Adverse Outcomes In Patients With Cancer Who Have Discrepancies In Serum Creatinine And Cystatin C-Based Estimated Glomerular Filtration Rate

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ABSTRACT

Intro: Accurate kidney function assessment is integral to safe medication dosing in patients with malignancy. Glomerular filtration rate (GFR) is typically estimated using serum creatinine (eGFR_{CRE}). However, patients with malignancy tend to have lower serum creatinine due to loss of muscle mass, and kidney function may be overestimated by eGFR_{CRE}. We hypothesized that discrepancies between eGFR_{CRE} and eGFR_{CYS} are common in patients with malignancy, putting them at risk for adverse side effects from medications that requires dose adjustment based on kidney function.

Methods: We conducted a retrospective cohort study of 1988 patients with malignancy who had concurrent creatinine and cystatin C measurement. eGFR discrepancy was defined as an eGFR_{CYS} more than 30% lower than eGFR_{CRE}. High-risk eGFR discrepancy was defined as eGFR_{CYS} more than 50% lower than eGFR_{CRE} plus eGFR_{CYS} less than 30mL/min/1.73m². Logistic regression was performed to identify predictors of high-risk eGFR discrepancies. We compared the rate of medication adverse events among vancomycin, trimethoprim/sulfamethoxazole, baclofen, and digoxin recipients who had eGFR discrepancy and those who did not.

Results: Total of 579 patient (29%) of the cohort had eGFR discrepancy, and 139 (7.0%) of patients had high-risk eGFR discrepancy. Predictors of eGFR discrepancies included white race (adjusted OR 1.57 (1.19 – 2.10) p=0.002), obesity (adjusted OR 1.54 (1.10 – 2.17) p=0.012), coronary artery disease (adjusted OR 1.34 (1.03 – 1.73) p=0.029), diabetes mellitus (adjusted OR 1.38 (1.07 – 1.79) p=0.014), cirrhosis (adjusted OR 1.86 (1.17 – 2.99) p=0.009), hypoalbuminemia (adjusted OR 5.89 (1.34 – 2.48) p<0.001) and anemia (adjusted OR 2.63 (1.91 – 3.64) p<0.001). Patients with eGFR discrepancy were more likely to have medication adverse side effects including vancomycin toxicity (66.8 vs. 39.8%, p<0.001), hyperkalemia due to trimethoprim-sulfamethoxazole (29% vs 13%, p<0.001), baclofen toxicity (25% vs. 0%, p=0.13), and digoxin toxicity (8.3% vs. 0%, p=0.30) compared to patients without eGFR
discrepancy. The rate/severity of medication adverse effects were even higher in patients with high-risk eGFR discrepancies.

**Conclusion:** It’s crucial to estimate GFR accurately in patients with malignancy since discrepancies between eGFR\textsubscript{CRE} and eGFR\textsubscript{CYS} may necessitate drug dose adjustment given higher risk of medication-related adverse effects. Our results suggest that direct patient harm can result from improper GFR estimation and an inappropriate drug dosing. Future studies are needed to improve and personalize the approach to GFR estimation in patients with malignancy.