CREATININE AND CYSTATIN-BASED ESTIMATED RENAL FUNCTION IN VANCOMYCIN MONITORING

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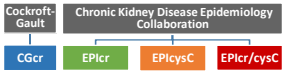
BACKGROUND AND AIM

Glomerular filtration rate (GFR) is usually estimated by using creatinine (cr) or cystatin C (cysC), but results are not always overlapping. Although CysC is not a reference marker, it has gained importance in drug monitoring.

The study evaluates the effect of using different equations for GFR estimation in vancomycin monitoring.

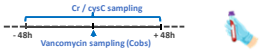
EQUATIONS:



METHODS

❑Study design and sample characterization

- Data from the last 5 years
- Age > 18 years (n=34)
- cr, cysC obtained within a range of 48h from observed vancomycin concentrations (Cobs) (n=47)



	Age (Years)	Weight (Kg)	cr (mg/dl)	cysC (mg/L)
mean±SD*	63.0 ± 16.4	64.5 ± 16.6	0.74 ± 0.49	1.70 ± 0.60
Range	28 - 90	38 - 110	0.18 – 2.12	0.74 – 3.82
n	34			47

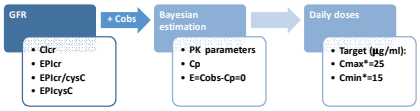
Sex (M/F)* 14/20 — Race (W/B)* 30/4

❑Estimation of GFR based on different equations

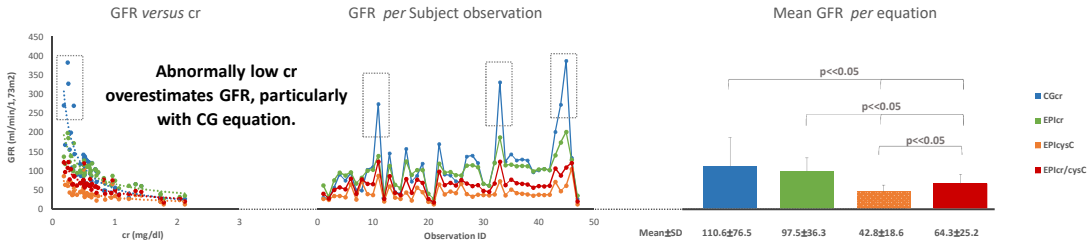
Equations	
CGcr	Clcr (ml/min)=((140-age) x weight / (72xcr)) x (0.85 if woman)
EPIcr (2009)	GFR (ml/min/1.73m²) = a x[(cr/b)^c)]x[0.993^Age]x[1.159 if black] Woman: a = 144; b = 0.7; c = 0.329 (if cr≤0.7) or 1.209 (if cr>0.7) Man: a = 141; b = 0.9; c = 0.411 (if cr≤0.9) or 1.209 (if cr>0.9)
EPIcysC (2012)	GFR (ml/min/1.73m²) = 133x[(cysC/0.8)^a)]x[0.996^Age]x[0.932 if woman] a = 0.499 (if cysC≤0.8) or 1.328 (if cysC>0.8)
EPIcr/cysC (2012)	GFR (ml/min/1.73m²) = a x[(cr/b)^c)]x[(cysC/0.8)^d)]x[0.995^Age]x[1.08 if black] Woman: a = 130; b = 0.7; c = 0.248 (if cr≤0.7) or 0.601 (if cr>0.7); d = 0.375 (if cysC≤0.8) or 0.711 (if cysC>0.8) Man: a = 135; b = 0.9; c = 0.207 (if cr≤0.9) or 0.601 (if cr>0.9); d = 0.375 (if cysC≤0.8) or 0.711 (if cysC>0.8)

❑Pharmacokinetics (PK) and statistical analysis

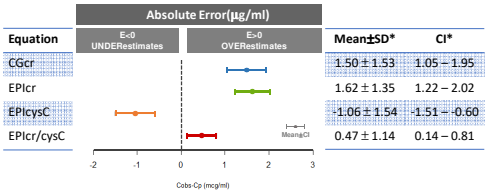
- PK bayesian estimation (PKS - Abbott®)
- Determination of Predicted concentration (Cp) and daily dose
- Absolute error (E), E=Cobs-Cp=0 → indicator of the adequacy of the equations
- Statistical inference at a confidence level of 95%



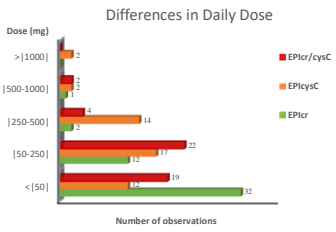
RESULTS



Estimated GFR showed statistically significant diferences (ANOVA 2-Way).



CGcr, EPIcr and EPIcr/cysC equations overestimated (E>0) renal function. Renal function was underestimated (E<0) with EPIcysC.



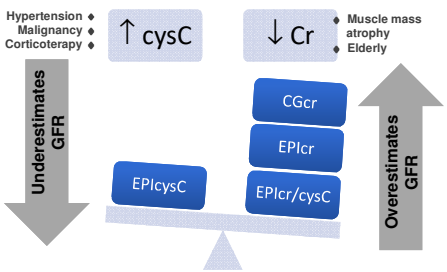
The estimated differences in daily doses ranged from 100 to 1600 mg/70Kg/day, considering CGcr equation as reference.

CONCLUSIONS AND RELEVANCE

The overestimation of GFR with equations dependent on cr, CGcr, EPIcr and, to a lesser extent, EPIcr/cysC, was marked in patients with abnormally low cr. Conversely, with EPIcysC equation, which depends on cysC, a biomarker independent of muscle mass, GFR was underestimated. This may be due to factors that increase cysC, without renal function impairment, such as hypertension, corticosteroid therapy and malignancy, all common in hospitalized patients, but poor data did not allow to explore this association.

The differences in the GFR estimates were clinically relevant on dosing adequacy, being suggestive that in the presence of abnormally low cr, equations with cysC are preferred.

Studies are needed to identify the variables responsible for the observed variability, in order to previously select the most appropriate equation for each case.



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*LIST OF ABBREVIATIONS: B – black; Cmax – maximum concentration; Cmin – minimum concentration; F – female; IC – confidence intervals; M – male; SD – standard deviation; W – white

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