From the [1]Endocrinology Sections, Saad Specialist Hospital, Al Khobar, Saudi Arabia; and the [2]Department of Endocrinology, Cleveland Clinic Foundation, Cleveland, Ohio.

Address correspondence to Wiam I. Hussein, MD, FACE, FACP, Section Head, Diabetes and Endocrinology, Saad Specialist Hospital, Al Khobar, Saudi Arabia. E-mail: husseinw@pol.net.

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References

1. Wertman E, Zilber N, Abramsky O: An association between multiple sclerosis and type I diabetes mellitus. *J Neurol* 239: 43–45, 1992
2. Edwards LJ, Constantinescu CS: A prospective study of conditions associated with multiple sclerosis in a cohort of 658 consecutive outpatients attending a multiple sclerosis clinic. *Mult Scler* 10:575–581, 2004

Poor Glucose Control in the Year Before Admission as a Powerful Predictor of Amputation in Hospitalized Patients With Diabetic Foot Ulceration

Although there is a strong association between lower-extremity amputation (LEA) and HbA_{1c} (A1C) in diabetic patients (1,2), little information is available on glucose control in the period preceding and following LEA (3). Our objective was to evaluate the predictors of LEA and to examine the role of blood glucose control during the year before and the year after admission. A total of 122 diabetic patients (82 men and 40 women aged 69.7 ± 10.9 years, disease duration 19.7 ± 10.4 years) consecutively admitted for diabetic foot ulcers to the Medicine Department of United Hospitals of Bergamo between January 2003 and December 2004 were enrolled in our observational study and assigned to one of three groups.

The prevalence of long-term diabetes complications was similar in each group; >75% had peripheral polyneuropathy, nephropathy, retinopathy, and ischemic cardiomyopathy, and >90% had peripheral vascular disease. Glycemic control was evaluated before and after admission using the mean of three A1C levels measured in the year preceding admission and in the year following discharge. Patients were reevaluated 1 year after admission and assigned to one of three groups: group A, major amputation ($n = 28$); group B, minor amputation ($n = 44$); and group C, no amputation ($n = 50$). Major amputation was defined as amputation above the ankle, and minor amputation was defined as amputation below the ankle.

Data are shown as means ± SD. Categorical variables were compared by χ^2 test, continuous variables by ANOVA.

In the year before admission, mean A1C levels were significantly higher in groups A (9.7 ± 1.5%) and B (9.1 ± 1.9%) than in the group C (7.9 ± 1.3%, $P < 0.001$ vs. A and $P < 0.05$ vs. B). Similarly at admission, A1C levels were higher in groups A (10.1%) and B (9.4 ± 1.8%) than in the group C (8.1 ± 1.5%, $P < 0.001$). A1C levels decreased in all groups after 1 year of follow-up: 8.4 ± 1% in group A, 7.9 ± 1.3% in group B, and 7.5 ± 1.2% in group C ($P < 0.05$ vs. A).

At admission, patients in groups A and B had a higher ulceration grade according to Wagner's classification (3.9 ± 0.4 and 3.7 ± 0.4, respectively) than those in group C (2.7 ± 1.1, $P < 0.001$). The prevalence of patients with LDL cholesterol levels <100 mg/dl was significantly lower in groups A (38%) and B (40%) than in group C (65%; $P < 0.01$ vs. A and $P < 0.05$ vs. B). More patients in group C (75%, $P < 0.05$) were on aspirin therapy than in groups A (61%) and B (59%). The frequency of optimal blood pressure control (≤130/80 mmHg) was ~50% in all groups. Patients in group A (21%, $P < 0.001$ vs. B and C) received less follow-up with a specialist in a diabetes clinic than patients in the groups B (50%) and C (56%).

Although hypertension and cholesterol levels were inadequately treated, and aspirin therapy underused in a large number of these patients, multivariate logistic regression analysis revealed that only A1C level and ulceration grade were independently associated with LEA.

In conclusion, poor metabolic control and inadequate treatment of modifiable risk factors are powerful predictors of LEA in patients hospitalized for diabetic foot ulcers. We suggest that all diabetic patients with poor metabolic control and risk factors associated with cardiovascular disease receive early referral for education and aggressive treatment with a diabetes clinic.

GIUSEPPE LEPORE, MD[1]
MARIA L. MAGLIO, MD[2]
CARLO CUNI, MD[3]
ALESSANDRO R. DODESINI, MD[1]
ITALO NOSARI, MD[1]
BRUNO MINETTI, MD[2]
ROBERTO TREVISAN, MD, PHD[1]

From the [1]Diabetes Unit, Ospedali Riuniti, Bergamo, Italy; the [2]Medicine Unit, Ospedali Riuniti, Bergamo, Italy; and the [3]Orthopaedic Surgery Unit, Ospedali Riuniti, Bergamo, Italy.

Address correspondence to Dr. Giuseppe Lepore, Diabetes Unit, A.O. Ospedali Riuniti, Largo Barozzi, 1, 24128 Bergamo, Italy. E-mail: glepore@ospedaliriuniti.bergamo.it.

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References

1. Moss SE, Klein R, Klein BEK: The 14-year incidence of lower-extremity amputations in a diabetic population: the Wisconsin Epidemiologic Study of Diabetic Retinopathy. *Diabetes Care* 22:951–999, 1999
2. Stratton IM, Adler AI, Neil AW, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR, the UK Prospective Diabetes Study Group: Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 321:406–412, 2000
3. Miyajima S, Shirai A, Yamamoto S, Okada N, Matsushita T: Risk factors for major limb amputations in diabetic foot gangrene patients. *Diabetes Res Clin Pract* 71: 272–279, 2005

Type 1 Diabetes and Autism Association Seems to Be Linked to the Incidence of Diabetes

We read with interest the article of Freeman et al. (1) reporting a higher prevalence of autism spectrum disorder in pediatric patients with type 1 diabetes in Toronto than in the general population (0.9% [95% CI 0.3–1.5 vs. 0.34–0.67]).

The finding was, however, not confirmed by Harijutsalo and Tuomilehto (2), who reported a prevalence of autism spectrum disorders in type 1 diabetic patients similar to that in the population aged <18 years in northern Finland

(0.135% [95% CI 0.5–2.8] vs. 0.139% [1.2–1.57]).

In Italy, we have "our own Finland," namely Sardinia. Italy has a peculiar epidemiology of type 1 diabetes. Sardinia has one of the highest incidences in the world (42.4/100 [95% CI 40.5–44.4]), while peninsular Italy has an overall incidence that is similar to other Mediterranean areas (8.4/100 [7.9–8.9], 11.2/100 [10.3–12.2] in North Italy, and 6.2/100 [5.8–6.7] in South Italy) (3). Only 2 of 1,373 patients aged <14 years from the Sardinian Registry of type 1 diabetes were diagnosed with autism spectrum disorders (0.1456% [0.13–0.16]), a finding similar to the Finnish data. On the contrary, a pattern similar to that observed by Freeman et al. (1) has been found in patients with type 1 diabetes aged <14 years from six Italian centers of pediatric diabetology equally distributed in the Italian Peninsula and in Sicily (0.72% [0.69–0.75]). The diagnosis of autism spectrum disorder was confirmed in all cases using the DSM-IV (Diagnostic and Statistic Manual of Mental Disorders-IV). Autism spectrum disorder includes autism, Asperger disorder, pervasive developmental disorders (not otherwise specified), Rett's syndrome, and childhood disintegrative disorder. Its prevalence in the general Italian population is estimated at 0.1%.

Our data seem to confirm the observation that the prevalence of autism in patients with type 1 diabetes is inversely associated to the incidence trends of diabetes in the observed areas. According to Daneman (4), if the relationship between autism and diabetes is based on shared genetic influences, this finding could be explained by the fact that, in areas with higher and rising incidence of type 1 diabetes without a parallel increase of the prevalence of autism, the rise in incidence of diabetes is due to a reduced contribution of high-risk HLA haplotypes (5).

Dario Iafusco, md[1]
Maurizio Vanelli, md[2]
Marco Songini, md[3]
Giovanni Chiari, md[2]
Francesca Cardella, md[4]
Annarita Fifi, md[5]
Fortunato Lombardo, md[6]
Annamaria Marinaro, md[7]
Annafranca Melia, md[8]
Alberto Marsciani, md[9]
Anna Vacca, md[10]
Franco Prisco, md[1]

From the [1]Department of Paediatrics, University of Naples, Naples, Italy; the [2]Department of Paediatrics, University of Parma, Parma, Italy; the [3]Department of Internal Medicine, Hospital "Brotzu," Cagliari, Italy; and the Italian Society of Paediatric Endocrinology and Diabetology Units of [4]Palermo, [5]Arezzo, [6]Messina, [7]Sassari, [8]Nuoro, [9]Rimini, and [10]Cosenza, Italy.

Address correspondence to Maurizio Vanelli, PhD, Full Professor of Paediatrics, University of Parma, Viale A. Gramsci, 14, 43100 Parma, Italy. E-mail: maurizio.vanelli@unipr.it.

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References

1. Freeman SJ, Roberts W, Daneman D: Type 1 diabetes and autism: is there a link? *Diabetes Care* 28:925–926, 2005
2. Harjutsalo V, Tuomilehto J: Type 1 diabetes and autism: is there a link? Response to Freeman et al. (Letter). *Diabetes Care* 29: 484, 2006
3. Carle F, Gesuita R, Bruno G, Coppa GV, Falorni A, Lorini R, Martinucci ME, Pozzilli P, Prisco F, Songini M, Tenconi MT, Cherubini V, the RIDI Study Group: Diabetes incidence in 0- to 14-year age-group in Italy: a 10-year prospective study. *Diabetes Care* 27:2790–2796, 2004
4. Daneman D: Diabetes and autism: is there a link? Response to Harijutsalo and Tuomilehto (Letter). *Diabetes Care* 29:485, 2006
5. Gillespie KM, Bain SC, Barnett AH, Bingley PJ, Christie MR, Gill GV, Gale EA: The rising incidence of childhood type 1 diabetes and reduced contributions of high risk HLA haplotypes. *Lancet* 364:1645–1647, 2004

A Proposal for the Cutoff Point of Waist Circumference for the Diagnosis of Metabolic Syndrome in the Japanese Population

In a community-based cohort of 692 Japanese individuals, Hara et al. (1) investigated the relationship between cutoff values used for the waist circumference to define central obesity and rates of detection of subjects displaying multiple risk factors of metabolic syndrome. Using the receiver-operator characteristic (ROC) curve, they proposed an optimal cutoff point of waist circumference for the diagnosis of metabolic syndrome in the Japanese population to yield maximal sensitivity plus specificity, with cutoffs of 85 cm in men and 78 cm in women.

In the Ohasama study, another Japanese general-population study (2,3), we also attempted to determine the most suitable cutoff level for waist circumference in terms of associations with insulin resistance (IR). We investigated relationships between the cutoff values used for waist circumference measured at the umbilical level and rates of subjects with IR among 329 residents (235 women) in Ohasama aged ≥35 years (mean age 64 years, mean BMI 24 kg/m^2) without antidiabetes medication. Subjects participated in the diabetes screening program conducted, in addition to the home blood pressure measurement program (2), from 2002 to 2004. The ROC curve for waist circumference to predict the presence of IR, as defined by a homeostasis model assessment of IR >1.73 (4), was plotted using SAS version 9.2 software (SAS Institute, Cary, NC).

According to the ROC curve, the cutoff level yielding maximal sensitivity plus specificity for predicting the presence of IR was 83 cm in men and 75 cm in women. Sensitivity and specificity using these cutoff values were 80 and 63%, respectively, in men and 85 and 58%, respectively, in women.

These results, together with those by Hara et al. (1), suggest that the cutoff point for waist circumstance in Japanese women, which is used to predict metabolic syndrome or IR, is lower than that proposed by the International Diabetes Federation (90 cm).

Takayoshi Ohkubo, md, phd[1]
Masahiro Kikuya, md, phd[2]
Kei Asayama, md, phd[1]
Yutaka Imai, md, phd[2]

From the [1]Department of Planning for Drug Development and Clinical Evaluation, Graduate School of Pharmaceutical Sciences and Medicine, Tohoku University, Sendai, Japan; and the [2]Department of Clinical Pharmacology and Therapeutics, Graduate School of Pharmaceutical Sciences and Medicine, Tohoku University, Sendai, Japan.

Address correspondence to Takayoshi Ohkubo, MD, PhD, Clinical Pharmacology and Therapeutics, Tohoku University Hospital, 1-1 Seiryo-cho, Aobaku, Sendai 980-8574, Japan. E-mail: tohkubo@mail.tains.tohoku.ac.jp.

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References

1. Hara K, Matsushita Y, Horikoshi M, Yoshiike N, Yokoyama T, Tanaka H, Kadowaki T: A proposal for the cutoff point of