

Developing and validating a warfarin dose prediction model for patients in sub-Saharan Africa

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Background: Warfarin remains the most used oral anticoagulant in sub-Saharan Africa. It has a narrow therapeutic index and highly variable clinical response for a given dose and thus optimal dose prediction is difficult.

Aims: To develop and validate a warfarin dose prediction model for use in sub-Saharan African populations.

Methods: Multivariable linear regression models were fitted using data from 364 patients. Starting with a list of potential variables, all possible linear models were fitted, with the optimal models chosen with reference to mean absolute error (MAE), mean absolute percentage error (MAPE) and logarithmic accuracy ratio. Bootstrap validation was applied to correct overfitting and the final models were externally validated in a cohort of 690 patients. In both development and external validation cohorts, we compared our models with current warfarin initiation practice (fixed dose of 35 mg/week) and two widely known dose prediction models.

Results: The final model included the three predictor variables age, weight and target International Normalized Ratio, and gave MAE of 11.7 (95% CI, 10.5-12.9) mg/wk, MAPE of 14.4% and a log accuracy ratio of 0.003. Ideal dose (predicted dose within 20% of actual dose) was achieved in 42.6% patients. In external validation, MAE was 12.4 (11.5-13.5) mg/wk, MAPE 14.7%, log accuracy ratio 0.006 and ideal dose was achieved in 41.4%. Based on all these metrics, our model performed better than the two well-known models, and compared to fixed dosing, it decreased the percentage of patients at high risk of sub-optimal anticoagulation by 8.3% and 11.9% in the development and validation cohorts respectively.

Conclusions: A dosing model has been developed for the first time for Black African patients starting warfarin in South Africa and Uganda. Its clinical utility is soon to be tested in a prospective study.

Keywords

dose prediction, warfarin, anticoagulation, Black African, personalized medicine