Title: *Impact of difference in estimated glomerular filtration rate based on creatinine and cystatin on the overall survival of patients with cancer*

Authors: Rayra Gomes Ribeiro, Renato A. Caires, George Marcelo T. Sapienza, Emmanuel A. Burdmann, Gilberto de Castro Júnior, Maria Del Pilar Estevez Diz, Verônica Torres Costa e Silva

Affiliation:

Instituto do Câncer do Estado de São Paulo (ICESP), Universidade de São Paulo (USP), São Paulo, Brazil

Background: Estimated glomerular filtration rate (eGFR) can differ according to whether serum creatinine (SCr) or cystatin C (Cys) is used for eGFR calculation, but the impact of these differences on adverse events of patients with cancer has not been demonstrated. We aimed to evaluate the impact of eGFR differences (eGFRdiff) between cystatin C–based eGFR (eGFRcys) and creatinine-based eGFR (eGFRcr) on the overall survival (OS) of patients with cancer admitted for treatment.

Methods: This is a prospective cohort of adult patients with solid tumors (diagnosed in the last 90 days) initiating treatment at a tertiary cancer center. eGFRcr and eGFRcys were calculated using the 2021 CKD-EPI equations. eGFRdiff was calculated: (eGFRcys-eGFRcr) *eGFRcr/100); If negative, eGFRcys < eGFRcr. SCr and Scys were measured through standardized assays at the University of Minnesota, the CKD-EPI Consortium laboratory of analysis. Measured (mGFR) was determined by the plasma clearance of 51Cr-EDTA.

Results: A group of 1,011 patients recruited from April 2015 to September 2017 was included for analysis and censored in March 2023. Patients were 50.6 ±13 y, 50.7% female. The most common cancer sites were breast (22.4%), gastrointestinal (21.9%), and male genital (21.2%); 15.5% had metastasis. ECOG 0, 1, and 2&3comprised 64%, 32%, and 6% of patients, respectively. Time of follow-up was 5.7 (2.5-6.5) y; overall mortality was 27.4%. Mean mGFR was 79.7 ± 21.1 ml/min/1.73m²; 17.2% had mGFR <60ml/min/1.73m². eGFRcr, eGFRcys, and eGFRcr-cys were 89.5 ± 19.9, 75.3 ± 23.8, 84.2 ± 22.2 ml/min/1.73m², respectively. eGFRdiff was lower than -30% in 22.5%, between -30 and +30% in 76.7%, and higher than+30% in 0.8% of patients. In the Cox regression model adjusted for age, sex, cancer site, metastasis, ECOG, and C-reactive protein, eGFRdiff lower than -30% was an independent predictor of reduced OS, even when adjusted for mGFR (Table).

Conclusion: This is the first study assessing the impact of eGFRdiff on the prognosis of patients with solid tumors. eGFRcys at least 30% lower than eGFRcr was associated with reduced OS. Our results endorse the utility of eGFRdiff as a predictor of worse outcomes in patients with cancer.

Table. Cox Regression Models	
Variables	**HR (95% IC)**
eGFRdiff > -30% **Between -30% and + 30% (reference)** > +30%	**1.56 (1.20 -2.03)** ---------- 0.0 (0.0 – 0.0
eGFRdiff adjusted for mGFR > - 30% **Between -30% and +30% (reference)** > + 30%	**1.50 (1.14 – 1.98)** --------- 0.0 (0.0 – 0.0)

Models were adjusted for age, sex, cancer site, metastasis, ECOG, and C-reactive protein. CI, confidence interval; HR, hazard ratio. eGFR difference: (eGFRcys -eGFRcr) * eGFRcr/100