Critical Review Form

Clinical Prediction or Decision Rule

Risk stratification nomogram for nephropathy after abdominal contrast-enhanced computed tomography, *Am J Emerg Med* 2011; 29:412-417

Objective: **"To develop (a) risk stratification nomogram for nephropathy inpatients receiving emergency A-CECT (abdominal contrast-enhanced CT) using clinical variables available before the procedure." (p. 413)**

Methods: **Retrospective chart review from August 2003-January 2007 at a single testing academic medical center ED with an annual census of 65000. Two trained emergency physicians abstracted the data from EMRs after identifying all patients receiving an abdominal CT with contrast who had pre- and post-contrast creatinine, were not already on dialysis and age <15 years. Data abstraction was limited to those variables that would be readily available at the ED bedside and included age, gender, history of DM, HTN, or cancer, type/volume of contrast material, baseline vital signs, and "laboratory results". All patients received non-ionic, low-osmolar contrast material administered as 2 ml/kg at 3 ml/sec. Initial serum creatinine (SCr) and all SCr over 3 days were recorded. CIN was defined as either an absolute increase of ≥ 0.5 mg/dl or a relative increase of 25% or more from baseline if the post-contrast creatinine exceeded 1.5 mg/dl.**

After univariate analysis, significant predictor variables were incorporated into a logistic regression model. Internal validation was conducted/tested using the bootstrap method to assess calibration accuracy (200 repetitions). The ROC AUC was computed with 95% CI. The odds ratios from the final prediction model were used to construct a nomogram to provide as risk-estimate for post-contrast nephropathy (below the nomogram below)

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).	Retrospective internal validation on the same data set using bootstrapping. Therefore, this is a level IV clinical decision rule with a risk of an over fitted model and therefore the results are not applicable to other populations.

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?	No. "We did not include variables other than those mentioned above because our intention was to develop a nomogram using only variables that are usually available before A-CECT for aiding in the decision to perform a A-CET before insult." (p. 416) However, there are many risk factors neglected that would be available at the bedside and that prior studies have found to be associated with CIN (anemia, proteinuria, previous CIN).
1b	Were all important predictors present in significant proportion of the study population?	Unknown. The investigators do not report the individual proportion of patients with risk factors.
1c	Does the rule make clinical sense?	Yes, but it might be difficult to apply at the bedside. Application available using smart phones or electronic medical records might be easier to use. In addition, the failure to incorporate the full set of variables previously described to lowers the content validity of the nomogram in question. (See II-1A).
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)?	No prospective validation so this is a Level IV CDR.
3	How well did the validation study meet the following criteria?	
3a	Did the patients represent a wide spectrum of severity of disease?	Uncertain since the investigators do not report what proportion of patients had mild, moderate, or severe CIN or what proportion required post-contrast dialysis.
3b	Was there a blinded assessment of the gold standard?	No. The gold standard was the post-contrast creatinine. Investigators do not state that chart reviewers were blinded to the study hypothesis or ancillary clinical data. Therefore, ascertainment bias is possible.
3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	The rule was not administered prospectively so we do not know whether clinicians would use the rule or interpret the predictor variables accurately.

3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	Not directly. The inclusion criteria mandated that all eligible patients have a pre- and post-CT creatinine, although the predictor variables in isolation or in aggregate probably impacted individual clinicians' decisions to obtain a post-CT creatinine. The patients in this trial probably represent a sub-population of ED patients that have more co-morbid illnesses and overall higher risk of CIN (spectrum bias).
4	How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?	• 5421 patients were identified but after excluding 4671 (25 without pre-CT Cr, 4606 without post-CT Cr, 5 dialysis patients, 35 under the age of 15) 750 patients were included in the model and bootstrapping validation. • Nephropathy was observed in 4.5% (34/750) • Age, DM, mean BP, and initial SCr were associated with nephropathy (Table 1 page 414) but the authors only included age and baseline Cr in the logistic regression modeling. • The final nomogram (below) had AUC 0.794 (95% CI 0.734-0.854) and the following diagnostic accuracy.
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 nomogram. Therefore, we are not sure if clinicians would (a) use the nomogram; (b) accurately and reliably interpret the nomogram's clinical implications; or (c) modify their clinical behavior in response to the nomogram.
2	What was the impact on clinician behavior and patient-important outcomes?	Cannot assess whether or how clinicians would use this nomogram since no impact analysis was performed in this derivation trial.

Predicted Prob CIN	Sen	Spec	LR+ (95%% CI)	LR- (95% CI)	Actual Incidence
≤ 1%	100	18	1.2(1.18-1.26)	NA	0%
1-5%	68	74	2.6(2-3.4)	0.44(0.27-0.71)	2.7%
≥ 15%	21	97	6.1(2.8-13.2)	0.82(0.69-0.98)	22.6%

Limitations

1) **No chart review methods (blinding/training/QA of chart reviewers). (Gilbert 1996, Worster 2004).**

2) **Use of logistic regression rather than recursive partitioning. The former will build a model that simultaneously maximizes sensitivity and specificity. For ED risk stratification, we generally prefer to maximize sensitivity at the expense of specificity so recursive partitioning is often preferred.**

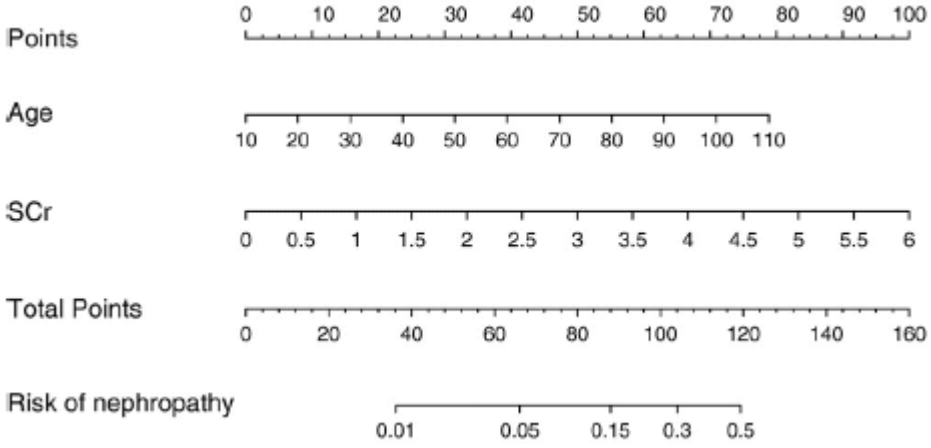
3) **Use of dichotomous likelihood ratios rather than interval LR's for continuous data.**

4) **Limited internal and external validity. Internal validity could be enhanced by incorporating more predictor variables initially, particularly those variables independently associated with CIN in other trials. External validity will necessitate assessment of the diagnostic accuracy in other populations.**

5) **Failure to report severity of CIN or patient-oriented outcomes.**

Bottom Line

Simple nomogram (see below) which (if validated) could assist clinicians in identifying ED patients at increased risk of post-CT CIN based upon age and baseline Cr alone in order for clinicians to consider alternative imaging strategies or prophylactic measures. Future research is still needed to validate the reliability (clinician ease-of-use and reproducibility when used prospectively) and diagnostic accuracy in different patient populations.



Instructions for nomogram

1. **Draw a straight line upward from age to point axis.**
2. **Draw another straight line upward from SCr to point axis.**
3. **Sum the points from #1 and #2. (point total)**
4. **Find the point total and draw a straight line downward to the "risk of nephropathy" axis.**