SERUM LEVELS OF AMINO ACIDS IN SUBJECTS WITH OR AT RISK OF ALZHEIMER'S DEMENTIA.

R FRATANGELO, A CRISTOFANO, N SAPERE, G LA MARCA, A ANGIOLILLO, M VITALE, G CORBI, T LOMBARDI, G SCAPAGNINI, G CORSO, G TEDESCHI, A DI COSTANZO.

Department of Medicine and Health Sciences "V. Tiberio", University of Molise, Campobasso

Introduction

Identifying people at risk of contracting Alzheimer Disease (AD) early and as accurately as possible is a priority for the medical community. In the present study we analyzed amino acid profile along the continuum from healthy subjects (HS), through patients suffering of subjective memory complaint (SMC) and/or mild cognitive impairment (MCI), up to those with AD.

Materials and methods

A total of 117 serum samples were analyzed. A mass spectrometry technique was used to quantify serum concentration of 16 amino acids (Fig 1): alanine, arginine, argininosuccinic acid, aspartic acid, citrulline, formiminoglutamic acid, glutamic acid, glycine, homocitrulline, hawkinsin, methionine, p henylalanine, ornithine, tyrosine, valine and leucine plus isoleucine (Xle). Data were analyzed using the SPSS (v. 17.0) statistical software package. Group differences (HS vs. SMC vs. MCI vs. AD) were evaluated by one-way multi- and uni-variate analysis of variance (ANOVA). The classification performance of selected metabolites was assessed using the multivariate receiver operating characteristic (ROC) curve and the area under the curve (AUC).
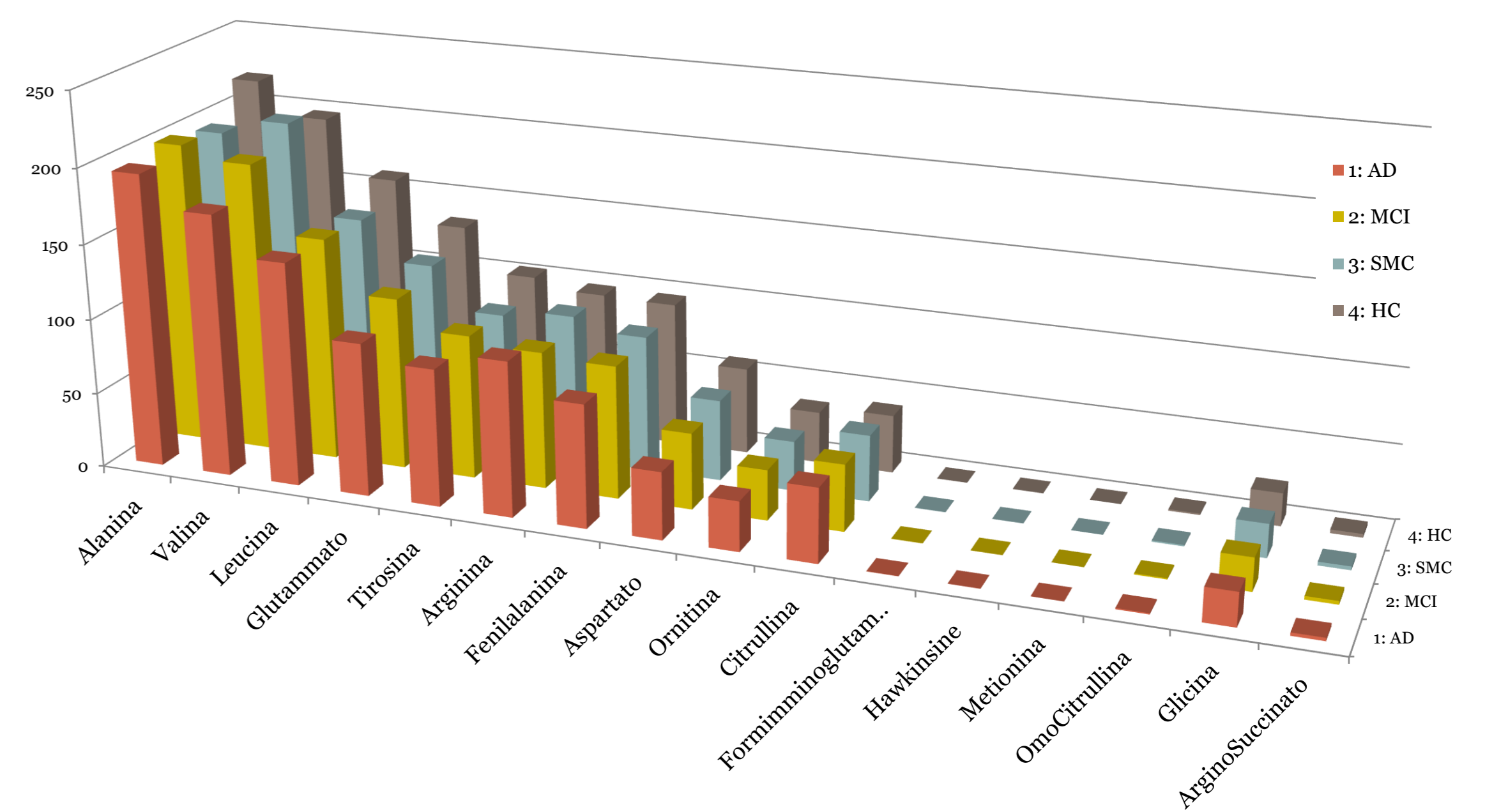
Fig 1. *Serum levels of amino acis among the four groups.*
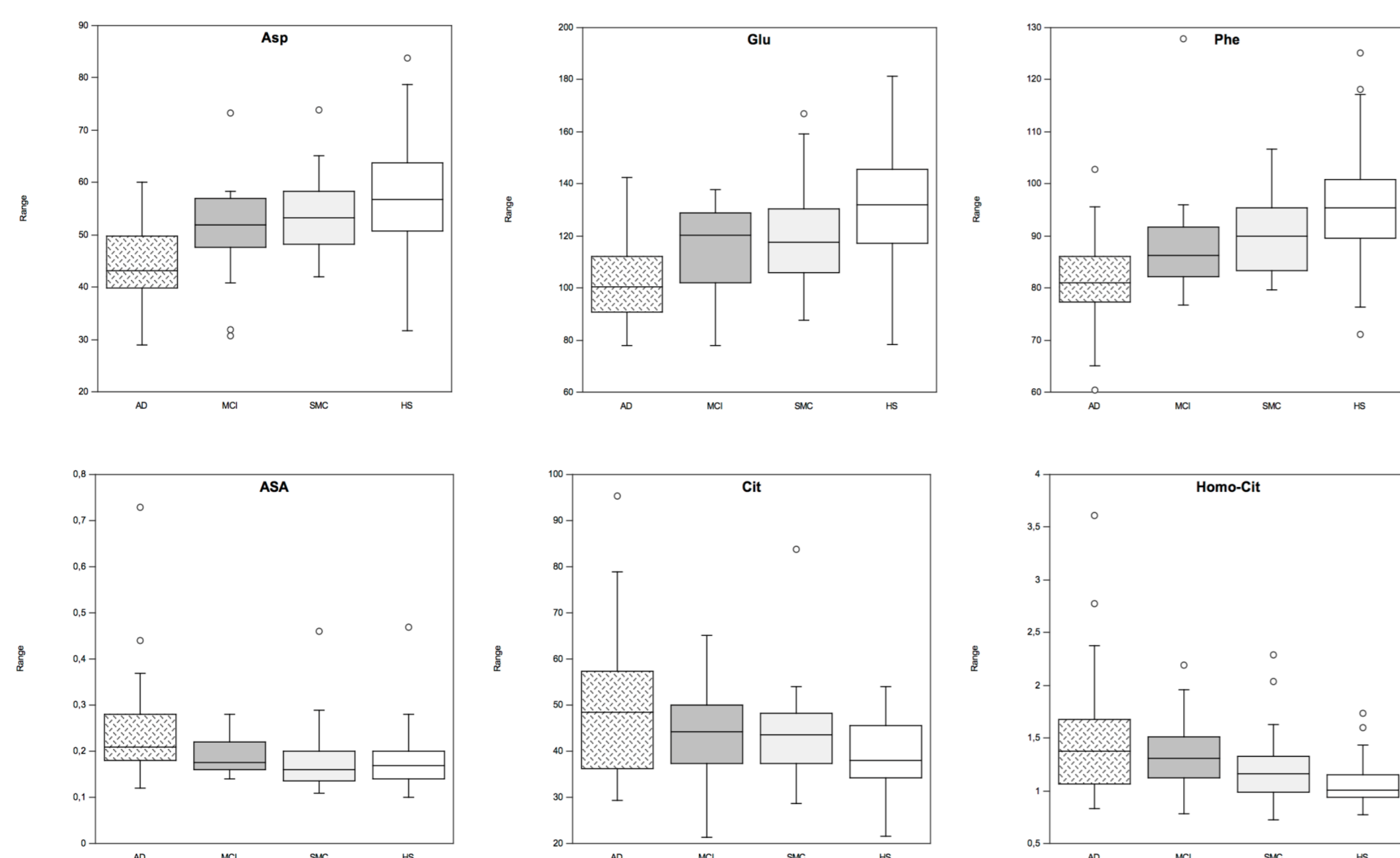
Fig 2. *Box-plots showing median (horizontal line in the box), 25th and 75th percentiles (edges of box), maximum and minimum values (whiskers) and outliers (°,*) of some amino acids concentrations (µmol/L) in the 4 groups of subjects.*

Fig 3. *Multivariate ROC curves analysis showing that the combination of ten biomarkers reached a very good power in discriminating AD form HS.*
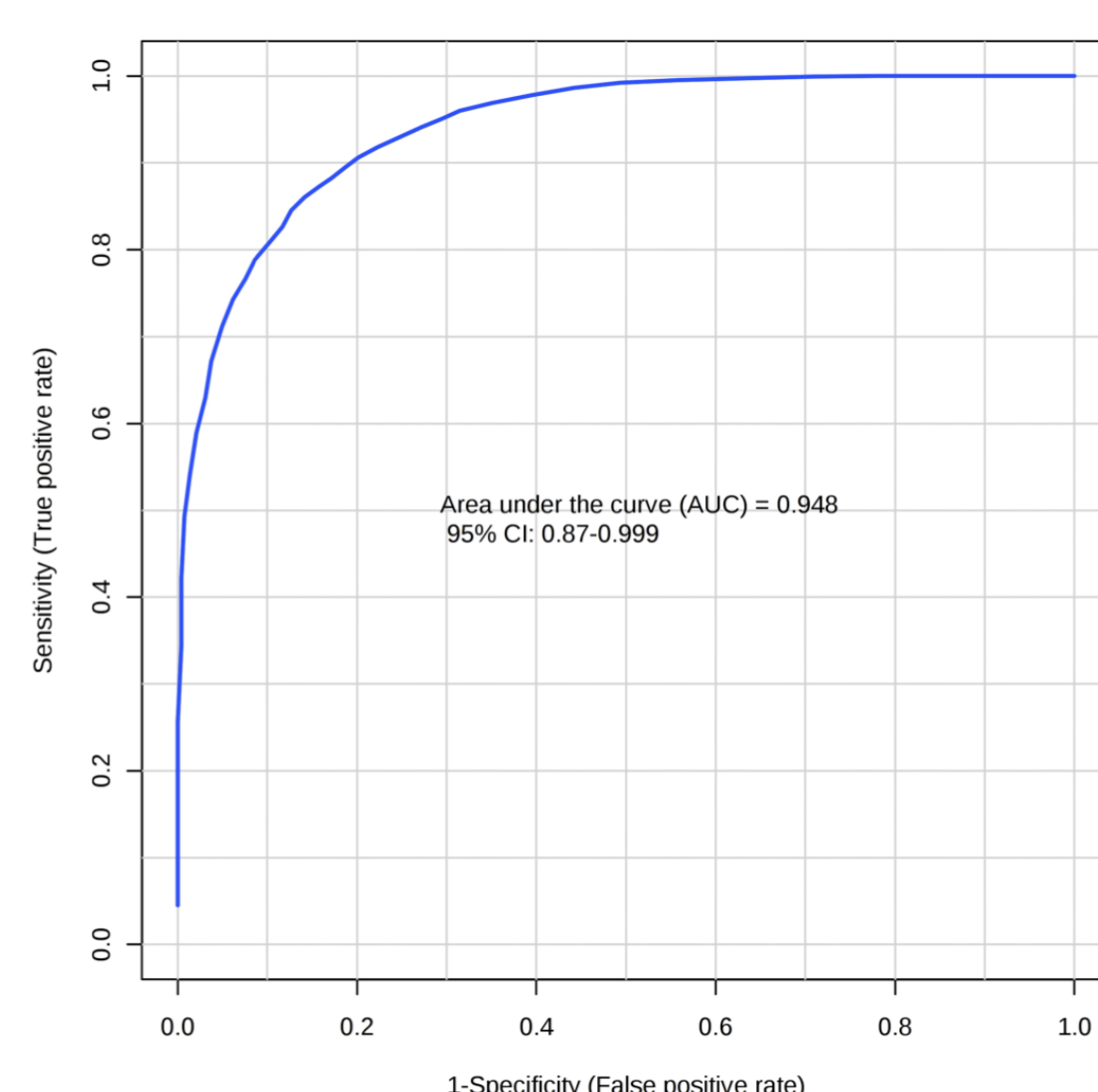
Results

Multivariate ANOVA resulted in a statistically significant difference among groups (F=2.577; df =108, 228; p<0.001). Univariate ANOVA and post hoc multiple comparisons showed that 11 amino acids (alanine, argininosuccinate, aspartate, citrulline, gluta mate, homocitrulline, hawkinsin, methionine, phenylal anine, tyrosine and valine) changed significantly among the four groups. Interestingly, the serum levels of glutamate, aspartate and phenylalanine progressively decreased from HS, through SMC and MCI, up to AD group, but only the comparisons HS vs. MCI, HS vs. AD and SMC vs. AD were statistically significant. On the contrary, serum concentrations of citrulline, homocitrulline and argininosuccinate showed a reverse trend (Fig 2).

Multivariate ROC curve analysis showed that the combination of ten biomarker (glutamate, aspartate, glutamate/citrulline, citrulline/p henylalanine, citrulline, Xle/phenylalanine, arginine/ph enylalanine, arginino-succinate, homocitrulline and phenylalanine) reached a very good power in discriminating AD from HS (AUC = 0,948, Fig 3).

Conclusion

The results of this study suggest that the serum levels of some amino acids could help to identify the patients before the phenotype conversion to AD.