LONGITUDINAL INFLUENCE OF THE EXTRACELLULAR WATER (ECW) / TOTAL BODY WATER (TBW) RATIO ON PROTEIN-ENERGY WASTING (PEW) IN PATIENTS WITH STAGE 5 CHRONIC KIDNEY DISEASE (CKD)

Anastasia Markaki[1], Periklis kyriazis[2], Athanasios Rizos[3], Vasilis Zafiropulos[1], Stamatia Skoulikidi[4], Marieta Pateinioti[4], Kostas Stylianou[5], John Kyriazis[3]

[1]Technological Educational Institute of Crete, Department of Nutrition and Dietetics, Sitia, GREECE
[2]The Transplant Institute, Beth Israel Deaconess Medical Center, Medicine, Boston, MA, USA
[3]General Hospital of Chios, Nephrology, Chios, GREECE
[4]General Hospital of Chios, Internal Medicine, Chios, GREECE
[5]University Hospital of Heraklion, Nephrology, Heraklion, Crete, GREECE

OBJECTIVES

PEW, which can be reliably assessed by the malnutrition-inflammation score (MIS), is associated with adverse clinical outcomes in stage 5 CKD patients. Fluid overload is also frequently present in these patients and reportedly has been associated with worsening nutritional status and reduced survival. In the present study, we examined a) whether changes in fluid status, as determined by the ECW/TBW ratio , influence changes of MIS over time and b) the interrelations between fluid overload, MIS and mortality in stage 5 CKD patients.

METHODS

Nutrition markers, body composition, using BIA, and MIS were assessed at baseline and at 6 and 18 months after enrollment, on 94 stage 5 CKD patients (45 on hemodialysis and 49 on peritoneal dialysis). Observation of this cohort was continued over 2.5 additional years. A higher score of the MIS (0 to 30) reflects a more severe degree of malnutrition and inflammation. Repeated measures mixed models and Cox models were evaluated, with adjustment for age, gender, cardiovascular disease and diabetes at baseline, mode of dialysis and dialysis vintage.

RESULTS

Table 1. Longitudinal change in outcome variables associated with a 1% longitudinal increase in ECW/TBW ratio , controlling for fixed factors

Variable	Estimate	95% CI		P	Pa
		Lower	Upper		
Biochemical					
Albumin (g/dl)	-0.01	-0.08	-0.007	0.047	0.649
Phosphorus (mg/dl)	-0.06	-0.10	-0.02	0.009	0.746
Creatinine (mg/dl)	-0.09	-0.16	-0.03	0.005	0.018
Prealbumin (mg/dl)	-0.002	-0.005	0.001	0.164	0.000
Parathormone (pg/ml)	4.03	-2.26	10.31	0.210	0.000
Inflammatory					
MIS	0.0.73	0.03	0.17	0.035	0.009
Anthropometric					
BMI (kg/m2)	-0.08	-0.15	-0.01	0.035	0.730
TSF (mm)	-0.02	-0.03	-0.003	0.022	0.624
MAC (cm)	-0.08	-0.17	0.00	0.059	0.034
MAMC (cm)	-0.01	-0.08	0.07	0.871	0.018
Body Composition					
FM (kg)	-0.18	-0.36	-0.004	0.045	0.060
FFM (kg)	0.17	0.02	0.32	0.027	0.088
Phase angle (°)	-0.17	-0.18	-0.16	0.000	0.305

• MIS, malnutrition -inflammatory score; BMI, body mass index; TSF, triceps skinfold thickness; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; FM, fat mass; FFM, fat-free mass.
• Pa for trend for ECW/TBW (%) -by-time interactions.

Figure 1. Box and whisker plots of MIS and ECW/TBW (%) measurements at baseline (month 0) and at 6 and 18 months after enrollment in the study population.
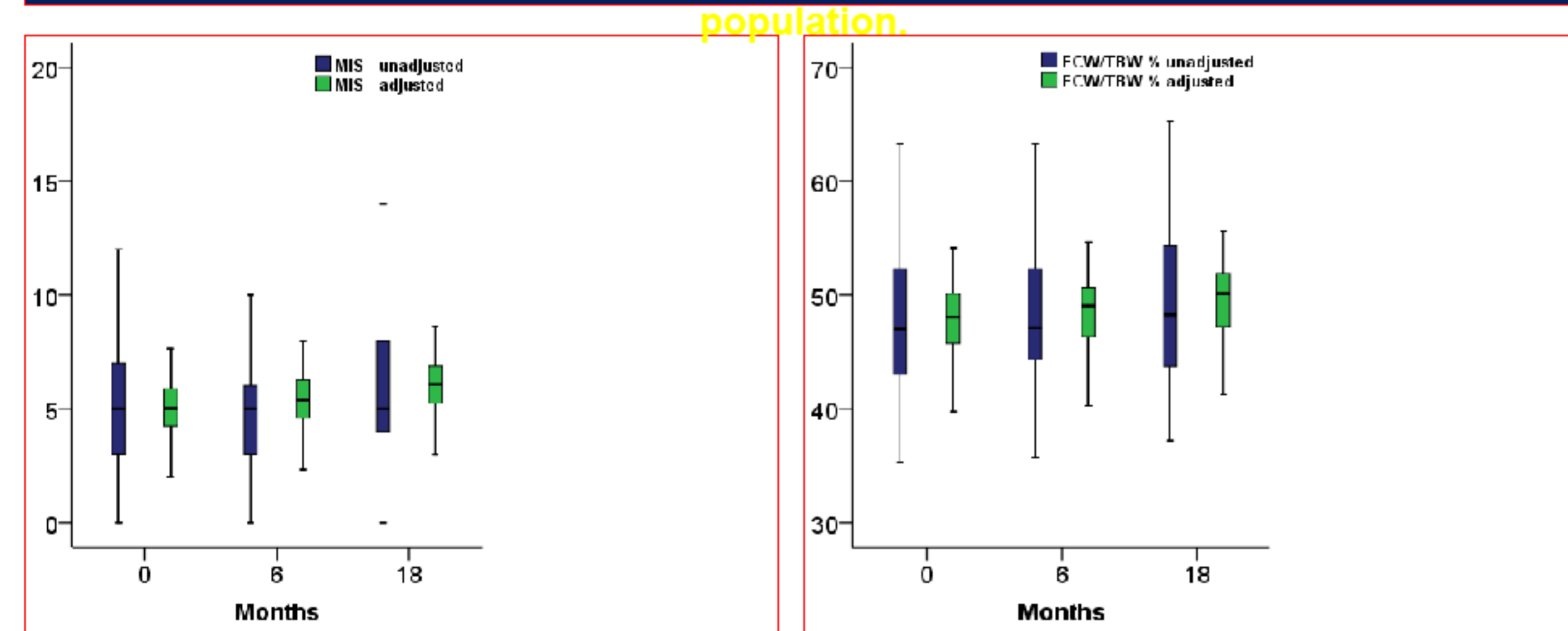
➢Longitudinal changes in ECW/TBW (%) were associated positively with changes in MIS (adjusted r = 0.073; p=0.035) [Table 1]. MIS increased significantly over time (linear estimate: 0.740 units/1.5 years; p = 0.001), as was also the case with ECW/TBW(%) (linear estimate: 0.98 units/1.5 years; p = 0.009) [Figure 1]. Each 1% increase in ECW/TBW ratio was associated with an increase in MIS of 0.016 units/1.5 years (p=0.02 for ECW/TBW(%) with time interaction), findings indicating that a person with 1% increase of ECW/TBW ratio over time would show about a 2.2 % faster rate of increase in MIS.

➢During the 4-year follow-up, 24 deaths were recorded. In adjusted (as mentioned above) Cox regression analysis, for each 1-unit increment in MIS, the all-cause mortality was increased by 18% (HR: 1.18; 95% CI, 1.01-1.39). The MIS - mortality association was lost after adjusting for ECW/TBW (%), whereas the latter emerged as an independent predictor of mortality in the final model. Specifically, 1% increase in ECW/TBW ratio was associated with a 9% increased risk of all-cause mortality (HR: 1.09; 95% CI, 1.01-1.18).

➢The area under the ROC curve (AUC) for predicting mortality was 0.677 (p=0.010) and 0.707 (p=0.003) for MIS and ECW/TBW (%), respectively. At an optimal ECW/TBW (%) cutoff of 48.9, the sensitivity and specificity of ECW/TBW (%) in predicting mortality were 67% and 64% , respectively.

CONCLUSIONS

These data show that:
a) the ECW/TBW ratio is a strong modulator of MIS over time
b) fluid overload may be a link between PEW and decreased survival and
c) maintenance of normal fluid status could ameliorate PEW and thus, improve survival in 5 stage CKD patients, a possibility that warrants further investigation.