Branched-Chain amino acids intake is negatively related to body adiposity in individuals at cardiometabolic risk

**ABSTRACT**

**Objective**
To assess the relationship between branched-chain amino acids intake in the current diet and the metabolic and body adiposity markers in a population at cardiovascular risk.

**Methods**
This is a cross-sectional study with 282 adults and elderly people from the Cardiovascular Health Care Program of the Universidade Federal de Viçosa. Sociodemographic, anthropometric and body composition data, as well as metabolic biomarkers were collected using standardized protocols. Dietary intake of branched amino acids was assessed using a 24-hour recall.

**How to cite this article**
Almeida AP, Fortes FS, Silveira BKS, Reis NA, Hermsdorff HHM. Branched-Chain amino acids intake is negatively related to body adiposity in individuals at cardiometabolic risk. Rev Nutr. 2020;33:e190208. https://doi.org/10.1590/1678-9865202033e190208
Results
Individuals with a higher branched-chain amino acids intake (≥2.6g/day, median value) had lower body fat (29.6 vs 32.2%; \(p=0.019\)) and higher serum ferritin (113.2 vs. 60.1mg/dL; \(p=0.006\)) and uric acid concentrations (4.4 vs. 4.0; \(p=0.023\)). In addition, a lower prevalence of overweight and excessive abdominal fat (\(p<0.05\)) was found in the individuals with higher branched-chain amino acids intake. They also had a higher daily intake of fiber, copper, zinc, magnesium, and iron, as well as a lower intake of total lipids.

Conclusion
In the present study, the intake of branched amino acids is negatively related to total and central adiposity, but more studies are needed to fully elucidate this possible relationship. (Brazilian Registry of Clinical Trials, code RBR-5n4y2g).

Keywords: Cardiovascular diseases. Feeding behavior. Isoleucine. Leucine. Overweight. Valine.

I N T R O D U C T I O N

Excess weight is the main risk factor for the development of Cardiovascular Diseases (CVD), being one of the biggest public health problems worldwide. It should be noted that eating habits are an important modifiable risk factor for such changes [1-5].

In this context, dietary Branched-Chain Amino Acids (BCAA), such as leucine, isoleucine, and valine, are essential for a healthy cellular and organ function [1,6-9]. The impact of BCAA intake on cardiometabolic risk factors, such as overweight and body fat, has been investigated in previous studies [10-12].

A recent meta-analysis [13] reported that a higher dietary intake of BCAA was inversely related to the prevalence of overweight and obesity in adults. The possible mechanisms for the effect of...
BCAA on body weight are still poorly understood, however it is known that BCAA, especially leucine, can act in ways to control cellular metabolism, providing a decrease in food intake and body weight [14-16]. However, few studies have assessed BCAA intake, especially in the Brazilian population and, to date, few studies have assessed the relationship of these nutrients with metabolic and adiposity markers in a population at cardiovascular risk [10]. Therefore, the aim of this article is to assess the relationship between BCAA intake, included in the current diet, and metabolic and adiposity biomarkers in a population at cardiovascular risk.

**METHODS**

A cross-sectional study with 282 patients included in the *Programa de Atenção à Saúde Cardiovascular da Universidade Federal de Viçosa* (PROCARDIO-UFV, Cardiovascular Health Care Program of the *Universidade Federal de Viçosa*), who had their first medical appointment until July 2016, with complete data concerning their BCAA intake. The PROCARDIO-UFV performs nutritional intervention to promote cardiovascular health in the academic community of the *Universidade Federal de Viçosa* (UFV), registered in the *Registro Brasileiro de Ensaios Clínicos* (ReBEC, Brazilian Registry of Clinical Trials), code RBR-5n4y2g [17].

The criteria for inclusion in the program are: age ≥20 years; both sexes; being a student, worker, or a dependent family member of UFV workers; present cardiovascular diseases or the occurrence of cardiometabolic risk factors such as overweight or obesity (Body Mass Index (BMI) ≥25 or 27kg/m²) or/and dyslipidemia (Triglycerides (TG) ≥150mg/dL; Total Cholesterol (TC) ≥ 200 mg/dL or/and High Density Lipoprotein (HDL-c) <40 or <50mg/dL for men and women, respectively), or/and blood pressure ≥130/≥85mmHg or diagnosed arterial hypertension or/and fasting blood glucose ≥100mg/dL or diagnosed diabetes mellitus. The data used were related to the first medical consultation at the PROCARDIO-UFV. Among the 417 users of the program, 282 were selected for having complete data on their BCAA intake.

The study was approved by the UFV’s Human Research Ethics Committee (Protocol number 066/2012/CEPH), in accordance with Resolution 466/2012 of the *Conselho Nacional de Saúde* (CNS, National Health Council/Ministry of Health, Brazil) and with the principles of the Helsinki Declaration. All study participants read and signed the informed consent form.

The participants responded to a 24-hour food recall (R24h), reporting all the food and drinks consumed the day before (weekday or weekend) the medical consultation, as well as their quantities. In the present study, the daily intake of calories, carbohydrates, proteins, lipids, fibers, vitamins A, C, D and E, selenium, copper, manganese, magnesium, zinc, calcium, iron, and sodium were assessed using the DietPRO software, version 5.0i [18].

The determination of BCAA intake (leucine, isoleucine, and valine) was performed using the National Nutrient Database for Standard Reference (USDA, 2015), as such data are not available in the Brazilian tables [19]. The foods reported in the R24h and not listed in the USDA table had their estimated composition considering the foods that showed nutritional composition and similar cooking methods. The preparations were broken down into their constituent ingredients and, if there was no choice of composition for the prepared food, the composition of the raw foods was used. The intake of each amino acid was performed in an electronic spreadsheet (Microsoft Excel®), developed especially for this purpose.
Anthropometric measurements (body weight, height, hip, and waist circumference) were measured using a standardized, previously established protocol [20]. Waist-to-Hip (WHR) and Waist-to-Height (WHTR) ratios were calculated. Total Body Fat (BF%) was assessed by tetrapolar electrical bioimpedance (Biodynamics 310 model, Washington, USA), according to the manufacturer's protocol. Excess weight was classified according to a BMI greater than or equal to 25 (adults) and 27 (elderly) kg/m$^2$ [21,22]. Excess abdominal fat was assessed using waist circumference values equal to or greater than 80 cm and 90 cm for women and men, respectively [23].

Fasting blood glucose, triglycerides, total and fraction cholesterol (Low Density Lipoprotein [LDL-c], High Density Lipoprotein [HDL-c], and Very Low Density Lipoprotein [VLDL-c]), ferritin, uric acid, total leukocytes, and Ultrasensitive C-Reactive Protein (Us-CRP) were determined at the Clinical Analysis Laboratory of the Health Department of the UFV, according to its standardized protocol.

Insulin resistance was estimated using the Homeostasis-Insulin Resistance Model (HOMA-IR), calculated as follows: HOMA-IR=[fasting glucose (mmol/L)] fasting insulin (μIU/ml)/22.5 and the triglycerides/glycemia (TyG) index, calculated using the formula: Ln [fasting triglycerides (mg/dl)xfasting glycemia (mg/dL)/2] [24].

The age, sex, educational level, relationship to the UFV, income, smoking, regular practice of physical activities, and intake of alcoholic beverages variables were collected by interviewing participants through a questionnaire.

The results were presented in absolute and relative frequencies, mean±standard deviation, and/or median (25$^{th}$–75$^{th}$ percentile). The normality of each variable was assessed using the Kolmogorov-Smirnov test. To assess the possible association of BCAA intake and other variables of interest, the sample of the present study was categorized according to the median BCAA intake (2.6g/day). The use of the median as a cut-off point for statistical analysis has been used before [25,26]. All food intake variables were adjusted for total caloric intake using the residual method [27].

The Student t and Mann-Whitney-U tests were used to compare the two groups, when appropriate. Pearson's Chi-square, linear trend chi-square or Fischer's exact test were used when appropriate to verify associations between sociodemographic and body composition variables, and the median BCAA intake. Spearman's correlation was used to assess the relationship between BCAA intake and other nutrients with variables of interest. All statistical analyses were performed using the SPSS 21.0® program, considering the level of statistical significance as 5%.

**RESULTS**

Of the individuals who had a higher BCAA intake (≥2.6g/day), 28.4% (n=40) were male, 28.2% (n=40) were employees of the university, and 75.9% (n=107) were not smokers (Table 1). Regarding food intake, those with a BCAA intake ≥2.6g/day had a higher intake of fibers, copper, zinc, magnesium, and iron (Table 2).

Individuals with the highest BCAA intake (≥2.6g/day) had higher concentrations of ferritin and uric acid, in addition to lower body fat and HDL-c values (Table 3).

Moreover, there was a higher prevalence of overweight and excessive abdominal fat in individuals with a lower BCAA intake (Figure 1). In addition, BCAA intake was negatively correlated with body fat (Figure 2).
Table 1. Sociodemographic characteristics, according to the Branched-Chain Amino Acids intake (median value).

| Variable                              | Lower BCAA intake (<2.6g/day (n=139)) | Higher BCAA intake (≥2.6g/day (n=142)) | p-values |
|---------------------------------------|---------------------------------------|---------------------------------------|----------|
|                                       | n     | %       | n     | %       |          |
| Sex                                   |       |         |       |         |          |
| Male                                  | 75    | 53.9    | 40    | 28.4    | <0.001*  |
| Female                                | 64    | 46.1    | 101   | 71.6    |          |
| Age                                   |       |         |       |         | 0.084    |
| Adults                                | 115   | 82.7    | 114   | 80.9    |          |
| Elderly individuals                   | 24    | 17.3    | 27    | 19.1    |          |
| Educational level                     |       |         |       |         | 0.260    |
| Illiterate- incomplete high school    | 26    | 19.7    | 36    | 27.1    |          |
| Complete high school                  | 26    | 20.5    | 19    | 14.3    |          |
| Complete or incomplete undergraduate  | 79    | 59.8    | 78    | 58.6    |          |
| Relationship to the UFV               |       |         |       |         | 0.032*   |
| Worker                                | 61    | 44.5    | 40    | 28.2    |          |
| Student                               | 50    | 36.5    | 62    | 43.6    |          |
| Worker’s dependent                    | 26    | 19.0    | 40    | 28.2    |          |
| Marital status                        |       |         |       |         | 0.159    |
| Single                                | 56    | 40.6    | 66    | 46.8    |          |
| Legally married or in a stable relation | 74  | 53.6    | 61    | 43.3    |          |
| Widowed or separated/divorced         | 8     | 5.8     | 14    | 9.9     |          |
| Income                                |       |         |       |         | 0.610    |
| Did not state                         | 11    | 7.9     | 16    | 11.4    |          |
| Up to 2 minimum wages                 | 34    | 24.7    | 32    | 22.9    |          |
| 2 to 4 minimum wages                  | 52    | 37.7    | 50    | 35.7    |          |
| 4 to 10 minimum wages                 | 33    | 23.9    | 38    | 27.1    |          |
| More than 10 minimum wages            | 8     | 5.8     | 4     | 2.9     |          |
| Smoking                               |       |         |       |         | 0.007*   |
| Never                                 | 81    | 58.3    | 107   | 75.9    |          |
| Ex-smoker                             | 51    | 36.7    | 29    | 20.6    |          |
| Smoker                                | 7     | 5.0     | 5     | 3.5     |          |
| Physical activities                   |       |         |       |         | 0.513    |
| No                                    | 63    | 45.7    | 67    | 47.2    |          |
| Yes                                   | 75    | 54.3    | 75    | 52.8    |          |
| Alcoholic beverage intake             |       |         |       |         | 0.384    |
| Does not drink                        | 51    | 37.2    | 63    | 45.3    |          |
| Socially                              | 82    | 59.9    | 73    | 52.5    |          |
| One or more drinks per day            | 4     | 2.9     | 3     | 2.2     |          |

Note: *p-values: <0.05 using the Chi-Square test.

DISCUSSION

Amino acids can play an important role in the development of CVD [10,28-35]. This relationship can be justified by the food source of these nutrients (legumes, oilseeds, eggs, fish, meat, milk, and dairy products). In fact, the cardiometabolic effects related to animal protein food sources are probably better explained by the non-protein components than by the protein components of these foods [36-38].
Table 2. Current dietary habits according to the branched-chain amino acids intake (median value).

| Intake/day | Lower BCAA intake <2,6g/day (n=139) | Higher BCAA intake ≥2,6g/day (n=142) | p-values |
|------------|-------------------------------------|--------------------------------------|----------|
| **Macronutrients** | | | |
| Carbohydrates (%CI) | 51.4 46.5-58.6 | 54.9 47.3-60.3 | 0.061 |
| Proteins (%CI) | 17.4 14.7-20.7 | 18.7 15.0-21.9 | 0.068 |
| Total lipids (%CI) | 30.3 24.4-34.9 | 26.8 23.0-33.4 | 0.008* |
| Fibers (g) | 21.5 15.6-29.9 | 25.3 17.5-33.5 | 0.019* |
| **Micronutrients** | | | |
| Vitamin E (mg) | 5.0 3.4-6.4 | 4.9 3.7-6.8 | 0.329 |
| Vitamin A (μg) | 502.8 298.8-790.9 | 464.1 297.8-620.8 | 0.211 |
| Vitamin C (mg) | 45.2 25.6-129.9 | 58.3 28.9-140.5 | 0.168 |
| Vitamin D (UI) | 30.2 16.3-87.3 | 32.5 18.6-70.1 | 0.813 |
| Selenium (μg) | 90.9 75.7-106.8 | 92.9 74.3-112.3 | 0.400 |
| Copper (mg) | 1.9 1.7-2.1 | 2.0 1.9-2.3 | 0.000* |
| Manganese (mg) | 3.8 3.0-4.9 | 3.7 2.7-5.3 | 0.994 |
| Zinc (mg) | 10.1 8.3-12.1 | 10.9 8.5-13.7 | 0.019* |
| Magnesium (mg) | 234.5 198.5-273.1 | 251.2 212.5-306.5 | 0.018* |
| Iron (mg) | 9.3 7.7-11.7 | 10.4 8.6-12.6 | 0.006* |
| Sodium (mg) | 2368.9 2056.7-2952.0 | 2336.9 1984.9-2692.7 | 0.144 |

Note: *p<0.05. Data presented median and quartiles (p25-p75).

Table 3. Adiposity indicators and cardiometabolic risk markers, according to branched-chain amino acids intake (median value).

| Intake/day | Lower BCAA intake <2,6g/day (n=139) | Higher BCAA intake ≥2,6g/day (n=142) | p-values |
|------------|-------------------------------------|--------------------------------------|----------|
| BMI (kg/m²) | 28.74 5.49 | 28.97 5.56 | 0.723 |
| Waist circumference (cm) | 96.24 14.84 | 97.35 14.14 | 0.525 |
| Waist-to-hip ratio | 0.92 0.09 | 0.93 0.09 | 0.627 |
| Waist-to-height ratio | 0.92 0.09 | 0.93 0.09 | 0.627 |
| Body fat (%) | 32.2 7.1 | 29.6 8.7 | 0.019* |
| Total leucocytes (1.000/mm³) | 6,270 1,551 | 6,375 1,837 | 0.647 |
| Ferritin (μg/L) | 60.1 26.6-152 | 113.2 56.1-230.7 | 0.006* |
| Urea (mg/dL) | 29.0 14.8-37.0 | 32.0 25.0-38.0 | 0.227 |
| Uric acid (mg/dL) | 4.0 3.2-4.8 | 4.4 3.5-5.8 | 0.023* |
| Blood glucose (mg/dL) | 90.0 83.0-100.7 | 93.0 85.0-108 | 0.122 |
| HOMA-IR | 2.1 1.3-2.9 | 2.2 1.3-3.3 | 0.370 |
| TyG index | 4.78 0.3 | 4.8 0.3 | 0.762 |
| Total cholesterol (mg/dL) | 210 41.1 | 200 44.2 | 0.074 |
| LDL-c (mg/dL) | 128 37.2 | 120 38.2 | 0.084 |
| HDL-c (mg/dL) | 48.0 39.0-58.0 | 43.1 36.0-54.0 | 0.040* |
| VLDL-c (mg/dL) | 27.90 20.4-40.0 | 26.4 19.3-41.4 | 0.451 |
| Total cholesterol / HDL-c | 4.34 3.57-5.07 | 4.34 3.45-5.47 | 0.597 |
| LDL-c / HDL-c | 2.55 1.99-3.34 | 2.59 1.99-3.38 | 0.883 |
| Triglycerides (mg/dL) | 147 100-210 | 139 101-238 | 0.956 |
| C-reactive protein (mg/dL) | 1.92 0.68-5.09 | 1.51 0.43-3.90 | 0.344 |

Note: *p<0.05. Data presented mean ± SD (standard deviation) or median and quartiles (p25-p75), when appropriate.

BCAA: Branched-Chain Amino Acids; BMI: Body Mass Index; HOMA-IR: Homeostasis-Insulin Resistance Model; LDL-c: Low Density Lipoprotein; HDL-c: High Density Lipoprotein; TyG: Triglycerides/Blood Glucose Index; VLDL-c: Very Low Density Lipoprotein.
The first relevant result of this study was the higher body fat (%) in those individuals with a lower BCAA intake. Other results also were towards the inverse relationship between BCAA intake and body adiposity, as well as the results of other cross-sectional studies, carried out in Brazil, China, Japan, the United Kingdom and the United States [10,14,15,39]. Probably, leucine is the most influential BCAA regarding energy balance [40]. When these amino acids are released into the gastrointestinal tract after the hydrolysis of dietary proteins, the production of anorexigenic hormones is stimulated and thus the production of orexigenic hormone is inhibited. In addition, leucine induces the activation of the pro-opiomelanocortin, hypothalamic neuropeptide, as well as negatively regulating neuropeptide Y signaling.

In the central nervous system, these signals can affect food intake, increasing satiation and satiety. Also, leucine can act directly on adipocyte, liver, and muscle cells, influencing the expression...
of fatty acid synthase (adipocytes) and lipid catabolism (adipocytes, liver and muscle cells), favoring, subsequently, the reduction of adiposity [40]. Leucine is also a potent activator of mTOR, a serine/threonine kinase involved in many cellular processes, which includes protein synthesis and cell growth. Central leucine administration can increase hypothalamic mTOR signaling and decrease food intake and body weight [14]. Another possible mechanism for the effect of BCAA on body weight is the improvement of glucose tolerance, since impaired glucose tolerance may be related as one of the possible causes of obesity [15].

As shown in Table 2, individuals with a higher BCAA intake also had a higher intake of fibers and minerals (iron, copper, zinc, and magnesium) \( (p<0.05) \), as well as a lower intake of total fats \( (p<0.05) \). We also observed a negative correlation between the percentage of body fat and the current intake of fibers, iron, zinc, and copper \( (r=-0.16 \text{ and } p=0.02; \ r=-0.206 \text{ and } p=0.003; \ r=-0.16 \text{ and } p=0.03; \ r=-0.16 \text{ and } p=0.02, \text{ respectively}) \). Therefore, the lower body fat in these individuals with a higher BCAA intake may also be related to a better quality of food in general.

Still, in the present study, serum ferritin and uric acid concentrations were significantly higher in the individuals with higher BCAA intake. However, these concentrations, even though higher, are still within normal values. They do not represent an increase in the cardiometabolic risk for these individuals [20,41,42].

In addition, HDL-c concentrations were lower in those individuals with higher BCAA intake. The opposite result was observed in the study by Cocate et al., in which HDL-c concentrations were higher in the third tertile, when compared to the first tertile of BCAA intake [10]. BCAA can act as signaling molecules to control energy homeostasis involving the disposition of glucose and lipid metabolism. Any changes in their intake could also lead to changes in the lipid profile [1,43], but additional studies that assess this relationship are necessary.

The present study has some limitations. First, its cross-sectional design makes impossible to infer about a cause-effect relationship in the results presented. However, the authors used the statistical tests that are suitable for this type of study and performed the interpretations of the results with scientific relevance. Another factor is the use of only a 24-hour recall, as it provides information only about the individual’s current and unusual intake. However, this food survey has been used in epidemiological studies that evaluated the relation between food intake and cardiometabolic risk factors with promising results and acceptance by the scientific community [44-47].

**CONCLUSION**

The results of the present study indicate that a higher BCAA intake (>2.6g/day) has an inverse association with excess weight and body fat, in addition to a positive association with biomarkers (ferritin and uric acid) in individuals at cardiometabolic risk. Further studies are needed to assess the relationship between BCAA intake and chronic diseases.

**ACKNOWLEDGMENTS**

To the Programa de Atenção à Saúde Cardiovascular da Universidade Federal de Viçosa (PROCARDIO-UFV, Cardiovascular Health Care Program of the Universidade Federal de Viçosa) patients, for their participation in this study, and for the professionals for the excellent support they provided. HHM Hermsdorff has a Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, National Council for Scientific and Technological Development) Research Productivity fellowship (1D-level).
CONTRIBUTORS

AP ALMEIDA contributed to research design, obtaining data, analysis and interpretation of data, writing the article and critical review of the manuscript for important intellectual content. FS FORTES contributed to research design, obtaining data, analysis and interpretation of data and writing the article. BKS SILVEIRA and NA REIS contributed to research design and data collection. HHM HERMSDORFF contributed to research design, analysis and interpretation of data and critical review of the manuscript for important intellectual content.

REFERENCES

1. Ruiz-Canela M, Toledo E, Clish CB, Hruby A, Liang L, Salas-Salvadó J, et al. Plasma branched-chain amino acids and incident cardiovascular disease in the PREDIMED trial. Clin Chem. 2016;62(4):582.

2. Dégano IR, Marrugat J, Grau M, Salvador-González B, Ramos R, Zamora A, et al. The association between education and cardiovascular disease incidence is mediated by hypertension, diabetes, and body mass index. Sci Rep. 2017;7(1):12370.

3. Zhao X, Han Q, Liu Y, Sun C, Gang X, Wang G. The Relationship between branched-chain amino acid related metabolomic signature and insulin resistance: a systematic review. J Diabetes Res. 2016;2794591.

4. Cummings NE, Williams EM, Kasza I, Konon EN, Schaid MD, Schmidt BA, et al. Restoration of metabolic health by decreased consumption of branched-chain amino acids. J Physiol. 2018;596(4):623-45.

5. Zheng Y, Ceglarek U, Huang T, Li L, Rood DH, et al. Weight-loss diets and 2-y changes in circulating amino acids in 2 randomized intervention trials. Am J Clin Nutr. 2016;103(2):505-11.

6. Siomkajlo M, Rybka J, Mierzchala-Pasierb M, Gamian A, Stankiewicz-Olczyk J, Bolanowski M, et al. Specific plasma amino acid disturbances associated with metabolic syndrome. Endocrine. 2017;58(3):553-62.

7. Rousseau M, Guénard F, Garneau V, Allam-Ndoul B, Lemieux S, Péruesse L, et al. Associations between dietary protein sources, plasma BCAA and short-chain acylcarnitine levels in adults. Nutrients. 2019;11(1):173.

8. Lynch CJ, Adams SH. Branched chain amino acids in metabolic signalling and insulin resistance. Nat Rev Endocrinol. 2014;10(12):723-36.

9. Giglio BM, Schincaglia RM, Silva AS, Fazani ICS, Monteiro PA, Mota JF, et al. Whey protein supplementation compared to collagen increases blood nesfatin concentrations and decreases android fat in overweight women: a randomized double-blind study. Nutrients. 2019;11(9):pii:E2051. https://doi.org/10.3390/nu11092051
17. Ministério da Saúde (Brasil). Registro Brasileiro de Ensaios Clínicos. Brasília: Ministério; 2013 [citado 2 fev 2017]. Disponível em: http://www.ensaiosclinicos.gov.br/rg/RBR-5n4y2g/.

18. Dietpro. Dietpro: soluções em Nutrição. Viçosa: Dietpro; 2019.

19. Department of Agriculture (United States). FoodData Central. Washington: Department; 2016 [cited 2016 Aug 8]. Available from: https://fdc.nal.usda.gov/

20. Silva HA, Carraro JCC, Bressan J, Hermsdorff HHM. Relação entre ácido úrico e síndrome metabólica em uma população com risco cardiometabólico. Einstein (Sao Paulo). 2015;13(2):202-8.

21. World Health Organization. Obesity: preventing and managing the global epidemic: report of a World Health Organization Consultation. Geneva: Organization; 2000(284):256.

22. Lipschitz DA. Screening for nutritional status in the elderly. Prim Care. 1994;21:55-67.

23. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120(16):1640-5.

24. Mohammadabadi F, Vafaiyan Z, Hosseini SM, Aryaei M, Eshghinia S. Assessment of insulin resistance with two methods: HOMA-IR and TyG index in Iranian obese women. Iran J Diabetes Obes. 2014;6(1):23-7.

25. Carraro JC, Hermsdorff HH, Mansego ML, Zulet MÁ, Milagro FI, Bressan J, et al. Higher fruit intake is related to TNF-α hypomethylation and better glucose tolerance in healthy subjects. J Nutrigenet Nutrigenomics. 2016;9(2-4):95-105.

26. Santos Epifânio AP, Balbino KP, Jorge MP, Ribeiro SMR, Moreira AVB, Oliveira JM, et al. Metabolic, inflammatory and oxidative stress markers in the nitric oxide variation of hemodialysis subjects. Nutr Hosp. 2018;35(1):176-84.

27. Willett W. Overview of nutritional epidemiology. In: Willett W. Nutritional epidemiology. 2nd. ed. New York: Oxford University Press; 1998:514.

28. Shin AC, Fasshauer M, Filatova N, Grundell LA, Zeliger E, Zhou JY, et al. Brain insulin lowers circulating BCAA levels by inducing hepatic BCAA catabolism. Cell Metab. 2014;20(5):898-909.

29. Du X, You H, Li Y, Wang Y, Hui P, Qiao B, et al. Relationships between circulating branched chain amino acid concentrations and risk of adverse cardiovascular events in patients with STEMI treated with PCI. Sci Rep. 2018;8:15809.

30. Prodhan UK, Milan AM, Thorstensen EB, Barnett MPG, Stewart RAH, Benatar JR, et al. Altered dairy protein intake does not alter circulatory branched chain amino acids in healthy adults: a randomized controlled trial. Nutrients. 2018;10(10):1510.

31. Zheng Y, Li Y, Qi Q, Hu X, Liang G, Zhang J, et al. Cumulative consumption of branched-chain amino acids and incidence of type 2 diabetes. Int J Epidemiol. 2016;45(5):1482-92.

32. Mangge H, Zelzer S, Prüller F, Schnedl WJ, Weihauer D, Enko D, et al. Branched-chain amino acids are associated with cardiometabolic risk profiles found already in lean, overweight and obese young. J Nutr Biochem. 2016;32:123-7.

33. Grajeda-Iglesias C, Aviram M. Specific amino acids affect cardiovascular diseases and atherogenesis via protection against macrophage foam cell formation: review article. Rambam Maimonides Med J. 2018;9(3):e0022. https://doi.org/10.5041/RMMJ.10337

34. Palmer ND, Okut H, Hsu FC, Ng MCY, Chen YDI, Goodarzi M, et al. Metabolomics identifies distinctive metabolite signatures for measures of glucose homeostasis: the Insulin Resistance Atherosclerosis Family Study (IRAS-FS). J Clin Endocrinol Metab. 2018;103(5):1877-88.

35. Tobis DK, Lawler PR, Harada PH, Demler OV, Ridker PM, Manson JE, et al. Circulating branched-chain amino acids and incident cardiovascular disease in a prospective cohort of US women. Circ Genom Precis Med. 2018;11(4):e002157. https://doi.org/10.1161/CIRCGEN.118.002157.

36. Merz B, Frommerierz L, Rist MJ, Kulling SE, Bub A, Watzl B. Dietary pattern and plasma BCAA-variations in healthy men and women: results from the KarMen Study. Nutrients. 2018;10(5):623.

37. Briggs MA, Petersen KS, Kris-Etherton PM. Saturated fatty acids and cardiovascular disease: replacements for saturated fat to reduce cardiovascular risk. Healthcare. 2017;5(2):29.
38. Haring B, Gronroos N, Nettleton JA, von Ballmoos MCW, Selvin E, et al. Dietary protein intake and coronary heart disease in a large community based cohort: results from the Atherosclerosis Risk in Communities (ARIC) Study. Plos One. 2014;9(10):e109552. https://doi.org/10.1371/journal.pone.0109552

39. Jennings A, MacGregor A, Pallister T, Spector T, Cassidy A. Associations between branched chain amino acid intake and biomarkers of adiposity and cardiometabolic health independent of genetic factors: a twin study. Int J Cardiol. 2016;223:992-8.

40. McAllan L, Cotter PD, Roche HM, Korpela R, Nilaweera KN. Impact of leucine on energy balance. J Physiol Biochem. 2013;69(1):155-63.

41. Klip IT, Voors AA, Swinkels DW, Bakker SJ, Kootstra-Ros JE, Lam CS, et al. Serum ferritin and risk for new-onset heart failure and cardiovascular events in the community. Eur J Heart Fail. 2017;19(3):348-56.

42. Zacharski LR, Shamayeva G, Chow BK, DePalma RG. Ferritin and percent transferrin saturation levels predict type 2 diabetes risk and cardiovascular disease outcomes. Curr Diabetes Rev. 2017;13(4):428-36.

43. Yang P, Hu W, Fu Z, Sun L, Zhou Y, Gong Y, et al. The positive association of branched-chain amino acids and metabolic dyslipidemia in Chinese Han population. Lipids Health Dis. 2016;15:120.

44. Silveira BKS, Novaes JF, Reis NA, Lourenço LP, Capobiango AHM, Leal ACG, et al. Sociodemographic and lifestyle factors are associated with diet quality in cardiometabolic risk subjects. J Food Nutr Res. 2019;7(2):141-7.

45. Meneguelli TS, Hinkelmann JV, Novaes JF, Rosa COB, Filgueiras MS, Silveira BKS, et al. Dietary inflammatory index is associated with excessive body weight and dietary patterns in subjects with cardiometabolic risk. J Food Nutr Res. 2019;7(7):491-9.

46. Almeida AP, Rocha DMUP, Moreira AVB, Lima HCFM, Hermsdorff HH. Personalized nutrition using PROCARDIO to reduce cardiometabolic risk in the academic community: a study protocol with preliminary results. J Am Coll Nutr. 2020;1-10.

47. Silva JT, Bersch-Ferreira ÂC, Torreglosa CR, Weber B, Levy RB. Development of a dietary index based on the Brazilian cardioprotective nutritional program (BALANCE). Nutr J. 2018;17(1):49.

Received: October 8 2019
Final version: May 5 2020
Approved: August 8 2020