Reviewer's report

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

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Reviewer: James Tattersall

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This paper describes a study to compare various methods for estimating GFR in 207 Chinese patients with CKD and type-2 diabetes. One of these methods is a novel neural network model, previously trained on an independent dataset of 307 CKD patients. The results of each prediction method was compared with a 'standard' GFR measured using the (99m) Tc-DTPA renal dynamic imaging method. The paper is nicely written. The study population is well-defined and includes approximately equal proportions of patients with stages 1-2, 3 and 4-5. The methods used in the study were adequate to validate the ability of the neural network model to predict the GFR measured by the (99m) Tc-DTPA renal dynamic imaging method in an independent set of patients. The results of the study show that the neural network model cannot predict GFR well enough to be clinically useful. The standard deviation of error was -25 to +47 ml/minute/1.73m2.

My main concern with the paper is that it assumes that the (99m) Tc-DTPA renal dynamic imaging is a valid reference method for GFR. This method is not recommended for GFR measurement and has not been validated for this purpose, to my knowledge. The method is designed to measure the proportional contribution of each kidney (split-function), not absolute GFR. Where the GFR calculated by (99m) Tc-DTPA renal dynamic imaging has been compared to an accepted 'gold-standard', the agreement has been rather poor. In one study in Chinese patients, the agreement between GFR calculated by (99m) Tc-DTPA renal dynamic imaging agreed with an accepted standard method (plasma clearance of (99m) Tc-DTPA) less well than the MDRD prediction [reference Ma YC, Zuo L et al]. The modified Gates method used in the study to return GFR from (99m) Tc-DTPA renal dynamic imaging, was originally calibrated by comparison with measured creatinine clearance, not GFR.

Specific points;
1) The methods section (page 7) states that 207 consecutive patients with type 2 diabetes attending the Third Affiliated Hospital of Sun Yet-sen University (Guangzhou, China) were enrolled in the study. The paper should state how many patients refused consent or dropped out of the study.

2) The methods section states that the stage of CKD was determined according to the KDOQI guidelines. This guideline states that GFR should be estimated from serum creatinine using the MDRD or Cockcroft and Gault method. These serum creatinine measurement should be calibrated against an international standard. Which method was used in the study? Which international standard was used? If MDRD method was used, was it the 4-variable or 6-variable method? In table 4, neither of the MDRD methods used in the study (4- or 6-variable) resulted in the same number of patients classified in each stage of CKD as the original classification (KDOQI method). This suggests the original classification was made using the Cockcroft and Gault method. Is this correct?

3) The methods section (page 8) states that an enzymatic method was used to calculate serum creatinine. How was this method calibrated with the international standard?

4) The methods section should state the inputs used for by the neural network model.

5) The methods section should provide more information on the modified gates method and on the DTPA renal dynamic imaging. As described in the literature, Gates’ method estimates GFR not corrected for surface area. How were the results normalized to surface area in the study?

6) The results show that the neural network model predicted a higher GFR than calculated using the DTPA renal dynamic imaging. The paper should discuss the reason for this. In theory there should have been no bias as the neural network model was trained using the same method of GFR measurement. Presumably there were significant differences between the subjects in the training and study groups.

7) The discussion section (page 15) states “Our results suggest that an RBF model based on a single measurement (SCr) can provide precise and accurate estimates of GFR.” The results of the study does not support this statement. The results show that the model was very imprecise at predicting at GFR measured using DTPA dynamic imaging. The ability of the model to predict true GFR was not tested as no ‘standard’ method was used.
Reference

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests