Improving dynamic models for predicting cancer progression: the use of joint modeling

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Abstract

Abstract: The Response Evaluation Criteria in Solid Tumors are used as standard guidelines for the clinical evaluation of cancer treatments. The assessment is based on the anatomical tumor burden: change in the size of target lesions and evolution of nontarget lesions (NTL). Despite unquestionable advantages of this standard tool, Response Evaluation Criteria in Solid Tumors are subject to some limitations such as categorization of continuous tumor size or negligence of its longitudinal trajectory. In particular, it is of interest to capture its nonlinear shape and model it simultaneously with recurrent progressions of NTL and overall survival. We propose different multivariate nonlinear joint frailty models for recurrent events and a terminal event with longitudinal data.
Furthermore, the biomarker is often characterized by an excess of zeros due to the subset of patients reaching the complete response of target lesions state. A biomarker distribution exhibiting inflated zeros and a continuous distribution of positive values is referred to as semicontinuous, i.e., it is zero-inflated and right-skewed. An appropriate model is needed for the longitudinal biomarker as well as an association structure with the survival outcome. We propose here a joint model for a longitudinal semicontinuous biomarker and a survival time. The semicontinuous nature of the longitudinal biomarker is specified by a two-part model, which splits its distribution into a binary outcome (first part) represented by the positive versus zero values and a continuous outcome (second part) with the positive values only. An application to advanced metastatic colorectal cancer data from the GERCOR study is performed where our two-part model is compared to one-part joint models. Our results show that treatment arm B (FOLFOX6/FOLFIRI) is associated with higher SLD values over time and its positive association with the terminal event leads to an increased risk of death compared to treatment arm A (FOLFIRI/FOLFOX6).

Keywords: *Joint models - survival analysis - recurrent events - Longitudinal data – Tumor response - Semicontinuous data - Two-part model - Zero inflation.*

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