Author’s response to reviews

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

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Dear editors,

This letter provides a detailed response to two reviewer point raised, describing what amendments have been made to the manuscript text and where these can be found.

Reviewer reports:

Reviewer 1-Antonio Sterpetti:

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 multidimensional 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.

Response 2: Limitation section, line 7-9, page 9

3- The Authors stated that in the Chinese 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.

Response 3: Discussion section, line 5-9, page 8

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.

Response 4: Limitation section, line 3-5, page 9

Reviewer 2- Noriyuki Hirahara, Ph.D., M.D.:

Well written

Response: None