Prominent Lipid Parameters Correlated with Trunk-to-Leg and Appendicular Fat Ratios in Severe Pediatric Obesity

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Abstract—Alterations in lipid parameters as well as in the fat distribution of the body are noteworthy during the evaluation of obesity stages. Total cholesterol (TC), triglycerides (TRG), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C) are basic lipid fractions. Fat deposited in trunk and extremities may give considerable amount of information. Ratios such as trunk-to-leg fat ratio (TLFR) and trunk-to-appendicular fat ratio (TAFR) are derived from distinct fat distribution in these areas. In this study, lipid fractions and TLFR as well as TAFR were evaluated and the distinctions among healthy, obese (OB) and morbid obese (MO) groups were investigated. Three groups [normal body mass index (N-BMI), OB, MO] were constituted. Ages and sexes of the groups were matched. The study protocol was approved by the Non-interventional Ethics Committee of Tekirdag Namik Kemal University. Written informed consent forms were obtained from the parents of the participants. Anthropometric measurements (height, weight, waist circumference, hip circumference, head circumference, neck circumference) were recorded during the physical examination. BMI values were calculated. Total, trunk, leg and arm fat mass values were obtained by TANITA Bioelectrical Impedance Analysis. These values were used to calculate TLFR and TAFR. Systolic (SBP) and diastolic blood pressures (DBP) were measured. Routine biochemical tests including lipid fractions were performed. Data were evaluated using SPSS software. p value smaller than 0.05 was accepted as significant. There was no difference among the age values and gender ratios of the groups. Any statistically significant difference was not observed in terms of DBP, TLFR as well as serum lipid fractions. Higher SBP values were measured both in OB and MO children than those with N-BMI. TAFR showed a significant difference between N-BMI and OB groups. Statistically significant increases were detected between insulin values of N-BMI group and OB as well as MO groups. There were bivariate correlations between LDL and TLFR as well as TAFR values in MO group. When adjusted for SBP and DBP, partial correlations were calculated for LDL-TLFR as well as LDL-TAFR. Much stronger partial correlations were obtained for the same couples upon controlling for TRG and HDL-C. Much stronger partial correlations observed in MO children emphasize the potential transition from morbid obesity to metabolic syndrome. These findings have concluded that LDL-C may be suggested as a discriminating parameter between OB and MO children.

Keywords—Children, lipid parameters, obesity, trunk-to-leg fat ratio, trunk-to-appendicular fat ratio.

I. INTRODUCTION

TRUNK adiposity was known to increase visceral adiposity, which in turn increases cardiovascular and cardiometabolic risk caused by obesity. Within this context, TLFR and TAFR ratios were frequently used. They were introduced as emerging early markers of childhood obesity and future cardiometabolic risks [1]-[5].

Adipose tissue makes a great contribution to information on lipid metabolism. Routinely, it is evaluated by four biochemical parameters: TC, TRG, LDL-C, and HDL-C. These parameters are important for the evaluation of obesity. TRG and HDL-C, two of these parameters, are accepted as two of metabolic syndrome (MetS) criteria, which should be considered during the transition stage from morbid obesity to MetS [6].

Both TLFR and TAFR were significantly associated with LDL-C, HDL-C, TRG in the elderly men in Japan. An increased TAFR was significantly associated with decreased adiponectin in OB children. Trunk fat, measured as TAFR, was associated with blood pressure during childhood and adolescence. TAFR was introduced as a valuable parameter for the evaluation of body fat distribution [7]-[10].

In relation with cardiovascular diseases (CVDs) and dyslipidemia, LDLs are atherogenic and represent a strong cardiovascular risk factor. Increased levels of LDL-C are recognized as a primary risk factor for atherosclerotic CVDs [11], [12].

It would be plausible to investigate the differences in the patterns of each lipid parameter between obesity and morbid obesity. Particularly, in morbid obesity some potential alterations that are not detected in OB individuals may be helpful as possible predictors for MetS.

The aim of this study was to investigate the associations between trunk adiposity and parameters of lipid profile, particularly LDL-C during childhood.

In this study, it was expected to find a parameter, which may serve as a discriminating factor between obesity and morbid obesity. Any MetS-related parameter, which exhibits a prominent feature in morbid obesity, may serve as a possible predictor for the future development of MetS in pediatric population.

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II. PATIENTS AND METHODS

A. Patients

The study was performed on three groups. In the first group, there were healthy children with N-BMI. This group (Group 1) served as the control group in this study. Second (Group 2) and third (Group 3) groups were composed of OB and MO children, respectively. 41, 42 and 43 children constitute N-BMI, OB and MO groups. Informed consent forms were obtained. The institutional ethical committee approved the study protocol.

B. Group Classification

Tables created by World Health Organization were used to determine the N-BMI or obesity classification of the groups [13]. Children, whose age- and sex-adjusted BMI percentiles were within the range of 15 and 85 were included in the first group. This range was 95 to 99 for OB children. Children with percentiles above 99 constituted MO group.

C. Body Fat Compartments and Ratio Calculations

Device designed for Bioelectrical Impedance Analysis was used to determine fat masses as well as fat percent values of the body fat compartments. Fat mass and percent values were recorded for total body fat, trunk fat, leg fat and arm fat. Fat distributed in legs and arms in combination was defined as the appendicular fat.

Two ratios were calculated: TLFR and TAFR.

D. Anthropometric and Blood Pressure Measurements

Weight, height, waist circumference (WC), hip circumference, head circumference and neck circumference measurements were performed. SBP and DBP values were measured and recorded.

E. Laboratory Tests

Biochemical analysis including TC, TRG, LDL-C and HDL-C tests were performed.

F. Statistical Evaluation

For the evaluation of the study data, statistical package program SPSS was used. Descriptive statistics including mean values and standard deviation were calculated. Analysis of variance and post hoc Tukey tests was performed to find the statistically significant differences between the groups. Pearson's bivariate correlation analysis was performed to calculate correlation coefficient and p value for statistical significance. Partial correlations were calculated using control variables. This analysis was also used to draw plots for linear regression.

III. RESULTS

Three groups were matched in terms of age and sex ratios ($p > 0.05$). Mean age ± standard deviation values for Group 1, 2 and 3 were found as 10.9 ± 4.2, 12.1 ± 3.2, and 10.6 ± 3.5 years, respectively. The corresponding female-to-male ratios for the same groups were calculated as 1.1, 1.2, and 1.1.

Table I showed BMI, WC, TLFR and TAFR. Statistically significant increases were noted in Group 2 and Group 3 compared to Group 1 in terms of BMI and WC. Values obtained for Group 3 were also higher than those found for Group 2.

Parameters related to lipid profile were listed in Table II. Any significant difference was not observed for TC, TRG, LDL-C and HDL-C among the groups.

TABLE I
VALUES FOR BMI, WC AND TLFR AS WELL AS TAFR OF THE GROUPS (MEAN ± SD)

Parameter		Group 1 N-BMI	Group 2 OB	Group 3 MO
BMI	kg/m^2	16.6 ± 2.2	25.0 ± 3.5	28.6 ± 5.6
WC	cm	60.3 ± 8.3	83.1 ± 12.3	89.6 ± 15.9
TLFR		0.96 ± 0.26	1.04 ± 0.20	1.01 ± 0.17
TAFR		0.73 ± 0.19	0.80 ± 0.15	0.78 ± 0.12

[BMI $^{1\text{-}2\,<0.01,\ 1\text{-}3\,<0.01,\ 2\text{-}3\,<0.01}$, waist C $^{1\text{-}2\,<0.01,\ 1\text{-}3\,<0.01,\ 2\text{-}3\,<0.05}$, TAFR $^{1\text{-}2\,<0.05}$]

Statistically significant bivariate correlations were observed between LDL-C and TLFR ($r = 0.396$; $p = 0.037$) as well as TAFR ($r = 0.413$; $p < 0.029$) (Figs. 1 and 2).

TABLE II
VALUES FOR LIPID PARAMETERS OF THE GROUPS (MEAN ± SD)

Parameter		Group 1 N-BMI	Group 2 OB	Group 3 MO
TC	mg/dL	156.3 ± 29.9	159.8 ± 28.0	156.1 ± 28.3
TRG	mg/dL	84.6 ± 43.1	101.7 ± 46.0	90.8 ± 40.8
LDL-C	mg/dL	83.1 ± 28.7	89.5 ± 27.6	86.3 ± 24.4
HDL-C	mg/dL	56.2 ± 12.9	52.8 ± 12.1	51.5 ± 8.5

Fig. 1 Bivariate correlation between LDL concentrations and TLFR in MO children

The correlations "LDL-C-TLFR and LDL-C-TAFR" were checked for some control variables (SBP, DBP, TRG, HDL-C), which were accepted as MetS components.

When adjusted for SBP and DBP, partial correlations between LDL-C and TLFR ($r = 0.421$; $p = 0.032$) as well as TAFR ($r = 0.438$; $p = 0.025$) were found to be much stronger than those detected for bivariate correlations (Figs. 3 and 4). On

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the other hand, when adjusted for TRG and HDL-C, partial correlations between LDL-C and TLFR (r = 0.475; p = 0.019) as well as TAFR (r = 0.473; p = 0.020) were found to be much stronger than those detected for partial correlations calculated for accepting blood pressure values as control variables as well as bivariate correlations (Figs. 5 and 6).
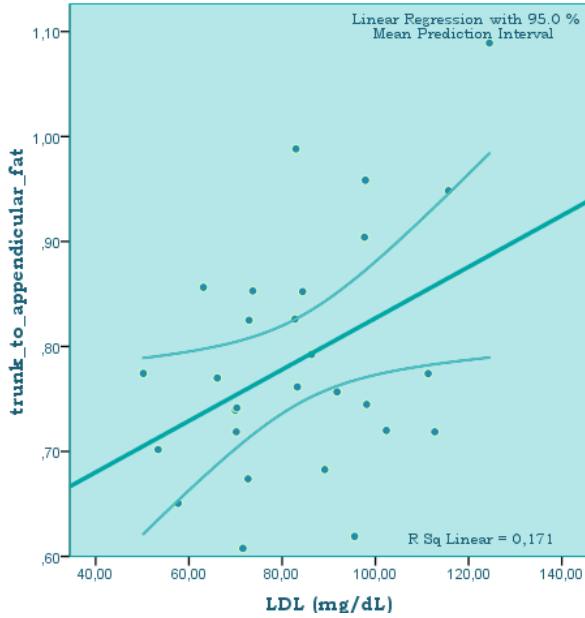

Fig. 2 Bivariate correlation between LDL concentrations and TAFR in MO children

Fig. 3 Partial correlation between LDL concentrations and TLFR in MO children controlled by SBP and DBP values

IV. Discussion

In this study, the associations between atherogenic LDL-C and trunk-to-leg as well as trunk-to-appendicular fat mass ratios were reported. Aside from simple correlations, associations emphasizing the effects of MetS components on this correlation were found by way of calculating related partial correlations.
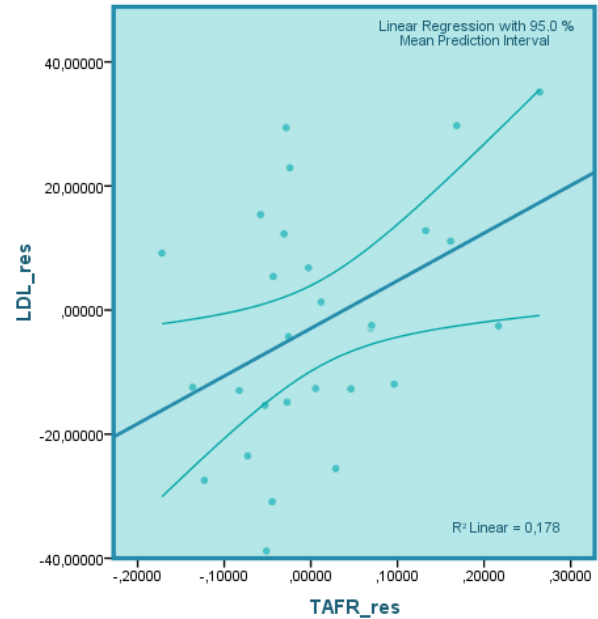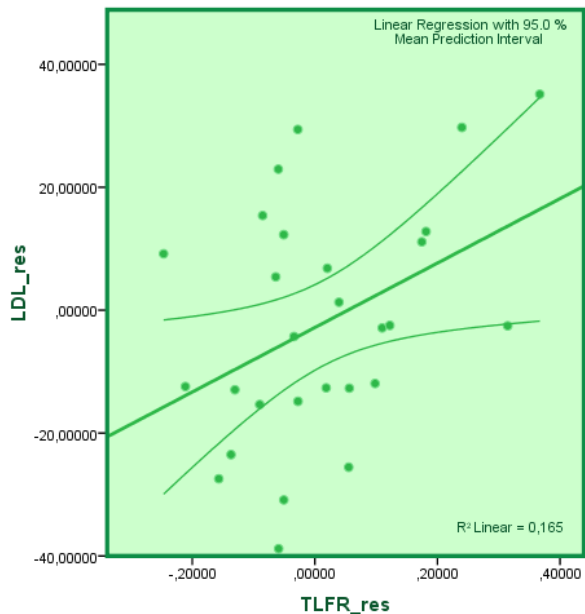

Fig. 4 Partial correlation between LDL concentrations and TAFR in MO children controlled by SBP and DBP values

Fig. 5 Partial correlation between LDL concentrations and TLFR in MO children controlled by TRG and HDL-C values
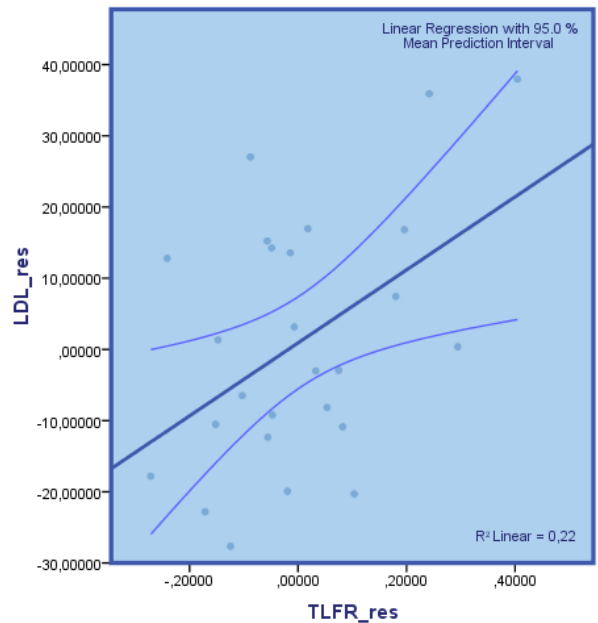
Body fat distribution is associated with cardiometabolic and cardiovascular risk in adults as well as in pediatric population. In healthy European population, larger leg fat mass is associated with a lower and trunk fat mass with a higher cardiovascular and metabolic risk [14]-[17].

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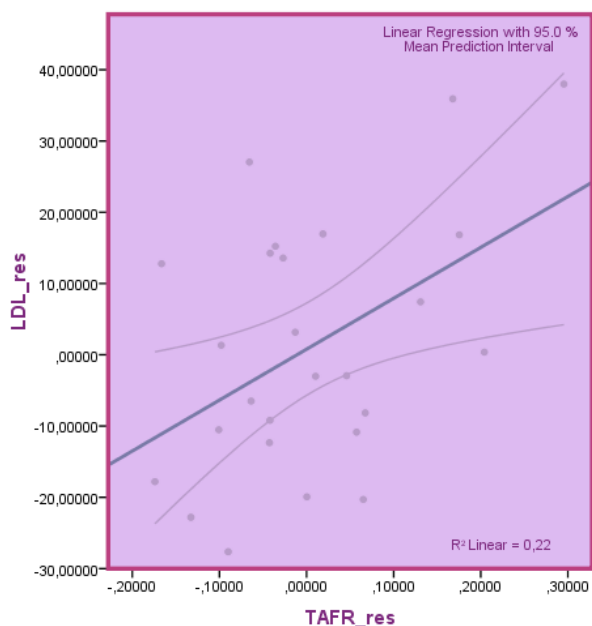Vol:16, No:10, 2022

Fig. 6 Partial correlation between LDL concentrations and trunk
TAFR in MO children controlled by TRG and HDL-C values

Higher proportion of TLFR was reported to contribute significantly to MetS. TLFR could be helpful in identifying and preventing MetS in OB population [18]. The results in our investigation agree with the findings of this Korean study.. Upon evaluation of the ratios (TLFR and TAFR), the contribution of trunk fat mass was pointed out and the associations with LDL-C were introduced.

TRG-rich lipoproteins may contribute to cardiovascular risk in patients undergoing LDL-lowering therapy [19]. The direct atherogenic effect of TRG was not confirmed [20]-[24], however, LDL-C was suggested as the main causal parameter for atherosclerotic CVDs [25]-[27].

The lack of association with HDL-C as well as TRG strengthens the findings of the study, because the state evaluated is morbid obesity, not MetS. In our study, LDL-C comes into prominence as the only lipid parameter that differs in transition from obesity to morbid obesity. Aside from simple relationships between LDL-C and trunk-related fat mass ratios, we have drawn attention to a set of correlations. The correlations were stronger Partial correlations were found to be stronger when bivariate correlations between LDL-C and TLFR as well as TAFR were controlled for SBP and DBP. It was even much stronger when they were further controlled for TRG and HDL-C. Considering the fact that each of the above control parameters was the member of MetS criteria team, these findings come out as the new insights contributing to the discussion on the tendency of morbid obesity to undergo transition towards the development of MetS, which is a cluster of conditions increasing the risk of many severe health problems such as type 2 diabetes mellitus, CVDs, and stroke.

It was suggested that LDL-C levels measured in the past may be informative for the prevention of coronary heart diseases in the future and maintaining optimal LDL-C concentrations during young adulthood may decrease the lifetime risk of developing atherosclerotic CVDs [28].

REFERENCES

[1] C. E. Cioffi, J. A. Alvarez, J. A. Welsh, and M. B. Vos, "Truncal-to-leg fat ratio and cardiometabolic disease risk factors in US adolescents: NHANES 2003-2006," *Pediatr Obes.*, vol.14, no.7, pp.e12509, Jul. 2019.
[2] L. B. Sherar, J. C. Eisenmann, P. D. Chilibeck, N. Muhajarine, S. Martin, D. A. Bailey, and A. D. Baxter-Jones AD. "Relationship between trajectories of trunk fat mass development in adolescence and cardiometabolic risk in young adulthood," *Obesity (Silver Spring)*, vol.19, no.8, pp.1699-1706, Aug 2011.
[3] E.N. Barbour-Tuck, M. C. Erlandson, L. B. Sherar, J. C. Eisenmann, N. Muhajarine, H. Foulds, H. Vatanparast, C. Nisbet, S. Kontulainen, and A. D. G. Baxter-Jones, "Relationship between trajectories of trunk fat development in emerging adulthood and cardiometabolic risk at 36 years of age," *Obesity (Silver Spring)*, vol.27, no.10, pp.1652-1660, Oct. 2019.
[4] I. Kishimoto, "Trunk-to-leg fat ratio-an emerging early marker of childhood adiposity, and future cardiometabolic risks," *Circ. J.*, vol.80, no.8, pp.1707-1709, Jul. 2016.
[5] K. Kouda, N. Dongmei, J. Tamaki, M. Iki, T. Tachiki, E. Kajita, Y. Nakatani, K. Uenishi, S. Kagamimori, Y. Kagawa, and H. Yoneshima, "Relative importance of central and peripheral adiposities on cardiometabolic variables in females: A Japanese population-based study," *J. Clin. Densitom.*, vol.20, no.1, pp.58-65, Jan-Mar 2017.
[6] P. P. Zimmet, K. G. AlbertiG, F. Kaufman, N. Tajima, M. Silink, S. Arslanian, G. Wong, P. Bennet, J. Shaw, S. Caprio, and IDF consensus group, "The metabolic syndrome in children and adolescents-an IDF consensus report," *Pediatr. Diabetes*, vol.8, no.5, pp. 299-306, 2007.
[7] K. Kouda, Y. Fujita, K. Ohara, T. Tachiki, J. Tamaki, A. Yura, J. S. Moon, E. Kajita, K. Uenishi, and M. Iki, "Associations between trunk-to-peripheral fat ratio and cardiometabolic risk factors in elderly Japanese men: baseline data from the Fujiwara-kyo Osteoporosis Risk in Men (FORMEN) study," *Environ. Health Prev. Med.*, Vol.26, no.1, pp.35, Mar 2021.
[8] K. Kouda, H. Nakamura, K. Ohara, Y. Fujita, and M. Iki, "Increased ratio of trunk-to-appendicular fat and decreased adiponectin: A population-based study of school children in Hamamatsu, Japan," J. Clin. Densitom., vol.20, no.1, pp. 66-72, Jan-Mar 2017.
[9] K. Kouda, H. Nakamura, Y. Fujita, K. Ohara, and M. Iki, "Increased ratio of trunk to appendicular fat and increased blood pressure: study of a general population of Hamamatsu children" Circ. J., vol.76, no.12, pp.2848-2854, 2012.
[10] K. Kouda, K. Ohara, Y. Fujita, H. Nakamura, and M. Iki, "Trunk-to-peripheral fat ratio predicts subsequent blood pressure levels in pubertal children with relatively low body fat-three-year follow-up study," Circ. J., vol.80, no.8, pp.1838-1845, Jul. 2016.
[11] J. Pöss, F. Custodis, C. Werner, O. Weingärtner, M. Böhm, and U. Laufs, "Cardiovascular disease and dyslipidemia: beyond LDL," *Curr. Pharm. Des.*, vol.17, no.9, pp.861-70, 2011.
[12] M. Rossi, E. Fabris, D. Barbisan, L. Massa, and G. Sinagra, "Lipid-lowering drug therapy: Critical approach for implementation in clinical practice," *Am. J. Cardiovasc. Drugs.*, 2021 Sep 13. Epub ahead of print.
[13] WHO World Health Organization (WHO). The WHO Child Growth Standards. 2016 June. Access: http://www.who.int/childgrowth/en/
[14] G. C. Chen, R. Arthur, N. M. Iyengar, V. Kamensky, X. Xue, S. Wassertheil-Smoller, M. A. Allison, A. H. Shadyab, R. A. Wild, Y. Sun, H. R. Banack, J. C. Chai, J. Wactawski-Wende, J. E. Manson, M. L. Stefanick, A. J. Dannenberg, T. E. Rohan, and Q. Qi, "Association between regional body fat and cardiovascular disease risk among postmenopausal women with normal body mass index," *Eur. Heart J.*, vol.40, no.34, pp.2849-2855, Sep. 2019.
[15] Y. Yan, J. Liu, X. Zhao, H. Cheng, G. Huang, J. Mi; China Child and Adolescent Cardiovascular Health (CCACH) Study Research Group, "Regional adipose compartments confer different cardiometabolic risk in children and adolescents: The China Child and Adolescent Cardiovascular Health Study," *Mayo Clin. Proc.*, vol.94, no.10, pp.1974-1982, Oct. 2019.
[16] N. Z. Mirhosseini, S. Shahar, M. Ghayour-Mobarhan, M. R. Parizadeh, N. A. Yusoff, and M. T. Shakeri, "Body fat distribution and its association with cardiovascular risk factors in adolescent Iranian girls," *Iran J. Pediatr.*, vol.22, no.2, pp.197-204, Jun 2012.
[17] W. Boorsma, M. B. Snijder, G. Nijpels, C. Guidone, A. M. Favuzzi, G.

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Mingrone, P. J. Kostense, R. J. Heine, and J. M. Dekker, "Body composition, insulin sensitivity, and cardiovascular disease profile in healthy Europeans," *Obesity (Silver Spring),* vol.16, no.12, pp.2696-2701, Dec. 2008.

[18] Y. M. Kim, S. Kim, S. H. Kim, and Y. J. Won, "Clinical and body compositional factors associated with metabolic syndrome in obese Koreans: A cross-sectional study," *Metab. Syndr. Relat. Disord.,* vol.16, no.6, pp.290-298, Aug. 2018.

[19] H. N. Ginsberg, C. J. Packard, M. J. Chapman, J. Borén, C. A. Aguilar-Salinas, M. Averna, B. A. Ference, D. Gaudet, R. A. Hegele, S. Kersten, G. F. Lewis, A. H. Lichtenstein, P. Moulin, B. G. Nordestgaard, A. T. Remaley, B. Staels, E. S. G. Stroes, M. R. Taskinen, L. S. Tokgözoğlu, A. Tybjaerg-Hansen, J. K. Stock, and A. L. Catapano, "Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies-a consensus statement from the European Atherosclerosis Society," *Eur. Heart J.,* 2021 Sep 2:ehab551. Epub ahead of print.

[20] B. G. Nordestgaard, "Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease: new insights from epidemiology, genetics, and biology," *Circ. Res.,* vol.118, no.4, pp.547–563, Feb. 2016.

[21] A. Chait, H. N. Ginsberg, T. Vaisar, J. W. Heinecke, I. J. Goldberg, and K. E. Bornfeldt, "Remnants of the triglyceride-rich lipoproteins, diabetes, and cardiovascular disease," *Diabetes,* vol.69, no.4, pp.508–516, Apr. 2020.

[22] K. Nakajima, and A. Tanaka, "Atherogenic postprandial remnant lipoproteins; VLDL remnants as a causal factor in atherosclerosis," *Clin. Chim. Acta,* vol.478, pp.200–215, Mar. 2018.

[23] M. Farnier, M. Zeller, D. Masson, and Y. Cottin, "Triglycerides and risk of atherosclerotic cardiovascular disease: an update," *Arch. Cardiovasc. Dis.,* vol.114, no.2, pp.132–139, Feb. 2021.

[24] E. K. Duran, and A. D. Pradhan, "Triglyceride-rich lipoprotein remnants and cardiovascular disease," *Clin. Chem.,* vol.67, no.1, pp.183–196, Jan. 2021.

[25] J. Bore´n, M. J. Chapman, R. M. Krauss, C. J. Packard, J. F. Bentzon, C. J. Binder, M. J. Daemen, L. L. Demer, R. A. Hegele, S. J. Nicholls, B. G. Nordestgaard, G. F. Watts, E. Bruckert, S. Fazio, B. A. Ference, I. Graham, J. D. Horton, U. Landmesser, U. Laufs, L. Masana, G. Pasterkamp, F. J. Raal, K. K. Ray, H. Schunkert, M. R. Taskinen, B. van de Sluis, O. Wiklund, L. Tokgozoglu, A. L. Catapano, and H. N. Ginsberg, "Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel," *Eur. Heart J.,* vol.41, no. 24, pp.2313–2330, Jun. 2020.

[26] M. S. Brown, and J. L. Goldstein, "The SREBP pathway: regulation of cholesterol metabolism by proteolysis of a membrane-bound transcription factor," *Cell,* vol.89, no.3, pp. 331–340, May 1997.

[27] B. A. Ference, H. N. Ginsberg, I. Graham, K. K. Ray, C. J. Packard, E. Bruckert, R. A. Hegele, R. M. Krauss, F. J. Raal, H. Schunkert, G. F. Watts, J. Bore´n, S. Fazio, J. D. Horton, L. Masana, S. J. Nicholls, B. G. Nordestgaard, B. van de Sluis, M. R. Taskinen, L. Tokgozoglu, U. Landmesser, U. Laufs, O. Wiklund, J. K. Stock, M. J. Chapman, and A. L. Catapano, "Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel," *Eur. Heart J.,* vol.38, no.32, pp.2459–2472, Aug. 2017.

[28] Y. Zhang, M. J. Pletcher, E. Vittinghoff, A. M. Clemons, D. R. Jacobs Jr, N. B. Allen, A. Alonso, B. K. Bellows, E. C. Oelsner, A. Zeki Al Hazzouri, D. S. Kazi, S. D. de Ferranti, and A. E. Moran, "Association between cumulative low-density lipoprotein cholesterol exposure during young adulthood and middle age and risk of cardiovascular events," *JAMA Cardiol.,* 2021 Sep 22. Epub ahead of print.