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Elevated Osteoprotegerin is Associated with Inflammation, Malnutrition and New Onset Cardiovascular Events in Peritoneal Dialysis Patients

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Backgrounds: Osteoprotegerin (OPG) is known to regulate bone mineral metabolism and is also associated with inflammation, cardiovascular disease (CVD) and mortality. Malnutrition-inflammation-atherosclerosis (MIA) syndrome is commonly found and closely linked to mortality in dialysis patients. The aim of this study was to investigate the associations between OPG and MIA syndrome in prevalent PD patients.

Methods: Prevalent patients on PD for more than 6months were prospectively followed up from March 2005 to May 2010. At baseline, OPG, hs-CRP, albumin, and %lean body mass (LBM) by urea kinetics were checked and subjective global asssessment was performed. New-onset cardiovascular events were evaluated during the study period. Based on the median level of OPG, patients were classified as lower OPG group and higher OPG group.

Results: Total 176 patients (age 52.0±11.8 years, male 50.6%, duration of PD 105.3±67.2 months) were recruited and followed. There was no difference in gender, vintage of dialysis, diabetes, Ca×P product, HOMA (homeostasis model assessment) index, dialysis adequacy, and residual renal function between higher and lower OPG group. In higher OPG group, age, hs-CRP level and Charlson's comorbidity index were higher, whereas serum albumin level, %LBM and subjective global assessment (SGA) score were significantly lower than lower OPG group. OPG levels were positively correlated with inflammatory markers, whereas negatively correlated with nutritional status. Cardiovascular events occurred in 51 patients during the study period. The rate of newly developed cardiovascular events was significantly common in higher OPG group (36/88, 40.9%) than lower OPG group (15/88, 17%, $p<0.01$). Cox regression analysis revealed that higher OPG level (per 1 increase in log OPG, RR: 2.34; 95% CI: 1.35 to 4.04; $p=0.002$) was a significant risk factor for cardiovascular events even after adjustments for age, sex, diabetes, and dialysis duration. Meanwhile, when %LBM and hsCRP levels were included in further adjustment, the significance of OPG level as a risk of cardiovascular events disappeared (RR: 2.0; 95% CI: 0.96 to 3.63; $p=0.06$, and RR: 1.79; 95% CI: 0.92 to 3.53; $p=0.09$).

Conclusion: OPG was significantly correlated with markers of systemic inflammation and malnutrition and a powerful predictor of CVD in PD patients. These findings suggest OPG might be a prognostic indicator of MIA syndrome in prevalent PD patients.

Key Words: Osteoprotegerin, Inflammation, Malnutrition, Cardiovascular disease, Peritoneal dialysis