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Anemia significantly increases Risk of Osteoporosis in Patients with Non-dialysis Chronic Kidney Disease

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Objectives: Anemia was frequently observed in chronic renal failure patients. The risk of osteoporosis is higher in patients with chronic anemia. Chronic anemia also showed a close relationship with bone mineral density (BMD). However, few studies has been done whether anemia affects bone mineral density with CKD patient. Therefore, the aim of our study is to evaluate the relationship between anemia and BMD in a large sample of non-dialysis CKD cohort.

Methods: We performed an observational study in 2,089 patients who measured hemoglobin and BMD with non-dialysis CKD enrolled in the KNOW-CKD. Anemia was defined as hemoglobin(Hb) levels of < 13.0 g/dL for males and 12.0 g/dL for females, respectively. BMD was estimated by dual energy x-ray absorptiometry system. The observed variable was decline of BMD during follow up.

Results: The mean age was 53.6 ± 12.2 years and 1,292(61.1%) patients were males. The BMD score was positively correlated with hemoglobin levels (**β**, 0.007; 95% CI, 0.003-0.012; P 0.002), but inversely with prevalence of anemia (**β**, -0.03; 95% CI, -0.042--0.008; P 0.004). In the multivariable logistic regression model, the prevalence of osteoporosis was significantly higher in the anemia group than that in the normal hemoglobin levels (odds ratio [OR], 1.67; 95% confidence interval [CI], 1.11-2.51, P=0.014). Among 881 patients except unavailable following BMD, 396 (19.7%) patients developed the decline of BMD during a median follow-up duration of 48 (interquartile range, 46-49) months. In the fully adjusted multivariable Cox models, risk of developing the decline of BMD was significantly higher in the anemia group (HR, 1.38; 95% CI, 1.02-1.87; P= 0.036) as compared to normal hemoglobin group.

Conclusions: We found that anemia is independently and significantly correlated with an increased risk of osteoporosis with non-dialysis CKD. Our study suggests that prompt correction of anemia in CKD patients could be beneficial to preserving bone mineral density.

Table 1. Multiple logistic regression analysis of factors associated with prevelance of osteoporosis

Table 1. Multiple logistic regression analysis of factors associated with prevelance of osteoporosis (cross- sectional analysis)

	Univariable analysis		Multivariable analysis*	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
	Reference		**Reference**	
Anemia	2.24 (1.66-3.02)	**<0.001**	1.67 (1.11-2.51)	0.014

*Adjusted for age, sex, BMI, CCI, smoking, eGFR, log-CRP, albumin, 25(OH) vitamin D, log-total cholesterol, log-PTH, iron replacement therapy, ESA replacement therapy, vitamin therapy, and calcium-containing phosphate binder

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; PTH, parathyroid hormone; ESA, erythropoiesis-stimulating agent.

logistic BMD_yn i.ANEMIA AGE i.SEX BMI1_B0 lncrp i.DRUG_IRONA_YN_B0 i.DRUG_ESA_YN_B0 C_ALB_B0 ln_VD25 TC ln_PTH i.DH_VD i.DH_CaP CCI_S1 i.SMK EPI_CR_B0

Table 2. Multivariable cox regression model for decline of bone mineral density

Table 2. Multivariable Cox regression model for decline of bone mineral density during follow-up

	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
	HR (95% CI)	**P-value**	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Normal	**Reference**		**Reference**		**Reference**		**Reference**	
ANEMIA	1.30 (1.10-1.54)	0.002	1.24 (1.02-1.50)	0.029	1.43 (1.07-1.91)	0.017	1.38 (1.02-1.87)	0.036

[a]Unadjusted model

[b]Adjusted for age, sex, BMI, CCI, and smoking

[c]Adjusted for Model 2 + hemoglobin, eGFR, log-CRP, albumin, 25(OH) vitamin D, log-total cholesterol, and log-PTH

[d]Adjusted for Model 3 + iron replacement therapy, ESA replacement therapy, vitamin therapy, and calcium-containing phosphate binder

* Variables are log transformed.

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; CRP, C-reactive protein; ESA, erythropoiesis-stimulating agent