The Fine & Gray model for competing risks with left truncated data or time-dependent covariates

Ronald B. Geskus[1]

[1] Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam, the Netherlands
[2] Cluster Infectious Diseases, Department of Research, Amsterdam Health Service, Amsterdam, the Netherlands

In the presence of competing risks, the effect of a covariate on the cause-specific hazard can be modelled via a standard Cox model. However, due to the competing event, there is no direct relation to its effect on the cause-specific cumulative incidence. Often, the cumulative scale is of greater interest. For example, since 1996 powerful anti-retroviral treatment has become available for HIV infected individuals. This may have changed the spectrum of causes of death. Calendar time is a time-dependent covariate: individuals who became infected before 1996 and were still alive in 1996 contribute to two different calendar periods.
Fine & Gray[1] introduced a model that directly quantifies the covariate effect on the cumulative incidence. They assumed proportionality in the “subdistribution hazard”, which describes the hazard belonging to the cause-specific cumulative incidence. The only difference between their definition of partial likelihood and standard partial likelihood is in the definition of the risk set: individuals who have the competing event remain in the risk set until their “potential” censoring time. An inverse probability of censoring weighting procedure is applied in case this censoring time is not known. Their weighting procedure did not consider the presence of time-dependent covariates. The following situations can be discriminated:

1. time-fixed covariates
2. time-fixed covariates, but left truncated data
3. external time-dependent covariates (like calendar period)
4. internal time-dependent covariates

Situation 1 was considered by Fine & Gray. Internal time-dependent covariates are difficult to relate to a cumulative scale, even in the situation of standard survival data with only one type of event. In situations 2 and 3, cause-specific cumulative incidence curves can be estimated using cause-specific hazards. Hence, a subdistribution hazard exists, suggesting that a regression on the subdistribution hazard can be performed with an appropiate weighting procedure. We derive the weights in these situations and apply the procedure to data on the effect on calendar period on cause of death in HIV infected individuals.

References

[1] Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. Journal of the American Statistical Association 1999; 94:496509.