Table 2 Relation between QT Interval and ECG leads with Early Repolarization

ECG leads	No. of patients	QT interval (ms)	QTc interval (ms)
Anterior (V_{1-4})	1064 (59.9)	401 ± 37	402 ± 17
Lateral (I, aVL, $V_{5,6}$)	73 (4.1)	398 ± 58	413 ± 19
Inferior (II, III, aVF)	54 (3.0)	392 ± 50	406 ± 17
Anterolateral (V_{1-4}, I, aVL, $V_{5,6}$)	118 (6.6)	406 ± 39	407 ± 18
Anteroinferior (V_{1-4}, II, III, aVF)	325 (18.3)	396 ± 45	404 ± 19
Inferolateral (II, III aVF, I, aVL, $V_{5,6}$)	141 (7.9)	398 ± 52	408 ± 17

Values are expressed as N (%) or mean ± SD.

Table 3 ECG Abnormality Complicated with Early Repolarization

ECG abnormality	No. of patients	Complication rate (%)
LVH	75	4.0
RVH	16	0.9
AF	15	0.8
PVC	24	1.3
Bradycardia	293	15.7
Tachycardia	85	4.5

LVH: left ventricular hypertrophy, RVH: right ventricular hypertrophy, AF: atrial fibrillation, and PVC: premature ventricular contraction
Bradycardia is defined as a sinus heart rate of 50 beats per min or lower; tachycardia, a sinus heart rate of 100 beats per min or higher.

implication of QT interval in early repolarization appears to be important, we need to pursue this study to evaluate the prognostic value of QT interval in early repolarization.

In contrast to ischemic ST-segment elevation that is caused by injured current, ST-segment elevation in early repolarization is unrelated to ischemic injury.[11] However, Haissaguree et al.[7] reported that early repolarization in inferolateral leads was associated with the generation of malignant ventricular arrhythmia in idiopathic ventricular fibrillation. To date, observation of early repolarization was also reported in Brugada syndrome[12] and arrhythmogenic right ventricular cardiomyopathy.[13] In addition, ST-segment elevation of early repolarization shared a similar pharmacological response with that in Brugada syndrome.[14,15] These similarities suggest that early repolarization may represent a non-ischemic ST-segment elevation related to the electrophysiological substrate.[16,17] An experimental study demonstrated that early repolarization could be arrhythmogenic in case loss of the epicardial action potential plateau generates a net repolarizing current that causes reentry.[15]

It may be meaningful to investigate whether or not early repolarization is present in coexistence with other ECG abnormalities to stratify the risk of early repolarization. In our patients, LVH, RVH, PVC, and AF were complicated with early repolarization. The left ventricular wall is thicker than the right ventricular wall. This might explain why LVH was more complicated than RVH. Of interest, heart rate seems to be related to the presence of early repolarization. Especially, sinus bradycardia was highly complicated with early repolarization. This finding suggests that transmural heterogeneity of ventricular repolarization may become pronounced when heart rate abnormally decreases.

Although early repolarization might be considered as a normal variant of the ECG phenotype, unless otherwise proven, the prognostic value of early repolarization remains undetermined in this study. Therefore, we need further investigation to determine whether or not our patients with early repolarization are at risk for ventricular arrhythmia.

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Original Article

Prevalence of childhood obesity from 1978 to 2007 in Japan

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Abstract ***Background***: There are few cross-sectional and longitudinal studies on identification of the age of onset of obesity. The purpose of the present study was therefore to investigate 30 years of cross-sectional and longitudinal changes in the prevalence of obesity from 1978 to 2007 in Japanese children and adolescents between 5 and 17 years of age, using population-based samples.

Methods: Subject data were obtained from the Annual Reports of the School Health Survey published by the Ministry of Education, Culture, Sports, Science and Technology, Japan. Obesity was defined as a body mass index (BMI) at or above the 95th percentile for age and gender based on the reference years from 1979 to 1981 in Japan. The BMI was calculated as weight in kg/(height in m)^2.

Results: Cross-sectional analysis of 5-, 8-, 11-, 14-, and 17-year-olds showed that the prevalence of obesity has gradually decreased since the early 2000s, with the highest prevalence in the late 1990s to early 2000s, except for in 17 year-old boys. Longitudinal studies showed that the critical periods for developing obesity were in late infancy (between 5 and 6 years of age) and in the high school period in boys, and mainly in late infancy in girls.

Conclusions: Intervention to prevent obesity should be focused on late infancy in both genders and male adolescents in Japan.

Key words obesity, population, prevention and control.

Obesity is considered a threat to public health, and the ongoing obesity epidemic represents a major public health concern worldwide.[1–3] In the Japanese adult population, the prevalence of obesity (body mass index [BMI] ≥ 25 kg/m^2) increased rapidly between 1984 and 2004 in men.[4] Men tend to develop obesity in their 40s or younger,[4] and tend to develop combined cardiovascular risks.[5] Obesity-associated risk factors arise in mildly to moderately obese conditions not only in adults but also in children in Japan,[7–10] indicating that primary prevention of obesity is important from childhood.

Analyzing the onset of obesity might identify periods of great vulnerability. There are few cross-sectional and longitudinal studies, however, on identification of the age of onset of obesity.[1,10] This information could be useful for determining when to prevent obesity.[1] Therefore, the aim of the present study was to investigate 30 years of cross-sectional and longitudinal changes in the prevalence of obesity from 1978 to 2007 in Japanese children and adolescents between 5 and 17 years, using population-based samples.

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Methods

Nationwide population-based data

The Ministry of Education, Culture, Sports, Science and Technology has performed the School Health Survey for height and weight since 1948. The data are collected by sampling with probability proportionate to size every year.[11] The Ministry collects information each year from 72 380 kindergartners aged 5 years (from 1645 kindergartens), 270 720 elementary school children aged 6–11 years (from 2820 schools), 225 600 junior high school adolescents aged 12–14 years (from 1880 schools), and 126 900 high school adolescents aged 15–17 years (from 2820 schools).[12] These samples corresponded to 4.7% of all children and adolescents in Japan in 2007.[12]

Measurements of height and weight in Japan

In Japan, all children and adolescents in kindergartens and schools undergo a mandatory medical examination, performed by school doctors and nurses. Height and weight are measured by school nurses in early April each year. Height is measured to the nearest 0.1 cm without shoes and weight is measured to the nearest 0.1 kg in underwear.

Collection and input of data for the present study

The frequency tables in the Annual Report of the School Health Survey[11] show frequency per thousand children for height (every 1 cm) and weight (every 1 kg) for each age and gender. Data are expressed to one decimal place.

The height and weight in the reports were input into a computer by personnel from a temporary-employment agency or secretaries of the National Hospital Organization Kagoshima Medical Center, and re-checked to ensure data were the same as the frequency tables. Financial support for the data input was provided by grants, as stated in the Acknowledgments section.

Definition of obesity

In the present study, obesity was defined as a BMI at or above the 95th percentile for age and gender based on the reference data in Japan. The BMI was calculated as weight in kg/(height in m)^2.

Reference data for the BMI percentile value for each age and gender

The prevalence of obesity (BMI ≥ 30.0) in adults is relatively low in Japan compared with that in Western populations, and thus a BMI ≥ 25 is usually used for the definition of obesity in Japanese adults.[3] Therefore, we used the Japanese data as a reference, and not the International data provided by Cole *et al.*[14] The percentile value of the BMI for each age and gender was determined from the frequency tables of height and weight from three successive years from 1979 to 81.[12] The prevalence of obesity in the reference years (1979–81) was 5% in all ages and genders. The cut-off points for obesity in the present study are shown in Table 1.

Cross-sectional surveillance of the prevalence of obesity

The prevalence of obesity was determined for 5-, 8-, 11-, 14-, and 17-year-old boys and girls between 1978 and 2007.

Longitudinal surveillance of the prevalence of obesity

We obtained data for the subjects between 5 and 17 years of age from 1978 for the present study. Subjects who were 5 years of age in 1978 were born in 1973, and we then made consecutive 4 year-interval cohorts, which were named as the 73–76, 77–80, 81–84, 85–88, 89–92, 93–96, and 97–00 birth cohorts.

Table 1 Cut-off points for obesity

Age (years)	Male	Female
5	17.65	17.68
6	17.80	17.80
7	18.31	18.27
8	19.48	19.22
9	20.66	20.10
10	21.74	21.09
11	22.35	22.13
12	23.00	23.20
13	23.46	23.94
14	23.94	24.56
15	25.28	25.45
16	25.26	25.39
17	25.47	25.32

Results

Prevalence of obesity in each age and gender in 2007

The prevalence of obesity in boys during the elementary school period (6–11 years of age in Japan) in 2007 was 4–5 points higher than that (5%) in the reference years (1979–81), while the prevalence in 5-year-old boys was 1.3 points higher than that in the reference years (Fig. 1). After a decrease in the prevalence of obesity during the junior high school period (12–14 years of age), the prevalence of obesity during the high school period (15–17 years of age) was approximately 6 points higher than that in the reference years.

A rapid increase in the prevalence of obesity was found in girls between 5 and 6 years of age, similar to that for boys (Fig. 1). The prevalence of obesity gradually decreased until the junior high school period, and then gradually increased during the high school period.

Cross-sectional surveillance of the prevalence of obesity

Changes in the prevalence of obesity for subjects who were 5, 8, 11, 14, and 17 years of age are shown in Figure 2. The increase in the prevalence of obesity was smallest in 5-year-old boys, and it then decreased after the mid-1990s (Fig. 2a). A rapid increase in the prevalence of obesity was present in 8-, 11-, and 14-year-old boys from the late 1980s to late 1990s; the prevalence of obesity of these ages then decreased after 2000. In contrast, the prevalence of obesity in 17-year-old boys had a prominent increase in 2002, and thereafter it increased to its highest point among these age groups in 2006.

The prevalence of obesity in 5-, 8-, 11-, and 14-year-old girls had a similar increase to that in boys from the late 1980s to late 1990s, and decreased after 2000 (Fig. 2b). The prevalence of

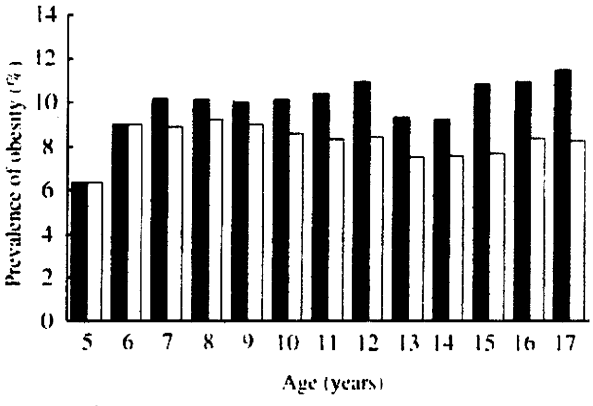

Fig. 1 Cross-sectional analyses of the prevalence of obesity in subjects between 5 and 17 years of age in (■) boys and (□) girls in 2007. A prominent increase in the prevalence of obesity occurred between 5 and 6 years of age in both genders. The prevalence of obesity increased again during high school in boys.

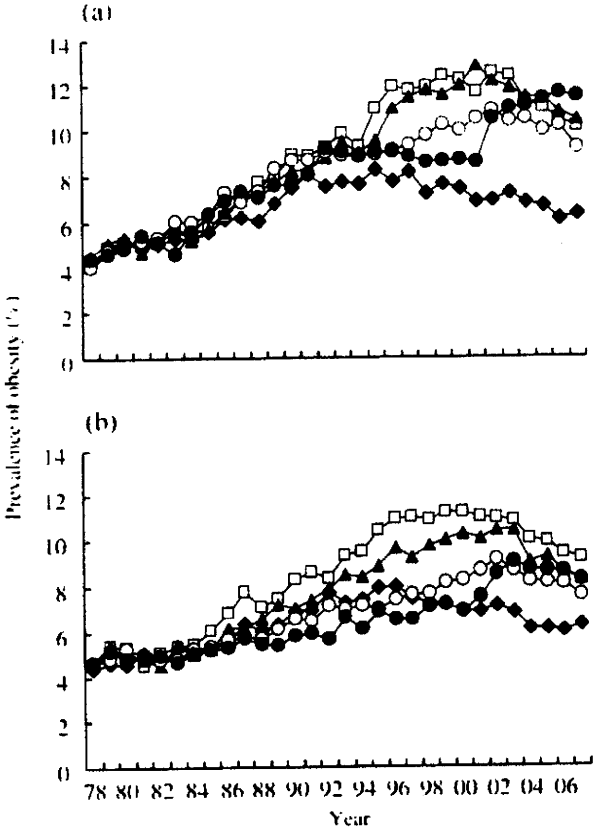

Fig. 2 Thirty year cross-sectional change in the prevalence of obesity in subjects (◆) 5, (□) 8, (▲) 11, (○) 14, and (●) 17 years of age from 1978 to 2007 in (a) boys and (b) girls. The prevalence of obesity gradually decreased from the early 2000s, with the highest prevalence occurring in the late 1990s–early 2000s, except for in 17 year-old boys.

obesity in 17-year-old girls increased in 2002, similar to that for boys, but it then decreased after this time.

Longitudinal surveillance of the prevalence of obesity

The longitudinal change in the prevalence of obesity in each cohort is shown in Figure 3. A sharp increase in the prevalence of obesity occurred between the ages of 5 and 6 in boys from the 1980s birth cohorts; the highest difference between 5- and 6-year-old boys was 3.7 points in the 93–96 birth cohorts (Fig. 3a). Among male birth cohorts, the more recent the cohort was, the higher the prevalence of obesity in almost all ages, until the 89–92 birth cohorts; the 89–92 birth cohort had the highest prevalence of obesity between the ages of 7 and 15 years. The prevalence of obesity in this cohort increased again at 15 years of age, after a decrease during the junior high school period. This tendency toward a higher prevalence of obesity was not present in the 93–96 and 97–00 birth cohorts.

A sharp increase in the prevalence of obesity also occurred between the ages of 5 and 6 in girls from the 1980s birth cohorts, and the highest difference was 3.5 points in the 93–96 birth cohorts (Fig. 3b). Among female birth cohorts, the prevalence of obesity in the 89–92 birth cohort was highest at the ages of 7–13 years, which was similar to that for boys. The prevalence of obesity during junior high and high school decreased in all cohorts except for the 85–88 cohort.

Discussion

In the present study, cross-sectional analysis demonstrated that the prevalence of obesity gradually decreased from the early 2000s, with the highest prevalence occurring in the late 1990s–early 2000s, except for in 17-year-old girls. Longitudinal studies showed that the critical periods for developing obesity were in late infancy (between 5 and 6 years of age) and the high school period in boys, and mainly in late infancy in girls, indicating that interventions to prevent obesity should be focused on these groups.

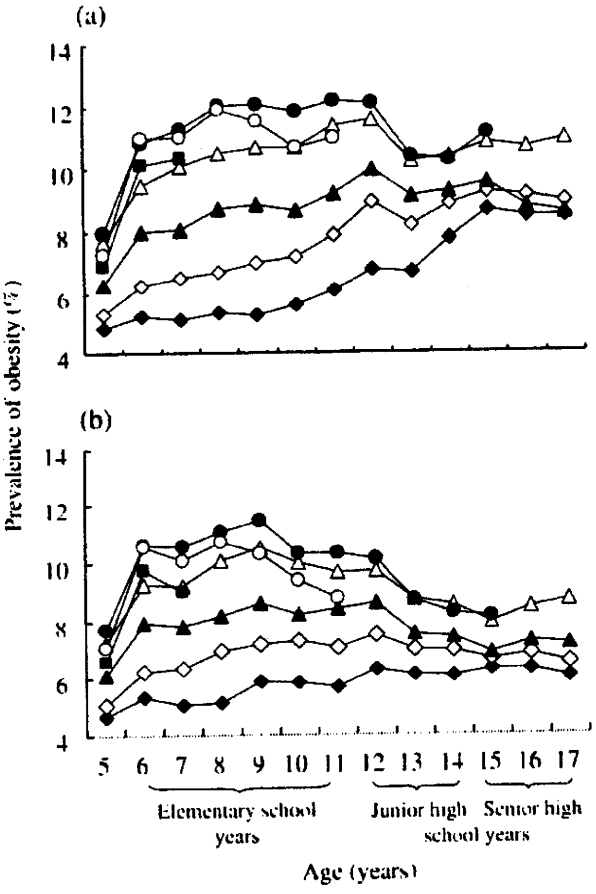

Fig. 3 Longitudinal changes in the prevalence of obesity in the 4 year-interval birth cohorts at each year of age in (a) boys and (b) girls. The (●) 89–92 birth cohort had the highest prevalence of obesity between the ages of 7 and 15 years in boys and between the ages of 7 and 13 years in girls. Birth cohorts: (◆) 73–76; (◇) 77–80; (▲) 81–84; (△) 85–88; (●) 89–92; (○) 93–96; (■) 97–00.

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ORIGINAL ARTICLE
Pediatric Cardiology and Adult Congenital Heart Disease

Cut-Offs for Screening Prolonged QT Intervals From Fridericia's Formula in Children and Adolescents

Daisuke Hazeki, MD; Masao Yoshinaga, MD, PhD; Hideto Takahashi, PhD; Yuji Tanaka, MD, PhD; Yasue Haraguchi; Mayumi Abe; Masami Koga; Toshiro Fukushige, MD, PhD; Masami Nagashima, MD, PhD

Background: The corrected QT interval (QTc) according to Bazett's formula ($QTc=QT/RR^{1/2}$) has been used in clinical practice. Bazett's formula, however, overcorrects the QT interval at fast heart rates and undercorrects it at low heart rates. Guidelines and some investigators have recommended using Fridericia's formula ($QTc=QT/RR^{1/3}$) in these cases, especially in tachycardic subjects. The aim of the present study was to determine cut-offs for QTc suitable for screening pediatric subjects with prolonged QT intervals, based on manually measured values corrected by Fridericia's formula in a large number of subjects.

Methods and Results: Three consecutive QT and RR intervals were measured in 4,655, 4,655, and 5,273 1st, 7th, and 10th graders, aged 6, 12, and 15 years, respectively. Each QT interval was corrected by Fridericia's formula, and mean values were calculated. Determination of the cut-offs for screening was based on the prevalence of abnormal electrocardiographic phenotypes of 1:1,164 and on the upper 0.025 percentile in the QTc distribution derived from previous studies. The tentative cut-offs suitable for screening subjects with prolonged QT intervals were 430 ms for 1st graders, 445 ms for 7th graders, and 440 and 455 ms for 10th grade boys and girls, respectively.

Conclusions: These tentative cut-offs can be used to screen subjects with prolonged QT intervals in the clinical setting. Further studies are needed to confirm their validity. (*Circ J* 2010; **74:** 1663–1669)

Key Words: Cut-off; Fridericia's formula; QT interval; Screening

Long QT syndrome (LQTS) is a rare disease characterized by prolonged ventricular repolarization and increased propensity to syncope and sudden cardiac death.[1–3] Because the QT interval is inversely related to heart rate, measured QT intervals are generally corrected for heart rate to identify prolongation.[4] Among many formulae investigated,[5] the corrected QT interval (QTc) according to Bazett's formula ($QTc=QT/RR^{1/2}$) has been used in clinical practice and in the medical literature.[2,4,6] Bazett's correction, however, overcorrects the QT interval at fast heart rates and undercorrects it at low heart rates.[2,4] Published diagnostic criteria using the QTc from Bazett's formula recommend additional diagnostic caution when scaling with tachycardic patients.[7] Under these circumstances, the guidelines of the International Conference of Harmonization,[4] as well as some authors,[8] recommend using Fridericia's correction ($QTc=QT/RR^{1/3}$). Cut-offs used to screen children and adolescents with prolonged QT intervals, corrected according to Fridericia's formula, have previously been reported using automatically measured data for QT and RR intervals (QT/RR data).[9] The accuracy of automatic QTc measurements, however, is questionable in many cases, and should be supplemented by manual readings.[8]

Editorial p1534

The estimated prevalence of symptomatic patients with LQTS is around 1 in 5,000 subjects.[2] The prevalence of abnormal electrocardiographic (ECG) phenotypes, namely that of abnormally prolonged QT intervals irrespective of the presence or absence of symptoms and/or family history, was estimated to be 1 in 1,164 among 7th graders aged 12 years.[10]

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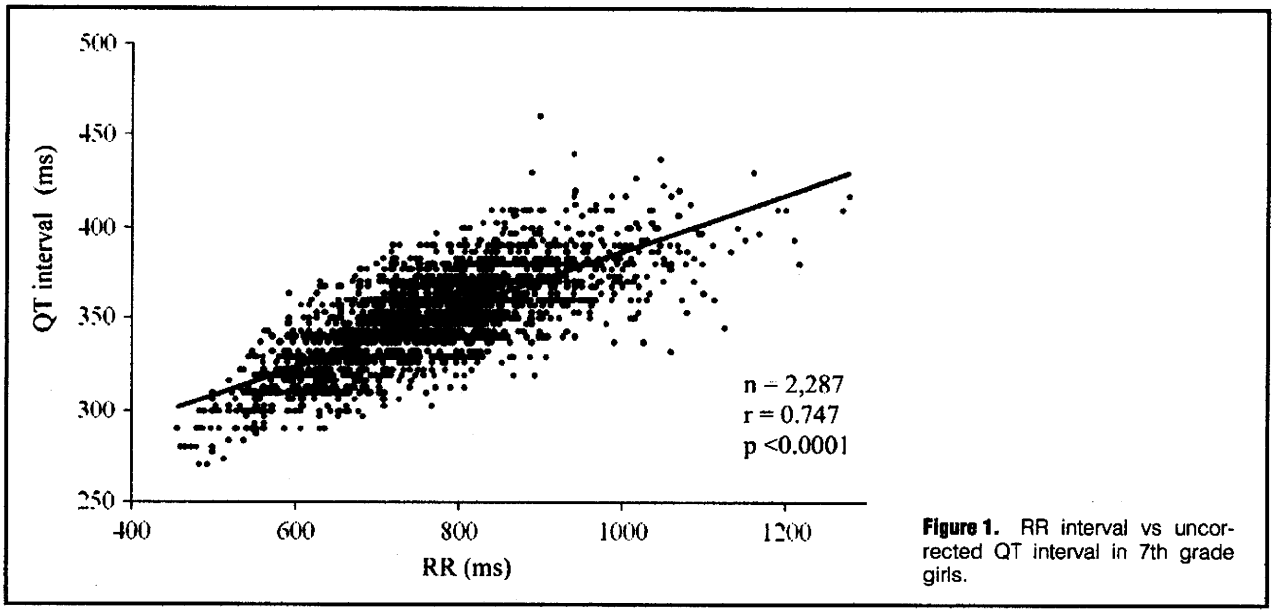

Figure 1. RR interval vs uncorrected QT interval in 7th grade girls.

No criteria have been proposed for the pediatric population using Fridericia's correction with manually measured data, although subjects in this age group are frequently tachycardic. No criteria have taken account of the prevalence of abnormal ECG phenotypes. Thus, the aim of the present study was to determine cut-offs for QTc suitable for screening children and adolescents with prolonged QT intervals, using manually measured QT/RR data corrected by Fridericia's formula. Determination of the cut-offs was based on the prevalence of abnormal ECG phenotypes and on the statistical distribution of the QTc intervals by grade and gender.

Methods

Subjects

Subjects were 1st, 7th, and 10th graders, aged 6, 12, and 15 years, respectively, in Kagoshima, Japan. Of these, the 1st and 7th graders were the same cohort. ECGs of 4,655 subjects (2,368 boys and 2,287 girls) were recorded when they were in the 1st grade in 1994 and again when they were in the 7th grade in 2000. The same 1st and 7th graders were the subjects of a previous report.[10] ECGs from 10th graders were obtained 3 years later, in 2003; only 2,735 subjects (1,312 boys and 1,423 girls) from this cohort re-entered the present study, either because they moved out of Kagoshima or because they entered private high schools. Children and adolescents in public schools participated only in the Kagoshima City Medical Association programs during the study period. In 2003, 2,538 new 10th graders were included, giving a total of 5,273 15-year-old subjects (2,598 boys and 2,675 girls). None of the subjects had any abnormal findings including arrhythmias with wide QRS, except for QT intervals. Information on the subjects (name, sex, and ECGs) was collected from the Screening Program for Heart Diseases in Kagoshima, operated by the Kagoshima City Medical Association. We obtained permission from the ethics committee of the National Hospital Organization Kagoshima Medical Center to use and analyze these data, on the condition that the confidentiality of all personal data would be maintained.

Measurement and Correction of QT Intervals

All resting ECGs were recorded at a speed of 25 mm/s at each school, by medical technologists from the Screening Program for Heart Diseases in Kagoshima. The QT interval of 3 consecutive beats was measured from the onset of the Q wave to the end of the T wave in lead V_5. The end of the T wave was defined as the isoelectric line intersecting a tangential line drawn at the maximal downslope of the positive T wave. Bifid T waves, but not U waves, were included in the QT measurement. When the notch was present in more than 3 leads[7,8] and the notch appeared at the same timing,[11] the T wave was defined as the bifid T wave. The QT/RR data from the 1st and 7th grade subjects in the previous report[10] were used in the present study. The data in the previous study[8] were measured by 2 authors (T.F. and M.Y.); the intrareader coefficient of variability for mean QT interval for the 2 authors was 1.7%, and the interreader coefficient of variability was 1.9%.[10] The QT/RR data for the 10th grade subjects were measured by 1 author (M.Y.) in the present study. The QT/RR data for each of 3 consecutive beats were corrected using Fridericia's formula ($QTc=QT/RR^{1/3}$) and the mean values for the 3 consecutive QTc were used.

Comparison of Bazett's Formula With Fridericia's Formula for QTc

To assess the effectiveness of the present study, association between the RR intervals and the uncorrected QT intervals, QTc from Bazett's and from Fridericia's formulas were determined using data of 7th grade girls.

Cut-Offs for Screening Subjects With Prolonged QT Intervals

In the previous study using the same cohort,[10] the prevalence of abnormal ECG phenotypes was 4 in 4,655 subjects (1 in 1,164) in the 7th grade and 0 in 4,655 in the 1st grade.[10] In another study using automatically measured data corrected using Fridericia's formula,[9] a long hiatus was identified at the statistical point of the upper 0.025 percentile in the distribution of QTc intervals in both genders in all groups (1st, 7th, and 10th graders). The hiatus was defined as the absence of subjects between neighboring QTc in the distribution of the

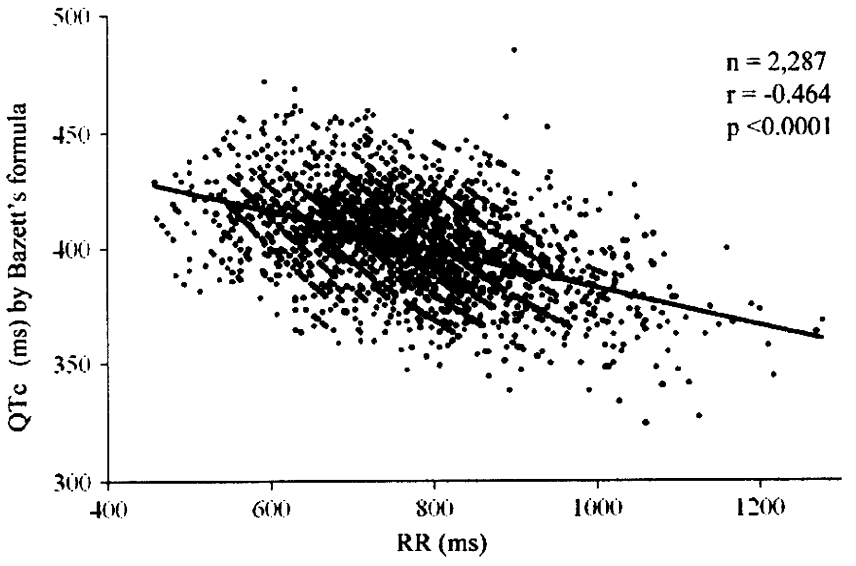

Figure 2. RR interval vs corrected QT interval (QTc) from Bazett's formula in 7th grade girls.

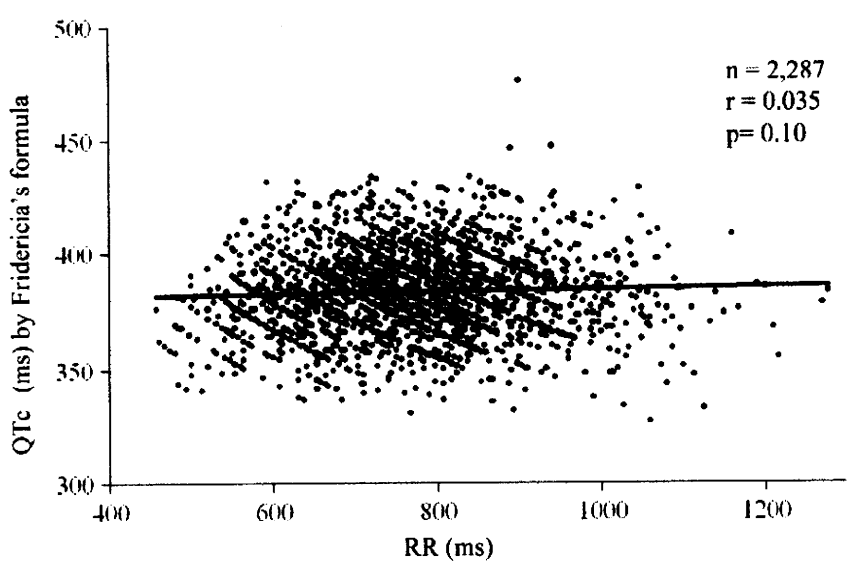

Figure 3. RR interval vs corrected QT intervals (QTc) from Fridericia's formula in 7th grade girls.

QTc. Cut-offs for screening were then determined by grade and gender, using 2 different methods. First, cut-offs were determined based on the long hiatus in the distribution of the QTc intervals near the statistical point of the upper 0.025 percentile (mean QTc+3.480756×SD). Second, cut-offs were determined to screen the 7th graders, at least at a rate of 1 in 1,164. Because the incidence of subjects with abnormal ECG phenotypes and/or symptomatic patients may increase with age,[2] the cut-offs should screen more than 1 in 1,164 for 10th graders. The cut-offs for 1st graders could be based only on the statistical distribution, because none of the cohort had abnormal ECG phenotypes in the 1st grade in the previous study.[10]

Statistical Analysis

Difference in the mean QTc between genders was examined using unpaired Student's t-tests. $P<0.05$ was considered statistically significant.

Results

Comparison of QTc From Bazett's and Fridericia's Formulas

Association between RR intervals and the uncorrected QT intervals, QTc from Bazett's and Fridericia's formulas were determined using the data of 7th grade girls. Because the QT intervals are affected by the RR intervals, namely by heart rates (**Figure 1**), the QT intervals are corrected by the RR intervals to minimize the effect of heart rates usually with Bazett's formula, but the QTc intervals from Bazett's formula were still affected by the RR intervals ($r=-0.464$, $P<0.0001$; **Figure 2**). Bazett's correction overcorrects at high heart rate (at short RR intervals) and undercorrects at low

Table. Number of Subjects vs Manually Measured QT/RR Intervals

	1st graders		7th graders		10th graders	
	Boys (n=2,368)	Girls (n=2,287)	Boys (n=2,368)	Girls (n=2,287)	Boys (n=2,598)	Girls (n=2,675)
RR interval (ms)	764±108	733±106	805±132	765±122	949±185	873±154
QT interval (ms)	332±23	327±22	353±25	350±25	360±29	358±27
HR (beats/min)	82±12	84±12	77±12	81±13	66±13	71±13
Mean QTc (ms)	367±18	364±18	380±18	384±18	368±20	376±20
0.025 percentile (ms)	430	427	443	447	438	446

Data are expressed as mean±SD.
HR, heart rate; QTc, corrected QT interval.

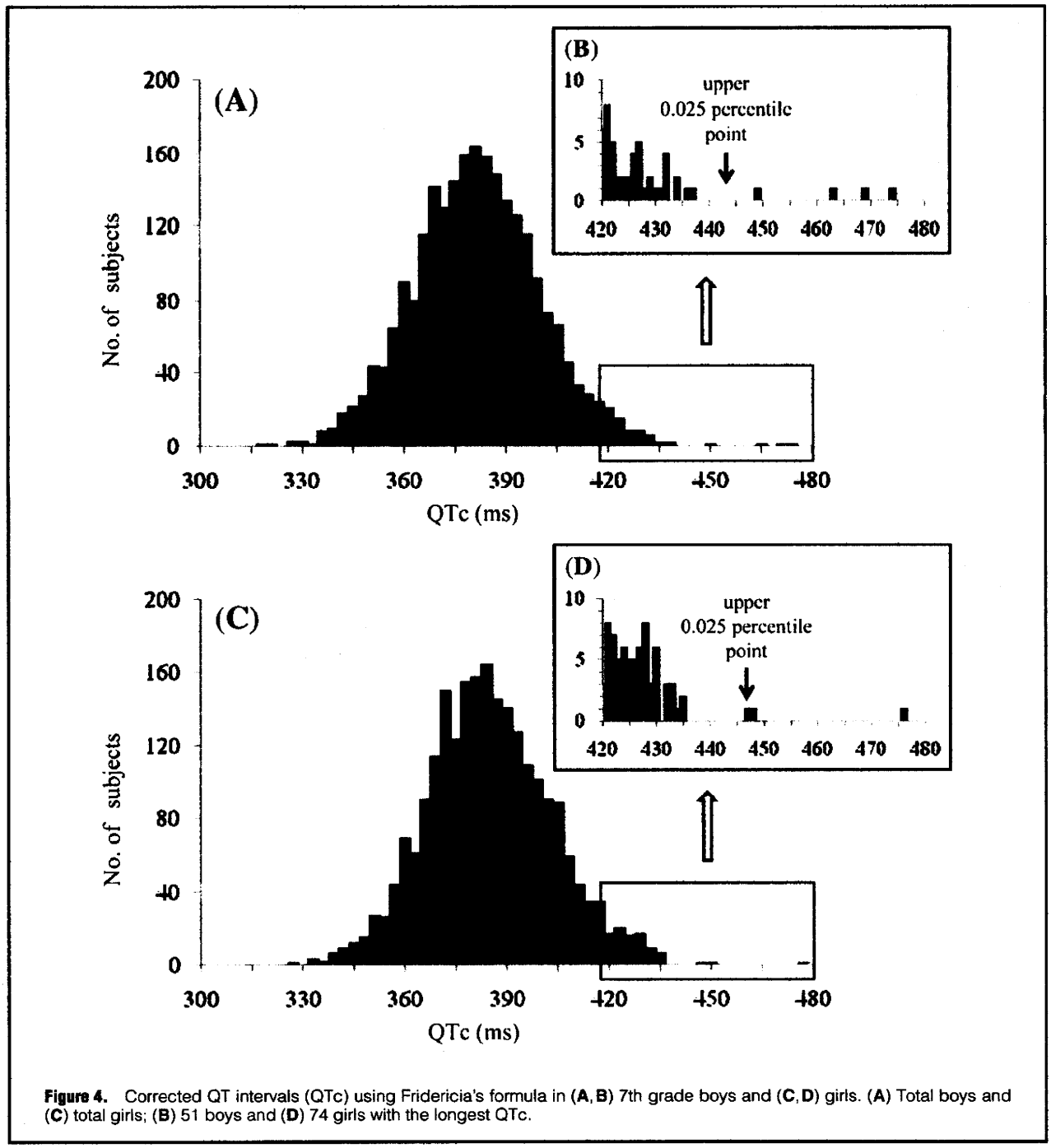

Figure 4. Corrected QT intervals (QTc) using Fridericia's formula in (**A**,**B**) 7th grade boys and (**C**,**D**) girls. (**A**) Total boys and (**C**) total girls; (**B**) 51 boys and (**D**) 74 girls with the longest QTc.

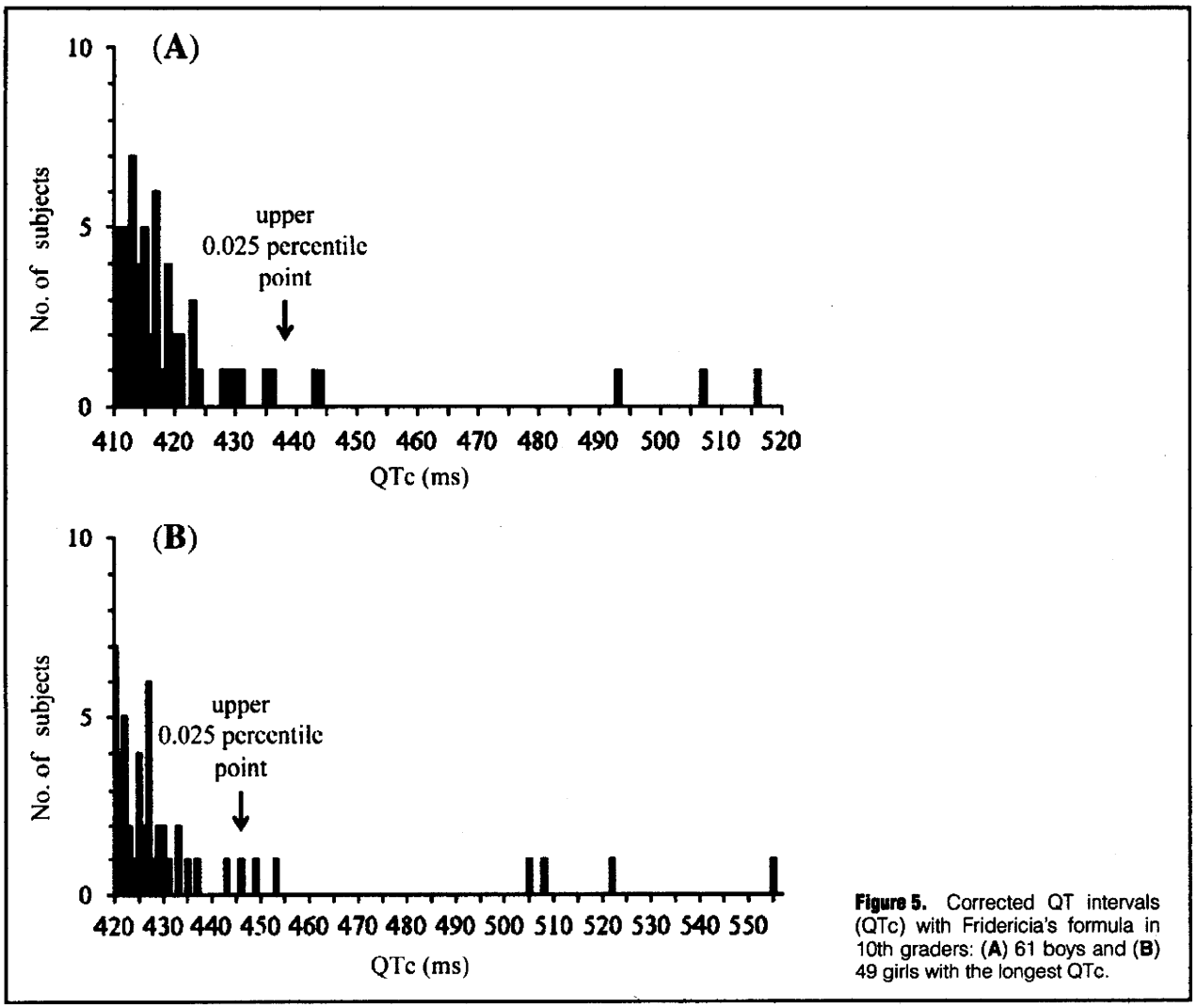

Figure 5. Corrected QT intervals (QTc) with Fridericia's formula in 10th graders: (**A**) 61 boys and (**B**) 49 girls with the longest QTc.

heart rate (at long RR intervals). In contrast, the QTc intervals with Fridericia's formula were not affected by the RR intervals (**Figure 3**).

Cut-Offs for Screening Subjects With Prolonged QT Intervals

The mean QT intervals increased in duration with age (**Table**). The mean heart rates of 10th grade boys were lower than those of 10th grade girls, and 7th grade boys and girls. Thus, the mean QTc for 10th grade boys was lower than that for 10th grade girls, and 7th grade boys and girls. There were gender differences in mean QTc in all grades ($P<0.0001$ for all groups). The upper 0.025 percentile cut-offs were around 430 ms for 1st graders, around 445 ms for 7th graders, and 0.440 and 0.445 ms for 10th grade boys and girls, respectively (**Table**).

The distribution of QTc in 7th graders contained the 1st long hiatus between 438 and 448 ms in boys, and between 436 and 446 ms in girls (**Figure 4**). Supposing a cut-off for QTc of 445 ms for 7th graders, this point is included in this hiatus, and the cut-off would identify 4 out of 2,369 boys (1 in 592) and 3 out of 2,286 girls (1 in 762). The 1st long hiatus in the distribution of QTc in 10th graders (**Figure 5**) occurred between 437 and 442 ms in boys and between 455 and 504 ms; tentative cut-offs could therefore be 440 and 455 for boys and girls, respectively, if the long hiatus is thought to be important. These cut-offs identified 5 out of 2,598 boys (1 in 520) and 4 out of 2,675 (1 in 669) girls, indicating a slightly higher incidence in 10th graders compared with 7th graders. Because there were no 1st graders with abnormal ECG phenotypes in the previous study,[10] 430 ms, near to the start of the upper 0.025 percentile, was tentatively used as a cut-off for 1st graders (**Figure 6**). The tentative cut-offs suitable for screening subjects with prolonged QT intervals are 430 ms for 1st graders, 445 ms for 7th graders, and 440 and 455 ms for 10th grade boys and girls, respectively.

Discussion

The present study identified tentative cut-off QTc for screening children and adolescents with prolonged QT intervals in the 1st, 7th, and 10th grades. These cut-offs were measured manually and corrected with Fridericia's formula for children and adolescents and can be used in the clinical setting to screen subjects with prolonged QT intervals, even those with high heart rates.

Bazett's formula remains the standard for clinical use worldwide, although it may over- or undercorrect when the heart rate is fast or slow, respectively.[2,3] Fridericia's formula

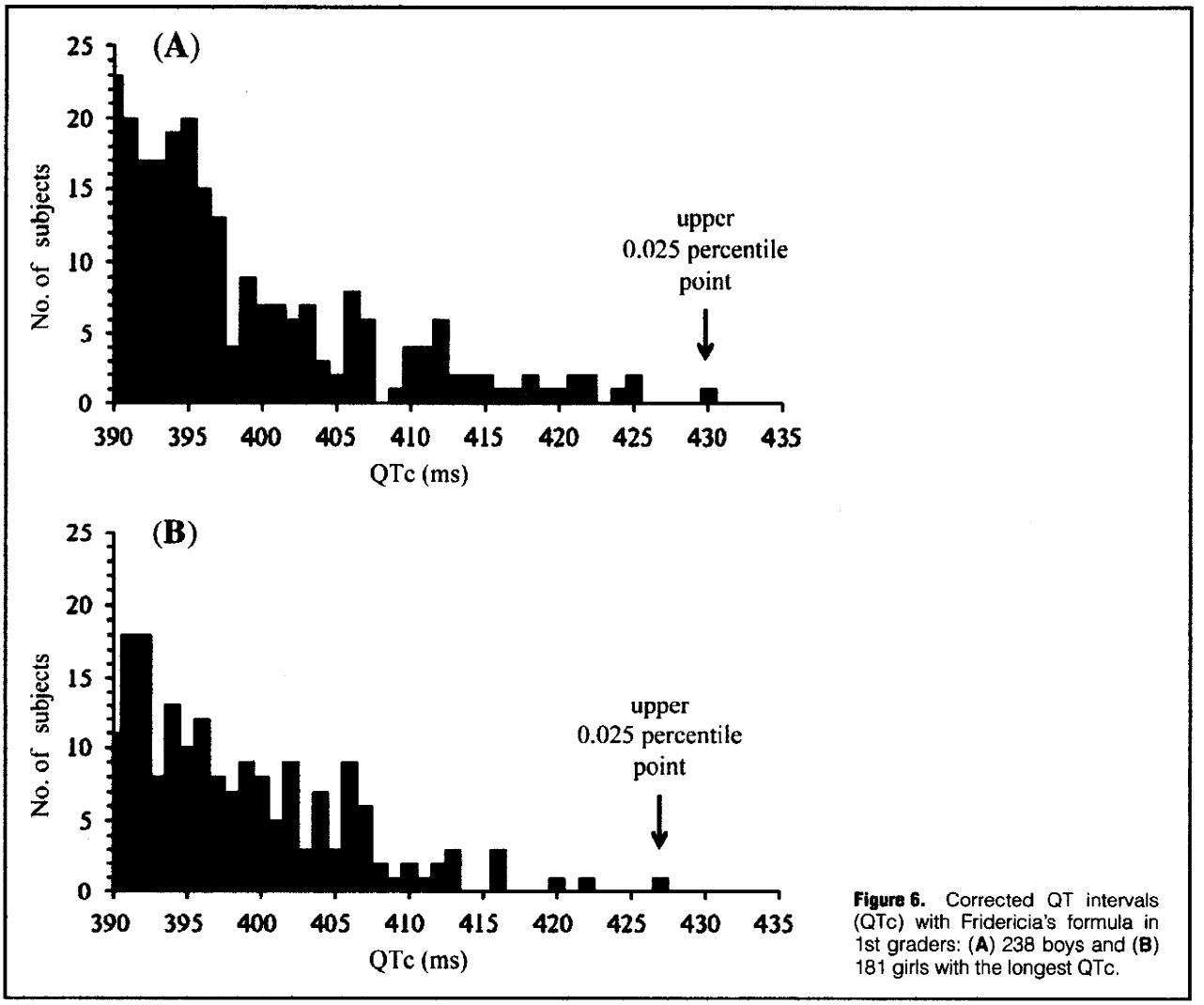

Figure 6. Corrected QT intervals (QTc) with Fridericia's formula in 1st graders: (**A**) 238 boys and (**B**) 181 girls with the longest QTc.

suffers from the same limitations at slow heart rate, but could provide a more accurate correction factor in subjects with tachycardia.[8] **Figure 2** clearly shows that Bazett's formula over- or undercorrects when the heart rate is fast or slow, respectively. **Figure 3** shows that Fridericia's formula overcorrects a little at low heart rate (at long RR intervals), because the correlation coefficient was slightly positive (r= 0.035), but the association was not significant. The former and the present data suggest that we may recommend using Fridericia's formula.

Clinically applicable pediatric cut-offs for QTc intervals for Fridericia's formula are needed. Aihoshi et al determined cut-offs for QTc corrected with Fridericia's formula to screen children and adolescents with prolonged QT interval, and these criteria have been used clinically in the Screening Program for Heart Diseases in some areas in Japan.[10,12] These values, however, were based on automatically measured data, and criteria using manually measured data are lacking. One of the reasons why Fridericia's formula has not been used nationwide may be the lack of clinically applicable pediatric cut-offs. To our knowledge, the present study is the first to derive cut-offs using manually measured data corrected with Fridericia's formula.

The cut-off for 10th grade boys was lower than that for 7th grade boys. This may be because the mean heart rate in 10th graders was significantly lower than that in 7th graders, although the mean QT interval was longer in 10th graders than that in 7th graders.

There were limitations to the present study. We produced only tentative cut-offs based on data for 1st, 7th, and 10th graders, aged 6, 12, and 15 years, respectively. Subjects in the 1st, 7th, and 10th grades are required to participate in the Screening Program for Heart Diseases in Japan, and ECG data are therefore available for children in these grades, provided that we obtain permission from the ethics committees to use and analyze these data. It would be more difficult to obtain a large sample of good ECG data from children in other grades, although cut-offs should be prepared for all ages in the future. Another limitation is that the tentative cut-offs in the present study have not been applied clinically to the Screening Program for Heart Diseases in Japan. We should determine whether these cut-offs are appropriate to screen all children who are genetically or clinically diagnosed with long QT syndrome.

In conclusion, these cut-offs can be used to screen pediatric subjects with prolonged QT intervals in a clinical setting, and further studies should be conducted to confirm the validity of these results.

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Original Article

Visceral Fat Accumulation in Japanese High School Students and Related Atherosclerotic Risk Factors

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***Aim*:** **To investigate the factors that influence visceral fat accumulation in adolescence, we performed a medical examination of high school students and assessed abdominal fat thickness and fatty change of the liver.**

***Methods*:** **A cohort of 374 Japanese high school students aged 15–16 years (193 boys and 181 girls) in public high schools in Chiba prefecture were enrolled. Anthropometric parameters, blood cell count, blood chemistry and adipocytokine levels were measured. Preperitoneal fat thickness (PFT) and echoic contrast of the liver were measured by ultrasonography.**

***Results*:** **Anthropometric parameters, systolic blood pressure, blood cell count, ALT, AST, FBS, γ-GTP, HDL-C, LpL, UA, adiponectin, resistin and leptin levels differed between sexes. Multivariate regression analysis revealed that leptin was the most appropriate marker for PFT in both sexes ($p<0.0001$). Visceral obesity, categorized as PFT exceeding 8 mm, was observed in 9.6% of all students. Boys with visceral obesity showed apparent liver dysfunction, hyperlipidemia, hyperinsulinemia, and high leptin and low adiponectin levels. Overall, 16.6% of boys and 30.4% of girls showed hepatorenal echo contrast positivity. Boys with visceral obesity and fatty liver had more risk factors for atherosclerosis.**

***Conclusions*:** **Physical examination of high school students is important for early detection of atherosclerosis.**

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Key words; Visceral fat accumulation, Ultrasonography, Adipocytokines, Sex

Introduction

The prevalence of obesity, as defined by the World Health Organization, is relatively low in Japan compared with western countries. According to a study by the Ministry of Health and Welfare, the percentage of young women with a body mass index exceeding 25 kg/m^2 was only 7%, and more than 20% of Japanese young women had a body mass index less than 18.5[1]. There are many studies about adolescent obesity in western countries[2], but it is unclear whether adolescent obesity occurs in Asian adolescents in the same manner because of the different environmental and genetic factors. Recently, the number of studies about metabolic responses in Asian adolescents has increased and some have evaluated the levels of biochemical data or compared the number of cardiovascular risk factors[3-5]; however, few studies have assessed

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actual visceral fat accumulation. We had an opportunity to obtain anthropometric data of apparently healthy high school students, many of who belonged to sports teams. This is particularly important because insufficient data from high school student health checkups are currently available in Japan. To our knowledge, this is the first study to report abdominal fat thickness and fatty change of the liver using ultrasonography in Japanese high school students. In addition, we attempted to determine the prevalence of visceral fat accumulation in these students and to evaluate the causal associations between visceral fat accumulation and various other factors, such as adipocytokine levels.

Subjects and Methods

Subjects

The 374 study subjects were 193 boys and 181 girls, in the first grade of three different public high schools in Chiba prefecture, who wished to have health checkups. Informed consent for the procedure was obtained from all participants. Height was measured to the nearest 0.1 cm without shoes and weight was measured to the nearest 0.1 kg including the same clothing. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Waist circumference was measured at the umbilical level without clothing to the nearest 0.1 cm. Blood pressure was determined by the conventional cuff method using a mercury sphygmomanometer after the students had rested for at least 15 minutes sitting on a chair. We measured blood pressure three times and the average of the second and third measurements was used. Blood samples were taken in the morning after an overnight fast to analyze the blood cell count and serum levels of AST, ALT, γ-GTP, FBS, FIRI, triglyceride, total cholesterol, high-density lipoprotein (HDL)-cholesterol and uric acid. All enzymatic and immunoassays were performed at a commercial laboratory center (SRL Inc., Tokyo, Japan). The levels of preheparin LpL mass were measured in fasting-state serum by an enzyme-linked immunosorbent assay. Adiponectin, leptin, desacyl-ghrelin, resistin and high sensitivity C-reactive protein (hs-CRP) were measured at the same laboratory (SRL); these adipocytokines and/or inflammatory markers were measured using a human adiponectin ELISA kit (Otsuka Pharmaceutical Inc., Tokyo, Japan), human leptin RIA kit (Linco Research, Inc., St Charles, MO, USA), desacyl-ghrelin ELISA kit (Mitsubishi Kagaku Iatron Inc., Tokyo, Japan), human resistin ELISA kit (Bio Vende Laboratory Medicine, Modrice, Czech Republic) and an N-latex CRPII kit (Dade Behring Inc., Marburg, Germany), respectively.

Ultrasonography

Fat thickness was measured by SonoSite MicroMaxx ultrasonography equipment (SonoSite, Inc., Bothell, WA, USA)[6] with a 3.75-MHz convex-type probe by the method of Suzuki *et al.*[7]. The probe was held perpendicular to the skin in the upper middle of the abdomen while the subject was in the supine position and a longitudinal scan was performed from the xiphoid process to the umbilicus. Scanning was performed with breath holding to keep the surface of the liver parallel to the skin as closely as possible. If the thickness was uneven, we used the maximum thickness of preperitoneal fat as the PFT, and the minimum thickness of the abdominal wall subcutaneous fat as the subcutaneous fat thickness (SFT). PFT was previously shown to be positively correlated with the visceral fat area obtained with computed tomography (CT) ($r=0.70$, $p<0.001$)[7] and we found that 8-mm-thick preperitoneal fat was equivalent to a visceral fat area of 100 cm^2, as measured by CT[8]. Therefore, we categorized the participants according to the presence of visceral obesity, which was defined as PFT >8 mm. We diagnosed fatty liver using hepatorenal echo contrast scans. Hepatorenal echo contrast was diagnosed based on a marked contrast between the hepatic and right renal parenchyma on a right intercostal sonogram performed along the midaxillary line. Fatty liver was graded stepwise based on the intensity of the ultrasonography findings as either none (no hepatorenal echo contrast), mild (hepatorenal echo contrast-positive), moderate (hepatorenal echo contrast-positive with hepatosplenic contrast-positive), and severe (hepatorenal echo contrast-highly positive with hepatosplenic contrast-positive), as previously described[9]. All ultrasonographic images were stored as photocopies and two specialists reviewed the photocopies and classified the findings without knowledge of the participants' data.

Statistical Analysis

Values are expressed as the means ± standard deviation. Statistical analyses, including Student's *t*-test, correlation analyses and linear regression analysis, were performed using SAS 8.0 software (SAS Institute Inc., Cary, NC, USA). A level of $p<0.05$ was considered significant.

Results

The general characteristics and laboratory param-

Table 1. Anthropometric and clinical characteristics

Characteristics		Boys (n=193)	Girls (n=181)	p value
Age (y)		15.2±0.03	15.6±0.02	0.46
Body composition	Height (cm)	169.7±5.9	158.7±5.5	<0.0001
	Weight (kg)	61.1±9.6	52.2±7.4	<0.0001
	Body mass index (kg/m^2)	21.2±3.1	20.7±2.5	0.092
	Waist circumference (cm)	72.3±7.3	71.2±6.4	0.138
	Waist/body height ratio	0.426±0.04	0.449±0.039	<0.0001
Fat thickness	PFT (mm)	4.21±2.8	4.73±2.35	<0.05
	SFT (mm)	5.10±3.20	8.11±3.11	<0.0001
Blood pressure	SBP (mmHg)	119.3±10.0	109.3±8.5	<0.0001
	DBP (mmHg)	64.9±9.1	63.9±7.8	0.030
Count of blood cells	WBC (μL)	6,265±1,543	6,440±142.4	0.275
	RBC ($\times 10^4/\mu$L)	524.2±28.7	460.0±31.1	<0.0001
	Hb (g/dL)	15.1±1.0	13.0±1.10	<0.0001
	Ht (%)	46.5±2.6	41.1±2.8	<0.0001
	PLT ($\times 10^4/\mu$L)	25.3±4.8	27.3±5.10	<0.0001

Results are the means ± standard deviation. Abbreviations: BMI, body mass index (weight in kilograms divided by the square of the height in meters); PFT, preperitoneal fat thickness; SFT, subcutaneous fat thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Ht, hematocrit; PLT, platelet.

Table 2. Clinical characteristics

Characteristics		Boys (n=193)	Girls (n=181)	p value
Blood biochemical data	AST (IU/L)	27.1±23.0	18.1±3.7	<0.0001
	ALT (IU/L)	20.0±19.1	11.4±3.7	<0.01
	γ-GTP (IU/L)	18.3±7.8	14.0±3.6	<0.01
	FBS (mg/dL)	87.4±6.3	85.5±5.5	<0.01
	FIRI (μIU/mL)	5.9±2.9	6.3±2.5	0.184
	LpL mass (ng/mL)	79.7±20.7	90.4±19.1	<0.0001
	TG (mg/dL)	51.7±27.1	47.7±22.7	0.120
	TC (mg/dL)	160.3±26.3	178.2±25.1	<0.0001
	HDL-C (mg/dL)	61.0±11.2	69.1±10.9	<0.0001
	Uric Acid (ng/mL)	6.1±1.0	4.4±0.8	<0.0001
	Adiponectin (μg/mL)	11.2±4.3	13.0±4.6	<0.0001
	Leptin (ng/mL)	2.0±2.0	6.7±4.1	<0.0001
	Deacyl-ghrelin (fmol/mL)	54.7±45.0	49.5±58.6	0.235
	Resistin (ng/mL)	4.4±2.2	5.0±2.1	<0.050
	hs-CRP (ng/mL)	342±981	272±815	0.014

Results are the means ± standard deviation: Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyltransferase; FBS, fasting blood sugar; FIRI, fasting immunoreactive insulin; LpLmass, lipoprotein lipase mass; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; hs-CRP, high sensitivity C-reactive protein.

eters of the subjects are shown in **Table 1**, **2**. Height, weight, waist circumference and blood pressure were significantly higher in boys and the waist to height ratio was significantly higher in girls. The red blood cell count, hemoglobin, hematocrit, AST, ALT, γ-GTP, FBS, total cholesterol and uric acid levels were significantly higher in boys, whereas the preheparin LpL mass and HDL-C level were significantly higher in girls. With regard to adipocytokine levels, adiponectin, leptin and resistin tended to be higher in girls. There were no significant differences in desacyl-ghrelin and hs-CRP levels between boys and girls.

Table 3. Correlations between individual risk variables and preperitoneal fat thickness by sex

Risk Variables	Boys				Girls			
	No	Regression Coefficient	SE	*p* value	No	Regression Coefficient	SE	*p* value
BMI	193	0.442	0.060	<0.0001	181	0.513	0.059	<0.0001
WC	191	0.213	0.024	<0.0001	181	0.200	0.024	<0.0001
WC/BH ratio	191	35.15	4.168	<0.0001	181	34.53	0.566	<0.0001
SFT	193	0.289	0.062	<0.0001	181	0.325	0.051	<0.0001
SBP	193	0.051	0.021	0.013	181	0.029	0.020	0.163
DBP	192	−0.007	0.023	0.744	181	−0.006	0.022	0.789
AST	193	0.004	0.009	0.684	181	−0.089	0.047	0.063
ALT	193	0.038	0.011	<0.001	181	−0.009	0.048	0.847
γ-GTP	193	0.097	0.026	<0.001	181	0.047	0.048	0.334
FBS	193	0.049	0.033	0.137	181	0.027	0.032	0.393
FIRI	193	0.213	0.069	<0.01	181	0.183	0.069	<0.01
LpL	189	−0.011	0.010	0.289	173	0.009	0.009	0.301
TG	193	0.026	0.007	<0.001	181	0.011	0.007	0.162
TC	193	0.014	0.008	0.068	181	0.006	0.007	0.342
HDL-C	193	−0.049	0.018	<0.01	181	−0.044	0.016	<0.01
UA	193	0.608	0.213	<0.01	181	0.217	0.221	0.327
Adiponectin	193	−0.089	0.048	0.064	181	−0.077	0.038	<0.05
Leptin	193	0.786	0.087	<0.0001	181	0.289	0.037	<0.0001
Desacyl-ghrelin	193	−0.007	0.005	0.134	181	−0.002	0.003	0.426
Resistin	189	−0.006	0.099	0.955	180	−0.046	0.082	0.578
hs-CRP	191	0.0002	0.0002	0.297	178	0.0001	0.002	0.596

Abbreviations: BMI, body mass index; WC, waist circumference; WC/BH ratio, waist circumference divided by body height; SFT, subcutaneous fat thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyltransferase; FBS, fasting blood sugar; FIRI, fasting immunoreactive insulin; LpLmass, lipoprotein lipase mass; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; hs-CRP, high sensitivity C-reactive protein.

Average PFT, i.e., visceral fat thickness measured by ultrasound, was 4.21 mm in boys and 4.73 mm in girls, and average SFT was 5.10 mm in boys and 8.11 mm in girls. The results of simple regression analysis between PFT and blood chemistry and adipocytokine levels are shown in **Table 3**. There was a positive correlation between PFT and BMI, waist circumference and the waist to height ratio, SFT and leptin in both sexes. Positive correlations between PFT and ALT, γ-GTP, FIRI, triglyceride, uric acid and leptin levels, and negative correlations with HDL-C were observed in boys. There were also positive correlations between PFT and FIRI and leptin, and negative correlations with HDL-C and adiponectin in girls.

To identify the factors associated with visceral fat accumulation, multivariate regression analysis was also performed using PFT as the dependent variable and each factor as independent variables. Leptin ($p<0.0001$) and TG ($p=0.03$) were independently associated with PFT in boys, and leptin ($p<0.001$) was independently associated with PFT in girls; therefore, leptin was the most appropriate marker for PFT in both sexes ($p<0.0001$) in **Table 4**.

In our study cohort, 20 boys (10.3%) and 16 girls (9.8%), i.e., 36 participants (9.6%), exhibited visceral obesity. BMI, waist circumference, waist to height ratio, and SFT were significantly higher in both sexes in subjects with visceral obesity than in subjects without. Boys with visceral obesity had significantly higher values for waist circumference, waist to height ratio, PFT, SFT, ALT, γ-GTP, FIRI, and total cholesterol, and lower HDL-C levels. In other words, they had liver dysfunction, hyperinsulinemia and hyperlipidemia. In addition, they had higher leptin and lower adiponectin and desacyl-ghrelin levels. Girls with visceral obesity had significantly higher values for waist circumference, waist to height ratio, PFT, SFT, and leptin levels, but there were no apparent differences in the other parameters between groups, as shown in **Table 5**.

In total, 32 boys (16.6%) and 55 girls (30.4%), i.e., 87 participants (23.3%), exhibited hepatorenal

Table 4. Multivariate linear regression for the associations between risk variables and preperitoneal fat thickness

Risk Variables	Boys			Girls		
	Regression Coefficient	SE	*p* value	Regression Coefficient	SE	*p* value
FIRI	−0.100	0.070	0.158	−	−	−
LPL	0.014	0.009	0.881	−	−	−
TG	0.016	0.007	0.033	−	−	−
HDL-C	0.004	0.018	0.812	−	−	−
Leptin	0.823	0.103	<0.0001	0.289	0.037	<0.0001

The model was developed with stepwise regression analysis and the initial explanatory valuables were FIRI, TG, leptin, HDL-C and LpL mass in boys and leptin in girls. Abbreviations: FIRI, fasting immunoreactive insulin; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LpLmass, lipoprotein lipase mass.

Table 5. Characteristics of subjects with and without visceral-type obesity

Characteristics	Boys (n=193)			Girls (n=181)		
	Visceral (n=20)	Non-visceral (n=173)	*p* value	Visceral (n=16)	Non-visceral (n=165)	*p* value
BMI (kg/m^2)	25.4±4.5	20.7±2.5	<0.001	23.6±3.0	20.4±2.3	<0.001
WC (cm)	83.2±11.4	71.0±5.5	<0.001	78.4±9.2	70.5±5.6	<0.01
WC/BH ratio	0.49±0.069	0.419±0.032	<0.001	0.493±0.050	0.445±0.035	<0.01
PFT (mm)	11.07±2.5	3.42±1.6	<0.0001	10.0±1.6	4.2±1.7	<0.0001
SFT (mm)	8.06±5.2	4.77±2.7	<0.05	10.7±2.4	7.9±3.1	<0.001
SBP (mmHg)	126.2±12.5	118.6±9.4	<0.01	112.6±11.1	109.0±8.2	NS
DBP (mmHg)	65.3±7.3	64.6±9.3	NS	64.3±8.2	63.9±7.8	NS
AST (IU/L)	27.8±13.4	27.0±24.0	NS	17.5±3.2	18.2±3.7	NS
ALT (IU/L)	34.5±31.3	18.3±16.5	<0.05	11.8±4.2	11.4±3.6	NS
γ-GTP (IU/L)	23.7±13.2	17.7±6.7	NS	15.7±3.6	13.8±3.6	NS
FBS (mg/dL)	89.2±7.5	87.2±6.2	NS	86.5±7.7	85.4±5.3	NS
FIRI (μIU/mL)	8.2±3.5	5.6±2.8	<0.01	7.45±3.4	6.14±2.4	NS
LpL mass (ng/mL)	70.9±14.6	80.7±2.1	<0.05	90.2±19.3	90.7±19.2	NS
TG (mg/dL)	73.5±34.7	49.2±25.0	<0.01	47.6±16.7	47.7±23.3	NS
TC (mg/dL)	172.3±23.4	158.9±26.3	<0.05	184.3±34.4	177.7±24.1	NS
HDL-C (mg/dL)	55.2±9.0	61.7±11.2	<0.05	64.9±12.1	69.5±10.8	NS
UA (mg/L)	6.6±1.0	6.1±0.9	<0.05	4.5±0.7	4.4±0.8	NS
Adiponectin (μg/mL)	8.9±2.9	11.5±4.4	<0.01	11.0±3.4	13.2±4.6	NS
Leptin (ng/mL)	5.2±3.83	1.7±1.3	<0.001	11.4±6.0	6.2±3.6	<0.01
Desacyl-Ghrelin (fmol/mL)	31.9±18.6	57.3±46.3	<0.0001	53.8±83.5	49.1±56.0	NS
Resistin (ng/mL)	4.4±1.9	4.4±2.2	NS	4.7±1.9	5.0±2.2	NS
hsCRP (ng/mL)	464.9±597.8	327.6±1,017.1	NS	230.0±430.3	280.9±851.3	NS

Abbreviations: BMI, body mass index; WC, waist circumference; WC/BH ratio, waist circumference divided by body height; SFT, subcutaneous fat thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyltransferase; FBS, fasting blood sugar; FIRI, fasting immunoreactive insulin; LpLmass, lipoprotein lipase mass; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; UA, uric acid; hs-CRP, high sensitivity C-reactive protein.

echo contrast positivity. Of the 36 participants with visceral obesity, six (16.7%) showed hepatorenal echo contrast positivity. Moderate fatty liver was investigated in five boys and one girl, but none of the participants had severe fatty liver. Boys with hepatorenal echo contrast positivity had higher values for waist circumference, waist to height ratio, SFT, γ-GTP, FIRI, and leptin levels. Girls with hepatorenal echo contrast positivity showed no significant differences from those without, except for ALT and uric acid levels, as shown

Table 6. Characteristics of subjects positive or negative for hepatorenal contrast

Characteristics	Boys (n=193)			Girls (n=181)		
	Hepatorenal contrast+ (n=32)	Hepatorenal contrast− (n=161)	p value	Hepatorenal contrast+ (n=55)	Hepatorenal contrast− (n=126)	p value
BMI (kg/m^2)	23.4±4.6	20.7±2.5	<0.01	20.7±2.6	20.7±2.5	NS
WC (cm)	78.1±11.9	71.1±5.4	<0.01	71.7±6.3	71.0±6.4	NS
WC/BH ratio	0.462±0.071	0.419±0.031	<0.01	0.449±0.038	0.449±0.039	NS
PFT (mm)	5.1±3.5	4.0±2.7	NS	4.9±2.5	4.6±2.3	NS
SFT (mm)	6.7±4.5	4.8±2.8	<0.05	7.8±3.1	8.2±3.1	NS
SBP (mmHg)	122.3±14.1	118.8±8.9	NS	110.3±10.0	108.9±7.8	NS
DBP (mmHg)	65.1±9.9	64.6±9.0	NS	63.7±7.6	64.1±7.9	NS
AST (IU/L)	32.0±31.1	26.1±21.1	NS	17.7±3.7	18.3±3.6	NS
ALT (IU/L)	32.3±37.9	17.5±11.1	NS	10.5±3.3	11.8±3.8	<0.05
γ-GTP (IU/L)	21.7±12.4	17.7±6.4	<0.05	13.4±2.8	14.3±3.9	NS
FBS (mg/dL)	89.2±6.5	87.1±6.3	NS	86.5±5.3	85.1±5.6	NS
FIRI (μIU/mL)	7.3±3.3	5.6±2.8	<0.01	6.4±2.5	6.2±2.5	NS
LpL mass (ng/mL)	84.8±22.0	78.6±20.3	NS	92.5±17.8	89.56±19.7	NS
TG (mg/dL)	53.7±31.8	51.4±26.2	NS	51.6±21.4	46.0±23.2	NS
TC (mg/dL)	157.1±26.1	160.9±26.3	NS	175.1±27.6	179.6±23.9	NS
HDL-C (mg/dL)	61.1±12.8	61.0±10.9	NS	68.3±10.7	69.5±11.01	NS
UA (mg/dL)	6.2±1.0	6.1±0.9	NS	4.2±0.9	4.5±0.7	<0.01
Adiponectin (μg/mL)	11.1±5.9	11.2±4.0	NS	12.3±4.3	13.3±4.6	NS
Leptin (ng/mL)	3.5±3.6	1.7±1.3	<0.01	6.2±3.9	6.9±4.2	NS
Ghrelin (fmol/mL)	48.0±42.5	56.0±45.5	NS	43.9±50.8	52.0±61.8	NS
Resistin (ng/mL)	4.3±2.2	4.4±2.1	NS	5.1±2.0	4.9±2.2	NS
hsCRP (ng/mL)	522.3±974.5	305.7±1,013	NS	211.8±719.5	304.5±863.6	NS

Abbreviations: BMI, body mass index; WC, waist circumference; WC/BH ratio, waist circumference divided by body height; SFT, subcutaneous fat thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyltransferase; FBS, fasting blood sugar; FIRI, fasting immunoreactive insulin; LpLmass, lipoprotein lipase mass; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; UA, uric acid; hs-CRP, high sensitivity C-reactive protein.

in **Table 6**. We compared the differences among hepatorenal echo contrast positivity with or without visceral fat accumulation and hepatorenal echo contrast negativity in **Table 7**. Difference among the three groups were compared by one-way analysis of variance (ANOVA) with Tukey-type multiple comparison. P-values less than 0.05 were considered significant. Boys with hepatorenal echo contrast positivity with visceral adiposity showed significantly higher values for waist circumference, waist to height ratio, PFT, SFT, high systolic pressure, γ-GTP, FIRI, and leptin levels, and lower values for LpL mass, HDL-C and adiponectin.

Discussion

Although the participants were enrolled from three different schools, there were no significant differences in BMI or the ratio of obesity between the participants and the entire student body, all of whom were measured (data not shown).

The anthropometric data and blood cell counts were within the normal limits by sex, and blood chemistry showed that, but AST, ALT, γ-GTP, FBS, total cholesterol, and uric acid levels were significantly higher in boys. On the other hand, preheparin LpL mass and HDL-C levels were significantly higher in girls. LpL hydrolyzes dietary and endogenous triglycerides, which are synthesized mainly in adipose and muscle tissue[10, 11]. LpL is mainly active on vascular cell surfaces and sensitive immunoassay systems have demonstrated that the presence of LpL in serum (preheparin mass) reflects LpL production. Several studies have reported that the serum preheparin LpL mass is decreased in visceral adiposity[12, 13] and is positively correlated with HDL-C levels and negatively correlated with triglyceride levels. In this study, the average preheparin LpL mass was 79.7 ng/mL in boys

Table 7. Comparison of boys with hepatorenal contrast positivity with and without visceral fat accumulation versus boys negative for hepatorenal contrast

Boys	Hepatorenal contrast (+) with visceral fat accumulation (A)	Hepatorenal contrast (+) without visceral fat accumulation (B)	Hepatorenal contrast (−) without visceral fat accumulation (C)	ANOVA (Tukeymethod, $p<0.05$)
N	5	27	161	
BMI (kg/m^2)	29.6±28.7	22.2±3.91	20.7±2.45	A-B, A-C, B-C
WC (cm)	95.8±5.68	74.7±9.47	71.7±5.43	A-B, A-C, B-C
WC/BH ratio	0.57±0.04	0.42±0.10	0.41±0.04	A-B, A-C
PFT (mm)	11.4±2.63	3.94±2.22	4.02±2.71	A-B, A-C
SFT (mm)	12.9±5.08	5.52±3.28	4.79±2.80	A-B, A-C
SBP (mmHg)	139.0±17.1	119.2±11.4	118.7±8.90	A-B, A-C
DBP (mmHg)	68.2±9.03	64.5±10.1	64.6±8.99	
AST (IU/L)	35.8±20.3	31.3±32.9	26.1±21.1	
ALT (IU/L)	66.8±44.4	25.8±33.7	17.1±11.1	A-B, A-C
γ-GTP (IU/L)	38.8±14.9	18.6±9.19	17.6±6.36	A-B, A-C
FBS (mg/dL)	91.4±9.58	88.8±5.94	87.0±6.27	
FIRI (μIU/mL)	11.6±2.70	6.45±2.80	5.60±2.79	A-B, A-C
LpL mass (ng/mL)	60.9±16.2	89.3±20.3	78.2±19.4	A-B, A-C
TG (mg/dL)	72.4±35.9	50.2±30.4	51.3±26.1	
TC (mg/dL)	182.0±13.6	152.4±25.3	160.9±26.3	
HDL-C (mg/dL)	48.2±7.66	63.4±12.0	60.9±10.8	A-B, A-C
UA (mg/dL)	6.84±0.78	6.06±1.06	6.12±0.94	
Adiponectin (μg/mL)	6.60±0.98	11.8±6.04	11.2±3.98	A-B, A-C
Leptin (ng/mL)	9.78±3.62	2.34±2.10	1.73±1.34	A-B, A-C
Ghrelin (fmol/mL)	28.6±16.6	51.6±45.0	56.0±45.5	
Resistin (ng/mL)	3.74±2.15	4.45±2.21	4.43±2.13	
hsCRP (ng/mL)	544.4±445.1	518.2±849.7	305.7±1,013	

Abbreviations: BMI, body mass index; WC, waist circumference; WC/BH ratio, waist circumference divided by body height; SFT, subcutaneous fat thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gam ma-glutamyltransferase; FBS, fasting blood sugar; FIRI, fasting immunoreactive insulin; LpLmass, lipoprotein lipase mass; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; UA, uric acid; hs-CRP, high sensitivity C-reactive protein.

and 90.4 ng/mL in girls, which were above the standard range for adults (40–70 ng/mL) and the level in girls was significantly higher than in boys ($p<0.0001$). This was consistent with an earlier study showing that women had higher LpL levels than men[14].

With regard to adipocytokines, the levels of adiponectin, leptin and resistin tended to be higher in girls. Adiponectin is secreted from adipose tissue and is abundantly present in the human plasma. Levels of adiponectin are generally higher in women than in men and are inversely correlated with BMI[15]. Adiponectin is also known as a modulator of the endothelial inflammatory response and is associated with coronary heart disease[16]. Our finding that the plasma adiponectin concentration was higher in girls than boys is physiologically relevant.

Leptin is another adipocyte-derived hormone that affects appetite and energy expenditure[17]. In obesity, the plasma leptin concentration is elevated and its production depends on the amount of adipose tissue[18]. In general, the plasma leptin level is higher in women than in men[19] and here we found that it was higher in girls than in boys.

Resistin is also an adipocyte-secreted hormone that is known to promote insulin resistance by inhibiting glucose uptake in muscle and adipose tissue. Serum concentrations of resistin are correlated positively with BMI and the waist to hip ratio in humans[20]; however, in our study, girls showed higher levels of serum resistin and insulin than boys, despite higher levels of adiponectin and leptin, which contradict each other. Recent studies have been made to understand the divergence in characteristics between murine resistin and human resistin[21], and further studies are clearly needed.

We also determined the levels of desacyl-ghrelin