Reviewer’s report

Title: Would artificial neural networks implemented in clinical wards help nephrologists in predicting epoetin responsiveness?

Version: 1 Date: 21 August 2006

Reviewer: Bengt Rippe

Reviewer’s report:

General

Reviewer #1 requested a more detailed description of the development and evaluation and validation of the neural network. He also wanted a further description on how multiple linear regression models were constructed and about the training of the networks. He showed some disappointment with the fact that no significantly new relationships were described in the present paper. He also pointed out the crucial influence of the route of administration (subcutaneous vs. i.v.) of Epo, and the fact that other descriptors were noted as significant, including pH, Kt/V, PTH and CRP, yet left out of the network.

As I can see, the authors have tried to respond to all the concerns of Reviewer #1. Yet, the article is indeed hard to follow, and one would really like to have some more general description of how ANN’s operate. I could, however, sympathize with the view of the authors that the implementation of ANN’s in clinical wards is needed, and that this paper may be regarded as confirmatory in nature. It is not providing any groundbreaking new insights! The minor suggestions by Reviewer #1 seem to have been followed rather closely by the authors.

Reviewer #2 suggests a discussion of ANN’s in a wider context and wants the authors to discuss the robustness of ANN’s to corrupting factors such as errors in data sampling in the time recordings etc. Reviewer #2 also wants the definition of Kt/V, ACE-I and ARB to be done. The authors seem to have expanded the sections on all these points to address the concerns of Reviewer #2. Furthermore, Reviewer #2 wanted the authors to discuss the conflicting data of Port et al (1), which, however, was now done (to some extent) after the revision.

Reviewer #3 is mostly concerned with linear regression plotting between epoetin dose against hemoglobin value for each patient, and the fact that the effect of any change in epoetin dose is fully appreciated only after about 3 months. The mathematical coupling of the epoetin dose with a contemporary Hb value would lead to an underestimate of the dose/Hb ratio during the first months, after any increase in dose, and an overestimate after a reduction in the Epo dose. Furthermore, Reviewer #3 wanted the authors to discuss the conflicting data of Port et al (1), which, however, was now done (to some extent) after the revision.

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According to my personal judgment, the article is indeed hard to read for someone who is not familiar with ANN’s. A minimal platform for understanding the paper is the article by Cross et al (Ref 33). Scientifically, however, the paper is sound and I cannot see any major flaws in it! Linguistically, it is acceptable. In terms of clarity, it seems to have improved from the former version. The suggestions and recommendations of the former reviewers, who, by the way, did a brilliant job (!), have been followed, if not fully, to a great extent. These changes seem all to have improved the paper.

According to my view, the paper is an important confirmation of the utility of using ANN’s as a non-linear adaptive learning machine for individualizing epoetin dosage in clinical practice. As pointed out by the authors, compared to other computer assisted non-linear adapting modeling, ANN’s are evidently easy to use and to access, and have a tolerance to both missing data and input errors in individual variables. My definite impression is that the reader, after all, will be left with this impression and find the article to be of interest.

According to my opinion, the paper, after the revision already performed, is acceptable for publication.
Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)