Development and Validation of a Prediction Model for Kidney Failure in Long-term Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)

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Purpose of study: Kidney failure is a rare but serious late effect following childhood cancer treatment. We aimed to develop a model using demographic and treatment characteristics to predict individual risk of kidney failure among five-year survivors of childhood cancer.

Methods: Childhood Cancer Survivor Study (CCSS) participants without history of kidney failure five years after cancer diagnosis (n=25,483) were assessed for subsequent kidney failure (i.e. dialysis or kidney transplantation, or death due to kidney disease) by age 40. Outcomes were self-reported and corroborated by the Organ Procurement and Transplantation Network and the National Death Index. A sibling cohort (n=5,045) served as a comparator. Piecewise exponential models accounting for race/ethnicity, age at diagnosis, nephrectomy, chemotherapy dosing, radiation dosimetry, congenital genitourinary anomalies, and early-onset hypertension estimated the relationships between potential predictors and kidney failure and were converted to integer risk scores. The St. Jude Lifetime Cohort Study (SJLIFE) and the National Wilms Tumor Study (NWTS) served as validation cohorts.

Results: Among CCSS survivors, 204 developed late kidney failure. Prediction models achieved an area under the curve (AUC) and concordance (C) statistic of 0.67 and 0.70 for kidney failure by age 40. Validation cohort AUC and C-statistics were 0.88/0.88 for SJLIFE (8 cases) and 0.67/0.64 for NWTS (91 cases). Risk scores were collapsed to form statistically distinct low- (n=17,762), moderate- (n=3,784), and high-risk (n=716) groups, corresponding to cumulative incidences in CCSS of kidney failure by age 40 of 0.6% (95% CI 0.4-0.7%), 2.1% (95% CI 1.5-2.9%), and 7.5% (95% CI 4.3-11.6%), respectively, compared with 0.2% (95% CI 0.1-0.5%) among siblings.

Conclusions: Prediction models can guide screening and interventional strategies for childhood cancer survivors at higher risk of late kidney failure.