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The association of carotid atherosclerosis, protein-energy wasting and inflammation status with mortality in patients on haemodialysis

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Background: Carotid atherosclerosis such as increased intima-media thickness (IMT) is associated with poor cardiovascular outcome. On the other hand, protein-energy wasting (PEW) or malnutrition, currently considered to be due to inflammatory process rather than poor nutritional intake, is highly prevalent in in chronic kidney disease (CKD) patients, particularly those on haemodialysis (HD). We investigated the association of carotid atherosclerosis, PEW and inflammation, and their joint role with prediction of mortality in chronic HD patients.

Methods: Carotid ultra-sound was performed in a total of 774 CKD patients stably undergoing HD therapy. Carotid atherosclerosis is defined as IMT$>$0.8mm as median value with hyperechoic plaque. Geriatric nutritional risk index (GNRI) which calculated from serum albumin levels, body weight and height as a surrogate marker of the PEW, and C-reactive protein (CRP) were measured at the same point. Patients were followed-up for 7 years.

Results: Declined GNRI and elevated CRP levels were independently associated with carotid atherosclerosis [odds ratio (OR) 0.96, 95% confidence interval (CI) 0.93–0.98, p=0.0082 and OR 1.30, 95% CI 1.04–1.64, p=0.019, respectively] accompanied with age (OR 1.03, 95% CI 1.01–1.05, p=0.0024) and hypertension (OR 1.78, 95% CI 1.12–2.91, p=0.013). During follow-up period (median of 67 months), 180 patients (23.3%) died. Carotid atherosclerosis [62.7% vs. 79.3% for 7-year survival rate, hazard ratio (HR) 1.57, 95% CI 1.12–2.16, p=0.0078], GNRI$<$91.2 as an established cut-off value (58.8% vs. 83.7%, HR 1.87, 95% CI 1.35–2.59, p=0.0002) and CRP$>$1.1 mg/l as a median value (65.8% vs. 88.6%, HR 2.87, 95% CI 2.00–4.22, p$<$0.0001) were identified as independent predictors of mortality after adjustment for other confounders. When patients were divided into groups according to number of these three risk factors, 7-year Kaplan-Meier survival rate was 92.7%, 91.1%, 56.8% and 37.2% among groups with no risk factor, any 1 risk factor, any 2 risk factors and all risk factors, respectively (p$<$0.0001 for trend). After adjustment for other confounders, patients with any 1, any 2 and all risk factors had 2.21-fold (95% CI 1.26–4.14), 5.44-fold (95% CI 3.13–10.1) and 7.19-fold (95% CI 3.67–14.6) higher risk for mortality compared to those without any risk factor, respectively (p$<$0.0001 for trend).

Conclusions: Presence of carotid atherosclerosis was closely associated with both declined GNRI and elevated CRP levels in CKD patients on HD. Combination of these predictors was also additively associated with an increasing risk of mortality. These results clearly manifested the so-called malnutrition, inflammation and atherosclerosis (MIA) syndrome in this high-risk population.