Association of adiposity and fitness with triglyceride-to-high-density lipoprotein cholesterol ratio in youth

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ABSTRACT

Background	:	The ratio of triglycerides-to-high-density lipoprotein cholesterol (TG/HDL-C) is considered a robust biomarker of metabolic syndrome (MetS) and is associated with several diseases, including type 2 diabetes mellitus (T2DM) and hypertension (HTN). This study examined the independent association of adiposity and fitness with the TG/HDL-C ratio.
Materials and Methods	:	This is a cross-sectional study comprising 403 (201 girls) Nigerian adolescents aged 11–19 years. Participants were evaluated for body mass index, cardiorespiratory fitness, and TG/HDL-C. Regression models adjusting for age and biological maturity were used to evaluate the association of adiposity and fitness with TG/HDL-C ratio. The TG/HDL-C ratios of 1.0 mmol/L and 1.1 mmol/L were used to stratify female and male participants into low- and high-risk groups, respectively.
Results	:	Of the 135 high-risk adolescents, 21.1%, 5.5%, 12.7%, 14.9%, and 0.5% were at risk of T2DM, systolic HTN, diastolic HTN, abdominal obesity, and MetS, respectively. The independent variables were significantly associated with TG/HDL-C ratio only in boys but not girls. In boys, high adiposity ($\beta = 0.193$; $P = 0.025$) and low fitness ($\beta = -0.169$; $P = 0.048$) were independently associated with the dependent variable. Unfit boys were 3.9 (95% confidence interval [CI] =1.37–10.94, $P = 0.011$) times more likely to develop elevated TG/HDL-C ratio than their fit peers. The likelihood of girls at risk of MetS developing a high TG/HDL-C ratio was 13.7 (95% CI = 3.89–48.32, $P < 0.001$) times compared to their counterparts without MetS.
Conclusions	:	Adiposity and fitness were independently associated with TG/HDL-C in boys but not in girls. Health promotion intervention focusing on lowering TG/HDL-C ratio among Nigerian adolescents should include an emphasis on healthy diet and endurance activity programs.
Keywords	:	Adolescents, body mass index, cardiorespiratory fitness, lipoprotein ratio, metabolic syndrome

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INTRODUCTION

Dyslipidemia, characterized by increased levels of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and decreased levels of high-density lipoprotein cholesterol (HDL-C), is a recognized modifiable risk factor for the development and progression of cardiovascular disease (CVD) and stroke.^[1] Among blood lipid profile parameters, the ratio of TG/HDL-C is considered a useful and robust biomarker of the metabolic syndrome (MetS), coronary atherosclerosis and atherogenic index of the plasma (AIP)^[2,3] in both adults^[4] and youth.^[5] It is established that moderately elevated levels of TG confer a greater risk of CVD than either diminishing levels of HDL-C or high levels of LDL-C.^[6] Since low levels of HDL-C is also predictive of CVD, evidently, a high ratio of TG/HDL-C would be a more devastating CVD risk than either TG or HDL-C alone.

A high ratio of TG/HDL-C is also associated with several disease conditions, including type 2 diabetes mellitus (T2DM),^[7] arterial stiffness,^[8] insulin resistance,^[9] hypertension (HTN),^[10] CVD, and mortality.^[11] Since MetS is a precursor of insulin resistance, T2DM and CVD, early identification of its risk factors, such as TG/HDL-C ratio, is important for primordial prevention. Despite the clinical importance of MetS and its sequelae, as well as the use of lipid ratios for CVD assessment in adults, only sparse data are available in the pediatric population,^[5] with limited information on African youth. Moreover, the association of behavioral risk factors such as fatness and fitness with the TG/HDL-C ratio needs to be explored. A better understanding of these relationships will help inform more effective intervention programs that could lead to improvement in fatness and fitness with a concomitant reduction in disease risk among youth.

Several studies have documented the adverse effect of adiposity (fatness) on health, indicating that elevated levels of fat are hazardous to the cardiometabolic health of both youth^[12-14] and adults.^[4,15] Physical fitness and physical activity are considered effective intervention factors that have beneficial effects on the overall risk of CVD. For instance, cardiorespiratory fitness (CRF) was found to favorably impact CVD and its components among adolescents.^[16,17] Despite the importance of these two behavioral risk factors of cardiometabolic disease (CMD), only scanty information is available on their relationship with the AIP or any lipoprotein ratio.^[3] To our knowledge, there has hardly been any previous study that evaluated the relationship between fatness and fitness with TG/HDL-C ratio in the pediatric population to date.

Adolescence is a critical period during which physiological and behavioral changes such as binge alcohol abuse, drug abuse, smoking, and excessive use of social media among others occur,^[18] which if not well managed, may lead to pediatric lifestyle noncommunicable diseases. Both pediatric obesity and low physical fitness are known to be increasing globally, and these expose youth to an increased risk of noncommunicable diseases of lifestyle. Therefore, early interventions to reverse this negative health trend are warranted in order to guarantee better health prospects later in life.

This study examined the association of fatness and fitness with the TG/HDL-C ratio among adolescent students in Kogi East, Nigeria. The study specifically determined the independent and combined associations of body mass index (BMI) and CRF with TG/HDL-C ratio among the participants. A secondary purpose was to identify CMD risk among Nigerian adolescents using TG/HDL-C ratio. Information on the interrelationships among these variables could be potentially relevant in planning effective health promotion and preventive strategies.

MATERIALS AND METHODS

Study design and participants

This study adopted a cross-sectional design consisting of 418 apparently healthy school girls and boys ages 11-19 years (who were early developers) drawn from four secondary schools in Kogi East Senatorial District, Kogi State, North Central Nigeria. The Lorentz formula for population greater than 10,000 was used to compute the minimum size, with a prevalence of 27% risk of abnormal TG/HDL-C ratio obtained as recommended.^[19] The minimum size calculated was 303 participants which was increased to 418 to account for possible attrition and to improve representativeness. Data for this project were collected during September 2019 to December 2019. Study participants were selected using the systematic sampling procedure. Every fourth student beginning from a particular number on the class list was selected to participate in the project. Eligibility criteria included participants with no history of CVD or any reported health problems, illness or had not participated in organized physical exercise programs at least 6 months before data collection. The purpose of the study and test procedures were fully explained to the participants after permission was duly obtained from the heads of participating schools. The study protocol was approved by the Ethical Review Committee of the College of Health Sciences (Ref. No. COHS/02/25/2020), Kogi State University, Nigeria. Written informed consent of parents/guardians and assent of participating students were also obtained before data collection. All tests were conducted from 9:00 am to 12:00 noon in compliance with the ethical guidelines of the Helsinki declaration.^[20]

Study setting

The study was conducted among school-going adolescents in the Kogi East senatorial district of Kogi State, Nigeria.

Kogi State, with its capital at Lokoja, is located in the North central geo-political zone of Nigeria. Like any typical state in Nigeria, secondary schools in Kogi State are in two main categories, public and private. Youths commonly assist their parents in their various occupations outside school hours. Information on youth physical fitness and other lifestyles in relation to their health in the study area is hardly available.

Physical characteristic measurements

Participants' physical characteristic measurements were conducted according to standard procedures.[21] Specifically, bare-foot body mass and stature were measured in light clothing without shoes and socks with the aid of a calibrated digital weighing scale (Model Sec-880, Seca Birmingham, UK) and wall-mounted stadiometer (Model Sec-206; Seca, Birmingham, UK) to the nearest 0.1 kg and 0.1 cm, respectively. BMI, used to estimate body fatness, was calculated by dividing body mass in kilograms by stature in meter square (kg/m²). Body fat was estimated from triceps and medial calf skinfolds with the aid of Harpenden skinfold calipers (Creative Health Products, Ann Arbor, MI, USA). Measurements were taken thrice on the right side of a participant's body, and the median was recorded. The revised regression equations for black children were used to estimate the percent body fat.^[22] Based on their BMI values, participants were categorized into healthy weight and overweight in accordance with FitnessGram revised data.[22]

Waist circumference was measured with a Lufkin retractable flexible anthropometric tape (W606PM Rosscraft, Canada) to the nearest 0.1 cm. The threshold for abdominal obesity of the 90th percentile for age and sex was determined as recommended by the International Diabetes Federation (IDF).^[23] All anthropometric measurements were conducted by an ISAK-Certified level 2 Anthropometrist (Lead author).

Fitness testing

The 20-m shuttle run test, a multistage aerobic capacity test that progresses in intensity was used to assess CRF. In this test, participants ran back and forth between two lines drawn 20 m apart. They were instructed to run until exhaustion in accordance with the audio signals emitted from the test compact disc and were given verbal encouragement throughout the test. Participants who failed to complete two successive shuttles were withdrawn from the test. The number of laps completed and the running speed of each participant was used to estimate their CRF.^[24] Specific details of the administrative procedures of this test and classification of participants into healthy fitness zone or high fitness and unfit or low fitness based on FitnessGram revised data have been previously described.^[22]

Resting systolic blood pressure (SBP) and diastolic blood pressure levels were measured on each participant's right arm using appropriate cuff sizes with an oscillometric device (HEM-705 CP; Omron, Tokyo, Japan) after sitting quietly for 5 min. Measurements were taken thrice at 2-min intervals, and the average of the three readings was recorded. The blood pressure cutoff point for HTN was based on the standards of the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents 2004.^[25]

Biochemical measurement

A 12-h overnight fasting blood glucose (FBG), HDL-C, and TG were obtained from capillary blood samples and analyzed with a CardioCheck Plus Analyzer (CCPA) (PTS Diagnostics, Indianapolis, IN, USA). Participants rested for 10 min, after which they took their turns for the test. Each participant's middle finger was cleaned with an alcohol wipe, after which a gentle pressure was applied to the finger with a lancet, and the finger stuck at the center. Meanwhile, gentle pressure was applied to the finger to produce a large drop of blood which was dispensed on the test strip, and test results were displayed within 90 s. The CCPA is a valid and reliable instrument for analyzing blood glucose (GLU) and lipids.^[26] Details of the protocol have been previously described.^[16] The TG/HDL-C ratio was calculated by dividing the TG in mmol/L by HDL-C in mmol/L.

Continuous metabolic risk score

A continuous metabolic risk score (MRS) was computed from the following variables: GLU, SBP, waist circumference (WC), HDL, and TG. Each of the variables was standardized by subtracting the mean value for each sex group from the individual's value and then dividing the product by the value of standard deviation (SD) (Z = value-mean/SD). The standardized HDL was inverted because it is inversely related to the MetS risk. The z-scores of the individual risk factor were summed to create a clustered MRS (continuous variable) for each participant, with a lower score indicating a more favorable metabolic risk profile. This approach has been used in the pediatric population.^[27,28] Participants with an MRS + 1SD above the overall mean were considered at increased risk of MetS.^[29]

Definition of cardiovascular disease risk abnormalities

CVD risk abnormalities for participants were determined using the standards of the IDF^[23] as follows: TG (\geq 1.7 mmol/L) or (\geq 130 mg/dl); HDL-C (\leq 1.04 mmol/L) or (\leq 40 mg/dl); and GLU (\geq 5.6 mmol/L) or (\geq 100 mg/dl). Study participants without risk factor abnormalities were classified as "no risk," while those with one or more risks were classified as "risk." In order to determine the threshold of TG/HDL-C that represents an increased risk for CMD, the sample was divided into tertiles, with the minimum value of the highest tertile as the cut-off point. The minimum of the highest tertile for the total sample was 1.0 (girls = 1.0; boys = 1.1). To date, there is no established specific cutoff point for TG/HDL-C in the pediatric population, and this approach is considered a robust estimate of the TG/HDL-C threshold and has been used by several investigators.^[9,30]

Pilot test

A pilot test was conducted before data collection. The purpose of the pilot test was to refine test administration procedures and determine the precision of the instruments for data collection and test reliability. Forty adolescents ranging in age from 12 to 15 years who did not form part of the actual study sample were selected to participate in the pilot test. All measurements were conducted in accordance with standard procedures, and test reliability was determined using Cronbach's alpha coefficients. In all cases, the alpha coefficients ranged from 0.864 to 0.899, indicating good internal consistency.^[31]

Statistical analysis

Data were coded and checked for normality before analysis with the Kolmogorov-Smirnov test. Descriptive data were presented as means, SD, frequencies, and percentage distributions. Significant differences between genders on all study variables were determined with the independent samples t-test. Person's product-moment correlation was used to assess the relationships between the dependent and independent variables. The associations of TG/HDL-C with BMI and CRF, and the relative importance of BMI and CRF were determined through multiple regression models. All analyses were adjusted for chronological age and biological maturity, with the later estimated from stature and chronological age using the regression equation of Moore et al.^[32] The equation estimates maturity off-set (MO) directly. Then, age at peak height velocity (APHV) was estimated as the difference between MO and chronological age. The independent association of fatness and fitness with the TG/HDL-C ratio was determined with the binary logistic regression model. Separate analyses were conducted for each gender. All statistical analyses were conducted with IBM SPSS (Version 20, IBM Corporation, Armonk, NY, USA) at a probability level of 0.05 or less.

RESULTS

Table 1 indicates the general characteristics of the participants stratified by gender. On average, girls were significantly heavier (P = 0.016), fatter (P < 0.001), displayed greater maturity status (P < 0.001),

BMI (P < 0.001), abdominal adiposity (P = 0.001), SBP (P = 0.010), and risk of MetS (P = 0.006) than boys. Boys had significantly better CRF (P < 0.001) and greater APHV (P < 0.001) than girls. There were no statistically significant gender differences in age (P = 0.558), TG/HDL-C (P = 0.091), and other variables, as indicated in Table 1.

Table 2 compares the CMD risk profiles of participants divided into "low" and "high" risk sub-groups based on the TG/HDL-C ratio. More high-risk individuals were identified among the girls than boys. For instance, girls were at increased risk of abdominal obesity, MetS, and systolic and diastolic HTN, while boys were vulnerable only of abdominal obesity, T2DM, and MetS. Regarding other health parameters, girls were also more disadvantaged than boys, as indicated in the table. The proportion of participants (combined) at risk of each of the CMD is displayed in Figure 1, which showed that most of the adolescents were at risk of T2DM (21%), followed by abdominal obesity (14.9%).

The zero-order correlation coefficients between the dependent and independent variables showed that the relationships were significant for fitness, FBG in boys and WC and MetS in both genders as well as for T2DM risk in boys [Table 3]. The relationships can be described as weak to moderate; the strongest relationship was between the dependent variable and MetS in both genders (Girls: r = 0.671, P < 0.001; Boys: r = 0.619, P < 0.001).

Results of the multiple regression models evaluating the extent to which fatness and fitness could predict TG/ HDL-C after controlling for age and maturity status are presented in Table 4. In boys, age (P = 0.022) explained 6% of the variation in the TG/HDL-C ratio in step 1. The addition of the independent variables in step 2 increased the total variance cumulatively to 9%, thus indicating that the independent variables explained an additional



Figure 1: Cardiometabolic disease risk by TG/HDL-C status. T2DM: Type 2 diabetes mellitus, Sys HTN: Systolic hypertension, Dia HTN: Diastolic hypertension, Abd OB: Abdominal obesity, TG/HDL-C: Triglycerides-to-high-density lipoprotein cholesterol

Variable	Combined (n=403)	Girls (<i>n</i> =201)	Boys (<i>n</i> =202)	t	Р
Age (years)	14.7±2.3	14.8±2.3	14.7±2.2	0.586	0.558
AHPV (years)	13.3±1.1	12.5±0.8	14.1±0.8	20.068	< 0.001
MO (years)	1.4±1.9	2.3±1.7	0.6±1.7	10.029	< 0.001
Stature (cm)	160.2±9.8	159.6±7.1	160.9±11.9	0.303	0.193
Body mass (kg)	53.1±12.5	55.5±12.1	50.8±12.5	3.784	0.016
Body fat (%)	15.5±7.0	19.8±7.4	11.2±2.9	15.31	< 0.001
BMI (kg/m ²)	20.5±3.5	21.7±4.0	19.3±2.6	6.929	<0.001
WC (cm)	65.8±8.8	67.2±9.4	64.4±8.0	2.273	0.001
20-MST (lap)	32.2±16.8	24.9±13.3	39.5±16.8	9.697	< 0.001
TG (mmol/L)	1.0±0.9	1.1±1.2	0.9±0.4	1.653	0.100
HDL-C (mmol/L)	1.3±0.4	1.3±0.3	1.3±0.4	1.090	0.276
TG/HDL-C (mmol/L)	0.9±1.2	1.0±1.6	0.8±0.5	1.697	0.091
SBP (mmHg)	105.6±16.6	107.8±16.7	103.5±16.2	2.587	0.010
DBP (mmHg)	69.9±14.5	70.4±15.3	69.5±13.5	0.595	0.552
FBG (mmol/L)	5.1±0.7	5.0±0.7	5.1±0.7	0.401	0.157
MetS	-7.7±2.2	-7.4±2.4	-8.0±2.0	2.773	0.006

APHV: Age at peak height velocity. MO: Maturity off-set, BMI: Body mass index, 20-MST: 20-m shuttle run test, TG: Triglycerides, HDL-C: High-density lipoprotein cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, MetS: Metabolic syndrome, WC: Waist circumference, AHPV: Age at peak height velocity

 Table 2: Comparison of cardiometabolic disease risks between participants with low and high triglycerides-to-high-density lipoprotein cholesterol ratio (*n*=403)

Variable		Girls		Boys			
	Low (<i>n</i> =134)	High (<i>n</i> =67)	Total (<i>n</i> =201)	Low (<i>n</i> =134)	High (<i>n</i> =68)	Total (<i>n</i> =202)	
Age (years)	14.3±2.5	15.9±4.4	14.8±2.3**	14.2±2.0	15.5±2.4	14.7±2.2**	
Body mass (kg)	54.7±13.4	57.0±8.1	55.5±12.1	50.4±11.9	51.6±13.6	50.8±12.5	
BMI (kg/m ²)	21.2±4.4	22.5±2.7	21.7±4.0*	19.1±2.4	19.7±2.9	19.3±2.6	
20-MST (lap)	27.4±13.6	19.8±10.8	24.9±13.3**	44.0±17.2	30.7±12.1	39.5±16.8**	
WC (cm)	64.2±8.1	73.2±8.9	67.7±9.4**	62.7±7.5	67.7±7.9	64.4±8.0**	
FBG (mmol/L)	5.0±0.8	5.1±0.6	5.0±0.7	5.0±0.6	5.4±0.8	5.1±0.7**	
SBP (mmHg)	104.2±17.5	114.9±12.2	107.8±16.7**	103.1±17.8	104.4±12.6	103.5±16.2	
DBP (mmHg)	66.9±15.4	77.2±12.7	70.4±15.3**	68.9±14.0	70.8±12.6	69.5±13.5	
MetS	-8.4±1.5	-5.5±2.6	-7.4±2.4**	-8.9±1.5	-6.4±1.7	-8.0±2.0**	

**P<0.001, *P<0.05. BMI: Body mass index, 20-MST: 20-m shuttle run test, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, MetS: Metabolic syndrome, WC: Waist circumference

Table 3: Correlations among triglycerides-tohigh-density lipoprotein cholesterol, body mass index, 20-m shuttle run test, and other health indicators (n=403)

Group	BMI	WC	20-MST	SBP	DBP	FBG	MetS
Girls Boys			-0.079 -0.310**				

**P<0.001, *P<0.05. BMI: Body mass index, 20-MST: 20-m shuttle run test, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, MetS: Metabolic syndrome, WC: Waist circumference

variance of 3% after controlling for the covariates. Although both independent variables made unique contributions, fatness ($\beta = 0.193$, P = 0.025) presented greater explanatory capacity. However, the girls' model was not statistically significant (P = 0.380).

Results of the logistic regression models assessing the impact of the independent variables and other health indicators on the dependent variable after controlling for age and maturity status indicated that only fitness displayed significant (odds ratio [OR] = 3.87, 95% confidence interval [CI] = 1.37-10.94, P = 0.011) negative effect in boys. In girls, three health indicators returned

significant positive associations with the dependent variable. These were MetS (OR = 13.70, 95% CI = 3.89–48.32, P < 0.001); WC (OR = 5.59, 95% CI = 1.00–31.02, P = 0.049); and BMI (OR = 0.26, 95% CI = 0.07–0.96, P = 0.44).

DISCUSSION

The main findings of this study include: The TG/HDL-C optimal cut-off value of 1.0 (girls = 1.0; boys = 1.1). The elevated TG/HDL-C cutoff values were used to identify adolescents at risk of MetS and selected CMDs. The study also demonstrated weak to moderate relationships between the dependent and independent variables and other health indicators. Indeed, the TG/HDL-C ratio was more strongly associated with MetS and WC than fatness and fitness. Fatness and fitness were independently and jointly associated with the dependent variable in boys but not girls, with fatness showing a stronger association.

The utility of the TG/HDL-C ratio to identify youth at risk of CMD is increasingly becoming popular in public health research and clinical practice.^[3,5,30] The TG/HDL-C ratios of 1.0 mmol/L found for adolescents in this study

Table 4: Standardized regression coefficients on
the relationships among triglycerides-to-high-
density lipoprotein cholesterol, fatness, and fitness

		Mod	el 1	Model 2		
Group	Predictor	В	Р	В	Р	
Girls	Age	0.127	0.649	-0.053	0.858	
	MŌ	-0.079	0.779	0.067	0.818	
	BMI	-	-	-0.038	0.635	
	20-MST	-	-	-0.149	0.061	
Boys	Age	0.542	0.022	0.123	0.673	
	MO	-0.339	0.149	0.150	0.611	
	BMI	-	-	0.193	0.025	
	20-MST	-	-	-0.169	0.048	

MO: Maturity off-set, BMI: Body mass index, 20-MST: 20-m shuttle run test

is comparable to the ratio of 1.1 mmol/L reported for 12.6-year-old Malaysian children^[3] and 1.25 mmol/L documented in 6–16-year-old Chinese children,^[33] but strikingly lower than the ratio of 3.3 mmol/L reported for 10–18-year-old Korean adolescents^[5] and 2.2 mmol/L noted for pubertal Venezuelan children.^[34] Potential reasons for the inconsistencies in results might be due to disparity in age, measurement protocols, and variation in ethnicity across studies.

In the present study, a high TG/HDL-C ratio was used to identify some CMDs [Figure 1]. Of the five CMDs, the prevalence of T2DM was highest, followed by abdominal obesity. These findings are supported by previous studies in children and adolescents.^[5,7,10]

Our study indicated strong correlations between the dependent variable, FBG, WC, and MetS. The strongest relationship was that between TG/HDL-C ratio and MetS. These results are consistent with previous research documenting a strong association between TG/HDL-C ratio and MetS.^[1-3] This substantial association may be because the dependent variable contains two of the diagnostic criteria of MetS. Moreover, there is accumulating evidence suggesting that TG/HDL-C ratio is a valid index for identifying MetS and CVD.^[1-3]

Our findings clearly indicated that both fatness and fitness were independent predictors of TG/HDL-C ratio in boys but not girls. The result in girls is surprising. The results also showed that in boys, the joint contribution of fatness and fitness in predicting the dependent variable is low (3%), but fatness presented greater explanatory power. These results, including that in girls, showed that fatness and fitness are not important explanatory variables for predicting the dependent variable in this cohort of adolescents.

This study has several limitations. First, the cross-sectional design precludes the determination of causality. Second, a preponderance of our study participants included ethnic Igala children of Kogi State, who do not represent the multiracial population in Nigeria. Furthermore, the TG/HDL-C ratio is known to be influenced by ethnicity

and genetic variations.^[35] Therefore, our findings cannot be extended to other population of Nigerian youth. Future studies in Nigeria should attempt to address this limitation by using a nationally representative sample.

CONCLUSIONS

This study has shown that unfavorable TG/HDL-C ratio is prevalent among Nigerian adolescents. Both fatness and fitness are independently associated with TG/HDL-C ratio in boys but not girls. The joint contribution of fatness and fitness in predicting the TG/HDL-C ratio is minimal, but fatness was the major determinant of the dependent variable in Nigerian boys. Nigerian adolescents with high TG/HDL-C ratios were at increased risk of CMDs, irrespective of gender. School and community-based health promotion efforts targeting favorable TG/HDL-C ratios should include an emphasis on healthy diet and endurance activities.

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Conflicts of interest

There are no conflicts of interest.

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