Tracking and prediction of arterial blood pressure from childhood to young adulthood in 868 patients with type 1 diabetes: A multi-center, longitudinal survey in Germany and Austria

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Running title: Type 1 diabetes and tracking of blood pressure

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ABSTRACT

Objective: Arterial blood pressure (BP) was followed in 868 patients with type 1 diabetes from 6.0 to 19.9 yrs of age in 95 centers in Germany and Austria.

Research Design and Methods: European BP reference data for 28,043 children and adolescents were used with respect to age and gender. Data were stratified in the 3 groups pre-pubertal, pubertal and post-pubertal.

Results: Up to 4% of the participants in the younger age groups and 13.9% of the post-pubertal patients exhibited BP values >97th centile. BP levels correlated to hemoglobin A1c and BMI z score. Tracking of BP revealed that children with elevated BP had higher BP in adolescence and young adulthood.

Conclusions: Patients with higher BP in childhood showed elevated BP later in life. We need to focus on the diagnosis of hypertension in children with type 1 diabetes, and to study the efficacy of early intervention.
OBJECTIVE
The objective of this survey was to follow arterial blood pressure (BP) and the prevalence of hypertension as a risk factor for cardiovascular disease (CVD) in a large cohort of young patients with type 1 diabetes. A total of 868 patients with type 1 diabetes from 6.0 to 19.9 yrs of age, treated in 95 Diabetes Centers and Pediatric Care Clinics in Germany and Austria, formed the study cohort for this report.

RESEARCH DESIGN AND METHODS
At the 1-4 annual clinical visits BMI (weight in kilograms divided by the square of height in meters), HbA1c and BP at rest were recorded. HbA1c measurements were standardized to the DCCT reference of 4.05-6.05% (1); BP levels were measured on a single occasion in a relaxed, sitting position at the upper arm with proper cuff size using sphygmomanometer or semi-automated Dinamap, Critikon. Data were collected from 1977 to 2006 with informed consent according to the Declaration of Helsinki, using a documentation database (DPV) as reported earlier (2,3). Of 1,353 patients who had been screened, 962 were enrolled, and data sets from childhood to young adulthood were completed for 868 participants (96% Caucasians, 4% other ethnicities; age at diagnosis 5.9±2.4 yrs; 432 females, 436 males). Patients with other diseases or permanent medication including antihypertensive drugs were excluded. European BP reference data for 28,043 children and adolescents were used with respect to age and gender (4). German reference data for BMI, obtained from 17,275 girls and 17,147 boys in a comparable time span were applied as reported earlier (5,3). BP and BMI values were derived using the LMS method box-cox-power-transformation, which adjusts the distribution of the parameters for skewness and allows individual data to be expressed as SDS or z score (6,7). Data were stratified in 3 groups according to age: 6.0-9.9 yrs (pre-pubertal), 10.0-15.9 yrs (pubertal) and 16.0-19.9 yrs (post-pubertal). Statistical analysis was performed using Pearson correlation, Kruskal Wallis test and Wilcoxon test. A $P$ value of $<0.05$ was considered significant. In addition, mixed multivariate models with systolic or diastolic blood pressure during adulthood as dependent variable and blood pressure during childhood (6-9.9 yrs), gender, migration background, age at onset, current age, observation period, BMI, smoking status and treatment center (random effect) as potential confounders were evaluated (SAS proc glimmix).

RESULTS
Within these 3 age groups, mean values (+SD) for HbA1c were 7.4±1.4%, 7.9±1.3%, 8.4±1.7%, for BMI z score 0.24±0.73, 0.37±0.78, 0.60±0.89, for systolic BP 106±7, 116±8, 127±11 mmHg, for diastolic BP 65±7, 68±7, 72±7 mmHg. Mean BP z scores in the 3 age groups increased with age (+0.09, +0.12, +0.52 for systolic BP, $P<0.000001$ and 0.63 to 0.69 for diastolic BP, $P<0.0001$). In the pre-pubertal and pubertal age groups, up to 4% of participants exhibited BP values $>97$th centile. However, 13.9% of patients in the post-pubertal group had BP levels $>97$th centile. BP values correlated to HbA1c and BMI z score ($r=0.2148$ and 0.3663, $P<0.0001$, respectively).

A mixed model with adult BP as dependent variable and adjustment for gender, migration background, age at onset, current age, observation period, BMI, smoking status and treatment center (random effect) revealed significant effects of childhood BP (age 6 – 9.9 yrs) as evidence for tracking ($P<0.000001$ for systolic and diastolic BP, Figure 1): Elevation of childhood BP by one SD increases adult BP z score by 0.43 (systolic) or 0.38 (diastolic).

CONCLUSIONS
In this survey we followed BP in patients with type 1 diabetes from childhood...
to young adulthood. Because patients with higher BP in childhood, or even hypertension, showed elevated BP later in life, early intervention is feasible. The use of BP determinations in patients with diabetes can, therefore, increase the prediction of a future CVD risk from childhood. It has been shown earlier, using ambulatory profiles of 24h BP, that daytime and nocturnal BP are more pronounced in the course of type 1 diabetes compared with healthy control subjects (8). Although we can only imagine the beneficial effects of lowering BP in the hypertensive individuals, preventing the development of atherosclerosis early in life is mandatory, because morbidity and mortality of CVD are increased up to 10-fold in patients with type 1 diabetes (9). In our study, BP values correlated significantly to HbA1c and BMI, which also exhibit adverse longitudinal changes in patients at risk for CVD (1,10). Along these lines, progression of carotid intima-media thickness, a measure of atherosclerosis, is strongly associated with age, blood pressure, and HbA1c in subjects with type 1 diabetes (1).

Moreover, by showing the advantage of having lower BP levels early in life on BP levels in young adulthood, this study provides additional evidence for the risk factor status in young patients with type 1 diabetes.

Taken together, we need to focus on the early detection of hypertension in children with type 1 diabetes and to study the efficacy of treatment in affected individuals early in life.
REFERENCES


FIGURE LEGEND

Figure 1. Tracking of systolic (A) and diastolic (B) blood pressure (BP) from childhood to young adulthood in patients with type 1 diabetes. Pre-pubertal (6.0-9.9 yrs.) BP z score quartiles are given together with mean pubertal (10.0-15.9 yrs.) and post-pubertal (16.0-19.9 yrs.) BP z scores in 868 patients with type 1 diabetes (432 females, 436 males). Patients were stratified according to their pre-pubertal BP z scores in 3 categories: BP z score <25th centile (n=217), 25-75th centile (n=438) and >75th centile (n=213).