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Evaluating the over-time prognostic performance of biomarkers for cancer prognoses using time-dependent receiver operating characteristic (ROC) curve

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Abstract

Biomarkers are important tools for early detection of a variety of disease related events, such as disease onset, recurrence, relapse or mortality due to a disease. In this work, I will demonstrate the biostatistical methodology of using sensitivity, specificity, predictive values, and the receiver operating characteristic (ROC) curve to evaluate biomarkers for prognosis of disease related events in a time-dependent fashion by using two examples in cancer studies. At first, I will show the process to assess the prognostic performance of biomarkers with a binary value, such as positive/negative. Under this situation, time-dependent sensitivity, specificity and predictive values were relevant parameters to use. In the first study, the goal of is to evaluate the prognostic accuracies of three pathological biomarkers – estrogen receptor (ER), progesterone receptor (PR), and human epidermal receptor 2 (Her2) – for prognosing breast cancer recurrences over 10 years of follow-up among 2,267 women in California and Utah with a previously diagnosed breast cancer (BC) enrolled in the Lifetime After Cancer Epidemiology (LACE) study. Using data from LACE, we found that Her2 has the best specificity for prognosis of BC recurrences over a 10 years period, but its sensitivity is lower than ER and PR over the same period of time. On the other hand, PR has a much better sensitivity over time than ER and Her2, but a lower specificity than the other two markers. Secondly, I will illustrate the statistical method for evaluating the prognostic performance of a biomarker as a continuous variable through another cancer study of a severe brain tumor, namely oligodendrogliomas. In this study, two continuously measured biomarkers, MIB-1 and MVD, were assessed and compared for their ability to prognose the overall survival and progression free survival for patients with diagnosed oligodendrogliomas of stage II or stage III. Using the time-dependent ROC method, our results indicate that the overall performance of MVD is significantly better than MIB-1. Finally, I will point out that the selection of an appropriate biomarker for disease/mortality prognosis should also be based on the feature of the disease, the type of prognosis (e.g., screening versus confirmative test), and certain economical factors (benefits versus cost).

Biography

Nan Hu has completed his Ph.D in 2010 from Department of Biostatistics at the University of Washington, School of Public Health. He is now an assistant professor of medicine at the University of Utah, and an investigator at Huntsman Cancer Institute. He has published more than 10 papers in reputed Statistics journals and Medical journals and served as Statistics reviewers for Statistic Sinica and several medical journals.