Abstract

“Estimation of cause-specific and subdistribution hazard ratios from a mixture model using penalized splines”

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For patients who survived a myocardial infarction, one possible strategy to prevent future cardiac events is to implant a defibrillator. As implantation of defibrillators is expensive and introduces the risk of infections for the treated patients, identification of adequate patients for implantation is inevitable. In a cohort of 2,343 individuals who survived a myocardial infarction and were observed for five years without implantation of a defibrillator, predefined risk stratification depending on the left ventricular ejection fraction and the presence of severe autonomic failure was assessed.

As only deaths from a cardiac reason can be prevented by the implanted defibrillators, death from a cardiac reason was considered as event of interest and deaths from other reasons as competing events. Consequently, data were analyzed by application of common competing risks analysis methods, such as cause-specific hazard regression, subdistribution hazard regression, and vertical modelling. Additionally, a recently published method allowing to estimate cause-specific and subdistribution hazard ratios from a mixture model assuming conditional event times to follow a generalized gamma distribution was intended to be applied to the data. As application failed due to convergence problems, which were also identified in simulated datasets, the approach was adapted by modelling the conditional event times considering penalized B-splines.

According to simulation studies, the spline approach appears to be superior to the parametric approaches regarding numerical stability and, due to higher flexibility compared to the parametric approaches, in the ability to reflect the true underlying cause-specific and subdistribution hazards. The approach was also applied to the cohort study data and results were compared to those obtained using other competing risks methods.