Beta cell function in type 1 diabetes determined from clinical and fasting biochemical variables

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Abstract

Aims/hypothesis

Beta cell function in type 1 diabetes is commonly assessed as the average plasma C-peptide concentration over 2 h following a mixed-meal test (CP_{AVE}). Monitoring of disease progression and response to disease-modifying therapy would benefit from a simpler, more convenient and less costly measure. Therefore, we determined whether CP_{AVE} could be reliably estimated from routine clinical variables.

Methods

Clinical and fasting biochemical data from eight randomised therapy trials involving participants with recently diagnosed type 1 diabetes were used to develop and validate linear models to estimate CP_{AVE} and to test their accuracy in estimating loss of beta cell function and response to immune therapy.

Results

A model based on disease duration, BMI, insulin dose, HbA_{1c}, fasting plasma C-peptide and fasting plasma glucose most accurately estimated loss of beta cell function (area under the receiver operating characteristic curve [AUROC] 0.89 [95% CI 0.87, 0.92]) and was superior to the commonly used insulin-dose-adjusted HbA_{1c} (IDAA1c) measure (AUROC 0.72 [95% CI 0.68, 0.76]). Model-estimated CP_{AVE} (CP_{EST}) reliably identified treatment effects in randomised trials. CP_{EST}, compared with CP_{AVE}, required only a modest (up to 17%) increase in sample size for equivalent statistical power.

Conclusions/interpretation

CP_{EST}, approximated from six variables at a single time point, accurately identifies loss of beta cell function in type 1 diabetes and is comparable to CP_{AVE} for identifying treatment effects. CP_{EST} could serve as a convenient and economical measure of beta cell function in the clinic and as a primary outcome measure in trials of disease-modifying therapy in type 1 diabetes.

Keywords

Adult Beta cell function Children Clinical trial Immune therapy Immune Tolerance Network Linear model TrialNet Type 1 diabetes

Abbreviations

AIC

Akaike’s information criterion

AUROC

: Area under the ROC curve

CP_{AVE}

: Average plasma C-peptide concentration over 2 h following a mixed-meal test

CP_{EST}

: Estimated CP_{AVE}

FCP

: Fasting C-peptide

FPG

: Fasting plasma glucose

IDAA1c

: Insulin-dose-adjusted HbA_{1c}

ITN

: Immune Tolerance Network

ROC

: Receiver operating characteristic

A list of members of the Type 1 Diabetes TrialNet Study Group and the Immune Tolerance Network Study Group can be found in the electronic supplementary material.

Electronic supplementary material

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Notes

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Contribution statement

JMW devised the study. JMW, NGB, LCG and LCH analysed the data and prepared the manuscript. All named authors contributed to collection, collation, analysis and interpretation of the data, helped to revise the manuscript and approved it for publication. Authors listed in the ESM contributed by performing the TrialNet and ITN clinical trials. JMW is the guarantor and takes full responsibility for the work as a whole, including the study design, access to data and the decision to submit and publish the manuscript.

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Duality of interest

SEG received funding from the Immune Tolerance Network (in turn funded by NIAID) for his role as principal investigator of the START trial (ITN-28). SG received a grant from NIDDK for unrelated work. All other authors declare that there is no duality of interest associated with their contribution to this manuscript.

Supplementary material

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