Reviewer’s report

Title: A Prediction Study of Warfarin Individual Stable Dose after Mechanical Heart Valve Replacement: Adaptive Neural-Fuzzy Inference System Prediction

Version: 0 Date: 22 Sep 2017

Reviewer: Antonio Sterpetti

Reviewer's report:

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In a retrospective study the Authors tried to identify a model to predict the right dosage for warfarin after mechanical heart valve replacement. A total of 13639 eligible patients were selected, divided in 4 groups. Nine input variables were selected. The Authors used an ANFIS models. An ANFIS model tries to overcome the concept of the importance of a single isolated variable, determining groups of patients with specific multiple characteristics. ANFIS model achieved the highest total ideal predicted percentage 63.7%.

In the dose subgroups, all the models performed best in the intermediate-dose group with the ideal predicted percentage 82.4~86.4%, and the use of the stratified training group slightly increased the prediction accuracy in low-dose group by 8.8% and 5.2%, respectively.

The Authors concluded that as a preliminary attempt, ANFIS model predicted the warfarin stable dose properly after heart valve surgery among Chinese, and also proved that Chinese need lower anticoagulation intensity INR (1.5-2.5) to warfarin by reference to the recommended INR (2.5-3.5) in the developed countries.

The study is very interesting. I completely agree that univariate and multivariate analyses lead to serious limitations in analyzing clinical data. The concept of multi-dimensional analysis should be routinely introduced in the analysis of clinical data.
I have few questions and advices to make, if I am allowed.

1- The Authors should clearly state that this is a retrospective study, and before any clinical application, results should be validated in a prospective study.

2- In my opinion there is a statistical flaw. Using ANFIS, like any multi-dimensional analysis, importance is given to variables that have influence in that determined retrospective study. In other word, in a retrospective study ANFIS is only a description of the phenomenon that has been analyzed and it cannot be used as a predictive model. This should be clearly stated in the limitations of the study.

3- The Authors stated that in the Chiese population a lower dose of warfarin is needed in comparison to those recommended in the western world. Probably this assumption should be in some way modified according to the obvious differences between the population in the present study and the population in other western world studies. The mean age of the patients in this study was 50 years and less than 1% of the patients had history of embolic disorders. In my opinion the majority of the patients did not have atherosclerosis as etiological factor. This is a major difference which should be stated.

4- In the 9 selected variables there was no mention to the life style, that I think is a major influencing factor. I saw many patients in warfarin therapy who had a diet very reach in vegetable (namely spinach) and warfarin had a minor effect on the coagulation cascade.

In conclusion I would like to congratulate the Authors for their interesting study,. I would like to encourage them to continue in their analysis, which has many clinical potentials in cardiac as well in general surgery.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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