Author's response to reviews

Title: Estimation of glomerular filtration rate by a radial basis function neural network in patients with type-2 diabetes mellitus

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Author's response to reviews: see over
July 29, 2013

Dr. Hayley Henderson  
Senior Executive Editor  
The BMC Nephrology Editorial Team  
e-mail: editorial@biomedcentral.com

MS: 2429087568207330, “Estimation of glomerular filtration rate by a radial basis function neural network in patients with type-2 diabetes mellitus”

Dear Dr. Henderson,

We have enclosed the revised version of our manuscript, “Estimation of glomerular filtration rate by a radial basis function neural network in patients with type-2 diabetes mellitus” (MS. MS: 2429087568207330), which we submitted for publication in BMC Nephrology.

We understand that referee 4 has raised some further concerns and we have provided point-by-point responses below, with references to the page numbers where changes were made. As requested, we have also highlighted all changes in the manuscript by use of the “Track Changes” feature of MS Word.

We thank you and reviewers for help in improving our manuscript and we hope that you find the revised manuscript acceptable for publication.

Sincerely yours,

Prof. Tan-Qi Lou

Referee 4:

Reviewer's report
Title: Estimation of glomerular filtration rate by a radial basis function neural
network in patients with type-2 diabetes mellitus

Version: 3 Date: 26 May 2013
Reviewer: James Tattersall

Reviewer's report:
Many of my concerns have been addressed in this revision. However, my major concern remains. It is not possible to reproduce or assess the validity and practicality of the neural network method used in this study. This is because the method is not explained adequately. The paper refers to a previous paper (ref 20), which describes the method and its validation. This paper was published only as an abstract and I have not been able to access it.

Response:
The full-text of a key reference for use of a radial basis function neural network to estimate glomerular filtration rate can be found in either EI (Engineering Village 2) or IEEE/IET Electronic Library (IEL):
http://www.engineeringvillage.com/controller/servlet/Controller?CID=quickSearchCitationFormat&database=1&SEARCHID=M2eed962713fe011cc01M2191prod3con1&intialSearch=true&showpatentshelp=false
http://ieeexplore.ieee.org/search/searchresult.jsp?newsearch=true&queryText=Application+of+radial+basis+function+neural+network+to+estimate+glomerular+filtration+rate+in+Chinese+patients+with+chronic+kidney+disease&x=35&y=18

I am also not convinced that the 99mTc-DTPA renal dynamic imaging method is an adequate gold-standard for GFR. the author has provided some references to support its validity, but there are others which show that this method is not particularly accurate. Therefore, the 99mTc-DTPA renal dynamic imaging may be practical and adequate for clinical use, but still controversial and inadequate as a gold-standard in studies.

Response:
We agree that diagnostic accuracy of the 99mTc-DTPA renal dynamic imaging method is debatable and we mentioned this as a possible limitation of our study in our original Discussion (page 15). In the revised manuscript, we provided additional justification for use of this method in the Methods (page 8) and expanded our discussion of this topic in the Discussion (pages 16-17).

Ma et al. (ref#31), Xie et al. (ref#32), and others have reported objections to this method. However, Ma et al. suggested that use of a proper reference GFR, better background subtraction, and soft-tissue attenuation correction may improve the accuracy of 99mTc-DTPA dynamic renal imaging. Xie et al. found that the CDK-EPI equation and the renal dynamic imaging method performed similarly in determining GFR for patients with elevated GFRs. Rehling et al. (ref#33) showed that a regression line between the values measured by inulin
clearance and renal dynamic imaging did not differ from the line of identity. Thus, the gamma camera uptake method with $^{99m}$Tc-DTPA is still recommended by Assadi et al. (ref#24) for routine practice.

Finally, the results of the study show that the neural networks model provided better precision and accuracy (only) for some groups of patients than the estimation by the traditional MDRD equations. However there was increased bias. So, it seems that the neural networks method offers only marginal benefit compared to the MDRD method for estimating GFR. I expect that it would be more complicated to apply the neural networks method than the MDRD method. It is not clear whether the benefits justify any increased complexity.

**Response:**

We agree that the artificial neural network (ANN) model had a greater bias than $^{99m}$Tc-DTPA renal dynamic imaging. However, a major advantage of the ANN model is that it can be modified and improved for different types of patients (e.g. patients with type-2 diabetes mellitus, as in our study), or by use of a six-variable genetic algorithm-optimized Back Propagation (GABP) network (Liu et al., 2013). Thus, the present study represents a foundation toward development of a better ANN model. As noted in our final paragraph, “We suggest that use of an RBF network model with more variables and testing of the model with additional data sets may ultimately provide more accurate and precise estimates of GFR.”

As mentioned in this previous article (Liu et al., 2013), an ANN model is a ‘black box’, and cannot be expressed as a simple mathematical equation. As a result, physicians may be initially reluctant to accept use of an ANN for calculation of GFR. However, a simple procedure together with ANN software could easily be provided to physicians to facilitate clinical application.


(https://www.plosone.org/article/info:doi/10.1371/journal.pone.0058242)