ROLE OF ISLET-CELL ANTIBODIES AS TIME-DEPENDENT COVARIATES IN THE DEVELOPMENT OF TYPE 1 DIABETES IN NONDIABETIC RELATIVES OF TYPE 1 DIABETIC PATIENTS

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Islet-cell antibodies (ICAs) are important markers of type 1 diabetes mellitus (T1DM). The issue regarding whether or not the measurement of ICAs should be completely replaced by biochemical markers detecting islet autoantibodies (AAs) for the prediction of T1DM has been the subject of endless debates. In light of this controversy, we assessed the role of ICAs as a predictive marker for T1DM progression in a longitudinal study in a cohort of 499 FDRs, consecutively enrolled between 1977 through 2001 from the Childrens Hospital of Pittsburgh Registry. Serums obtained at the time of enrollment and about every two years were assayed for five autoantibodies: human and rat ICAs, glutamic acid decarboxylase (GAD) 65, insulin A (IA)- 2 AA, and insulin AAs (IAAs). The temporal relationships between the ICAs positivity and the onset of T1DM were analyzed using nonparametric tree-structured model with time-dependent covariates and also a Cox model. The tree-structured model provide a novel analytical approach to this area of research. We find that the ICAs provide important information in the prediction of T1DM. These results confirm the earlier result from a cross-sectional study where a cohort of 1484 first-degree relatives (FDRs) of T1DM probands from the same registry was analyzed (Pietropaolo, Yu , et. al, Pediatric Diabetes 2005:00: 1-9).