Reviewer’s report

Title: A novel differential diagnostic model based on multiple biological parameters for immunoglobulin A nephropathy

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Reviewer: Francois Berthoux

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To the Authors:
This paper is potentially interesting but is very confusing for a nephrologist.
The goal is very clear: make the diagnosis of IgA nephropathy without renal biopsy; this is a big challenge!!
Background: the picture of renal biopsy complications is too dark and does not correspond to the reality!!

Material and methods:
The method with two sets of patients is correct: first establishing the model on 58 IgAN (biopsy-proven) and 63 non-IgAN. We need guaranty that the initial histopathological diagnosis is correct: we need to have the results of immunofluorescence with quantitation of IgA mesangial deposits in all 121 patients; we need to have the exact histopathological diagnosis for the non-IgAN and the score of the Oxford classification for all IgAN (M 0/1; E 0/1; S 0/1; and T 0/1/2).
The supplement 3 with the 57 parameters should be included as Table.

Results:
You should produce for each parameter (57) the data (mean+/-SD and median with extremes) for the 2 groups and comparisons by T and U tests. After, you may keep only those significant (P<0.05) or better highly significant (P<0.001) due to the big number of variables.
For each parameter, you may produce in a Table the C statistics for the ROC curves: AUC with 95% CI and P value. After you may select/keep only those highly significant (P<0.001).
For logistic regression, you should present univariate analyses with all the preselected variables. After, all significant or highly significant variables should be included in a multivariate analysis for prediction of IgAN. The really significant and independent variables should be used for the model.
We should see the results of all these MAJOR steps.
For the model, it should be define what is acceptable as accuracy parameters for a clinician: here specificity is more important than sensitivity; in my view specificity should not be below 0.90 (1false diagnosis out of 10) and ideally 0.95+. 
The validation set presented is an internal validation on retrospective cohort; an external independent validation will be needed in the future.

Figures:
ROC curves without C statistics are useless.
Figure 2 and Figure 6 are difficult to understand.
Figure 5: no legend for blue color!

Tables:
Table 1: all definitions should be given for each item: hypertension, nephritic Sd, nephrotic Sd, Proteinuria, Haematuria, normal renal function; etc; is Gross/Macroscopic hematuria included?
Table 3: what is “constant”?
Table 4: there is not a unique definition of accuracy; you should produce all accuracy parameters: Se, Sp, NPV, PPV, etc...

References:
Ref 3 is incomplete.
Ref to CT/NMR/PET-Scan, and CKD-EPI are useless with comments in background.