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Are Young Age and Insulin Treatment Enough to Diagnose IDDM?

In a paper recently published in *Diabetes Care*, V.A. Koivisto et al. (1) addressed the issue of cardiovascular disease in IDDM patients in Europe. The study was based on cross-sectional data from 16 European countries (EURODIAB IDDM Complications Study) (2). The target population was all individuals with IDDM in the participating centers. The eligibility criteria were an age range of 15–59 years, a diagnosis of diabetes before 36 years of age, and unbroken record of insulin treatment.

We have published in a recent issue of *Diabetes Care* (3) our experience with IDDM in adults in a community-based study in Israel. To determine the clinical characteristics of insulin-treated NIDDM and IDDM diabetic patients, we examined all known insulin-treated diabetic patients from three community clinics (registered population, 9,573 adults). Fasting plasma C-peptide levels were measured in all insulin-treated patients; insulinopenia was diagnosed when plasma C-peptide was <0.132 nmol/l. A total of 588 diabetic patients were found, 100 of whom were insulin-treated; of those, only 25 were insulinopenic. The mean ages (range) of the IDDM and NIDDM groups were 49.5 (24–75) and 62.0 (29–86) years, respectively; the mean ages at diagnosis of diabetes were 26.9 (4–60) and 46.9 (17–73) years, respectively. Moreover, 43% of the IDDM patients were diagnosed at ≥36 years of age, whereas 22% of the insulin-treated NIDDM patients were diagnosed at ≤36 years of age. Interestingly, only 66% of our insulinopenic patients received insulin as a first treatment, while 21% of insulin-treated NIDDM patients received insulin as a first treatment.

If our patients were to be classified according to the EURODIAB inclusion criteria, 43% of the insulinopenic IDDM patients would be excluded, and 22% of the insulin-treated NIDDM patients would be included in the IDDM group. Since most insulin-treated patients, at least in our study, actually had NIDDM (3), it is possible that a large number of patients included in the EURODIAB study were insulin-treated NIDDM patients. Also, Laakso and Pyörälä (4), who studied insulin-treated patients in Scandinavia, found that 50% of insulin-treated patients were positive for endogenous insulin secretion.

Thus, the measurement of endogenous insulin secretion capacity in insulin-treated patients is of great value to differentiate between IDDM and insulin-treated NIDDM individuals. Despite the added technical burden and the increase in cost, fasting plasma C-peptide measurements should be included in large epidemiology studies dealing with IDDM.

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Reply to Maislos and Weitzman

Maislos and Weitzman (1) criticize the definition of IDDM used in the EURODIAB study, suggesting that this could result in diagnostic misclassification. It is clear that there is no one universally accepted diagnostic test that will completely differentiate between IDDM

and NIDDM, which is unsurprising given the considerable heterogeneity of the two conditions.

Weitzman recommends using plasma C-peptide as the diagnostic criterion, but fails to provide a reference for the cutoff point used in his study. There is a considerable range of C-peptide levels in diabetic patients, with a clear overlap between insulin-treated and non–insulin-treated patients (2). Finding an appropriate cutoff point for C-peptide to differentiate between IDDM and NIDDM would be difficult, even if laboratory variation is not taken into account, and would of course result in some degree of misclassification. Further, the supposition that C-peptide levels provide a good indicator of insulin concentrations has been challenged (3).

In the EURODIAB IDDM Complications Study, a diagnosis of diabetes had to be made before 36 years of age, with a continuous need for insulin therapy within a year of diagnosis (not an unbroken record of insulin treatment, as Weitzman indicates). This is a pragmatic definition, as many clinics still do not have access to sophisticated laboratory tests, and the diagnosis of IDDM has to be largely clinical, according to current World Health Organization criteria (4). Our study aimed to recruit a representative sample of IDDM patients, as currently identified in clinical practice. The mean BMI in our patients varied from 23.5 to 24.1 kg/m^2 in men and women without or with cardiovascular disease, respectively (4). Thus, the majority of our patients were nonobese, which is typical for IDDM but not for NIDDM patients. We do not agree that C-peptide measurement provides major advantages in the definition of IDDM on an epidemiological basis.

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Severe Hypertrophic Cardiomyopathy in an Infant of a Diabetic Mother

Hypertrophic cardiomyopathy (HCM) is commonly found in fetuses of diabetic mothers (1,2), but it is still open to question whether it can be reversed by tight maternal glycemic control. We present a severe case of HCM in an infant of a diabetic teenage mother, who was 16 years old when pregnancy was diagnosed after 20 weeks of amenorrhea. The duration of type I diabetes was 8 years. Maternal HbA_{1c} ranged from 7 to 8% (normal range 3.7–6.7%) in the previous year and during the first two trimesters of gestation; after an intensive insulin regimen at 1.9 U · kg^{-1} · d^{-1}, it was optimized in the third trimester (HbA_{1c} 6.5%). Fetal macrosomy was detected ultrasonographically at 28 weeks of gestation. Delivery took place by cesarean section at 35 weeks of gestation. The newborn girl was large for gestational age (3.650 kg); she presented a moderate asphyxia (Apgar score 5 at 1'; 7 at 5'), tachypnea (respiratory rate 60/min), subcyanosis (PaO_2 50 mmHg), and transitory hypoglycemia (1.38 mmol/l). She presented a moderate systolic ejection murmur on the mesocardial area with a normal second heart sound; a fourth sound was appreciable on the apical area. Echocardiography performed by bidimensional and Doppler technique showed a hypertrophic cardiomyopathy involving the interventricular septum (15 mm in diastole, n.v. <4 mm), the left ventricular posterior wall (6 mm, n.v. <4 mm), and the right ventricular anterior wall (6.5 mm, n.v. <4 mm); a moderate dynamic obstruction of the left ventricular outflow, evaluated at about 40 mmHg, was present (Fig. 1). Abnormal patterns of diastolic flow through the mitral valve, represented

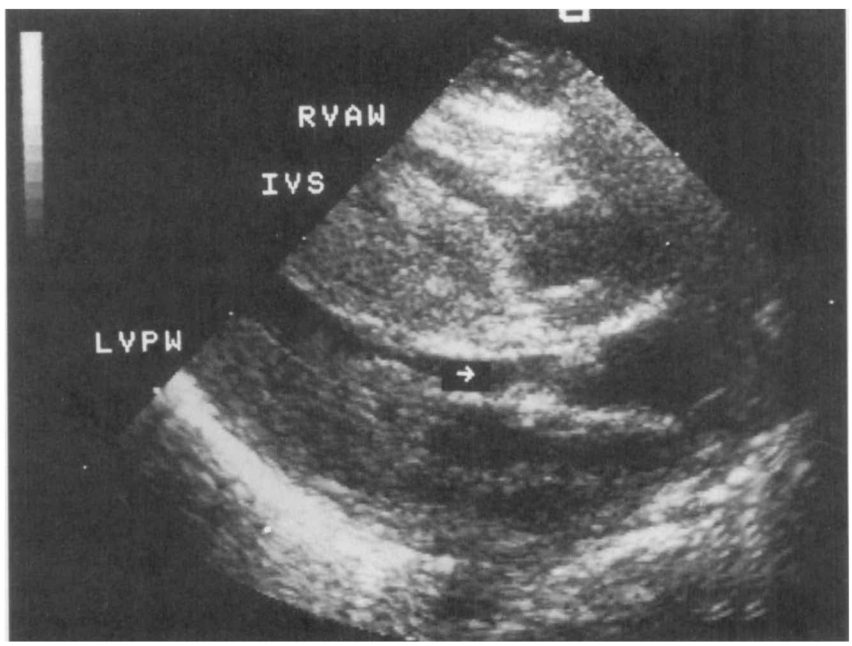

Figure 1—*Bidimensional echocardiographic image showing the severe thickening of the ventricular myocardium (IVS, interventricular septum; LVPW, left ventricular posterior wall; RVAW, right ventricular anterior wall). The arrow indicates narrowing of the left ventricular outflow tract.*