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Interpretation Approaches

Prediction of response to antiretroviral therapy by human experts and by the EuResist data-driven expert system (the EVE study)


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Background. Rules-based algorithms developed by expert panels are routinely used to interpret HIV-1 genotype for drug resistance monitoring in clinical practice. The EuResist expert system is a novel data-driven expert system based on the combination of three engines trained on a large number of treatment change episodes (TCEs) and each computing optional patient and virus features in addition to the minimal information made of baseline viral load and genotype plus therapy. The output provided is the probability of achieving 8-week virological success.

Methods. The performance of the EuResist system in predicting short-term success was compared with that of ten individual major HIV-1 drug resistance experts recruited worldwide. A series of 25 past patient cases with drug-resistant HIV-1 genotype were extracted from the EuResist database validation dataset and provided to the experts and to the EuResist engine. To simulate clinical practice, all current and past patient data were made available to the experts, including viral load, CD4 counts, previous treatment history, previous HIV-1 genotypes. The experts were allowed to consult any rules-based interpretation system and asked to provide a qualitative and quantitative estimate of the probability of short-term treatment success. The agreement among experts was evaluated by computing the multirater free-marginal kappa statistics for the qualitative prediction and the coefficient of variation for the quantitative prediction. The agreement between human experts and the expert system for the quantitative prediction was evaluated by Pearson correlation. The tradeoff between specificity and sensitivity for labeling a treatment as successful was evaluated by receiver operating characteristics (ROC) analysis

Results. In addition to the baseline TCE defining information, a median (IQR) of 15 (8-25) viral load measurements, 14 (10-30) CD4 counts and 1 (0-3) genotypes were available from past patient histories. There were 15 treatment successes and 10 treatment failures. In the classification task, the number of mislabeled cases was six for EuResist and 6-13 for the human experts (mean±SD 9.1±1.9). Based on ROC analysis, EuResist was not better than the mean prediction computed from the human experts, nor was it better than any of the individual experts. The only significantly different performance was that between the best and worst expert as measured by the area under the ROC curve (p = 0.011). The quantitative estimates computed by EuResist were significantly correlated with the mean quantitative estimates provided by the experts (Pearson r = 0.694, p = 0.0001). However, the agreement among the experts was moderate (for the classification task, kappa = 0.335; for the quantitative prediction, mean±SD coefficient of variation = 55.9±22.4%).

Conclusions. Predicting treatment response remains a difficult task even with the help of rules-based interpretation systems plus expert advice. Although tested on a limited number of cases, the EuResist engine performed as well as a panel of human experts in predicting short-term success, thus it may be considered as a treatment-decision support tool for clinical practice.

No conflict of interest

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