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PS 14 Genetics and epidemiology of diabetic nephropathy

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ACE I/D polymorphism predicts end stage renal disease and or mortality in type 1 diabetic patients except for those with already advanced nephropathy: the follow up of the Genesis/Genediab Studies

M. Fysekidis[1,2], S. Hadjadj[3], R. Roussel[1,2], N. Bellili[2], S. Madani[2], F. Fumeron[2], H. Leblanc[4], J. Gautier[4], L. Weekers[5], B. Bauduceau[6], G. Charpentier[7], M. Virally[8], F. Alhenc-Gelas[9], P. Lefebvre[5], M. Marre[1,2];
[1]Diabetology, Bichat Hospital, APHP, Paris, France, [2]Inserm, U695, Paris, France, [3]Division of Diabetes,, CHU, Poitiers, France, [4]Diabetology, St Louis Hospital, APHP, Paris, France, [5]CHU du Sart Tilman, Division of Diabetes, Liège, Belgium, [6]Department of Endocrinology, Army Hospital, St Mande, Begin, France, [7]Diabetology, CHU Sud Francilien, Corbeil-Essones, France, [8]Diabetology, Lariboisiere Hospital, APHP, Paris, France, [9]U652, INSERM, Paris, France.

Background and Aims: Angiotensin Converting Enzyme (ACE) activity controls renal hemodynamics and its insertion /deletion (I/D) polymorphism was reported to affect development and progression of diabetic nephropathy in type 1 diabetes(T1D).We tested its impact on the risk for End Stage Renal Failure (ERSD) and mortality in prospective follow up of two cohorts of 856 T1D patients from France and Belgium (Genesis/Genediab).
Materials and Methods: Of the 533 participants of the Genediab study 332 agreed in prospective follow up as well as 524 out of 588 of the Genesis study .They were originally included between 1994 and 2000 on the basis of having insulin treatment before the age of 35 years and backround retinopathy.They had a follow up untill 31/12/2006 for the occurrence of ESRD or death. The tested hypothesis was that the 182 participants with II genotype will display less events than the others. Survival analysis was performed and adjustements were made using the Cox model.
Results: At baseline 463 subjects had no nephropathy, 222 incipient, 205 established and 186 advanced (plasma creatinine > 150 µmol/l) nephropathy. Age, sex ratio, HbA1c and diabetes duration were similar between groups.There was an expected association between nephropathy stage and ACE I/D polymorphism at baseline (χ^2 for trend II vs ID/DD :6,6. $p<0,05$). During follow up 141 events occurred the odds ratio for participants with II genotypes vs others was 0,55(95% CI 0,32-0,94). However, only 23 events occurred in participants without nephropathy at baseline,13 with incipient nephropathy,34 those with established and 79 among those with advanced nephropathy(nephropathy stage effect :$p < 0,0001$).When both nephropathy stage and ACE I/D genotype effects entered together in the Cox model the II genotype effect disappear OR 0.820 (95% CI 0,45-1,51; p=0,48) due to the lack of II genotype effect among the participants with advanced nephropathy at the baseline. Treatment with ACE inhibitors did not alter the result.
Conclusion: The ACE II genotype protects from the development and progression of diabetic nephropathy, and from the risk for ESRD and mortality as well. However its effect disapears in people with already advanced nephopathy.