Predicting Cisplatin-Induced Kidney Injury: A Milestone in Onconephrology

By Prakash Gudsoorkar

One of the central challenges in oncology is striking the right balance between effectively eradicating cancer cells and safeguarding patient well-being. Cisplatin, a linchpin in chemotherapy regimens, is well-documented for its efficacy but equally notorious for its nephrotoxic potential. This toxicity can drastically affect patient outcomes and quality of life. In a groundbreaking study published in *The BMJ*, Gupta and colleagues (1) developed and externally validated a risk-prediction model for severe cisplatin-associated acute kidney injury (CP-AKI). This research represents a pivotal advancement in personalized cancer care.

To develop their risk-prediction model, Gupta and colleagues (1) conducted an extensive multicenter cohort study across six major academic cancer centers in the United States, meticulously examining data from 24,717 individuals treated with intravenous cisplatin therapy from 2006 to 2022. The primary outcome was moderate-to-severe AKI, defined by a twofold or greater increase in serum creatinine or the initiation of kidney replacement therapy within 14 days after administration, aligning with the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for stage 2 or 3 AKI, thus focusing on the most clinically significant form of AKI. As secondary outcomes, the authors also investigated broader and stricter definitions of CP-AKI, along with the composite outcome of major adverse kidney events within 90 days, which further deepens our comprehension of the renal implications of post-cisplatin administration.

The authors implemented rigorous inclusion and exclusion criteria and collected detailed data on demographics, comorbidities, baseline laboratory values, and concomitant nephrotoxic chemotherapies. The study identified independent predictors of CP-AKI through multivariable logistic regression within a derivation cohort and subsequent external validation. The analysis of continuous variables using restricted cubic splines, backward elimination for variable selection with a p value threshold of 0.1, and multiple imputation for missing data culminated in a primary model that achieved a c-statistic of 0.75, greatly outperforming previous risk models for CP-AKI, which had c-statistics ranging from 0.60 to 0.68. The increased accuracy in predicting CP-AKI could facilitate closer monitoring and early intervention strategies for those at the highest risk.

Consider two hypothetical patients with cancer, each of whom is about to receive cisplatin therapy, as shown in the Table.

Table. Hypothetical patients with cancer

	Patient 1	Patient 2
Age (years)	25	60
Cancer type	Testicular	Lung
Hypertension	No	Yes
Diabetes mellitus	No	Yes
Cisplatin dose (mg)	100	150
Serum creatinine (mg/dL)[a]	0.8	1.4
Serum magnesium (mg/dL)[a]	2.0	1.0
Serum albumin (g/dL)[a]	4.0	2.5
Hemoglobin (g/dL)[a]	14.0	11.2
White blood cell count (K/mm^3)[a]	10.0	14.0
Platelet count (K/mm^3)[a]	250	125

[a]Indicates laboratories drawn before cisplatin administration.

By entering their clinical characteristics into the online risk calculator (https://kidneycalc.org/cp-aki-calculator/), the greatly different risks of CP-AKI between these two patients can be appreciated, as shown in the Figure.

The authors also found a strong association between CP-AKI severity and 90-day mortality, highlighting the clinical importance of these findings.

Despite its strengths, the study had some limitations, including the potential for limited generalizability, as it used data only from major US-based academic centers. Nevertheless, the study's merits, such as its extensive sample size (considerably larger than all prior studies combined), stringent definition of CP-AKI (prior studies used much more liberal definitions for CP-AKI), and the practical applicability of its online risk-prediction model, are noteworthy. The model's reliance on readily accessible clinical variables for risk assessment broadens its utility across various clinical settings, empowering health care practitioners to proactively identify patients with high risk with tailored nephroprotective strategies.

In summary, the research by Gupta and colleagues (1) signifies a substantial leap toward personalized medicine in oncology, presenting an innovative and practical tool for predicting severe CP-AKI in cisplatin recipients. This model hopes to enhance patient outcomes, reduce health care costs, and elevate the overall standard of cancer care. Looking forward, the prospective validation of this predictive model in a wider range of clinical environments and its integration into clinical workflows are crucial steps. Such measures will harness the model's full potential to alleviate the nephrotoxic effects of cisplatin therapy, propelling the onconephrology field forward. ■

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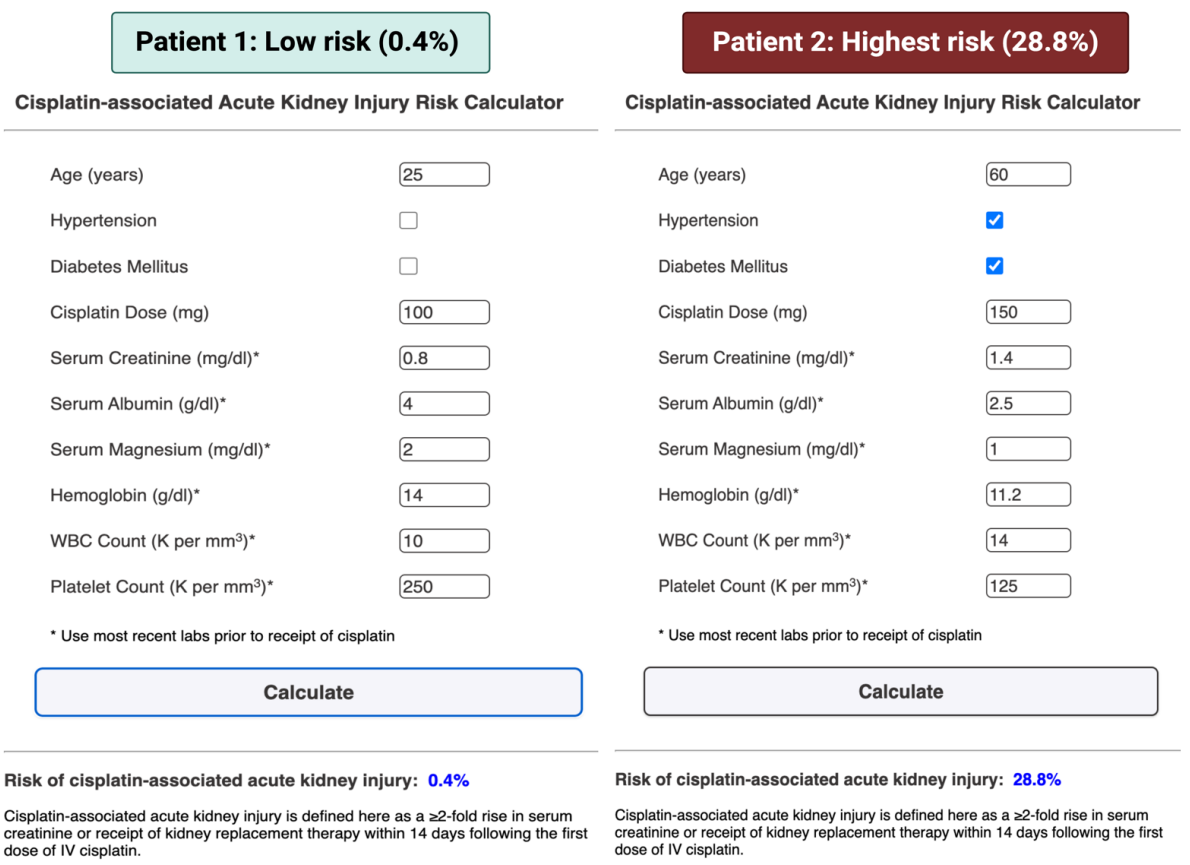
Reference

1. Gupta S, et al. Derivation and external validation of a simple risk score for predicting severe acute kidney injury after intravenous cisplatin: Cohort study. *BMJ* 2024; 384:e077169. doi: 10.1136/bmj-2023-077169

Figure. Results of the CP-AKI risk calculator among hypothetical patients



IV, intravenous; WBC, white blood cell.