Factors affecting β-cell function in type 1 diabetes

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BACKGROUND: Type 1 Diabetes (T1D) is a progressive autoimmune disease resulting from destruction of insulin-producing pancreatic β-cells. C-peptide secretion is currently the only available clinical biomarker to measure residual β-cell function in T1D and the primary end point to assess therapeutic efficacy of immune intervention trails. However, there is great heterogeneity in natural history of C-peptide decline after diagnosis in T1D and factors influencing this decline are not well understood.

AIM: The aim of this project was to investigate factors affecting β-cell function in T1D from diagnosis up to 5 years.

METHODS: We collected data on C-peptide of over 4,000 T1D patients recruited from several European centres representing all age groups at disease onset (childhood, adolescence and adulthood).

We investigated the shape of C-peptide decline over time from T1D onset in relation to age at diagnosis, haemoglobin A1c (HbA1c) levels, Body Mass Index (BMI) and insulin dose. The influence of age of onset on β-cell function at baseline was investigated, in addition to the shape of C-peptide decline over 5-years of follow up in a longitudinal analysis. Linear regression models were also used to identify baseline predictors of 1-year Fasting C-peptide (FCP) decline.

	≤5		>5 and ≤10		>10 and ≤18		≥18	
Year	FCP (nM)	Δ%	FCP (nM)	Δ%	FCP (nM)	Δ%	FCP (nM)	Δ%
0	0.15 (0.17)	0	0.19 (0.23)	0	0.28 (0.34)	0	0.30 (0.38)	0
1	0.10 (0.17)	34	0.14 (0.16)	26.3	0.26 (0.31)	7.1	0.30 (0.36)	0
5	0.028 (0.035)	83.3	0.052 (0.096)	73.7	0.093 (0.17)	67.5	0.17 (0.33)	46.7

TABLE 1. FCP by age of onset group and year of follow up

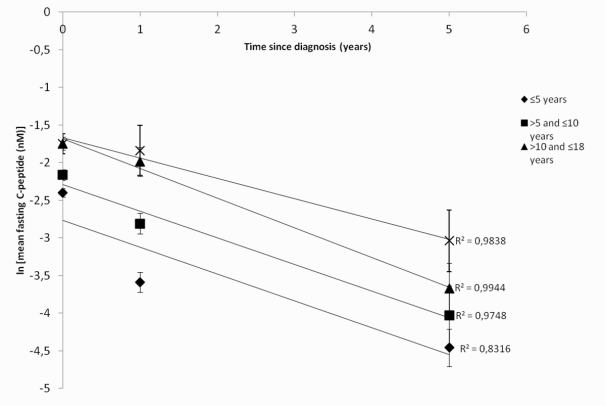

FIGURE 1. Log-linear decline of FCP over 5-years by age of onset

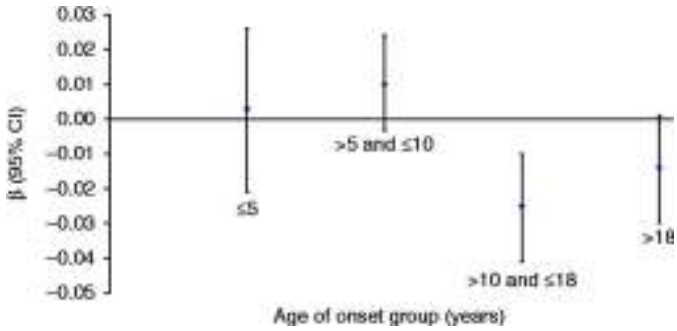

FIGURE 2. Association between 1kg/m2 change in BMI and Δ C-peptide by age of onset group

RESULTS: FCP data at diagnosis were available in 3,668 patients stratified according to age at diagnosis in four groups (<5 years, n=344; >5 years<10 years, n=668; >10 years<18 years, n=991; >18 years, n=1.655). There was a significant age-dependent increase in FCP at diagnosis (p<0.001) (Table 1). The subsequent decline in FCP over time was log-linear with a greater rate in younger age groups (p<0.0001) (Figure 1).

In those with an age of onset of >10 years and ≤18 years BMI was a significant predictor of C-peptide decline over 1-year (Figure 2), whereas in those diagnosed ≥18 years gender was the most important predictor. No associates of 1-year FCP decline were identified for younger age of onset groups.

CONCLUSION: This study reveals an inverse correlation between age at T1D onset and FCP at diagnosis with a more rapid decline in β-cell function in very young patients. In addition, our data suggest that increased body weight is associated with more rapid disease progression after diagnosis of T1D in an age group 10–18 years. These observations can inform the design of clinical trials using C-peptide values as an endpoint for the effect of a given treatment.