

# CD4 lymphopenia is associated with aortic arch calcification in patients with end-stage renal disease

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## INTRODUCTION

Vascular calcification is preceded by atherosclerosis and/or chronic kidney disease-mineral and bone disorder (CKD-BMD) in patients with end-stage renal disease (ESRD). All-cause and cardiovascular mortality can be predicted from the degree of aortic arch calcification on chest X-rays. The T cell phenotype is associated with cardiovascular disease (CVD) and T-cell infiltration is thought to be involved in vascular calcification sites. However the association between T cell phenotype and vascular calcification remains unclear.

## METHODS

**•Patients** :The patients with ESRD (CKD stage5 or 5D) and older than 20 years admitted to Osaka Minami Medical Center from June 2013 to December 2016 participated in this study.

*The exclusion criteria were as follows;*

Patients with acute kidney injury, active infection, HCV, HBV, malignancy, use of immunosuppressants, and chronic inflammatory disease such as rheumatoid arthritis, systemic lupus erythematosus, and vasculitis were excluded.

**•Flowcytometry** :Flowcytometric analysis was performed to detect CD3<sup>+</sup>T cells, CD4<sup>+</sup>T cells, CD8<sup>+</sup>T cells, CD4 to CD8 ratio, the proportion of CD28<sup>+</sup> cells on CD4<sup>+</sup>T cells, and the proportion of CD28<sup>+</sup> cells on CD8<sup>+</sup>T cells by using Peripheral Blood Mononuclear Cells.

**•Aortic Arch Calcification** :The patients were assigned to groups depending on whether they had none - mild or moderate - severe AAC on chest X-rays. Calcification was graded as follows: none (no visible calcification), mild (small spots of calcification or single thin calcification of the aortic knob), moderate (one or more areas of thick calcification) severe (circular calcification of the aortic knob).

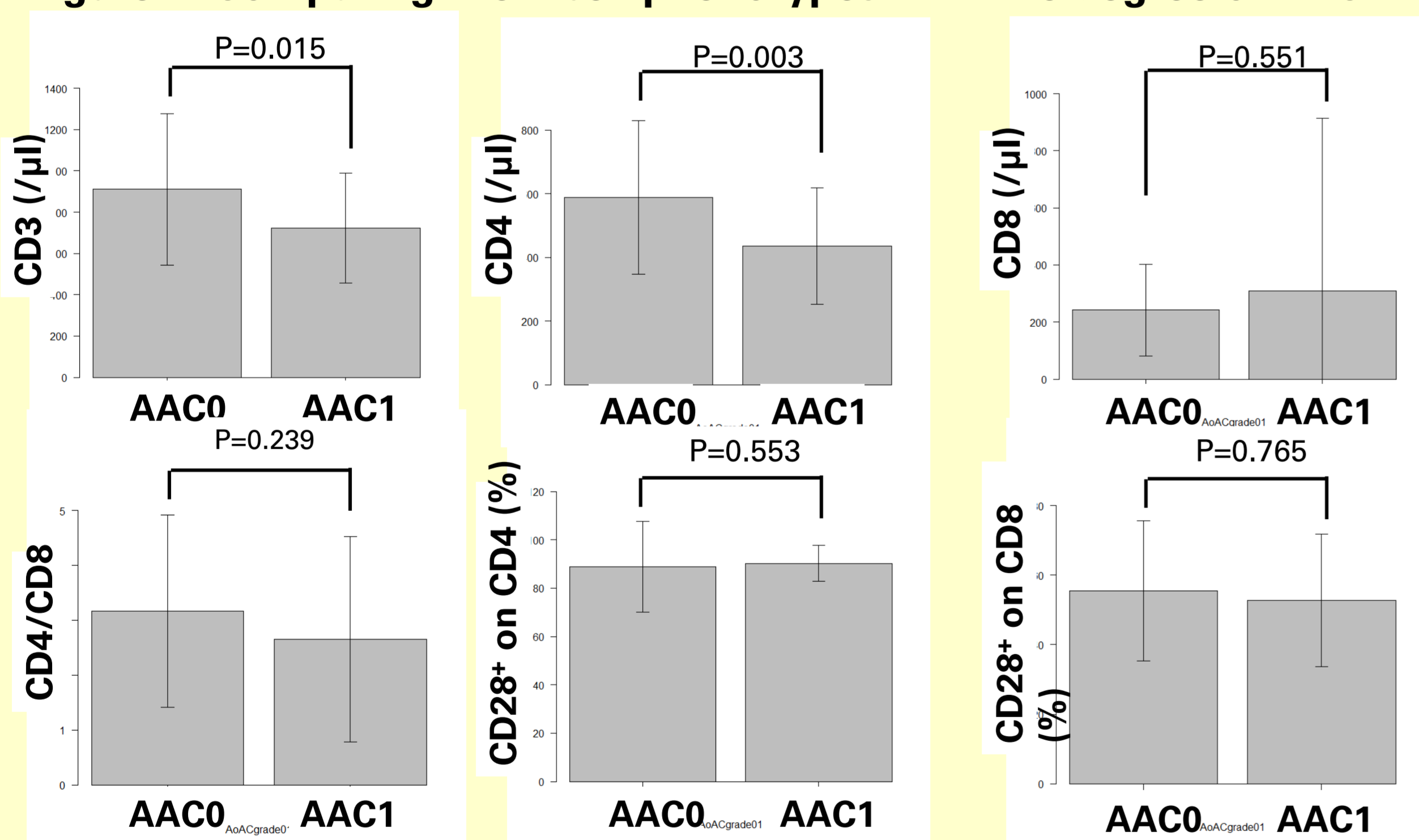
**•Statistics** :We performed multivariate logistic regression analysis to detect the factors determining AAC and ROC analysis for the predictive power of T cell phenotypes and AAC.

## RESULTS

**Table 1. Characteristics of the study population**

	All (n=71)	None to mild calcification (AAC0, n=31)	Moderate to severe calcification (AAC1, n=40)	P
Age (years)	68 (12)	62 (15)	72 (8)	<0.001
Female n, (%)	26 (37)	11 (36)	15 (38)	1.000
Diabetes n, (%)	37 (52)	13 (42)	24 (60)	0.156
CVD n, (%)	26 (37)	8 (26)	18 (45)	0.137
Systolic blood pressure (mmHg)	143 (17)	140 (19)	142 (15)	0.232
Adjusted Ca (mg/dl)	9.3 (0.5)	9.3 (0.5)	9.3 (0.6)	0.880
IP (mg/dl)	5.1 (1.3)	5.4 (1.5)	4.8 (1.1)	0.078
intact PTH (pg/ml)	206 [11, 1672]	202 [11, 1321]	209 [32, 1672]	0.862
Hb (mg/dl)	10.1 (1.1)	10.4 (1.3)	9.8 (0.9)	0.054
Albumin (g/dl)	3.3 (0.5)	3.4 (0.5)	3.3 (0.6)	0.827
TCHO (mg/dl)	171 (40)	187 (41)	160 (36)	0.010
CRP (mg/dl)	0.11 [0.01, 1.03]	0.10 [0.01, 1.03]	0.12 [0.01, 0.37]	0.981
Dialysis n, (%)	31 (44)	13 (42)	18 (45)	0.814

**Figure 1. Comparing the T cell phenotypes with the degree of AAC**

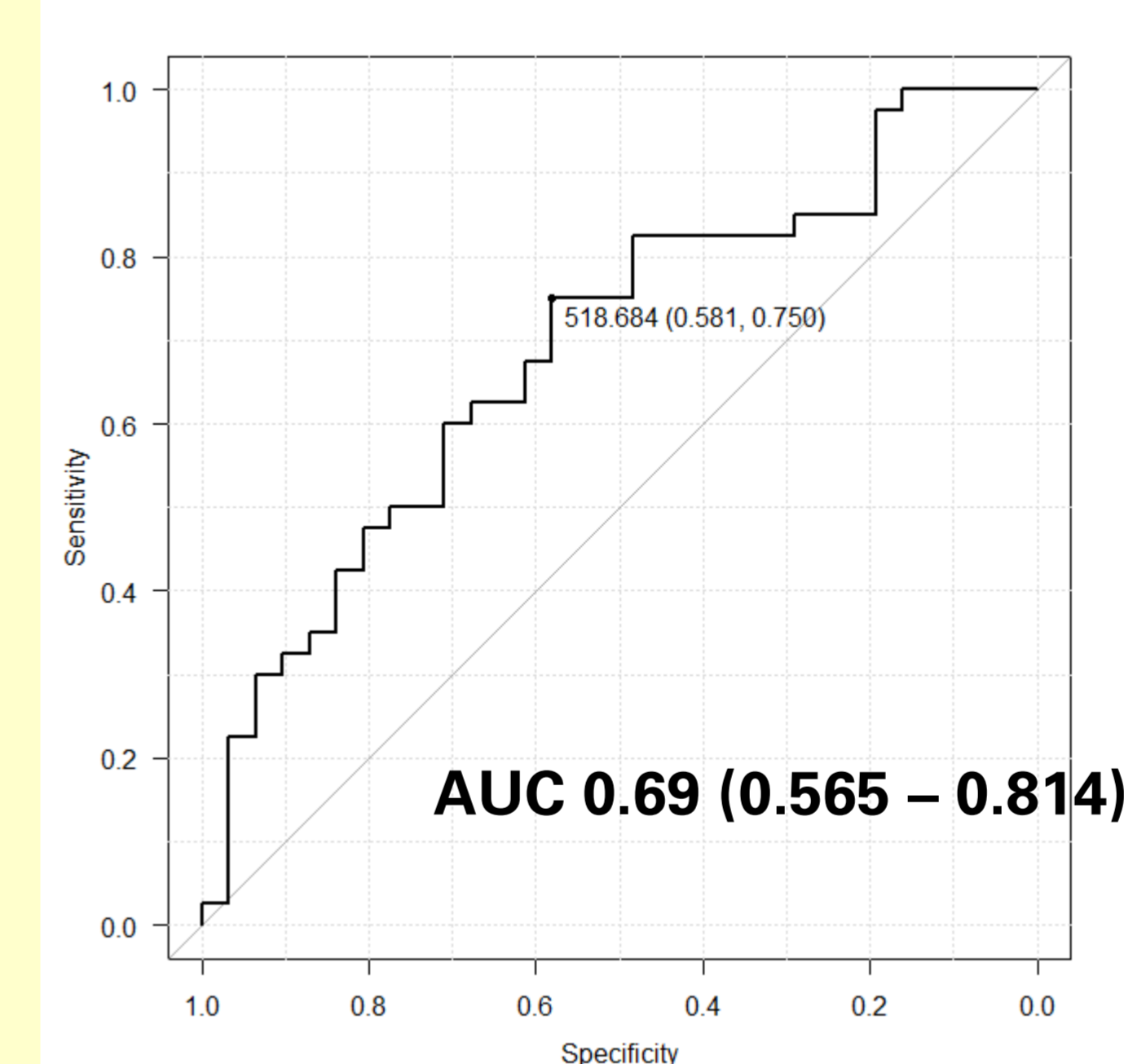


**Table 2. Multivariate logistic regression of immunological predictors of AAC**

Immune phenotype	Odds ratio (95%CI)	P
CD3 (/ $\mu$ l)	0.998 (0.996 to 1.000)	0.068
CD4 (/ $\mu$ l)	0.997 (0.994 to 1.000)	0.027
CD8 (/ $\mu$ l)	1.000 (0.998 to 1.000)	0.715
CD4/CD8	0.868 (0.636 to 1.180)	0.371
CD28 <sup>+</sup> on CD4 (%)	1.020 (0.954 to 1.080)	0.636
CD28 <sup>+</sup> on CD8 (%)	1.000 (0.976 to 1.030)	0.788

Adjusted by age, the history of cardiovascular disease, Log CRP, and dialysis

**Figure 2. ROC analysis for the predictive power of CD4 counts and AAC**



## DISCUSSIONS

- CD4 lymphopenia is observed in ageing, the presence of cancer and cardiovascular disease<sup>(1)</sup>. However, T cell accumulates in gut associated lymphoid tissue<sup>(2)</sup>.
- T cell infiltration is also observed at the atherosclerotic site<sup>(3)</sup>.
- One of the reason for the association of CD4 lymphopenia with aortic arch calcification in this study may be that atherosclerosis progresses when mineralization occurs.
- It is known that poor prognosis is caused by vascular calcification in CKD patients<sup>(4)</sup>, some of which may be mediated by CD4 lymphopenia because CD4 lymphopenia is observed in poor condition such as ageing, cancer, and cardiovascular disease.

## CONCLUSIONS

CD4 lymphopenia in peripheral blood is associated with aortic arch calcification in patients with ESRD.

## REFERENCES:

1. Ducloux, et al. J Am Soc Nephrol. 2003
2. Martinet, et al. Immun ageing. 2014
3. Tall, et al. Nat Rev Immunol. 2015
4. Gorriz, et al. c J Am Soc Nephrol. 2015