MP547

CYSTATIN C AND BETA-2 MICROGLOBULIN - VALUABLE BIOMARKERS OF RESIDUAL RENAL FUNCTION IN PERITONEAL DIALYSIS

Carla Leal Moreira[1], Liliana Cunha[1,2], Maria João Carvalho[1], José Carlos Oliveira[3], Olívia Santos[1], António Cabrita[1], Anabela Rodrigues[1]

1 – Nephrology Department, Centro Hospitalar do Porto; 2 – Nephrology Department, Hospital Fernando Fonseca; 3– Clinical Pathology Department, Centro Hospitalar do Porto.

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Introduction

Standard residual renal function (RRF) evaluation remains dependent of 24h urine collection. Serum biomarkers Cystatin C (CysC) and Beta-2 microglobulin (ß2M) accuracy for estimating RRF has been studied in peritoneal dialysis (PD) patients. Hoek et al in the Netherlands, proposed a simple equation based on serum CysC levels and found that it outperformed the Modification of Diet in Renal Disease formula. Yang et al, in China, developed a hyperbolic model based on serum levels of CysC, concluding it can reliably estimate RRF in patients on CAPD. T Shafi, in USA, also developed equations using CysC and ß2M, respectively.

Aim: Evaluate CysC and ß2M equations accuracy to estimate RRF in a sample of PD patients.

Methods

We conducted a cross-sectional study enrolling all 52 stable patients in our outpatient peritoneal dialysis clinic between September and December of 2016. Anuric patients (diuresis <200ml/24h) were excluded (n=12). RRF was measured by average clearance of urea and creatinine (CLCrU) in 24-h urine collection and compared to estimated RRF (eRRF) applying CysC based equations published by Hoek, Yang and T Shafi, and ß2M using T Shafi's equation.

Agreement between CysC equations, ß2M equation and CLCrU was performed using Bland-Altman plot test. Accuracy of these biomarkers in estimating RRF was tested calculating the area under the curve (AUC) and the cutoff value for RRF was 2.0 mL/min/1.73m2.

Statistical analysis was performed using Stata/IC 14.0.

Results

In our sample of 40 patients, male patients represented 50% (n=20), mean age was 53.7 ± 12.9 years-old. Patients main baseline characteristics are described in *table 1*.

Serum CysC level was not significantly associated with peritoneal or urinary CysC excretion, age, gender, diabetes, body mass index, body cell mass, lean total mass, normalized protein catabolic rate or PD modality.

In contrast, serum CysC levels did correlate with renal (rho- 0.77, p<0.00001) and peritoneal CLCr (rho 0.44, p=0.004), and ß2M level (rho 0.76, p<0.00001). Serum ß2M level also correlated with both renal (rho -0.71, p<0.0009) and peritoneal CLCr (rho 0.50, p=0.005), and an association was found with PD modality (z=3.22, p=0.001).

The mean CLCrU was of 5.2±3.4 (mL/min/1.73m2), the eRRF was of 3.7 ± 1.0 for Hoek's equation, 6.4 ± 1.2 for Yang's CysC equation, 5.7 ± 1.2 for T Shafi's CysC equation, 7.4 ± 3.1 for T Shafi ß2M equation. The mean bias in eRRF was lowest for T Shafi's CysC equation (-0.49, p<0.0001), followed by Yang's CysC equation (-1.21, p<0.0001) and Hoek's CysC equation (1.48, p<0.0001), while ß2M equation showed the largest variability in bias (-2.22, p=0.56), *Figure 1*. Each equation's accuracy to estimate RRF is expressed in *Figure* 2.

Patients Characteristics	*Mean(SD)/Median(IQR) or N(%)*
N	40
Age, mean (SD)	53.7 (12.9)
Males	20 (50%)
Hypertension	38 (95%)
Diabetes mellitus	4 (10%)
Chronic kidney disease etiology	
Diabetic nephropathy	3 (8%)
ADPKD	2 (5%)
Chronic GN	22 (55%)
Nephroslerosis	1 (2%)
Others	12 (30%)
Charlson Comorbidities Index, median (IQR)	3 (2, 4.5)
Time on PD (months), median (IQR)	20.9 (11.5, 37.3)
PD modality	29 (72%)
Weekly peritoneal CrCL (L/1,73m^2), median(IQR)	38.2 (34.3, 45.5)
Weekly renal CrCL (L/1,73m^2), median (IQR)	39.3 (26.9, 72.1)
D/P ratio 4h, median (IQR)	0.8 (0.7, 0.8)
CLCrU (ml/min/1.73m^2), mean (SD)	5.2 (3.4)
UF Peritoneal (L), median (IQR)	1.3 (0.8, 1.8)
nPCR (g/Kg), median (IQR)	1.1 (0.9, 1.3)
Serum CysC mg/L, median (IQR)	5.5 (4.3, 6.3)
Peritoneal CysC mg/L, median (IQR)	12.1 (5.6, 17.7)
Urinary CysC mg/L, median (IQR)	4.7 (2.1, 8.0)
Serum Creatinine mg/dL, median (IQR)	8.5 (2.8)
ß2M (mg/L), median (IQR)	22.4 (7.4)

Table 1: Baseline characteristics of the patients.
Data presented as mean ± SD (standard deviation), median (interquartile range), or percent frequency, as appropriate. GN: glomerulonephritis; ADPKD: autossomal dominant policystic kidney diasese; PD: peritoneal dialysis; CLCrU: clearance of urea and creatinine in 24-h urine collection; UF: Ultrafiltration; nPCR: normalized protein catabolic rate.

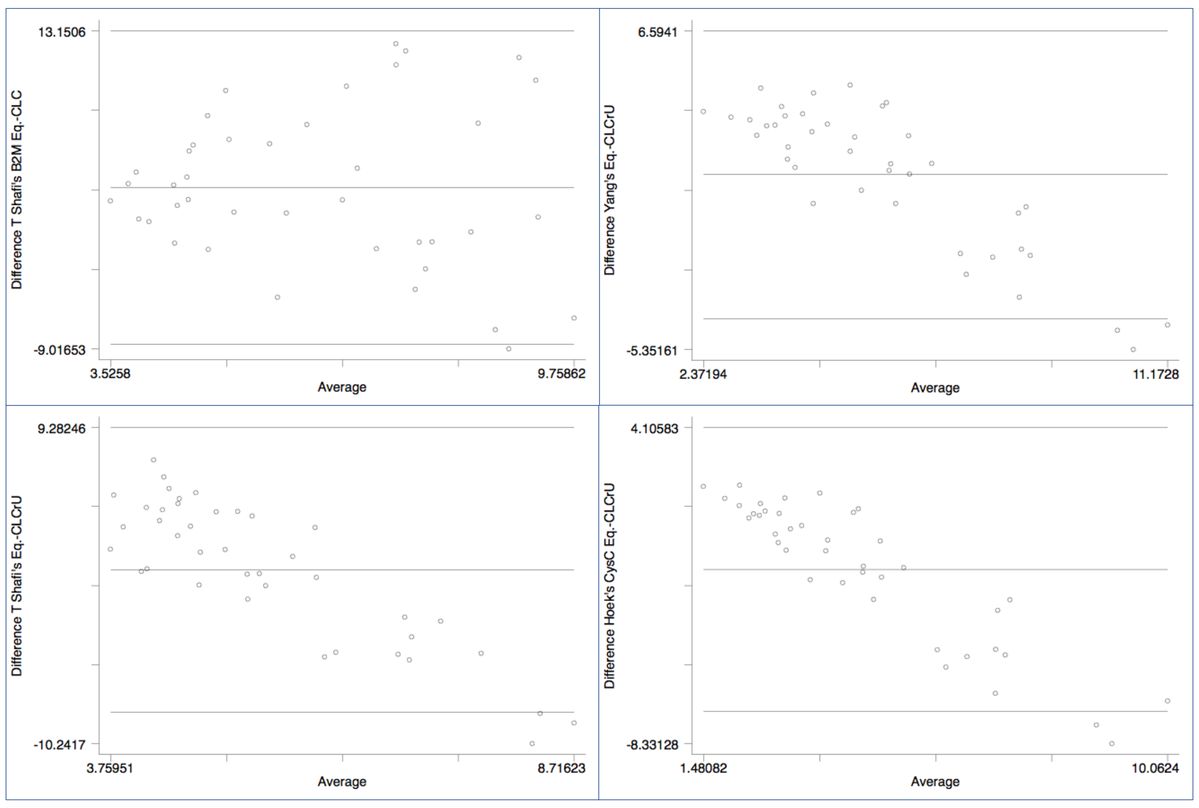

Figure 1. Agreement between endogenous filtration markers equations (CysC and ß2M) and measured CLCrU. Expressed in ml/min/1.73m^2.

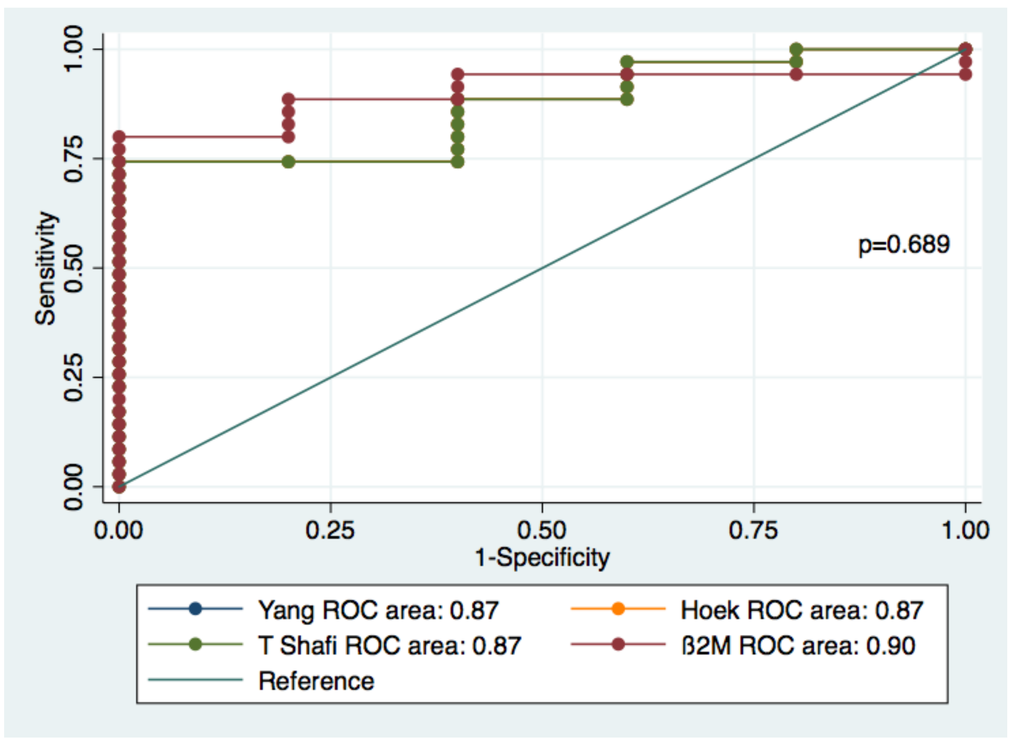

Figure 2. Receiver Operating Curves (ROC) for all three equations using serum CysC and the one equation using ß2M. A *p* value <0.05 was considered statistically significant.

Conclusions

- Serum CysC can be used as a surrogate of RRF, and T Shafi's CysC equation disclosed the best combination of AUC and bias from measured RRF in this group of patients.
- T Shafi's CysC and ß2M equations, and Yang's equation underestimated, while Hoek's equation overestimated measured RRF in this PD sample.
- Compared to ß2M, CysC showed better performance as a serum biomarker of measured RRF.

References:
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