PLASMA LIPIDOMICS IN CHRONIC KIDNEY DISEASE AND HEMODIALYSIS PATIENTS

Flore Duranton[1], Nathalie Gayrard[1], Alain Ficheux[1], Anne-Dominique Lajoix[2], Klaus M. Weinberger[3,4], Harald Mischak[5] and Angel Argilés[1,6]

1. **RD-Néphrologie**, Montpellier, France
2. **BC2M (EA7288),** Université de Montpellier, France
3. **BIOCRATES Life Sciences AG**, Innsbruck, Austria
4. **Mosaiques Diagnostics**, Hannover, Germany
5. **sAnalytiCo Ltd,** Belfast, United Kingdom
6. **NDSG Sete**, France

INTRODUCTION AND AIMS

Changes in circulating lipid profiles may reflect impaired metabolism and be associated with clinical conditions. Blood lipid levels have been reported to be modified in hemodialysis (HD) patients.

Still, the association between chronic kidney disease (CKD) and blood lipid profiles is not clear. In a cross-sectional study in CKD and HD patients, we analyzed plasma lipids.

METHODS

77 patients with CKD stage 2-3 (n = 23), 4-5 (n = 29) or end stage renal disease treated with chronic hemodialysis (HD, n = 25) were sampled at baseline and followed-up for 3.5 years.

Blood samples were taken in study visits or before dialysis sessions in non-fasting conditions and were analyzed by targeted flow-injection analysis - tandem mass spectrometry (FIA-MS/MS) for quantification of phosphatidylcholines (PC), lysophosphatidylcholines (LPC) and sphingomyelins (SM). Free and total fatty acid (FA) were analyzed by gas chromatography - tandem mass spectrometry (GC-MS/MS).

A total of 219 lipid species (80% of targeted compounds) were found in >50% of plasma samples and further analysed. The levels of lipid species and families (sum of species) were compared to healthy controls from external sources (1,2).

The association between CKD severity and diabetes with lipid families or individual species was analyzed by ANOVA. The association between lipid families and combined outcome (mortality or dialysis initiation) was assessed by Cox proportional hazards models.

RESULTS

PLASMA LIPIDS AND CKD STAGE

Compared to published controls (1,2), CKD patients had enriched plasma PC levels (notably C30:2) and SM levels (notably, C14:0, C20:2 and C22:3) and a tendency to lower LPC (notably C16:0 and C18:0), figure 1.

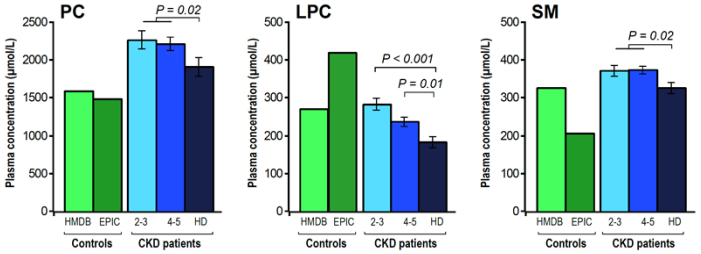

Figure 1. Plasma concentration in lipid families from CKD patients at different stages and controls (1,2). Mean levels and available standard errors are displayed. HMDB samples were obtained in fasting conditions.

The plasma level of PC, LPC and SM families was decreased in HD patients (P < 0.05, figure 1). In contrast, free and total FA levels were not associated with CKD stage.

Out of the 45 species significantly associated with HD compared to non-HD CKD patients, 44 were found to have lower levels, while free elaidic acid (trans C18:1w9) concentration was increased (+70% in HD vs CKD2-3, P < 0.001). The level of linoleic and alpha-linolenic acid (essential FA) were not modified by CKD stages or diabetes.

PLASMA LIPIDS AND SURVIVAL

Outcome was known for 73 (95%) patients after a median follow-up of 3.0 (IQR: 1.4 ; 3.3) years. There was a total of 31 events (20 deaths and 11 dialysis initiations).

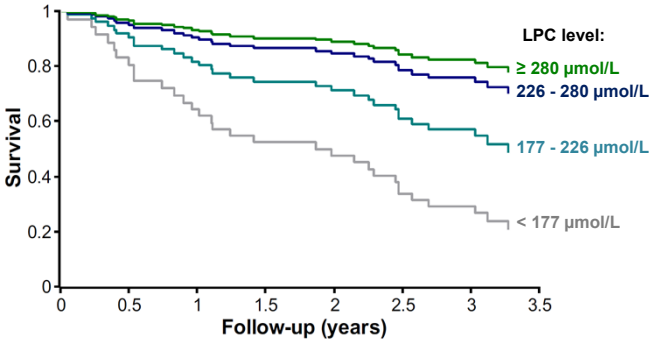

Figure 2. Survival curves by quartiles of LPC level.
The median and IQR of LPC was 226 (177 ; 280) µmol/L.

LPC level was associated with better combined outcome (figure 2). Patients with low LPC had a higher risk of mortality or dialysis initiation.

For an increase of 50 µmol/L, the hazard ratio was 0.6 [0.4 ; 0.8], P < 0.001. The association remained significant (P = 0.04) when accounting for age and CKD group (both NS).

CONCLUSIONS

Patients with CKD have increased levels of plasma PC and SM which tend to be normalized in HD patients. In contrast, CKD patients have lower LPC levels which are further decreased in HD patients and correlate with adverse outcome. These changes could be related to metabolic dysfunctions.

References

1. Psychogios N, Hau DD, Peng J, et al. The Human Serum Metabolome. PLoS ONE 2011;6(2):e16957.
2. Schmidt JA, Rinaldi S, Ferrari P, et al. Metabolic profiles of male meat eaters, fish eaters, vegetarians, and vegans from the EPIC-Oxford cohort. Am J Clin Nutr 2015;102(6):1518-26.

Contact: RD - Néphrologie, 2 rue des Mûriers, 34090 Montpellier, France; duranton@rd-n.org