Metabolomic characterisation of peritoneal dialysis effluent using NMR spectroscopy

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INTRODUCTION and OBJECTIVES

Peritoneal dialysis (PD) has been widely used by patients with end-stage renal disease. However, chronic exposure of the peritoneal membrane to bioincompatible PD solutions, and peritonitis and uremia during long-term dialysis result in peritoneal membrane injury and thereby contribute to membrane changes, ultrafiltration (UF) failure, inadequate dialysis and technical failure. Although the peritoneal equilibration test (PET) is a highly reproducible procedure, it allows to classify patients just in four classes: high, high average, low average or low transporters. Metabonomics encompasses the comprehensive and simultaneous profiling of multiple metabolite levels and their systematic and temporal changes and could be used to accurately obtain the quantitative biochemical information on PD effluent evaluated and eventually to assess the success of PD therapy and functionality of peritoneal membrane. In particular, H-nuclear magnetic resonance (NMR) spectroscopy is a rapid and non-invasive technique that gives qualitative and quantitative information about the endogenous metabolites.

AIM OF OUR STUDY WAS TO CHARACTERIZE BY NMR THE PERITONEAL EFFLUENT METABOLITES COMPOSITION AND EVALUATE ITS ASSOCIATION WITH PET RESULTS.AND RENAL FUNCTION (EGFR, CKD-EPI), ANEMIA AND IMMUNOSUPPRESSIVE REGIMENS.

METHODS

Peritoneal effluent from 21 patients (14 M and 7 F, age 55.3 ± 11.8 years, dialysis duration 2.7 ± 1.8 years) were collected and frozen at -80C° until the NMR measurements were performed. All patients executed a PET to determine the creatinine dialysate/plasma transport status. NMR spectra were recorded on a Bruker Avance 500 MHz (11.74 T) spectrometer. To assess quality, samples were collected twice.

All the data were pre-processed prior to analysis and Glucose and Lactate region were removed. Data were normalized to the internal standard. Exploratory multivariate analysis was performed using principal components analysis (PCA). PCA was performed on data normalized to zero mean and unit variance. Classification tree analysis (J48 algorithm) was performed to evaluate the predictive ability of PCs of patients transport status.

RESULTS

Figure 1 shows the distribution of samples and the 4 most influential PC loadings corresponding to: Threonine (1.38); Alanine (1.59); Acetic Acid (2.1); Creatinine (3.15). Patients were divided as high, high average, low average or low transporters. Using the first 10 PCs a decision tree has been created to classify between High and Low transporter. As depicted in Figure 2 we found that using only the 2nd PC, the model was able to correctly classify 19 of 21 patients (AUC=0.76).

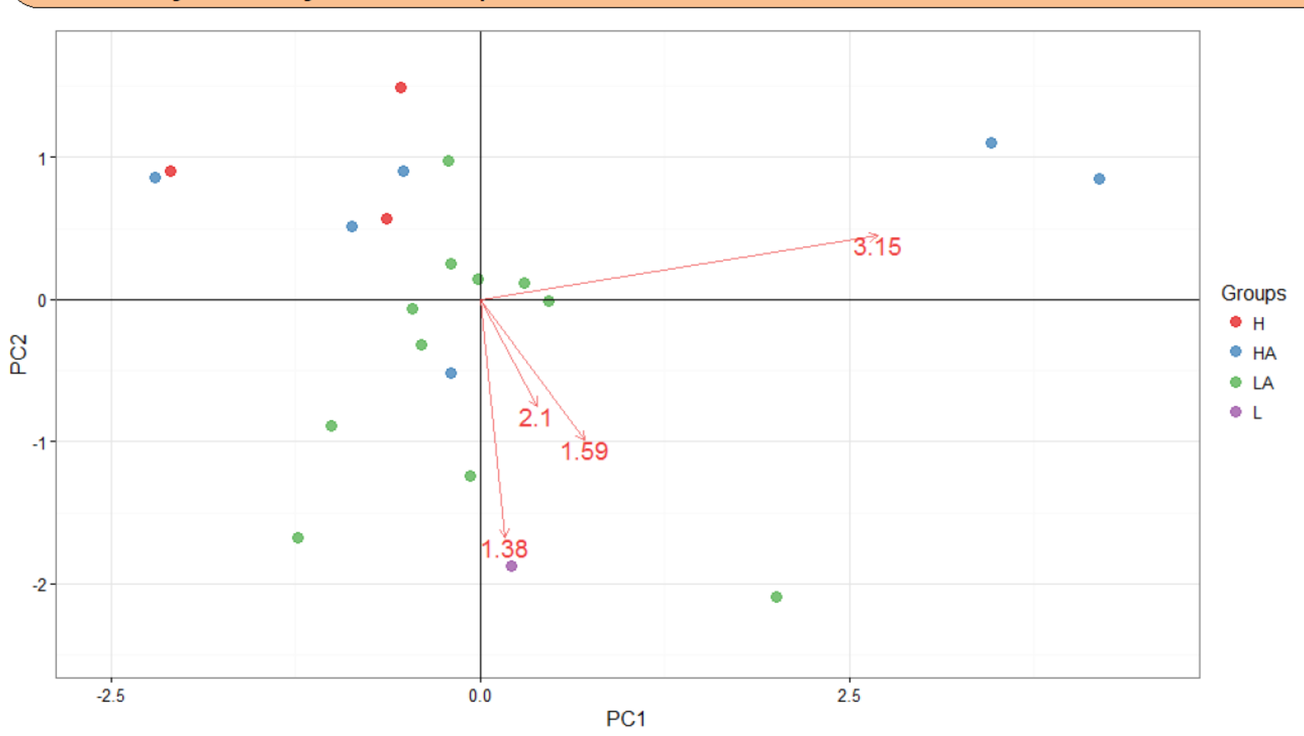

Figure 1. Scatter plot of the 21 patients in the space of the first 2 PC and the 4 most influential PC loadings.

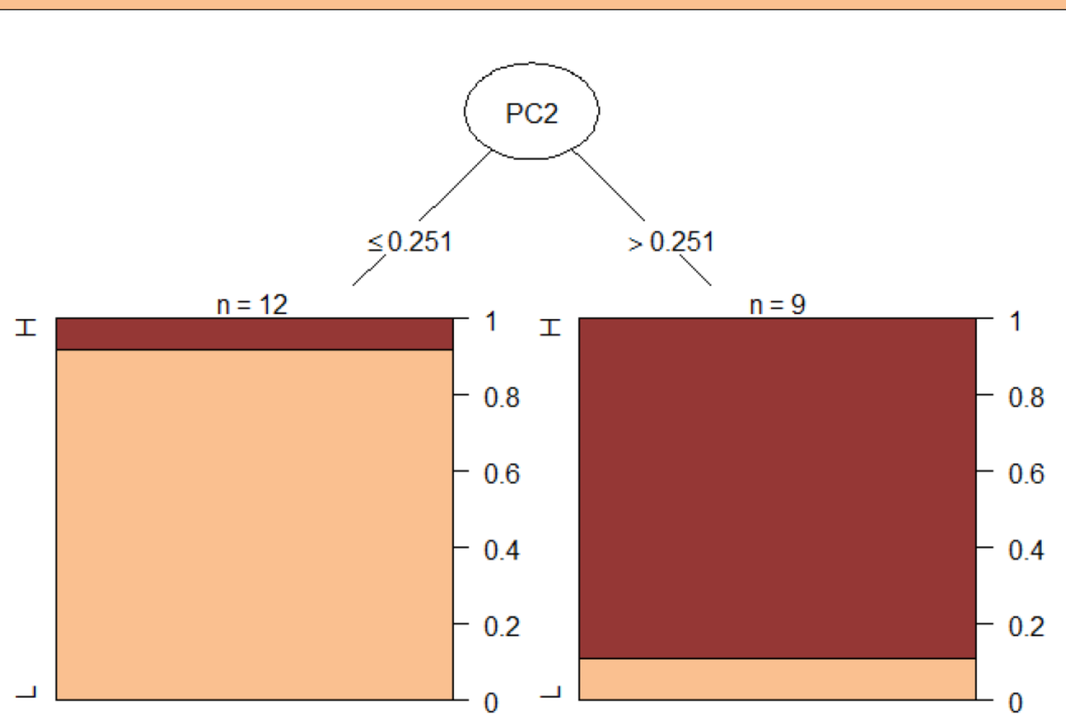

Figure 2. Decision tree for the classification of patients as High/High-Average (H) or Low/Low-Average (L) transporter.

CONCLUSIONS

RESULTS OF NMR SPECTRA FROM PERITONEAL EFFLUENT SEEMS TO BE HIGHLY CORRELATED WITH PET RESULTS.

THE HOLISTIC STUDY OF THE METABOLOME MAY OFFER THE POSSIBILITY TO CHARACTERIZE SINGLE PATIENT PD PERFORMANCE AS WELL AS A NUMBER OF ADVANTAGES INCLUDING LOW-COST AND HIGH-THROUGHPUT EXPERIMENTS

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