integrable martingale, and $V_h^{(n)}(t)$ converges in probability to $\xi_h(t)$. The optimal variation process $[Z, Z](t)$ is still a consistent estimator of Σ along the sequence of local alternatives (Anderson, Borgan, Gill and Keiding (1991, Chap.V2)), where Σ is the covariance matrix of $Z(t)$. We therefore have for any fixed time t,

$$Z^{(n)}(t) \xrightarrow{D} N(\xi(t), \Sigma(t)) \qquad \text{as } n \to \infty.$$

It follows that, under the sequence of local alternatives (3.3), the test statistic $\mathbf{X}^2(t)$ given by (3.2) has, asymptotically, a noncentral χ^2 distribution with $q-1$ degrees of freedom and noncentrality parameter $\zeta(t) = \xi(t)^T \Sigma(t)^- \xi(t)$, where, $\xi(t) = (\xi_1(t), \ldots, \xi_q(t))$. Therefore, asymptotic local optimality is achieved when the noncentrality parameter $\zeta(t)$ gets its maximum value. It is not hard to see that

$$\begin{aligned}\zeta(t) &= \sum_{h=1}^q [\xi(t)_h(t)]^2 / E \int_0^t K(s)^2 q^{-1} \lambda(s) dN..(s) \\ &= \{(\varphi_h - \varphi)^2\} [\int_0^t K^{(n)}(s) \gamma(s) \lambda(s) Y^{(n)}(s) ds]^2 / E \int_0^t {}^{(n)}(s)^2 \lambda(s) Y^{(n)}(s) ds \\ &\le \{\sum_{h=1}^q (\varphi_h - \varphi)^2\} \int_0^t K^{(n)}(s) \gamma(s) \lambda(s) Y^{(n)}(s) ds.\end{aligned}$$

The last inequality follows from Cauchy-Schwarz, with equality if and only if $K^{(n)}(s)$ is proportional to $\gamma(s)$. Thus, a test with weight process $K^{(n)}(s)$ asymptotically proportional to $\gamma(s)$ is the asymptotic locally optimal test.

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