Skin autofluorescence is a predictor of cardiovascular disease in chronic kidney disease patients

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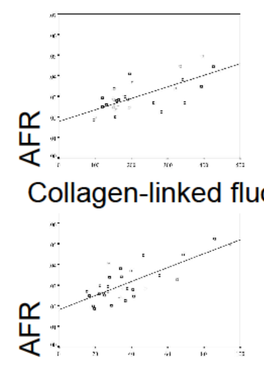
OBJECTIVES

Accelerated formation and tissue accumulation of advanced glycation endproducts (AGEs), reflecting cumulative glycemic and oxidative stress, occurs in age-related and chronic diseases like diabetes mellitus (DM) and renal failure, and contributes to vascular damage. Skin autofluorescence (AFR), a noninvasive measurement method, reflects tissue accumulation of AGEs. AFR has been reported to be an independent predictor of mortality in Caucasian hemodialysis patients. We assessed the relationship between levels of AFR and the prevalence of cardiovascular disease (CVD), and clarified the prognostic usefulness of skin AFR levels in Asian (non-Caucasian) hemodialysis (HD) patients.

METHODS

This study was conducted on 64 chronic CKD patients undergoing 3- to 4-h sessions three times a week with standard bicarbonate HD. Blood samples were collected before a HD session on Monday or Tuesday. The following hematologic and biochemical tests were done using standard laboratory techniques: hemoglobin (Hb), albumin (Alb), low-density lipoprotein (LDL), triglyceride (TG), parathyroid hormone (PTH), C-reactive protein (CRP), or HbA1c. Levels of these parameters have been reported to be associated with CVD in CKD patients . AGE accumulation was assessed based on the skin autofluorescence using the autofluorescence reader (AGE reader; DiagnOptics, Groningen, the Netherlands). The AFR illuminates a skin surface of ~1 cm2 at the lower arm, guarded against surrounding light, with an excitation light source between 300 and 420 nm. The amount of ultraviolet light exposure is small and the autofluorescence reader has already been tested in several studies without any adverse effect.



Collagen-linked fluorescence

pentosidine

Meerwaldt R et.al. 2005
J Am Soc Nephrol

Table 1. Patient background (n=64)

Male	73.40 %		(n=47)
age (years)	60.90 ±	13.20	
HD duration (years)	4.79 ±	3.87	
Diabetes	56.30 %		(n=36)
Hypertension	89.00 %		(n=57)
Dyslipidemia	10.90 %		(n=7)
CAVI	9.16 ±	1.53	
ABI	1.09 ±	0.16	
Alb (g/dl)	3.74 ±	0.49	
LDL (mg/dl)	93.40 ±	31.70	
TG (mg/dl)	130.00 ±	86.30	
PTH (pg/ml)	167.00 ±	115.00	
CRP (mg/dl)	0.26 ±	0.34	
Hb (g/dl)	11.00 ±	1.37	
HbA1c (%)	6.56 ±	1.44	
AFR	3.40 ±	0.91	

Table 2. Baseline characteristics of HD patients according to 3-year follow-up monitoring

	no-CVD n=43	de novo CVD n=21	*P*	
male {%}	29 {67.4}	18 {85.7}	0.12	
age (years)	63.81±2.10	67.54±3.12	0.31	
HD duration (years)	3.94±0.58	6.52±0.81	0.01>	**
diabetes {%}	18 {41.9}	7 {33.3}	0.51	
hypertension {%}	38 {88.4}	19 {90.5}	0.8	
Dyslipidemia	3 {6.9}	4 {19.1}		
Albumin (g/dl)	3.77±0.08	3.68±0.13	0.41	
LDL (mg/dl)	90.41±5.44	100.79±8.49	0.31	
TG (mg/dl)	126.30±15.14	140.61±24.12	0.61	
PTH (pg/ml)	164.82±20.01	175.00±32.50	0.79	
CRP (mg/dl)	0.22±0.07	0.35±0.11	0.34	
Hb (g/dl)	11.17±0.23	10.63±0.35	0.21	
HbA1c (%)	6.14±0.39	7.97±0.72	0.04	*
AFR	3.19±0.13	3.88±0.18	0.01>	**

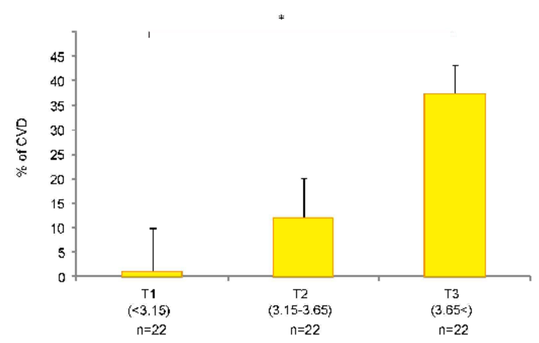
Values are numbers with percentages in parentheses or the mean ± SD. *p<0.05, ** p<0.01 CVD, cardiovascular disease

Table 3. Multiple logistic analyses for CVD in HD patients according to clinical characteristics and parameters in univariate and multivariate models.

	Univariate model					Multivariate model				
	OR	95% CI		*p*		OR	95% CI		*p*	
male	2.89	0.81 -	13.82	0.11						
age	1.02	0.98 -	1.06	0.31						
HD duration	1.25	1.04 -	1.72	0.01>	**	1.34	1.05 -	2.08	0.01>	**
diabetes	0.18	-0.35 -	0.75	0.51						
hypertension	0.11	-0.71 -	1.11	0.8						
dyslipidemia	0.57	-0.23 -	1.43	0.17						
Albumin	0.63	0.13 -	2.27	0.15						
LDL	1.01	0.99 -	1.03	0.06						
TG	1.00	0.99 -	1.01	0.62						
PTH	1.00	0.99 -	1.01	0.79						
CRP	1.00	0.99 -	1.01	0.62						
Hb	0.75	0.47 -	1.17	0.2						
HbA1c	1.09	0.57 -	2.15	0.09						
AFR	2.70	1.31 -	6.78	0.01>	**	2.96	1.26 -	8.16	0.01>	**

OR, odds ratio; CI, confidence interval. **p<0.01.

Fig 1. Prevalence of CVD according to AFR tertiles. Values are numbers with percentages or the mean ± SE.
T, tertile. CVD, cardiovascular disease.
T1: AFR<3.15, T2: AFR 3.15-3.65, T3: AFR>3.65 * p<0.01 for trend.



RESULTS

The demographic characteristics of the study group are summarized in Table 1. Twenty-one patients experienced *de novo* CVD events during follow-up monitoring. The baseline characteristics of HD patients with and without *de novo* CVD after the 3-year follow-up are summarized in Table 2. In the present study, CVD was defined as acute myocardial infarction, apoplexy, peripheral artery disease accompanied by toe necrosis, angina pectoris, or sudden cardiac death.

Levels of HbA1c and AFR were significantly higher in patients with CVD than those without CVD (7.97 ± 0.72 *vs* 6.14 ± 0.39 % and 3.88 ± 0.18 *vs* 3.19 ± 0.13, respectively, p<0.05). The HD duration of *de novo* CVD patients was significantly longer than that in non-CVD patients. Multivariate logistic regression analyses of the risk factors for *de novo* CVD were carried out (Table 3).

Univariate analyses in all subjects showed that the prevalence of *de novo* CVD correlated with HD duration and AFR level (p<0.01). Multivariate logistic regression analyses of risk factors showed that the prevalence of *de novo* CVD in HD patients was independently associated with HD duration and AFR.

Patients in the upper tertile of AFR level had a significantly higher prevalence of CVD (p<0.01 for trend) (Figure 1).

CONCLUSIONS

The present study suggests that AFR values may play an important role in the diagnosis and detection of CVD in HD patients. Our study supports the importance of AFR enhancement in the pathogenesis of vascular disease.

Non-invasive measurement of AFR could become a rapid tool for risk assessment and provide a novel approach for monitoring the role of AFR in disease.

References

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L3) Dialysis. Cardiovascular complications.
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