Acute kidney injury (AKI) is a worldwide epidemic that results in 2 million deaths per year along with imposing significant economic burden. Several reports have highlighted a higher prevalence of acute renal failure associated with critical illness, with a significant proportion of patients needing acute renal replacement therapy (RRT) [1]. Severe AKI requiring RRT is associated with higher rates of in-hospital mortality and increased risk of chronic dialysis among survivors. There is lack of specific therapy for AKI, and no differences in survival with existing RRT modalities (continuous vs. intermittent) or with increasing intensity of treatment have been demonstrated. Hence, there is a need to identify those who are at a high risk for developing AKI. Kiers et al. [2] reported that predictive models by Thakar and colleagues offer the best discriminative value to predict the development of AKI after cardiothoracic surgery and are applicable for all patients undergoing cardiac surgery.

In those with established AKI, mortality prediction models are valuable for risk stratification, clinical decision-making, comparing quality of care and facilitating AKI clinical trial enrollment. Several studies have studied the risk factors for mortality after AKI. The Stuivenberg Hospital Acute Renal Failure and Liano scores were initially derived from a single center, and later tested in a multi-center cohort in which the Stuivenberg Hospital Acute Renal Failure II score performed better than the Liano score [3, 4]. The Vellore score was developed using both community and hospital AKI cohorts in the tropics. Two other studies have derived risk scores for in-hospital mortality using a multi-centric database, and inclusion criteria were based on serum creatinine measurements [5]. Demirjian et al. [6] developed an AKI-specific risk prediction model for 60-day mortality in patients supported by RRT using the VA/NIH acute renal failure trial network database.

In this issue of the Journal, Ohnuma et al. [7] compared the ability of various mortality prediction models in a retrospective, multi-centric cohort of 343 Japanese patients with AKI requiring continuous renal replacement therapy in 14 ICUs captured between January and December 2010. Overall, the mortality rate of this cohort (58.6%) was slightly higher than other established scoring systems. All included scores had an area under the re-
ceiver operator curve <0.80. Among these scores, Demirjian score had the highest discriminatory ability and Lia
no’s model had better calibration ability. Validation co-
hort consisted of critically ill patients, majority of whom
were on respiratory and vasopressor support with sepsis
being the predominant cause of AKI. Although this study
attempts to address an important question and reveals
some interesting findings, its limitations deserve men-
tion. While the study aimed at performing an external
validation of existing scores, it excluded patients with
AKI not requiring continuous renal replacement therapy
(including those who were started on intermittent dialy-
sis), which may impact overall model performance. The
authors acknowledged the relatively small sample size of
the study, missing data, and inability to calculate calibra-
tion using Hosmer-Lemeshow test due to lack of inter-
cept. It also needs to be emphasized that there are differ-
ces among the outcomes of the original prediction
models (in-hospital mortality, 60-day mortality, etc.) and
these equations were derived from observational cohorts
(except for Demirjian score) that are subject to inherent
biases.

Evaluating the performance of a predictive model is
challenging. Whereas calibration refers to how close the
predicted risk of outcomes is to the actual risk, the pre-
diction score’s ability to distinguish those with and with-
out outcomes defines discrimination. It is difficult to
have a prediction score with good discrimination and
good calibration. For instance, if the predicted values for
those with outcomes are higher than those without out-
comes, the model can discriminate perfectly, even if the
predicted risk does not match the proportion with out-
comes. In the prognostic setting, the predictors are as-
essed before outcome occurs and therefore discrimina-
tory ability is valuable as it is insensitive to the random
nature of the outcomes [8]. Since calibration implies the
agreement between predictions and actual outcomes,
models with high calibration will help inform clinical de-
cision making.

Ohnuma et al. [7] inform us about the utility of the
available risk prediction models in AKI in Japanese pop-
ulation but it also provides an opportunity to revisit the
areas that warrant further examination. AKI requiring
RRT portends both serious short-term and long-term
consequences. Earlier and accurate diagnoses of kidney
damage using tissue specific biomarkers may help in
prompt institution of treatment of AKI and is an area of
active research. Predictive models in AKI may be used in
conjunction and to validate novel biomarkers. Indeed,
urine IL-18 and plasma NGAL were found to improve
AKI prediction in cardiac surgery cohorts [9]. Similarly,
NGAL was found to predict AKI in a cohort of critically
ill patients. Given that these cohorts reflect relative ho-
mogeneity in the context of surgical course and patient
characteristics, there is an unmet needs for studies evalu-
ating biomarker performance in multiple institutions with
diverse patient population with varying etiology of AKI.
We hope future studies integrating biomarkers will en-
able incremental prognostic information beyond that
found by clinical and laboratory evaluation.

Recent literature demonstrates that AKI survivors
have significant risk of advanced kidney disease as well
as mortality. Poukkonen et al. [10] utilized the Finnish AKI
dataset to develop models predicting 1-year mortality af-
after AKI. But, there is lack of reliable predictive scores for
ascertaining long-term prognosis (including renal out-
comes such end stage renal disease), which would help us
identify high-risk populations needing close follow-up.
Previous studies had small sample size and the increasing
availability of electronic health record data can be lever-
aged to include data from a larger number of patients in
clinical practice to predict outcomes in this cohort. Such
efforts have been made to predict AKI in hospitalized
patients and future studies can develop models to predict
outcomes in those with AKI using such data [11]. These
would reflect real-world data and might be more gener-
izable.

It is unequivocal that there is a substantial need for
strategies to prevent the development of AKI, to hasten
the kidney function recovery and to mitigate the adverse
outcomes following AKI. Although predictive models
cannot replace clinical acumen, they act in conjunction
and aid risk stratification. While we hope that a combina-
tion will facilitate novel diagnostic tools and interven-
tions in AKI, additional studies are warranted to accu-
rately predict long-term outcomes in those with severe
AKI.

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