Critical Review Form

Clinical Prediction or Decision Rule

Probability of reduced renal function after contrast-enhanced CT: a model based on serum creatinine level, patient age, and estimated GFR, *AJR* 2009; 193: 494-500

Objective: **"To develop a model to predict the probability of reduced renal function after CECT (contrast-enhanced CT) either indirectly based on patient age, sex, and race and on pre-CT estimated glomerular filtration rate and to determine the relationship between patients with changes in creatine level that characterize contrast-induced nephropathy and patients with a reduced GFR after CECT." (p. 495)**

Methods: **Single-center chart review for all outpatients who had CECT between June 2004-December 2005, identified from a review of the radiology information system. Chronic kidney disease patients were excluded. From 140,000 CECT exams during this period, 6000 were randomly selected. Only the first CECT for each patient was included in the data and 49 dialysis and 113 patients <18 years old were excluded leaving 5309 unique patients in the data set. The final data set excluded those without a creatine both within 180 days prior to the CECT and 4 days after the CECT leaving 963 adults for analysis.**

Estimated GFR was computed using the MDRD equation recommended by the National Kidney Foundation (not the Cockcroft-Gault equation). The logistic regression model was built using 2/3 (n=642) of the sample for the derivation set and 1/3 (n=321) for the validation set. Backward selection of variables was used with p > 0.05 used for removal of variables. The Hosmer-Lemeshow goodness of fit model was used to assess model fit. Model discriminatory accuracy was assessed with ROC AUC. A fraction of charts were manually abstracted in order to assess the reliability of the electronic extraction technology.

Guide		Comments
I.	**Is this a newly derived instrument (level IV)?**	
A.	Was validation restricted to the retrospective use of statistical techniques on the original database? (If so, this is a Level IV rule & is not ready for clinical application).	Validated on a subset of the cohort-not the same patients but not as unique population either so a Level III CDR.
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	

1a	Were all important predictors included in the derivation process?	Uncertain. The authors do not detail what variables were included in building their models. If included, important variables such as previous CIN, proteinuria, or nephrotoxic medications may have increased the model's discriminatory capacity.
1b	Were all important predictors present in significant proportion of the study population?	Uncertain. The authors provide no demographic information or breakdown of risk factor prevalence for this study cohort.
1c	Does the rule make clinical sense?	No. This is an exponential probability calculator which is not user-friendly at the bedside. In addition, the lack of POEM and uncertain content validity (see II-1A above) limit one's confidence in this model.
2	Did validation include prospective studies on several different populations from that used to derive it (II) or was it restricted to a single population (III)?	Level III (see I-A above)
3	How well did the validation study meet the following criteria?	
3a	Did the patients represent a wide spectrum of severity of disease?	Yes. **TABLE 1: Study Group Patients (n = 963) With Reduced Renal Function Before and After Contrast-Enhanced CT (CECT)** No. (%) of Patients With Reduced Renal Function Estimated GFR Criteria[a] / Before CECT / After CECT / Testing Group (n = 642) / Training Group (n = 321) < 60 mL/min/1.73 m^2 / 156 (16.2) / 203 (21.1) / 135 (21.0) / 68 (21.2) < 45 mL/min/1.73 m^2 / 57 (5.9) / 85 (8.8) / 57 (8.9) / 28 (8.7) Note—GFR = glomerular filtration rate. [a]The estimated GFR was calculated using the four-variable Modification of Diet in Renal Disease Study equation (see Appendix 1).
3b	Was there a blinded assessment of the gold standard?	All patients had pre-and post-CECT Cr by inclusion criteria, but no blinding of data abstractors is reported.
3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	No. The predictor variables were not assessed prospectively. However the variables selected in these models are not prone to significant interpretation variation: age, gender ethnicity, creatine level.

3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	No, by design all patients had a pre- and a post-CT Cr.
4	How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?	• The derivation and validation sets did not differ in proportion with GFR <60 or GFR <45 (renal dysfunction severity). • To predict post-CECT GFR <60 multiple models are described in the manuscript, but the following model had the highest discriminatory ability (ROC AUC = 0.908) with the greatest simplicity (**see attached Excel calculator to compute this for you**): $y = 0.037A + 0.86G + 6.46Cr - 10.13$ Where A = patient's age G = gender (male = 0, female = 1) Cr=pre-CT creatinine $Probability_{GFR<60} = [e^y/(1+e^y)]$ • In comparing the change in serum Cr with GFR the discrepancy rate was 21.6% for GFR <60 and 15.2% for GFR <45. • Chart abstraction revealed differences in chart reviewers' and electronic medical record pre-CT Cr in 14/48 (29.2%) of cases abstracted.
III.	**Has an impact analysis demonstrated change in clinical behavior or patient outcomes as a result of using the instrument? (Level I). If so, consider the following:**	

1	How well did the study guard against bias in terms of differences at the start (concealed randomization, adjustment in analysis) or as the study proceeded (blinding, co-intervention, loss to follow-up)?	There have been no impact factor analyses performed for this instrument. Therefore, we are not sure if clinicians would (a) use the instrument; (b) accurately and reliably interpret the instrument's clinical implications; or (c) modify their clinical behavior in response to the instrument's results.
2	What was the impact on clinician behavior and patient-important outcomes?	The probabilities were not computed prospectively so if and how accurately clinicians compute the probabilities, as well as whether they use the information is unknown. However, computed as estimated post CECT GFR "may ultimately help determine which patients might be at unacceptably high risk of CIN so that alternative imaging studies without iodinated contrast material can be used." (p. 498)

Limitations

1) **No chart review methods.**

2) **No patient demographics (external validity).**

3) **No description of variables considered (internal validity).**

4) **No report of goodness of fit so this model may be over-fitted to the data.**

5) **Complicated exponential equation which is a difficult decision aid to use at bedside (see the attached Excel sheet which will calculate the post-contrast probability of GFR< 60 for you).**

6) **No patient-oriented outcomes (dialysis, prolonged LOS, etc).**

Bottom Line

This exponential equation derived from a poorly described cohort of outpatients without recognized underlying renal disease may predict post-contrast CT glomerular filtration rates <60 mL/minute/1.73 m^2 or <45 mL/minute/1.73 m^2, but further research is needed to assess the internal validity (additional risk factors), external validity (same results when applied to different populations), and reliability of this equation. In addition, user-friendly derivatives of this exponential approach should be evaluated prospectively to describe their impact on clinician behavior and patient-oriented outcomes.