Subgroup Identification for Time-to-event Data Based on AFT Model

CURRENT STATUS: POSTED

Sheng-li An
asl0418@126.com Corresponding Author

Pei Kang
Department of Biostatistics, School of Public Health, Southern Medical University

Ying-xin Liu
Department of Biostatistics, School of Public Health, Southern Medical University

Fu-qiang Huang
Department of Biostatistics, School of Public Health, Southern Medical University

DOI:
10.21203/rs.2.18979/v1

SUBJECT AREAS
Health Economics & Outcomes Research

KEYWORDS
accelerated failure time model, adaptive design, change-point algorithm, false discovery rate, precision medicine, subgroup identification
Abstract
Considering the problem of identifying subgroup in a randomized clinical trial with respect to survival time, we present an analysis strategy to find subgroup of enhanced treatment effect. We fit univariate accelerated failure time (AFT) models with covariate-treatment interactions to identify predictive covariates. The false discovery rate is controlled by Benjamini-Hochberg procedure. Then a composite score conversion is employed to transform the set of identified covariates for each patient into a univariate score. To classify patient subgroups, a change-point algorithm is applied to searching for the threshold cutoff instead of using the median. Moreover, we adopted a biomarker adaptive design to check whether the treatment effect exists within certain subgroup. The simulation results show that the change-point method is remarkably superior to the median cutoff particularly when the subgroup sizes vary considerably. Furthermore, the 2-stage adaptive design has good power properties in detecting treatment effect while the type I error is generally controlled. As an illustration, we apply the proposed methods to an AIDS study. In conclusion, when the sample size is sufficient and the censoring rate is mild, the AFT model combined with change-point algorithm performs well in identifying subgroup. Keywords: accelerated failure time model; adaptive design; change-point algorithm; false discovery rate; precision medicine; subgroup identification

Full-text
Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.