**CYSTATIN C REDUCTION RATIO AS A MARKER OF HEMODIALYSIS ADEQUACY: STRONG ASSOCIATION WITH SURVIVAL**

**BACKGROUND AND OBJECTIVES:**

Assessment of dialysis adequacy in hemodialysis patients has previously focussed on normalised urea clearance (Kt/V) or urea reduction ratio. Middle molecule removal is thought to be important and techniques which enhance this, especially hemodiafiltration, may improve survival. However, no standard method for assessing the effectiveness of middle molecule clearance has however been established. We aimed to study the impact of reduction ratios of Cystatin C reduction (CysCRR) and β2-microglobulin β2MRR) on long-term survival.

**DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS:**

Pre- and post-dialysis cystatin C and β2-microglobulin levels were measured in relation to a single HD session in 325 unselected prevalent haemodialysis patients allowing calculation of CysCRR and β2MRR, akin to urea reduction ratio. Demographic, clinical and dialysis-related parameters were also collected. Patients were then followed up for survival over a period of almost eight years. The association of CysCRR and β2MRR with unadjusted and adjusted survival was explored using Kaplan Meier analysis and Cox Proportional Hazards Models.

 **RESULTS:**

Mean CysCRR was 51 ± 11%. Mean and β2MRR was 64 ± 10%. Both were associated with improved survival in univariate analysis (CysCRR HR=0.967: p=0.001 and Β2MRR HR=0.973: p =0.025). CysCRR was also strongly associated with survival adjusted for age, sex, body weight, dialysis vintage, Charlson Comorbidity Index, residual urea clearance , the use of hemodiafiltration, dialysis session duration, and equilibrated Kt/V (HR 0.965: p <0.001). An increase of 10% in CysCRR reduced mortality risk by around 35%. Patients with CysCRR s in the upper tertile ie above 56.7% had significantly better survival. The association between β2MRR and adjusted survival was not significant (p=0.062).

**CONCLUSIONS:**

CysCRR was associated with long term survival in prevalent hemodialysis patients, and may have utility as an indicator of dialysis adequacy. The association of CysCRR with survival was present even after correcting for the confounding effects of small solute (urea) clearance. It may provide a composite assessment of small solute and middle molecule clearance and take some account of residual renal function. Further work should explore potential modifiable factors.