Change in Skin Autoflourescence over One Year Predicts Mortality at Five Years in a Prospective Cohort of People with Chronic Kidney Disease Stage 3

Renal Risk in Derby

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Introduction

Tissue advanced glycation end product (AGE) accumulation is a marker of cumulative metabolic stress assessed by a simple, non-invasive measurement of skin autofluoresence (SAF). This has been shown to predict mortality in haemodialysis patients[1] and in earlier CKD in some studies, but the impact of change in SAF over time has not previously been reported. In this study we sought to investigate the associations of SAF and change in SAF over time with mortality in people with CKD stage 3.

Methods

1741 people with CKD 3 (confirmed by two eGFR values) were recruited from primary care.[2] Participants attended for baseline, year 1 and year 5 study visits and underwent clinical assessment, blood and serum biochemistry. SAF was recorded from the forearm at each visit using an AGE reader (Diagnoptics Technologies B.V. Groningen, the Netherlands, Fig. 1). 3 Recordings of SAF were taken from each participant at each study visit. . The mean of these values was used in analyses. Mortality data were collected from hospital and national records (Office of National Statistics).

Fig. 1 Measuring SAF using the AGE reader

Results

At baseline, mean eGFR was 53.5 ml/min/1.73m^2, mean age 73 years and mean SAF 2.7 arbitrary units (AU). There was a small decrease in mean SAF at 1 year (-0.1 AU; p<0.001) but 310 (20.1 %) participants evidenced an increase of >10%.

299 (17.2%) participants died prior to the conclusion of year 5 follow-up. Splitting the cohort into tertiles of baseline SAF showed significant differences in the Kaplan-Meier survival function (Fig. 2, Log-rank p < 0.001).

Cox proportional hazards analysis (Table 1) showed that both baseline SAF (HR 1.38) and change in SAF (HR 1.53) over the first year were independent determinants of mortality at 5 years in addition to age (HR 1.77), male gender (HR 1.53), baseline eGFR (HR 0.98) and previous cardiovascular disease (HR=1.56).

Results

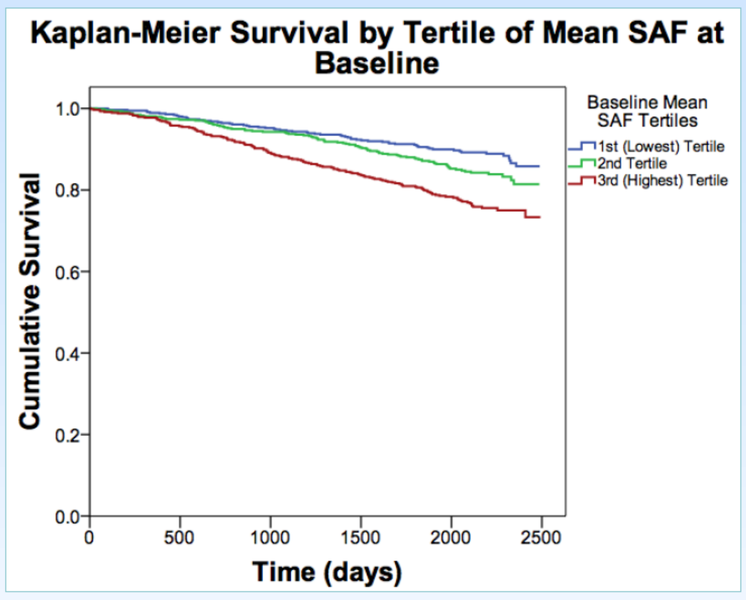

Fig. 2 Kaplan-Meier survival curves by baseline SAF tertile

Table 1. Cox Proportional Hazards Analysis – Associations of All-Cause Mortality at 5 Years

Variable	Constant	HR (95% CI)	p
Age	**0.75**	**1.08 (1.06-1.10)**	**<0.001**
Gender	**0.42**	**1.53 (1.13-2.07)**	**0.007**
eGFR	**-0.03**	**0.98 (0.96-0.99)**	**<0.001**
Log (uACR)	0.06	1.06 (0.96-1.17)	0.2
SAF	**0.32**	**1.38 (1.06-1.78)**	**0.016**
Haemoglobin (g/dl)	-0.06	0.94 (0.85-1.04)	0.2
Albumin	-0.04	0.96 (0.92-1.01)	0.09
Diabetes	-0.02	0.98 (0.69-1.39)	0.9
Smoker or Ex-Smoker	0.18	1.19 (0.88-1.61)	0.2
Previous CVD	**0.44**	**1.56 (1.16-2.08)**	**0.003**
Change in SAF at Y1	**0.42**	**1.53 (1.16-2.00)**	**0.002**

Variables in bold are significantly associated with mortality at 5 years

In a sensitivity analysis of participants without diabetes, change in SAF at 1 year remained an independent determinant of mortality (HR 1.5), adjusted for age, gender, baseline eGFR, previous cardiovascular disease and baseline SAF.

Conclusion

Our data show for the first time that an increase in SAF over 1 year is an independent predictor of mortality in CKD stage 3 in addition to baseline SAF. Serial measures of SAF may therefore be useful in predicting risk and monitoring interventions for reducing AGE accumulation.

References

1. Meerwaldt R. et al. JASN 2005; 16(12):3689-93
2. McIntyre N.J. et al. Nephron Clin Prac 2011; 199(4):269-76

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