Impaired Glucose Tolerance and Bone Mineral Content in Overweight Latino Children With a Family History of Type 2 Diabetes

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OBJECTIVE — Research on the skeletal status of pre-diabetic (type 2 diabetic) children is warranted. We examined the hypothesis that bone mineral content (BMC) and bone mineral density (BMD) will be lower in children with impaired glucose tolerance (IGT) versus normal glucose tolerance (NGT).

RESEARCH DESIGN AND METHODS — Total body BMC and BMD of 184 overweight Latino children (106 boys, 78 girls, 11.9 ± 1.7 years) with a family history of type 2 diabetes were measured using dual-energy X-ray absorptiometry. Glucose tolerance was assessed by 2-h glucose after an oral glucose tolerance test. Area under the insulin curve (AUC) assessed the cumulative insulin response to oral glucose. Acute insulin response to glucose (AIR) was determined by an intravenous glucose tolerance test.

RESULTS — Partial correlations revealed an inverse relationship between BMC and AIR ($r = -0.29$, $P = 0.00$), AUC ($r = -0.28$, $P = 0.00$), fasting insulin ($r = -0.16$, $P = 0.04$), and 2-h insulin ($r = -0.16$, $P = 0.04$). There was no significant difference in BMC or BMD between children with IGT ($n = 46$) or NGT ($n = 138$). Stepwise multiple linear regression revealed that 89% of the variance in BMC is attributed to lean mass (87%), age (1%), and AIR (1%). BMD was explained by lean mass (69%), Tanner stage (3%), and AUC (2%).

CONCLUSIONS — The findings of this study suggest that in overweight children, lean mass is the primary predictor of BMC and BMD, whereas age, Tanner stage, and the acute and cumulative insulin responses to oral glucose make subtle independent contributions to the total variances. In addition, poor glycemic control does not seem to be detrimental to bone mass of pre-diabetic children.

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The relationship between diabetes and osteopenia has received considerable attention in the last 55 years, initiated with the findings of Albright and Reifenstein (1,2) who first demonstrated loss of bone mineral by evaluation of conventional X-rays of diabetic patients in 1948. However, despite the large quantity of publications since that year, the pathogenesis, nature, and magnitude of this problem remains unsettled.

Krakauer et al. (3) concluded that the metabolic effects of poor glycemic control lead to increased bone resorption and bone loss in young diabetic adults. With improvements in glycemic control, studies (3–5) have found increased values of serum osteocalcin in diabetic patients. These studies suggest that during periods of poor glycemic control, increased rates of bone resorption are not accompanied by proportional increases in rates of bone formation. In contrast, Barrett-Connor and Holbrook (6) found higher bone mineral density (BMD) in diabetic (type 2) older women than in those with normal glucose tolerance (NGT), independent of obesity. In men, they found no differences in bone density by glycemic status (6). Similarly, Marugame et al. (7) recently found no association between impaired glucose tolerance (IGT) and alveolar bone loss but found a positive relationship between type 2 diabetes and alveolar bone loss in a group of Japanese men, suggesting that duration and severity of disease may be important factors in the possible deficits in bone density.

It is likely that the controversies regarding whether bone disease is a complication of diabetes may be due to the cross-sectional nature of the majority of studies. For this reason, we have decided to examine the bone mineral status of a group of overweight children who are currently participating in the University of Southern California (USC) Study of Latino Adolescents at Risk (SOLAR) diabetes project with the intention to follow them

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Abbreviations: AIR, acute insulin response to glucose; AUC, area under the insulin curve; BMC, bone mineral content; BMD, bone mineral density; CDC, Centers for Disease Control and Prevention; GCRC, General Clinical Research Center; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; SOLAR, Study of Latino Adolescents at Risk; USC, University of Southern California.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

longitudinally and to carefully monitor their skeletal as well as metabolic changes. The present cross-sectional investigation is the first of a series of reports that will address the relationship between pre-diabetes (i.e., IGT) and bone mass in children. The recent global emergence of type 2 diabetes in children combined with puberty being a time of rapid skeletal growth and a critical period for the attainment of peak bone mass makes this study unique and its purpose imperative.

In this article, we assessed the combined and independent contributions of age, Tanner stage, lean mass, fat mass, fasting/2-h glucose and insulin, and the acute insulin response to glucose (AIR) and the cumulative insulin responses to oral glucose (i.e., area under the insulin curve [AUC]) to bone mineral content (BMC) and BMD in a group of Latino children to address the hypothesis that children with IGT will have lower BMC and BMD than children with NGT.

RESEARCH DESIGN AND METHODS

— A cohort of overweight Latino children with a positive family history of type 2 diabetes was established with the intention to follow them longitudinally in the USC SOLAR diabetes project. The current investigation reports the cross-sectional findings from the first 184 children in this cohort.

A total of 184 children (106 boys, 78 girls) were recruited to the SOLAR project through clinics, health fairs, newspaper announcements, and word of mouth. The children were required to meet the following inclusion criteria: *1*) age 8–13 years; *2*) BMI ≥85th percentile for age and sex based on the Centers for Disease Control and Prevention (CDC) standards (8) and an initial telephone prescreening; *3*) Latino ancestry (all four grandparents Latino by self-report); and *4*) family history of type 2 diabetes in at least one parent, sibling, or grandparent. Children were of Mexican-American (71%), Central American (16%), or mixed Mexican–Central American (13%) heritage. Children were excluded if they had prior major illness including type 1 or type 2 diabetes, took medications, or had a condition known to influence body composition, bone mass, insulin action, or insulin secretion (e.g., pregnancy, glucocorticoid therapy, or hyper- or hypothyroidism). The SOLAR study was approved by the Institutional Review Board, Health Science Campus, USC. Informed consent and assent were obtained from all parents and children, respectively.

Outpatient screening visit

Children arrived at the USC General Clinical Research Center (GCRC) at ~8:00 A.M. after an overnight fast. Weight and height were measured followed by a physical examination conducted by a board-certified pediatric endocrinologist (Marc J. Weigensberg). Physical examinations included Tanner staging in girls (breast stage) and boys (pubic hair stage) as well as testicular volume measurements in a subsample (n = 84) of boys. A medical history was conducted including parental interview detailing family history of diabetes. After these procedures, an oral glucose tolerance test was conducted. Children who met the following screening criteria were invited back for further testing during an inpatient GCRC visit: *1*) BMI ≥85th percentile for age and sex according to the CDC standards (8) based on height and weight measures at the GCRC and *2*) absence of type 1 or type 2 diabetes using the American Diabetes Association guidelines (9). Note that for the purposes of this study, we used the CDC definitions for weight status in children (i.e., at risk of overweight/obesity is a BMI age/sex percentile >85th). All children met the BMI criteria, and none of the 184 children screened positive for diabetes.

Inpatient visit

Of the 184 children completing the outpatient visit, all returned to the GCRC within 15 ± 10 (± SD) days. Children were admitted to the GCRC in the early afternoon and then completed tests for bone mass and body composition using dual-energy X-ray absorptiometry. Children were served dinner and an evening snack, with only water permitted after 8:00 P.M. The following morning, insulin sensitivity and AIR were determined from an intravenous glucose tolerance test.

Weight, height, and anthropometry

Height (by a wall-mounted stadiometer) and weight (by a balance beam medical scale) were recorded at each visit to the nearest 0.1 cm and 0.1 kg, respectively, and the average of the two measurements was used for analysis. BMI and BMI percentiles for age and sex were determined based on established CDC normative curves using EpiInfo 2000, Version 1.1.

Bone mineral and body composition

A whole-body dual-energy X-ray absorptiometry scan was performed to determine whole-body BMC (units: grams), BMD (units: grams/cm^2), and whole-body composition using a Hologic QDR 4500W (Hologic, Bedford, MA). The whole-body scan requires the subject to be placed supine with the arms and legs positioned according to the manufacturer's specifications. Quality control was performed daily using a phantom, and measurements were maintained within the manufacturers precision standards of ≤1%.

Cardiorespiratory fitness

A subsample (n = 146) of participants completed an all-out progressive continuous treadmill protocol (10). After being familiarized with the exercise equipment, the children practiced walking on the motorized treadmill until they were able to walk without holding the railings. Children walked for 4 min at 0% grade and 4 km/h, after which the treadmill grade was raised to 10%. Each ensuing work level lasted 2 min, during which the grade was increased by 2.5%. The speed remained constant until a 22.5% grade was reached, at which time the speed was increased by 0.6 km/h until the subject reached exhaustion. Respiratory gases were collected and measured via open circuit spirometry and analyzed on a MedGraphics CardiO_2 combined V_{O_2}/ECG Exercise System. Heart rate was measured continuously using a Polar Vantage XL heart rate monitor (Port Washington, NY). $V_{O_{2max}}$ was achieved if individuals satisfied two of the following three criteria: respiratory exchange ratio >1.0, heart rate ≥195, and a leveling or plateauing of V_{O_2} defined as an increase of oxygen uptake <2 ml · kg^{-1} · min^{-1} with a concomitant increasing workload.

Oral glucose tolerance test

A topical anesthetic (EMLA cream; AztraZeneca, Wilmington, DE) was applied to the antecubital area of one arm, and a flexible intravenous catheter was placed in an antecubital vein. Subjects ingested 1.75 g oral glucose solution per kilogram body weight (to a maximum of 75 g) at "time 0." Blood was sampled and assayed for glucose and insulin at times −5 min ("fasting") and 120 min ("2 h") relative to glucose ingestion. IGT was defined by "2-h glucose ≥140 mg/dl," as recom-

mended by the American Diabetes Association Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (11). AUC was determined with the trapezoidal method (12). Incremental insulin AUC was calculated by dividing the AUC by 180 min and subtracting the fasting insulin value.

Frequently sampled intravenous glucose tolerance test

At 6:30 A.M., the EMLA cream was applied, followed ~1 h later by flexible intravenous catheter placement in bilateral antecubital veins. Two fasting blood samples were drawn at −15 and −5 min for determination of basal glucose and insulin. At time 0, glucose (25% dextrose, 0.3 g/kg body wt) was administered intravenously. Blood samples were collected at time points 2, 4, 8, 19, 22, 30, 40, 50, 70, 100, and 180 min. Insulin (0.02 units/kg body wt, Humulin R [regular insulin for human injection]; Eli Lilly, Indianapolis, IN) was injected intravenously at 20 min. Values for glucose and insulin were entered into the Minmod Millenium 2002 computer program (Version 5.16, Richard N. Bergman) for determination of insulin sensitivity and the acute insulin response to glucose (13).

Glucose and insulin assays

Blood samples during the oral glucose tolerance test were centrifuged, and plasma was placed on ice and analyzed within 1 h at the Los Angeles County USC Medical Center Core Laboratory with a Dimension Clinical Chemistry system using the hexokinase method (Dade Behring, Deerfield, IL). Blood samples from the intravenous glucose tolerance test were centrifuged, and plasma was stored on ice before storage at −80°C. Aliquots were assayed in duplicate for glucose using the glucose oxidase method and a Yellow Springs Instruments 2700 Analyzer (Yellow Springs Instruments, Yellow Springs, OH). Insulin was assayed in duplicate using an enzyme-linked immunosorbent assay kit from Linco (St. Charles, MO).

Statistical analysis

All analyses were performed using SPSS version 11.0 (SPSS, Chicago, IL), with a type I error set at $P < 0.05$. Partial correlations (controlling for lean mass, age, and Tanner stage) were performed to determine the associations between BMC and BMD and the independent variables. Children with NGT versus IGT were compared using ANOVA or general linear models when covariates were included. As determined by the Kolmogorov-Smirnov test of normality, BMC and BMD were not normally distributed and were log transformed; multiple linear regression analysis was repeated with log-transformed dependent variables.

Table 1—*Descriptive statistics of participants*

	IGT	NGT
n	46	138
Sex (M/F)	26/20	80/58
Age (years)	12.1 ± 1.8	11.8 ± 1.7
Tanner stage	2.4 ± 1.4	2.2 ± 1.3
Tanner 1	16 (35)	51 (37)
Tanner 2	14 (30)	44 (32)
Tanner 3	2 (4)	16 (12)
Tanner 4	11 (24)	14 (10)
Tanner 5	3 (7)	13 (9)
Testicular volume (ml)*	8.8 ± 6.8	6.6 ± 5.7
Weight (kg)	61.1 ± 19.8	64.2 ± 19.4
Height (cm)	148.3 ± 12.5	149.2 ± 11.2
BMI (kg/m^2)	27.0 ± 5.2	28.3 ± 5.4
Fat mass (kg)	22.8 ± 10.0	24.8 ± 10.0
Percent fat (%)	36.7 ± 6.7	38.4 ± 6.4
Lean mass (kg)	35.8 ± 10.1	37.0 ± 10.2
$V\text{O}_{2max}$ (ml/min)†	2,107.7 ± 501.8	2,204.9 ± 605.2
$V\text{O}_{2max}$ (ml · kg^{-1} · min^{-1})†	35.1 ± 7.0	35.1 ± 6.9
BMC (g)	1,501.4 ± 410.9	1,553.5 ± 449.2
BMD (g/cm^2)	0.92 ± 0.1	0.92 ± 0.1
Bone area (cm^2)	1,600.1 ± 309.1	1,658.1 ± 296.3
Fasting glucose (mg/dl)	93.9 ± 8.0	91.4 ± 8.7
2-h glucose (mg/dl)	150.7 ± 10.6‡	118.4 ± 11.5
Fasting insulin (μU/ml)	17.6 ± 18.3	16.1 ± 10.1
2-h insulin (μU/ml)	210.5 ± 169.5‡	128.8 ± 116.2
Insulin sensitivity [×10^{-4} min^{-1}/(μU/ml)]	2.2 ± 1.4	2.2 ± 1.5
AIR (μU/ml)	1,457.2 ± 1,322.3	1,805.7 ± 1,258.8
AUC (pmol/l)	318.4 ± 216.4	301.3 ± 201.6
Incremental AUC (pmol/l)	291.0 ± 205.1	264.0 ± 168.8

Data are means ± SD or *n* (%).*Testicular volume values represent 84 boys (18 IGT, 66 NGT). †$V\text{O}_{2max}$ values represent 146 subjects (39 IGT, 107 NGT). ‡Significantly greater than NGT at $P < 0.0001$.

RESULTS — A summary of the adolescents' characteristics based on glycemic control (i.e., IGT vs. NGT) is shown in Table 1. Mean BMC was 1,501.4 ± 410.9 g in IGT and 1,553.5 ± 449.2 g in NGT children; BMC had a range of 748–3,199 g. BMD values ranged from 0.71 to 1.34 g/cm^2 and were identical (mean of 0.92 g/cm^2) in IGT and NGT children. Bone area was 1,600.1 ± 309.1 cm^2 in IGT and 1,658.1 ± 296.3 cm^2 in NGT children. There were no significant differences in BMC, BMD, or bone area in IGT versus NGT children when the analysis was repeated separately by sex (data not shown). Mean 2-h glucose and 2-h insulin were significantly greater in IGT than NGT children. There were no other significant differences in groups.

Table 2—*Partial correlations with BMC and BMD (controlling for lean mass, age, and Tanner stage)*

	BMC	BMD
Fasting glucose	−0.06	−0.05
2-h glucose	−0.02	−0.05
Fasting insulin	−0.16*	−0.17*
2-h insulin	−0.16*	−0.17*
Insulin sensitivity	0.10	0.12
AIR	−0.29†	−0.22‡
AUC	−0.28†	−0.31†
Incremental AUC	−0.24‡	−0.25‡

*$P < 0.05$; †$P < 0.0001$; ‡$P < 0.001$.

Table 3—*Partial correlations with BMC and BMD (controlling for lean mass, age, and Tanner stage)*

	IGT (n = 46)		NGT (n = 138)	
	BMC	BMD	BMC	BMD
Fasting glucose	−0.00	−0.04	−0.07	−0.05
2-h glucose	−0.26	−0.19	0.14	0.06
Fasting insulin	−0.23	−0.19	−0.08	−0.13
2-h insulin	−0.03	−0.10	−0.12	−0.16
Insulin sensitivity	0.12	0.13	0.06	0.08
AIR	−0.58*	−0.51†	−0.14	−0.03
AUC	−0.36‡	−0.39‡	−0.20‡	−0.22‡
Incremental AUC	−0.34‡	−0.38‡	−0.20‡	−0.22‡

*$P < 0.0001$; †$P < 0.001$; ‡$P < 0.05$.

Table 2 reports partial correlations (controlling for lean mass, age, and Tanner stage) between the glucose/insulin variables and BMC and BMD. Fasting and 2-h glucose levels were not significantly correlated with BMC or BMD. Fasting and 2-h insulin levels were both inversely correlated with BMC ($r = -0.16$) and BMD ($r = -0.17$). AIR and AUC were also inversely correlated with BMC and BMD. The inverse relationships between insulin AUC and BMC and BMD were stronger than the inverse correlations between incremental insulin AUC and BMC and BMD.

Table 3 reports partial correlations of the independent variables with BMC and BMD based on glucose tolerance. Of the 184 subjects, 138 (75%) had NGT and 46 (25%) had IGT. All significant relationships were negative. In NGT children, the relationships between AIR and BMC and BMD were not significant. In IGT children, however, there were strong inverse correlations between AIR and BMC ($r = -0.58$, $P = 0.000$) and BMD ($r = -0.51$, $P = 0.001$). Although the relationships between insulin AUC and incremental insulin AUC and BMC and BMD were significant and negative in both NGT and IGT children, these inverse relationships were magnified in IGT children.

Figure 1 compares the adjusted means and SEs of BMC in IGT versus NGT children. Although IGT children had lower adjusted BMC (1,527 ± 22.3 g) than NGT children (1,545 ± 12.8 g), these differences were not significant.

Stepwise multiple linear regression analyses were performed to examine the independent influence of age, Tanner stage, lean mass, fat mass, $V_{O_{2max}}$, fasting/2-h glucose, fasting/2-h insulin, insulin sensitivity, AIR, and AUC on log-transformed whole-body BMC and BMD. Multiple regression coefficients and partial/total R values are presented in Table 4. Lean mass (87%), age (1%), and AIR (1%) explained a total of 89% of the variance in BMC with no contribution by the other variables. BMD was explained by lean mass (69%), Tanner stage (3%), and AUC (2%) for a total of 74% of the variance. Fat mass, $V_{O_{2max}}$, fasting/2-h glucose, fasting/2-h insulin, and insulin sensitivity did not make significant contributions to the vari-

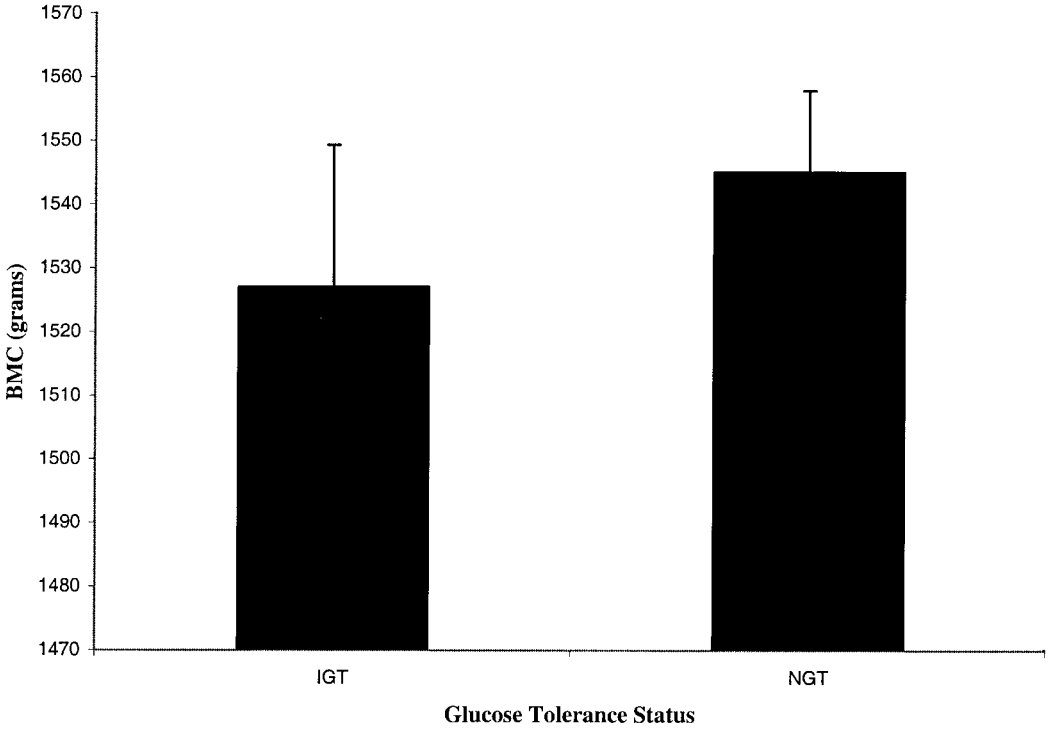

Figure 1—*BMC in IGT an NGT children (adjusted for lean mass, age, and Tanner stage). Data are adjusted means ± SE. Differences between IGT and NGT are nonsignificant.*

Table 4—*Multiple linear regression model for total body*

	Log BMC		Log BMD	
	β ± SE	R^2	β ± SE	R^2
Intercept	6.22 ± 0.05		−0.45 ± 0.03	
Age (years)	0.02 ± 0.006*	0.01	NS	
Tanner stage	NS		0.02 ± 0.005†	0.03
Lean mass (kg)	0.00002 ± 0.00†	0.87	0.000008 ± 0.00†	0.69
Fat mass (kg)	NS		NS	
$V_{O_{2max}}$ (ml/min)	NS		NS	
Fasting glucose (mg/dl)	NS		NS	
2-h glucose (mg/dl)	NS		NS	
Fasting insulin (μU/ml)	NS		NS	
2-h insulin (μU/ml)	NS		NS	
Insulin sensitivity [$\times 10^{-4}$ min^{-1}/(μU/ml)]	NS		NS	
AIR (μU/ml)	−0.00002 ± 0.00†	0.01	NS	
AUC (pmol/l)	NS		−0.00007 ± 0.00‡	0.02
Total R^2	0.89		0.74	

β, multiple regression unstandardized coefficient. *$P \leq 0.001$; †$P < 0.0001$; ‡$P \leq 0.01$.

ances in BMC or BMD. When the analysis was repeated without log transformations, the results did not materially change (data not shown).

CONCLUSIONS — Our findings with respect to lack of significant differences in BMC and BMD in IGT versus NGT subjects, although the first in a group of pre-diabetic (type 2) children, are in agreement with those of previous researchers who have examined the same hypothesis in different populations. Wakasugi et al. (14) found no relationship between the level of HbA_{1c} and deficits in bone mass of type 2 diabetic adults. Pascual et al. (15) found no correlation between BMD and HbA_{1c} in children with type 1 diabetes but acknowledged the fact that HbA_{1c} may not be an ideal marker for poor glycemic control because it represents only the patients' glycemic status of the last 3 months; it is noteworthy that changes in bone metabolism take place over a longer period. Although IGT (i.e., 2-h glucose ≥140 mg/dl) is an important precursor of diabetes (11), it is difficult to speculate the duration of this condition in our IGT children; nevertheless, we believe that inadequate duration of the pre-diabetic state may have contributed to the lack of significant differences in BMC and BMD of the two groups. Other research has shown that insulin-dependent diabetic children have a normal spine BMD during the first year of disease (16,17); a decreased BMD has been observed in those with long-standing diabetes (17). We are aware that there are also individual differences in susceptibility to disease; in other words, not all subjects with IGT will worsen to diabetes, and another possible explanation for the lack of significant differences in BMC and BMD between IGT and NGT may be because only IGT children with the potential to progress to diabetes may be at risk for osteopenia.

Although differences in BMC and BMD in IGT versus NGT children were not significant, Table 1 and Fig. 1 highlight the fact that IGT children had lower unadjusted (Table 1) and adjusted (Fig. 1) means of BMC, which in growing children is a better measure than BMD (18). Mean 2-h insulin was significantly greater in IGT than in NGT children (210.5 vs. 128.8 μU/ml). Furthermore, partial correlations (Table 2) reveal that 2-h insulin was inversely correlated with both BMC and BMD. Therefore, in light of the greater levels of 2-h insulin in IGT children and the inverse relationship between 2-h insulin and BMC and BMD, it makes sense that IGT children had lower BMC than NGT children. We therefore believe that this adjusted trend toward lower bone mass may continue if our IGT children remain hyperglycemic and hyperinsulinemic.

We (19,20) and many others (21–25) have shown that body size is the strongest single determinant of BMD, a relationship that is attributed to weight bearing and to the conversion of androstenedione to estrogen in adipose tissue (26,27). Consistent with our previous findings in Asian adolescents (19), lean body mass was the best covariate of BMC and BMD in this group of overweight Latino children. When lean mass was replaced with fat mass in the regression models, age (50%) and Tanner stage (41%) became the primary covariates of BMC and BMD, respectively; fat mass became a secondary covariate of BMC (17% of the total variance) and BMD (10% of the total variance). These findings are similar to the conclusions of others who have shown that lean mass and not fat mass independently predicts whole-body (28) and lumbar spine (29) BMD. Our results regarding the strong independent contribution of lean mass to bone mass provides additional evidence on the importance of mechanical impact and muscular forces for the growing skeleton. Further, it indirectly substantiates that skeletal muscle is also capable of aromatizing androstenedione to estrogen (30).

Because previous studies (31,32) of type 1 diabetic children with poor metabolic control have reported reductions in linear growth velocity and a diminished pubertal growth spurt, we thought it is necessary to also examine whether there are differences in height and Tanner stage in our two groups. As such, we found no significant differences in height or Tanner stage between IGT and NGT children (Table 1). Furthermore, it is noteworthy that testicular volume was highly correlated ($r = 0.90$, $P < 0.0001$) with Tanner stage (based on pubic hair) in boys. Because of this strong correlation and the lack of tes-

ticular volume data on the entire sample of boys, we chose to stage pubertal development based on pubic hair, and we believe that this was an accurate measure of puberty in boys. When we examined testicular volume values in IGT ($n = 18$) versus NGT ($n = 66$) children, we found no significant differences.

Other subtle contributors to the total variances in BMC and BMD of this population were the acute and cumulative insulin responses to oral glucose. Although some research (6,33) has suggested a link between hyperinsulinemia and better bones, reduced levels of IGF-I, a polypeptide synthesized by bone cells, reported in hyperglycemic, hyperinsulinemic, type 1 diabetic, and type 2 diabetic conditions (34–37) could alternatively cause osteopenia (34,37–39). In in vitro studies, receptors for insulin and IGF-I are present on osteoblastic cells (40,41), and both substances have a direct stimulatory effect on the recruitment of osteoblastic cells (42). We are in agreement with others (4,34,38) who have concluded that type 2 diabetes and the hyperinsulinemic state typically associated with obesity and insulin resistance in these patients could cause low bone mass (independent of body size) and that this relationship is possibly mediated by deficiency in insulin-like growth factors. Studies have found low (43), normal (44,45), and high (46) IGF-I levels in obese subjects. Whether or not overweight children with IGT have abnormal IGF-I levels should be investigated in longitudinal studies of this population.

Studies have shown that trabecular bone has high turnover and responds to factors such as endocrine changes to a greater extent than does cortical bone (24,32,47). Previous research on the association between diabetes and osteopenia has also shown site specificity. Roe et al. (48) found that in diabetic children, cortical but not trabecular BMD was lower than that in control subjects. In contrast, Lettgen et al. (49) found lower trabecular BMD but no differences in cortical or total BMD in diabetic versus nondiabetic children. Therefore, although it would seem more logical that trabecular bone would be more sensitive to metabolic changes, measurement of both cortical (femoral neck) and trabecular (lumbar spine) bone is necessary in our future work.

We conclude that IGT does not seem to predispose young pre-diabetic children to osteopenia. However, the lower unadjusted and adjusted means for BMC in children with IGT as well as the independent inverse relationship of acute and cumulative insulin responses to oral glucose on BMC and BMD suggest that, independent of body size, the skeleton of adolescents at risk for type 2 diabetes may not be protected, possibly because of the yet unproven role of IGF deficiency on bone accretion during growth. Because diabetic status may be altered in this population, examination of changes in the skeleton of these children over time may provide some answers into whether possible deficits in peak bone mass is a consequence of type 2 diabetes.

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