Tracking and Prediction of Arterial Blood Pressure From Childhood to Young Adulthood in 868 Patients With Type 1 Diabetes

A multicenter longitudinal survey in Germany and Austria

INA KNERR, MD, PHD[1]
AXEL DOST, MD, PHD[2]
RUDOLF LEPLER, MD[3]
KLEMENS RAILE, MD[4]
EDITH SCHOBER, MD, PHD[5]
WOLFGANG RASCHER, MD, PHD[1]
REINHARD W. HOLL, MD, PHD[6]
ON BEHALF OF THE DIABETES DATA ACQUISITION SYSTEM FOR PROSPECTIVE SURVEILLANCE (DPV) SCIENTIFIC INITIATIVE GERMANY AND AUSTRIA

OBJECTIVE — Arterial blood pressure was followed in 868 patients with type 1 diabetes aged 6.0–19.9 years in 95 centers in Germany and Austria.

RESEARCH DESIGN AND METHODS — European blood pressure reference data for 28,043 children and adolescents were used with respect to age and sex. Data were stratified into three groups: prepubertal, pubertal, and postpubertal.

RESULTS — Up to 4% of the participants in the younger age-groups and 13.9% of the postpubertal patients exhibited blood pressure values >97th centile. Blood pressure levels correlated with A1C level and BMI *Z* score. Tracking of blood pressure revealed that children with elevated blood pressure had higher blood pressure in adolescence and young adulthood.

CONCLUSIONS — Patients with higher blood pressure in childhood showed elevated blood pressure 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.

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The objective of this survey was to follow arterial blood pressure 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 years of age, who were 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 each of the first through fourth annual clinical visits, BMI (calculated as weight in kilograms divided by the square of height in meters), A1C, and blood pressure at rest were recorded. A1C measurements were standardized to the Diabetes Control and Complications Trial reference of 4.05–6.05% (1); blood pressure 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, Tampa, FL). Data were collected from 1977 to 2006 with informed consent according to the Declaration of Helsinki, using the diabetes data acquisition system for prospective surveillance (DPV), as previously described (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% Caucasian and 4% other ethnicity; age at diagnosis 5.9 ± 2.4 years; 432 female and 436 male). Patients with other diseases or permanent medication, including antihypertensive drugs, were excluded. European blood pressure reference data for 28,043 children and adolescents were used with respect to age and sex (4). German reference data for BMI, obtained from 17,275 female subjects and 17,147 male subjects in a comparable time span, were applied as reported earlier (3,5). Blood pressure and BMI values were derived using the least median of squares (LMS) Box-Cox power transformation method, 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 three groups according to age: 6.0–9.9 years (prepubertal), 10.0–15.9 years (pubertal), and 16.0–19.9 years (postpubertal). Statistical analysis was performed using Pearson correlation, Kruskal-Wallis test, and Wilcoxon's signed-rank test. A *P* value of <0.05 was considered significant. In addition, mixed multivariate models with systolic or diastolic blood pressure during adulthood as the dependent variable and blood pressure during childhood (6–9.9 years), sex, 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 three age-groups, mean ± SD values for A1C were 7.4 ± 1.4, 7.9 ± 1.3, and 8.4 ± 1.7%; for BMI *Z* score 0.24 ± 0.73, 0.37 ± 0.78, and 0.60 ± 0.89; for systolic blood pressure (SBP) 106 ± 7, 116 ± 8, and 127 ±

From the [1]Children's and Adolescents' Hospital, University of Erlangen-Nuremberg, Erlangen, Germany; [2]University Children's Hospital, Jena, Germany; [3]Children's Hospital Wilhelmstift, Hamburg, Germany; [4]University Children's Hospital, Berlin, Germany; [5]University Children's Hospital, Vienna, Austria; and the [6]Division of Applied Information Technology, University of Ulm, Ulm, Germany.
Address correspondence and reprint requests to Ina Knerr, MD, PhD, Children's and Adolescents' Hospital, University of Erlangen-Nuremberg, D-91054 Erlangen, Germany. E-mail: ina.knerr@uk-erlangen.de.
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Abbreviations: CVD, cardiovascular disease; DBP, diastolic blood pressure; SBP, systolic blood pressure.

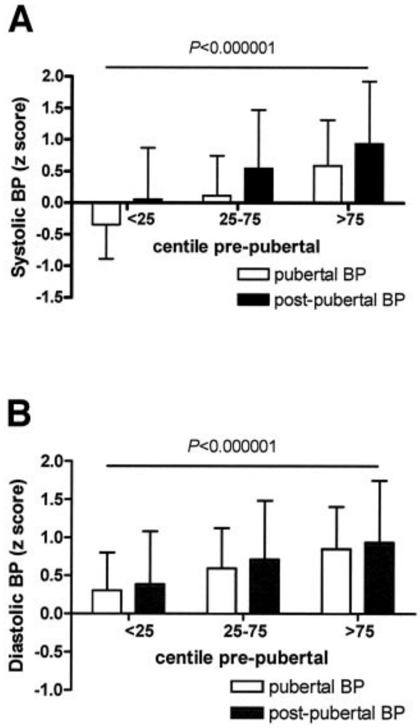

Figure 1—*Tracking of systolic* (A) *and diastolic* (B) *blood pressure (BP) from childhood to young adulthood in patients with type 1 diabetes. Prepubertal (6.0–9.9 years) blood pressure Z score quartiles are given together with mean pubertal (10.0–15.9 years) and postpubertal (16.0–19.9 years) blood pressure Z scores in 868 patients with type 1 diabetes (of whom 432 were female and 436 male). Patients were stratified according to their prepubertal blood pressure Z scores in three categories: blood pressure Z score <25th centile* (n = *217), 25th–75th centile* (n = *438), and >75th centile* (n = *213).*

11 mmHg; and for diastolic blood pressure (DPB) 65 ± 6, 68 ± 7, and 72 ± 7 mmHg. Mean blood pressure *Z* scores in the three age-groups increased with age (increases of 0.09, 0.12, and 0.52 for SBP, *P* <0.000001, and 0.63 to 0.69 for DBP, *P* <0.0001). In the prepubertal and pubertal age-groups, up to 4% of participants exhibited blood pressure values >97th centile. However, 13.9% of patients in the postpubertal group had blood pressure levels >97th centile. Blood pressure values correlated to A1C level and BMI *Z* score ($r = 0.2148$ and 0.3663, respectively; *P* <0.0001).

A mixed model with adult blood pressure as the dependent variable and adjustment for sex, migration background, age at onset, current age, observation period, BMI, smoking status, and treatment center (random effect) revealed significant effects of childhood blood pressure (age 6–9.9 years) as evidence for tracking (*P* <0.000001 for SBP and DBP) (Fig. 1). Elevation of childhood blood pressure by 1 SD increases adult blood pressure *Z* score by 0.43 (systolic) or 0.38 (diastolic).

CONCLUSIONS— In this survey, we followed blood pressure in patients with type 1 diabetes from childhood to young adulthood. Because patients with higher blood pressure in childhood, or even with hypertension, showed elevated blood pressure later in life, early intervention is feasible. The use of blood pressure 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 24-h blood pressure, that daytime and nocturnal blood pressure is more pronounced in the course of type 1 diabetes compared with that in healthy control subjects (8). Although we can only imagine the beneficial effects of lowering blood pressure 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, blood pressure values correlated significantly with A1C level and BMI *Z* score, which also exhibit adverse longitudinal changes in patients at risk for CVD (1,10). Similarly, progression of carotid intima-media thickness, a measure of atherosclerosis, is strongly associated with age, blood pressure, and A1C in subjects with type 1 diabetes (1).

Moreover, by showing the advantages of having lower blood pressure levels early in life on blood pressure levels in young adulthood, this study provides additional evidence for the importance of monitoring blood pressure as a risk factor in young patients with type 1 diabetes. In conclusion, 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.

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