



# CAROTID PLAQUE COULD PREDICT THE RATE OF RENAL FUNCTION DECLINE IN PATIENTS WITH CHRONIC KIDNEY DISEASE 3 AND 4

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## Objectives

- Patients with chronic kidney disease (CKD) are at extraordinarily high risk of adverse cardiovascular (CV) outcome.
- The presence of carotid plaque is a surrogate marker of systemic atherosclerosis and closely associated with adverse CV outcomes. However the prevalence of carotid plaque as well as its relationship with renal decline rate and progression to dialysis is unknown in chronic kidney disease (CKD) patients
- The aims of this study were
  - (1) to evaluate the association between carotid plaque as well as carotid intima-media thickness (cIMT) with renal decline rate in patients with advanced CKD stage 3 and 4.
  - (2) to assess whether carotid plaque and/or cIMT are independently associated with the commencement of dialysis.

## Methods

- Since January 2008, our hospital has been implementing the atherosclerosis surveillance program using carotid ultrasonography (US) in patients with CKD with eGFR <60 mL/min/1.73m<sup>2</sup> at the time of diagnosis with CKD
- The eGFR was calculated using the 4-variable MDRD formula, and the rate of eGFR decline was calculated by regression analysis as an eGFR slope.
- The cIMT was defined as the distance between the leading edges of the lumen interface and the media-adventitia interface, and carotid plaque was defined as a focal structure encroaching into the arterial lumen of at least 0.5 mm or 50% of the surrounding cIMT, or demonstrates a thickness >1.5mm as measured from the media-adventitia interface to the intima-lumen interface.

## Results

- This prospective longitudinal observational study enrolled 411 CKD stage 3a, 3b and 4 patients.
- Mean cIMT was 0.89 ± 0.17 mm and carotid plaque was observed in 282 (68.6%) patients.
- Baseline eGFR and eGFR decline slope was 44.5 ± 11.6 mL/min/1.73m<sup>2</sup> and -2.87 ± 3.76 mL/min/1.73m<sup>2</sup>/yr.

Table 1. Baseline characteristics according to eGFR

Characteristics	Total (n=411)	eGFR stage			P
		3a (n=224)	3b (n=126)	4 (n=61)	
eGFR slope (mL/min/1.73m <sup>2</sup> /yr)	-2.87 ± 3.76	-1.97 ± 3.19	-3.46 ± 4.04	-4.54 ± 4.26	<0.001
eGFR (mL/min/1.73m <sup>2</sup> )	44.5 ± 11.6	53.4 ± 4.8	38.2 ± 4.6	24.2 ± 3.8	<0.001
Age (year)	69.5 ± 12.1	69.5 ± 12.3	70.4 ± 12.4	67.5 ± 11.2	0.290
Male, n (%)	189 (46.0)	116 (51.8)	52 (41.3)	21 (34.4)	0.007
Ever - smoking (%)	172 (41.8)	90 (40.2)	56 (44.4)	26 (42.6)	0.907
Diabetes mellitus, n (%)	258 (62.8)	121 (54.0)	82 (65.1)	55 (90.2)	<0.001
Hypertension, n (%)	352 (85.6)	185 (82.6)	112 (88.9)	55 (90.2)	0.065
Systolic BP (mmHg)	134.6 ± 24.3	132.9 ± 20.6	136.2 ± 28.3	138.0 ± 27.7	0.243
Diastolic BP (mmHg)	74.0 ± 13.6	74.0 ± 12.3	75.4 ± 15.2	71.3 ± 14.3	0.146
Body mass index (kg/m <sup>2</sup> )	24.5 ± 3.6	24.4 ± 3.6	24.4 ± 3.5	24.7 ± 3.8	0.836
Hemoglobin (g/dL)	11.6 ± 2.0	12.4 ± 1.7	10.9 ± 1.9	9.9 ± 1.5	<0.001
Albumin (g/dL)	3.9 ± 0.5	4.0 ± 0.4	3.8 ± 0.6	3.6 ± 0.6	<0.001
UPCR (g/g)	0.91 ± 1.60	0.49 ± 1.10	1.10 ± 1.65	2.10 ± 2.33	<0.001
<b>Carotid data</b>					
IMT (mm)	0.89 ± 0.17	0.87 ± 0.16	0.89 ± 0.14	0.94 ± 0.24	0.037
Plaque, n (%)	282 (68.6)	141 (62.9)	93 (73.8)	48 (78.7)	0.006
Plaque calcification, n (%)	266 (64.9)	153 (68.3)	71 (56.7)	42 (71.0)	0.466

Figure 1. Subjects with more decreased eGFR had significantly higher cIMT and prevalence of carotid plaque.

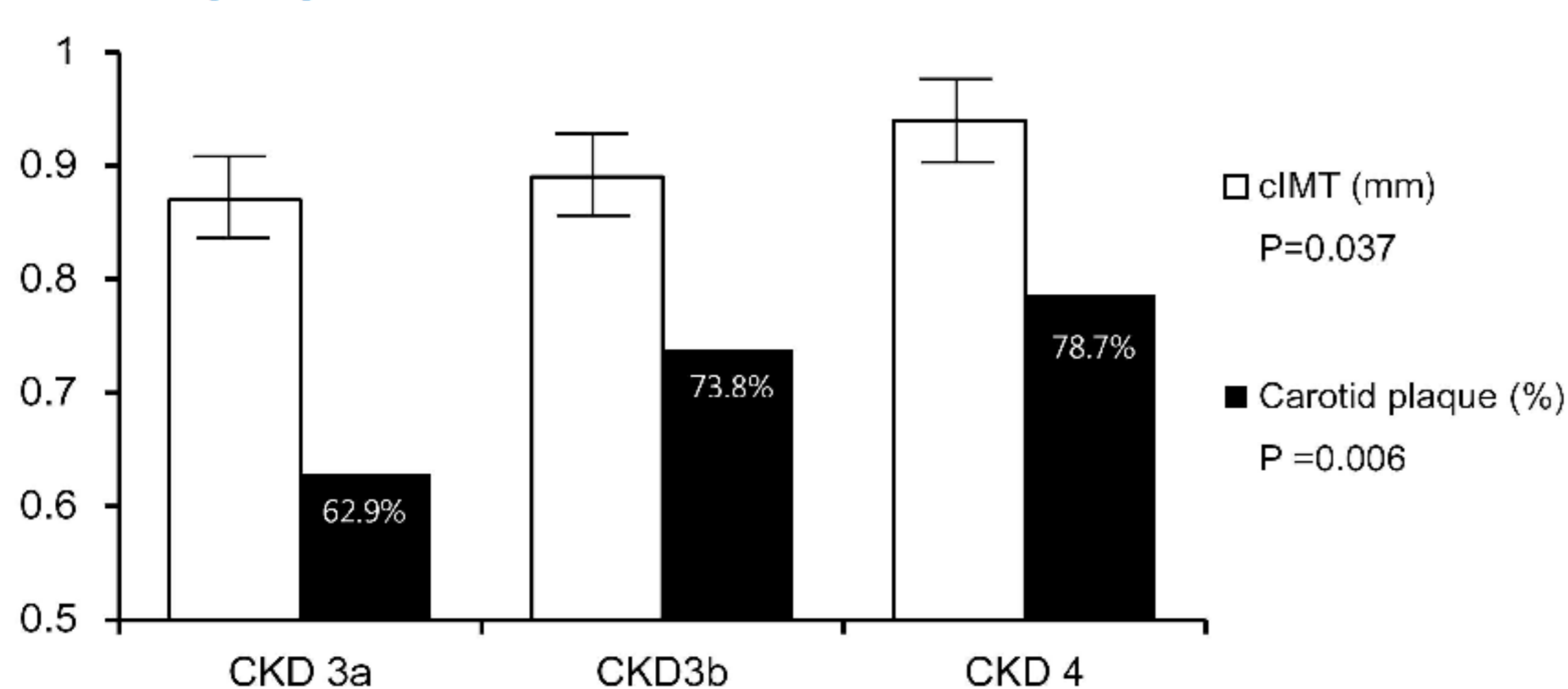


Figure 2. Rate of renal function decline was closely associated with carotid plaque as well as cIMT.

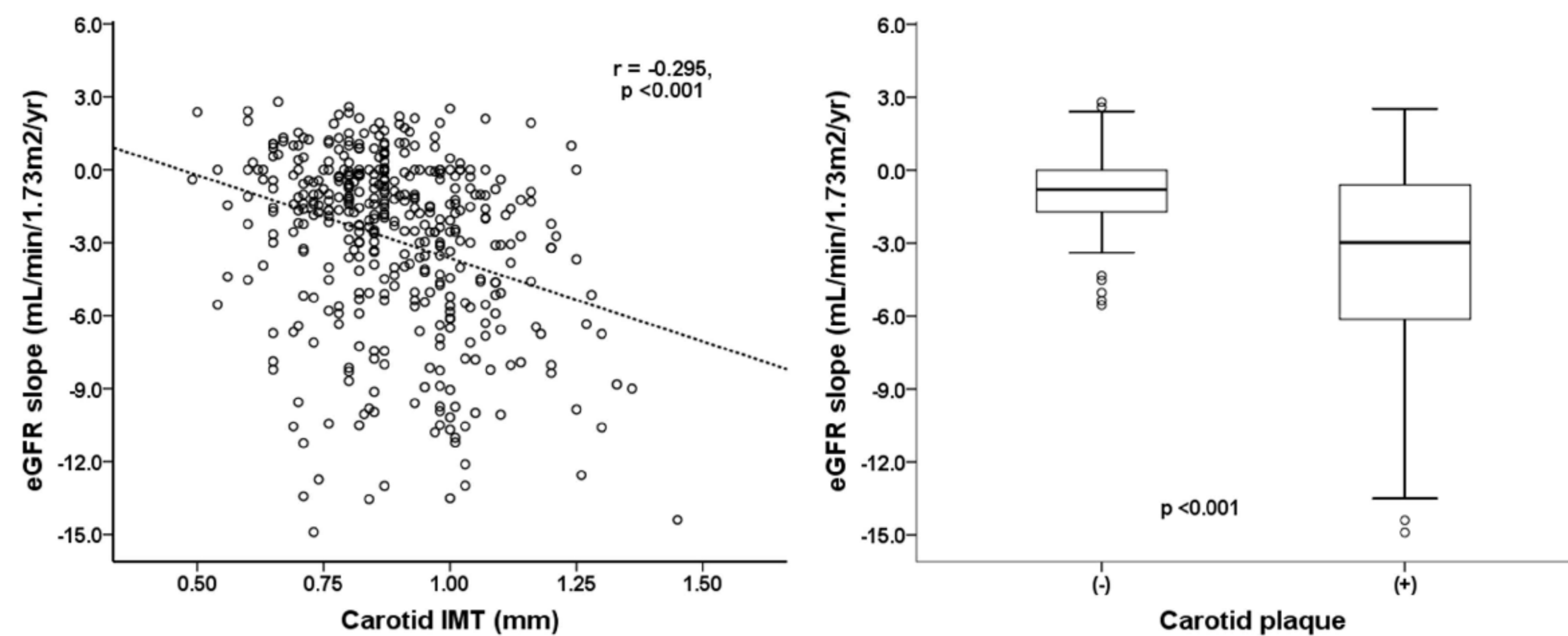


Table 2. Clinical factors affecting eGFR slope

Parameters	Univariate analysis		Multivariate analysis	
	Unstandardized Coefficient β	P	Unstandardized Coefficient β	P
Age (year)	0.04 (-0.02, 0.04)	0.779	-	-
Male, n (%)	-0.15 (-0.88, 0.56)	0.680	-	-
Diabetes mellitus, n (%)	-1.99 (-2.72, -1.26)	<0.001	-0.77 (-1.52, -0.03)	0.033
Hypertension, n (%)	-1.21 (-2.46, -0.18)	0.022	-0.38 (-1.34, 0.58)	0.445
Smoking	-0.59 (-1.39, 0.21)	0.155	-	-
Systolic blood pressure (mmHg)	-0.04 (-0.05, -0.02)	<0.001	-0.01 (-0.03, 0.01)	0.333
Diastolic blood pressure (mmHg)	-0.04 (-0.06, -0.02)	0.002	-0.02 (-0.05, 0.2)	0.259
<b>Laboratory parameters</b>				
Hemoglobin (g/dL)	0.51 (0.33, 0.72)	<0.001	0.13 (-0.08, 0.33)	0.226
Albumin (g/dL)	2.10 (1.41, 2.71)	<0.001	0.61 (-0.16, 1.38)	0.120
eGFR (mL/min/1.73m <sup>2</sup> )	0.09 (0.06, 0.12)	<0.001	0.02 (-0.02, 0.05)	0.310
UPCR (g/g)	-0.81 (-1.03, -0.58)	<0.001	-0.50 (-0.75, -0.24)	<0.001
<b>Carotid data</b>				
IMT (mm)	-6.36 (-8.44, -4.27)	<0.001	-4.36 (-6.56, -2.17)	<0.001
Plaque	-2.63 (-3.37, -1.88)	<0.001	-1.48 (-2.27, -0.69)	<0.001

- Statistically significant variables associated with more rapid renal progression rate were diabetes mellitus (p=0.033), greater proteinuria (<0.001), increased cIMT (p<0.001) and the presence of carotid plaque (p < 0.001).

Figure 3. Kaplan-Meier estimates of renal survival according to carotid plaque (Lt) and cIMT (Rt).

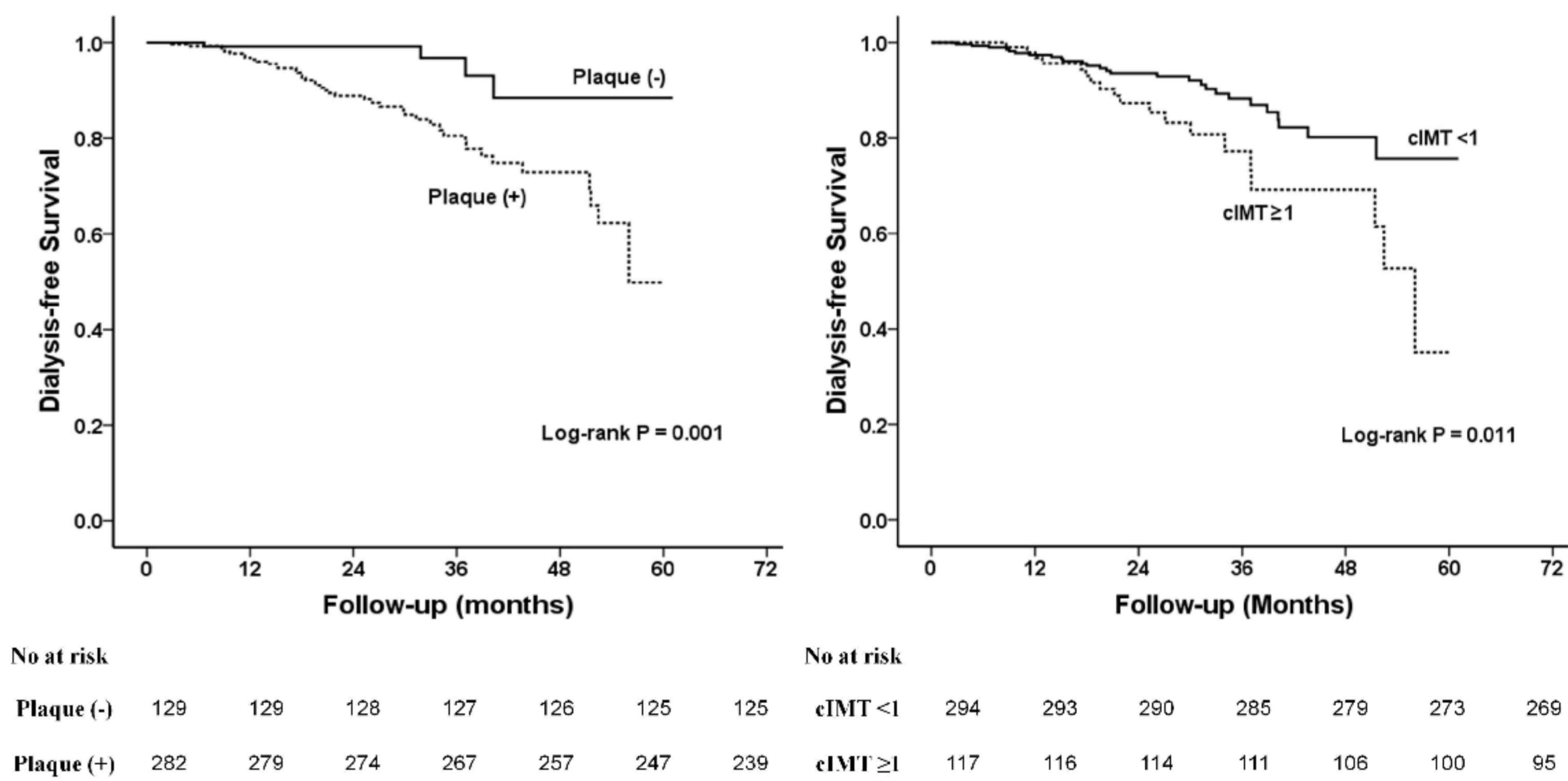


Table 3. Predictors of progression to dialysis using multivariate Cox Proportional hazards model

Variable	Unit	Hazard Ratio	95% CI	p
Age	1 year increase	1.02	0.96, 1.05	0.138
Male	vs. female	1.13	0.64, 2.01	0.668
Smoking	ever vs. never	2.25	1.05, 4.81	0.049
Diabetes	presence	2.33	0.63, 8.68	0.167
SBP	per 10 mmHg	1.05	0.91, 1.22	0.151
Hemoglobin	per 1g/L	0.89	0.69, 1.15	0.377
Albumin	per 1g/dL	0.58	0.27, 1.25	0.164
Baseline eGFR	per 1mL/min/1.73m <sup>2</sup>	0.88	0.85, 0.93	<0.001
UPCR	per 1g/g	1.20	1.01, 1.44	0.044
Carotid IMT	≥ 1.0 vs. <1.0 mm	2.50	0.51, 2.50	0.549
Carotid Plaque	presence	3.30	1.01, 10.77	0.048

During the 2.5-year follow-up, 47 (11.4%) started dialysis therapy. Patients with carotid plaque had a worse dialysis-free survival than those without carotid plaque.

## Conclusions

The presence of carotid plaque was closely associated with rapid decline of renal function and progression to dialysis in CKD stage 3 and 4 patients. Detecting carotid plaque may help identify patients at high-risk for rapid progression of renal dysfunction.

