KSN 2018
Seoul, Korea · May 17 - 20

Abstract Type : Poster
Presentation No. : PNO 032

Prognostic impact of serum osteoprotegerin on renal disease progression in non-dialytic patients with chronic kidney disease

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Objectives: In patients with chronic kidney disease (CKD), osteoprotegerin is considered to be an important regulator of bone metabolism and vascular calcification. However, the role of osteoprotegerin on the progression of renal dysfunction has not yet been well defined. The purpose of this study was to investigate the prognostic impact of osteoprotegerin in declining renal function in patients with CKD.

Methods: We analyzed 2238 patients who were collected from 2011 to 2017 using The KoreaN Cohort Study for Outcome in Patients with Chronic Kidney Disease (KNOW-CKD) dataset. A total of 1454 patients were enrolled after excluding 784 patients whose osteoprotegerin values were not measured. Primary outcomes included the incidence of end stage renal disease and ≥ 50% decline in estimated glomerular filtration rate (eGFR).

Results: During an average follow-up of 3.40 years, 361 patients had eGFR reduction of more than 50% or progressed to end stage renal disease. A multivariable-adjusted logistic regression model confirmed that osteoprotegerin was significantly associated with renal outcome [Odds ratio (OR), 1.10; 95% confidential interval (CI), 1.03-1.18; p=0.003]. In the Cox regression analysis after adjustment of confounding factors, OPG level was independently associated with primary renal outcome [hazard ratio (HR), 1.09; 95% confidence interval (CI), 1.05-1.13; p<0.001].

Conclusions: Osteoprotegerin level is independently associated with declining of renal function in patients with CKD. These findings suggest that serum osteoprotegerin may be a predictor of progression to end stage renal disease in CKD patients.

Table 1.Multivariable logistic regression analysis for the relationship between serum osteoprotegerin and total renal event in patient with CKD

Multivariable logistic regression analysis for the relationship between serum osteoprotegerin and total renal event in patient with CKD

	Doubling of Cr or 50% decline of GFR,		Dialysis or transplantation		Renal events	
	OR(95% CI)	p-value	OR(95% CI)	p-value	OR(95% CI)	p-value
Unadjusted	1.08(1.05-1.12)	< 0.001	1.26(1.21-1.31)	< 0.001	1.22(1.18-1.27)	< 0.001
Model 1	1.12(1.08-1.18)	< 0.001	1.36(1.29-1.42)	< 0.001	1.32(1.26-1.38)	< 0.001
Model 2	1.11(1.06-1.16)	< 0.001	1.33(1.27-1.40)	<0.001	1.29 (1.23-1.36)	< 0.001
Model 3	1.03(0.97-1.10)	0.328	1.14(1.06-1.23)	0.001	1.10 (1.03-1.18)	0.003

Model 1: age, sex, current smoker
Model2 : DM, HTN, BMI≥25, MI, CHF, PVD, CVD
Model 3: Model 2 + eGFR, Hb, Alb, Ca, P, PTH, 25OHvitD, uPCR≥0.5g/gCr, 24hr urine Ca, 24hr urine P, hsCRP
*Variables are log transformed.
Abbreviations : DM, diabetes mellitus; HTN, hypertension; BMI , body mass index; MI ,myocardiac infarction; CHF , Congestive heart failure; PVD, peripheral vascular disease; CVD, cerebral vascular disease; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; Alb, albumin; PTH, parathyroid hormone; uPCR , urine protein creatinine ratio, AACS, abdominal aorta caclfication score; hsCRP , high sensitive c-reactive proetin

Table 2. Cox regression analysis for the relationship between serum osteoprotegerin and renal event in patient with CKD

Cox regression analysis for the relationship between serum osteoprotegerin and renal event in patient with CKD

	Doubling of Cr or 50% decline of GFR,		Dialysis or transplantation		Renal events	
	OR(95% CI)	p-value	OR(95% CI)	p-value	HR(95% CI)	p-value
Unadjusted	1.13(1.11-1.16)	< 0.001	1.15(1.13-1.16)	< 0.001	1.15(1.13-1.16)	< 0.001
Model 1	1.15(1.13-1.18)	< 0.001	1.16(1.14-1.18)	< 0.001	1.16(1.14-1.18)	< 0.001
Model 2	1.12(1.09-1.15)	<0.001	1.13(1.11-1.16)	<0.001	1.13(1.11-1.15)	< 0.001
Model 3	1.10(1.04-1.16)	0.001	1.09(1.04-1.13)	<0.001	1.09(1.05-1.13)	< 0.001

Model 1: age, sex, current smoker
Model2 : DM, HTN, BMI≥25, MI, CHF, PVD, CVD
Model 3: Model 2 + eGFR, Hb, Alb, Ca, P, PTH, 25OHvitD, uPCR≥0.5g/gCr, 24hr urine Ca, 24hr urine P, hsCRP
*Variables are log transformed.
Abbreviations : DM, diabetes mellitus; HTN, hypertension; BMI , body mass index; MI ,myocardiac infarction; CHF , Congestive heart failure; PVD, peripheral vascular disease; CVD, cerebral vascular disease; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; Alb, albumin; PTH, parathyroid hormone; uPCR , urine protein creatinine ratio, AACS, abdominal aorta caclfication score; hsCRP , high sensitive c-reactive proetin