Editorial

Nomogram development and validation

Michael W. Kattan

Department of Quantitative Health Sciences, The Lerner Research Institute, Cleveland Clinic, Ohio, USA

Correspondence to: Michael W. Kattan, PhD. Department of Quantitative Health Sciences, The Lerner Research Institute, Cleveland Clinic, 9500 Euclid, JJN3-01 Cleveland, OH 44195, USA. Email: kattanm@ccf.org.

Comment on: Cai YJ, Dong JJ, Dong JZ, *et al*. A nomogram for predicting prognostic value of inflammatory response biomarkers in decompensated cirrhotic patients without acute-on-chronic liver failure. Aliment Pharmacol Ther 2017;45:1413-26.

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Cai *et al.* (1) have conducted a very elegant study regarding the prediction of survival in decompensated cirrhotic patients without acute-on-chronic liver failure. The development and validation of their nomogram was well done. Of course, future studies are always needed, and some suggestions can be made for how those might be done.

Updated nomogram development

An update to the Cai *et al.* (1) nomogram might consider making several changes. First, it would be very interesting to see what happens when NLR and LMR are left continuous. Dichotomizing them loses tremendous information and presumably prognostic power. Instead, they could be left continuous and allowed to have nonlinear effects, as was apparently done with age, although Cai *et al.* (1) do not specify the mechanism by which that was performed.

Harrell *et al.* (2) provide the argument against univariable screening for choosing the predictors in a nomogram. Cai *et al.* (1) used the predictors that were significant in univariable analysis for use in the multivariable model, and this univariable screening approach, although intuitive, does not necessarily produce the best prediction model. Harrell's argument is that subject matter experts should really make the call as to which predictors belong in the prediction model.

And for presentation purposes, the new nomogram can safely omit the axis for the linear predictor. No end user needs to see that clutter.

Updated nomogram validation

The key for any prediction model is how well it validates. Curiously, the best evidence for the Cai *et al.* (1) model is in the supplemental information, Table S3 and Figures S3, S4. Validation information should always take precedence over development information, such as that presented in Figure 2.

A key component in nomogram validation is Harrell's c-index. This measure has been around a very long time and is prominent in most all medical prediction model validation studies. However, it would appear that the measure has been modified by Cai *et al.* (1) without providing the details. Cai *et al.* (1) obtain different c-indexes for the 6-month, 1-year, and 3-year predictions. Using a Cox model, this should not have been possible if the original Harrell c-index were computed since there can be no rank order difference for those three predictions, and the time horizon for the outcome (e.g., 6 months *vs.* 3 years) does not enter into the Harrell calculation for the c-index.

A true validation cohort is ultimately needed to assess predictive performance (3). In the Cai *et al.* (1) study, only a single center's data was available. This is a common limitation and does not diminish the important first step that the authors have made in getting this nomogram in the literature and available for others to assess. However, it was not clear how Cai *et al.* (1) formed their validation cohort, presumably by splitting somehow the single center's dataset.

An interesting clinical question will lie in the predicted probability cutoff for decision making. The decision curve analysis performed by Cai *et al.* (1) was an important contribution. However, if a very low predicted probability of survival is necessary for clinical decision making, the calibration curves of the validation cohort suggest these predictions will not occur commonly with the currently

nomogram, especially in the short-term prediction setting.

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